The Significance of P Wave Duration and P Wave Dispersion for Risk Assessment of Atrial Tachyarrhythmias in Patients with Corrected Tetralogy of Fallot

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Background: The aim of the present study was to determine the potential role of P wave duration and P wave dispersion for risk assessment of atrial tachyarrhythmias in patients with corrected tetralogy of Fallot (ToF).

Methods: The maximum P wave duration, minimum P wave duration, and the P wave dispersion from the 12-lead surface electrocardiogram of the patients and controls were measured. Electrophysiological study was performed only in the patient group.

Results: The study group consisted of 25 patients with corrected ToF with a mean age of 16.4 ± 4.25 years and 25 age-matched healthy control subjects. Patients underwent repair at a mean age of 4.6 ± 3.41 years (range: 1–19), and the mean duration of follow-up of 11.8 ± 1.7 years (range: 9–15) after surgery. On electrophysiological study sinus node dysfunction was detected in 3 patients (12%), atrial tachyarrhythmias—atrial flutter or fibrillation—in 5 patients (20%), both sinus node dysfunction and atrial flutter in 1 patient (4%), and AV conduction delay in 1 patient (4%). P wave dispersion is significantly higher in patients with atrial tachyarrhythmia inducible by electrophysiological study than in other patients ($P < 0.05$). A P wave dispersion value of >35 ms has a high predictive accuracy (sensitivity = 83% and specificity = 89%) for inducible atrial tachyarrhythmia in patients with corrected tetralogy of Fallot.

Conclusion: P wave dispersion is an easily measured electrocardiographic marker with a good sensitivity and specificity for predicting atrial arrhythmias in patients after correction of ToF.

A.N.E. 2004;9(4):339–344

atrial tachyarrhythmia; P wave duration; P wave dispersion; correction of tetralogy of Fallot

The long-term success of correction of tetralogy of Fallot (ToF) is hampered by the occurrence of arrhythmias. Considerable attention has been focused on ventricular arrhythmia in an adult after ToF repair.^{1,2} However, atrial tachyarrhythmias (AT) in these patients received little attention. Recently, prevalence of AT has been reported to be as high as 34% after the repair of ToF.³ There is a general agreement that the supraventricular arrhythmias more often generate symptoms and require treatment more frequently than ventricular arrhythmias.⁴

P wave dispersion and maximum P wave duration have been used to evaluate the discontinu-

ous propagation of sinus impulse and the prolongation of atrial conduction time. The clinical significance of P wave duration has been demonstrated in many clinical conditions including left atrial hypertension,⁵ left atrial enlargement,⁶ and paroxysmal atrial fibrillation.⁷ Prolonged P wave duration and P dispersion have been reported to represent an increased risk for atrial fibrillation in patients with no underlying heart disease.⁷ Dilaveris et al.⁸ and Ozer et al.⁹ were the first to comment on the relationship of P wave dispersion with hypertension.

The purpose of this study was to search for simple electrocardiographic markers derived from the 12-lead surface electrocardiogram that could be

used for prediction of AT in patients after correction of ToF and correlate with electrophysiological study.

METHODS

Twenty-five patients with correction of ToF and 25 age-matched healthy control subjects were included in this study. Patients' selection was performed according to the symptoms of presyncope, syncope, palpitation, or elapse of at least 10 years after surgery. None of the control subjects had any cardiac symptoms, and all clinical, electrocardiogram, chest radiograph, and echocardiographic examinations were normal. The exclusion criteria from this study were using antiarrhythmic drugs, complete bundle branch block, congestive heart failure, acid-base imbalance, detectable cardiovascular, or other systemic disease. The time interval from operation to electrophysiological study ranged from 9 to 15 years (mean: 11.8 ± 1.77 years). This study included 12-lead surface ECG, 24-hour continuous ambulatory monitoring (Holter), echocardiography, and electrophysiological study. Electrophysiological study was performed in all patients but not in control subjects.

Holter Monitoring

All patients and controls underwent Holter monitoring. Modified chest leads V3 and V5 were recorded with RZ153 digital recorders and the tapes were analyzed by the same cardiologist using Holter for windows system (Rozinn Electronics, Inc., Glandale, NY). Any combination of at least two of sinus bradycardia, abrupt sinus pauses (>1 second in the absence of respiratory variation), and escape beats was coded as sinus node dysfunction. Atrial fibrillation, atrial flutter, and ectopic atrial rhythm were diagnosed using conventional criteria.

Echocardiographic Examination

Echocardiographic examination of all patients and controls was performed using General Electric Vingmed System Five Performance echocardiographic scanner (General Electric, Horten, Norway). Left atrial dimensions were measured from the standard long-axis view.

Electrophysiological Study

Continuous 12-lead ECG monitoring was maintained during the electrophysiological study, and conscious sedation was achieved using intravenous midazolam. Electrode catheters were advanced into the heart through right femoral vein with using two introducer sheaths. A sequence of atrial pacing studies was performed with the electrode catheter positioned in the high right atrium near the superior vena cava-right atrial junction. An EP Medsystems electrophysiologic system (West Berlin, New Jersey, USA) was used. The A-H interval was measured from the onset of atrial activation (A) to the first rapid deflection of the His bundle potential (H). The H-V interval was measured from the first rapid deflection of the His bundle potential (H) to the onset of ventricular activity on the surface ECG. Atrioventricular (AV) conduction was evaluated by determining the heart rate at which second degree AV block occurred during progressively increased atrial pacing at rates from 120 to 200 beats/min increments. Sinus node function was also evaluated by measuring sinus node recovery time (SNRT) at varying duration of atrial pacing. The absolute SNRT was measured from the last pacing artifact that was effective in capturing the atrium to the onset of the first spontaneously occurring P wave of sinus origin. The corrected SNRT was determined by expressing the absolute SNRT as a percentage of the resting P-P interval. During electrophysiological study, single-, double-, and triple-programmed atrial and ventricular premature stimuli were introduced into atrial and ventricular-paced rhythm during basal state and isoproterenol infusion. Patients were classified by electrophysiological study results as having no inducible atrial or ventricular tachycardia, sinus node dysfunction, AV conduction delay, atrial tachyarrhythmias (atrial flutter or fibrillation), nonsustained ventricular tachycardia, or sustained ventricular tachycardia. Informed consents were obtained from the parents of the subjects.

12-Lead Surface ECG

A 12-lead surface ECG was obtained from all control subjects in the supine position who were instructed to breathe freely but not to speak or cough. Digital ECGs were recorded digitally with an EP Medsystems electrophysiologic system. An acceptable ECG was defined by the ability to measure

the P wave duration in at least 8 of the 12 electrocardiographic leads simultaneously recorded. The measurement was performed manually with a cursor when each ECG was magnified and displayed on a high-resolution computer screen. The onset of the P wave was defined as the junction between the isoelectric line and the beginning of the P wave deflection and the offset of the P wave was defined as the junction of the end of the P wave deflection and the isoelectric line. The maximum (Pmax) and minimum (Pmin) P wave duration in any of the 12 ECG leads were calculated for each control subjects. P wave dispersion was calculated as the difference between the Pmax and Pmin durations (P wave dispersion = Pmax – Pmin). The average values of Pmax and P wave dispersion were measured by two investigators. Intraobserver and interobserver coefficients of variation (SD of differences between two observations divided by the mean value and expressed as percentage) were found to be 2.2% and 2.6% for Pmax and 2.7% and 2.8% for P wave dispersion, respectively.

Statistical Analysis

Results are expressed as mean value $\pm$ SD. The Kolmogorov-Smirnov test was used to assess distribution normality for each variable. Data were compared between groups using independent sample *t*-test (normally distributed subjects) and Mann-Whitney U test (not normally distributed subjects). Correlations between the parameters were explored with Pearson's correlation coefficients. To determine the prognostic value of P dispersion, relative risk ratios were calculated. All statistical calculations were performed with commercially avail-

able computer software. The level of significance was set at 0.05 (two-sided).

RESULTS

Twenty-five patients with correction of ToF, with a mean age of 16.4 ± 4.25 years (range: 11–32) and 25 control subjects, with a mean age of 15.8 ± 1.88 years (range: 11–18) were included in this study. There were 20 males and 5 females in the patient group and 17 males and 8 females in the control group. Patients underwent repair at a mean age of 4.6 ± 3.41 years (range: 1–19,) and the mean duration of follow-up of 11.8 ± 1.77 years (range: 9–15) after surgery. No significant difference was found between groups for age and sex ($P > 0.05$) (Table 1).

Echocardiographic Examination

Left ventricle end-diastolic diameter (LVEDD) and left ventricle end-systolic diameter (LVESD) were found to be significantly lower in the patient group than in healthy control subjects. Otherwise no significant difference was found between groups for left ventricle ejection fraction (LVEF) and left ventricle shortening fraction (LVSF) (Table 1). LVEDD was weakly and negatively correlated with P wave dispersion ($r: -0.342$, $P < 0.05$). No significant correlation was found between other echocardiographic and electrocardiographic indices. LVEDD, LVESD, LVEF, and LVSF were similar in patients with AT and arrhythmia-free group (LVEDD: 42.5 ± 6.5 vs 43.1 ± 5.4 , LVESD: 24.3 ± 7.6 vs 24.8 ± 4.6 , LVEF: 73.5 ± 11.6 vs 72.5 ± 6.9 , LVSF: 42.8 ± 9.1 vs 41.7 ± 6.3 ,

Table 1. Demographic and Echocardiographic Characteristics of the Patients and the Controls

	Patients Mean $\pm$ SD (range)	Controls Mean $\pm$ SD (range)	P Value
No	25	25	
Gender (M/F)	20/5	17/8	
Age	16.4 ± 4.25 (11–32)	15.8 ± 1.88 (11–18)	0.883
LVEDD (mm)	42.9 ± 5.6 (34–52)	46.4 ± 4.2 (38–54)	0.022
LVESD (mm)	24.7 ± 5.3 (19–36)	27.3 ± 3.7 (18–35)	0.044
LVEF (%)	72.8 ± 8 (53–87)	71.8 ± 5 (63–85)	0.676
LVSF (%)	41 ± 6 (28–56)	41 ± 4 (34–53)	0.566

LVEDD = Left ventricle end diastolic diameter; LVESD = Left ventricle end systolic diameter; LVEF = Left ventricle ejection fraction; LVSF = Left ventricle shortening fraction.

Table 2. P Wave Maximum, Minimum, P Dispersion, and Left Atrial Diameter Values in Patients and Control Subjects

	Patients (n = 25) Mean $\pm$ SD (range)	Controls (n = 25) Mean $\pm$ SD (range)	P Value
P maximum (ms)	94.48 $\pm$ 13.25 (61–118)	86.20 $\pm$ 10.16 (66–108)	0.017
P minimum (ms)	67.80 $\pm$ 13.23 (45–92)	68.92 $\pm$ 8.72 (53–85)	0.725
P dispersion (ms)	26.68 $\pm$ 10.82 (10–49)	17.28 $\pm$ 8.71 (5–37)	0.01
Left atrial diameter (mm)	29.16 $\pm$ 4.16 (22–35)	26.52 $\pm$ 3.45 (20–34)	0.018

respectively; $P > 0.05$). We detected symptom-free low LVEF (53%) in 1 patient with AT.

Holter Monitoring

On Holter monitoring, atrial premature beats were recorded in 3 patients, ventricular premature beats in 4 patients, combined atrial and ventricular premature beats in 3 patients, and sinus node dysfunction in 1 patient. None of the patients showed atrial fibrillation or flutter.

Electrophysiological Study

Sinus node dysfunction was detected in 3 patients (12%), AT—atrial flutter or fibrillation—in 5 patients (20%), both sinus node dysfunction and atrial flutter in 1 patient (4%), AV conduction delay in 1 patient (4%), and nonsustained ventricular tachycardia was detected in 6 patients (24%). During electrophysiological study, AT was induced by burst-programmed atrial pacing in 3 patients and double-programmed atrial stimulation in 2 patients. The mean A-H interval, mean H-V interval, and the mean corrected SNRT was measured 102 ± 22 ms, 58 ± 10 ms, and 394 ± 245 ms, respectively. There were no patients with sustained ventricular tachycardia.

12-Lead Surface ECG

Pmax ($P < 0.05$), P wave dispersion ($P = 0.01$), and left atrial diameter ($P < 0.05$) were found to be significantly higher in the patient group than in healthy control subjects. Otherwise Pmin was similar in the two groups ($P < 0.05$). Values of Pmax, Pmin, P wave dispersion, and left atrial diameters are shown in Table 2.

Maximum P wave duration was correlated with P dispersion ($r: 0.550$, $P < 0.001$), left atrial dimension ($r: 0.353$, $P < 0.05$), and duration after surgery ($r: 0.418$, $P < 0.05$). Left atrial dimension was correlated with duration after surgery ($r: 0.427$, $P < 0.05$) and age at repair ($r: 0.474$, $P < 0.05$). Pmax, Pmin, and left atrial dimensions were similar in patients with AT and arrhythmia-free group. Only P wave dispersion was found to be significantly higher in patients with AT than in the arrhythmia-free group ($P < 0.05$). Values of Pmax, Pmin, P dispersion, and left atrial diameter of the patients with AT and arrhythmia-free group are shown in Table 3.

A P dispersion cut point of >35 ms resulted in a sensitivity of 83%, a specificity of 89%, and a negative predictive value of 94% in differentiating post-operative ToF patients with AT from those without AT.

Table 3. P Wave Maximum, Minimum, P Dispersion, and Left Atrial Diameter Values in Patients with Atrial Tachycardia (AT) and Arrhythmia-Free Group

	Patients (n = 19) Arrhythmia-Free Group	Patients (n = 6) AT Group	P Value
P maximum (ms)	92.26 $\pm$ 13.45	101.5 $\pm$ 10.65	0.140
P minimum (ms)	68.15 $\pm$ 12.74	66.66 $\pm$ 15.92	0.816
P dispersion (ms)	24.10 $\pm$ 9.2	34.83 $\pm$ 12.36	0.031
Left atrial diameter (mm)	29.26 $\pm$ 4.18	28.83 $\pm$ 4.44	0.831

DISCUSSION

Supraventricular arrhythmias have received comparatively little attention, although they are not uncommon after correction of ToF.^{3,10} In our study atrial flutter or fibrillation have not been found on Holter recordings. On electrophysiological study AT—atrial flutter or fibrillation—were detected in 5 patients (20%) and both sinus node dysfunction and atrial flutter in 1 patient (4%). We detected nonsustained ventricular tachycardia in 24% of our patients by electrophysiological study. Holter recordings were poor guides for the diagnosis of AT or nonsustained ventricular tachycardia in our patients. In a collaborative study of 380 young patients with atrial flutter, aged 1 to 25 years, only 8% had repaired ToF.¹¹ On the other hand, the incidence of atrial arrhythmias was found in 34% of adults patients with surgically repaired ToF by using Holter monitoring.³ The development of atrial tachyarrhythmia in the adult late after ToF repair identifies patients at risk and is associated with older age at repair.¹⁰ In our study, the mean duration of follow-up was 11.8 years after surgery. Difference of the frequency of AT in these studies may be explained by the age of the patients. For example, Ross-Hessellink et al.³ found that the age at follow-up was significantly higher in patients with atrial fibrillation or flutter.

Sustained ventricular tachycardia is much less common; it is seldom seen in children and is more frequent in adults.⁴ In the present study, most of our patients are children or adolescents and this may be the reason for the fact that we did not find any sustained ventricular arrhythmia.

The pathophysiology of atrial arrhythmias in ToF-repaired patients might be multifactorial. Atriotomy and atrial sutures may play a role in the development of atrial arrhythmias. Relationship between atriotomy scar region and intraatrial reentry tachycardia was showed in patients with surgically corrected congenital heart disease including 3 patients with ToF.¹² Association between left atrium dimension and the risk for recurrent tachyarrhythmias in patients with paroxysmal atrial fibrillation and flutter is well known.¹³ In one series of patients with correction of ToF, arrhythmias were most likely found in patients with left atrial enlargement.³ In the present study, left atrial diameters were significantly higher in the patient group than in the control group, but were not found to be higher in the AT group. We found left atrial

dimension to be positively correlated with Pmax, duration after surgery, and age at repair. Probably, increased Pmax is a result of left atrial enlargement. Duration after surgery and age at repair seemed to be important parameters in large left atrial dimension. Also, these parameters are important for the development of arrhythmia in postoperative ToF patients. The risk of development of AT in the adult late after ToF repair was shown to be associated with older age at repair. Progressive myocardial fibrosis with increasing age and age at repair are a purported substrate for ventricular arrhythmias after ToF,¹⁴ and may similarly play a role in the pathogenesis of AT in these patients.¹⁰ Our patients who developed AT are limited and we could not find any relationship between left atrial enlargement and AT.

The prolongation of P wave duration is thought to be an accepted indicator of interatrial conduction disturbance that can occur independently of an increase in atrial size.¹⁵ Prolonged P wave duration is commonly used for the prediction of atrial fibrillation.^{7,16} Prior studies have demonstrated that individuals with clinical paroxysmal atrial fibrillation have significantly longer intraatrial and interatrial conduction time of sinus impulses, which is not only electrophysiologically determined^{17,18} but also shown as P wave prolongation in 12-lead surface electrocardiograms.^{19,20} Aytemir et al.¹⁶ found that Pmax and P wave dispersion are significantly higher in patients with paroxysmal atrial fibrillation compared to healthy controls. Dilaveris et al.⁷ found Pmax to be a significant independent predictor of recurrent paroxysms of atrial fibrillation. We found that Pmax was significantly higher in the patient group than in the control group and Pmax was correlated with P wave dispersion, left atrial dimension, and duration after surgery. Pmax is a component of P wave dispersion and relationship between these parameters was not a surprise.

In the present study, decrease in the LVEDD on echocardiographic examination was not a surprise in the postoperative ToF patients. In addition, P wave dispersion was significantly higher in patients compared to the controls. Probably, we found negative correlation between LVEDD and P wave dispersion due to these relationships.

P wave dispersion has already been used for the prediction of atrial fibrillation.⁷ Similar to Pmax and left atrial dimension, P wave dispersion was significantly higher in the patient group than in the control group. In opposition to the other

parameters, P wave dispersion was found to be significantly higher in patients with AT inducible by electrophysiological study than an arrhythmia-free group in postoperative ToF patients. This result is the principal new finding of this study and P wave dispersion cut point of >35 ms resulted in a sensitivity of 83%, a specificity of 89%, and a negative predictive value of 94% in differentiating postoperative ToF patients with AT from those without AT. From these findings we speculate that prolonged inhomogeneous intraatrial conduction might be one of the causes of AT in corrected ToF patients. But P wave dispersion does not extremely investigate except atrial fibrillation and we do not know the exact mechanism for these P wave changes. Further investigation into the mechanism of this phenomenon is needed.

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 AT. However, electrophysiologic studies are highly complex, time consuming and expensive, and could not be used as a screening test for the general population. Consequently, the identification of simple electrocardiographic predictors for the development of atrial fibrillation appears to be the most practical approach. A novelty of our study is the development of a new electrocardiographic index that was defined as P wave dispersion. Therefore, we could suggest that, this is a simple, noninvasive, electrocardiographic marker that could distinguish patients with AT from arrhythmia-free patients after ToF operation.

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