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Full Length Research Paper

Assessment of a trial electromechanical delay in patients with mitral valve prolapse

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Atrial arrhythmias are seen frequently in symptomatic patients with mitral valve prolapse (MVP). The purpose of our study was to evaluate whether the atrial electromechanical delay (AEMD) measured by tissue Doppler imaging (TDI) is prolonged in patients with MVP. A total of 40 patients with MVP (16 males/24 females, 33.4 ± 6.1 years), and 40 controls (18 males/22 females, 34.2 ± 4.2 years) were included in the study. Inter-AEMD and intra- AEMD were measured by TDI. P-wave dispersion (PWD) was calculated from the 12-lead electrocardiogram. Inter-AEMD and intra-AEMD were significantly longer in patients with MVP than in the controls (31.6 ± 12.1 vs 24.7 ± 5.4 ms, p = 0.001 and 8.1 ± 5.3 vs. 5.7 ± 1.9 ms, p = 0.008; respectively). PWD was significantly longer in patients with MVP than in the controls (41.3 ± 7.1 vs 34.7 ± 4.3 ms, p<0.0001). The left atrial (LA) diameter, anterior and posterior mitral leaflet thicknesses were significantly higher in patients with MVP than in the controls. (35.4 ± 3.0 vs 31.9 ± 3.0 mm, p<0.0001 and 3.6 ± 0.9 vs 2.8 ± 0.7 mm, p<0.0001 and 2.9 ± 0.7 vs 2.2 ± 0.4 mm p<0.0001; respectively). Inter-AEMD was positively correlated with PWD, mitral leaflet thickening and LA diameter. We showed that AEMD is significantly prolonged in patients with MVP, and speculated that this prolongation may reflect the increase of the risk of atrial arrhythmias in MVP subjects.

Key words: Mitral valve prolapse, atrial electromechanical delay, P-wave dispersion.

INTRODUCTION

Mitral valve prolapse (MVP) is one of the most common diagnosed valvular heart disorder in the general population, which is estimated to be affecting 2 to 3% of the society. MVP is usually defined as the displacement of one or both of the mitral leaflets more than two millimeters into the left atrium (LA) during systole (Freed et al., 1999; Devereux et al., 2001). Atrial arrhythmias such as atrial fibrillation (AF) have been reported to occur frequently in symptomatic patients with MVP (Zuppiroli et al., 1994; Lévy, 1992; Baedeker, 1988; Berbarie and Roberts, 2006; Ohki et al., 2001; Grigioni et al., 2002; Avierinos et al., 2002). The exact mechanisms underlying atrial arrhythmias in patients with MVP are obscure. Atrial electromechanical delay (AEMD) has been defined as the temporal delay between the detected onset of electrical activity and the realization of force in the myocardium and has been evaluated using tissue Doppler imaging (TDI) (Ozer et al., 2005; Cui et al., 2008). The assessment of AEMD is a novel, simple and inexpensive method alternative to invasive electrophysiological studies. Recent studies have demonstrated that AEMD is prolonged in patients with paroxysmal AF when compared with the controls (Cui et al., 2008; Omi et al., 2005) The aim of our study was to investigate whether AEMD is prolonged in patients with MVP and to assess whether it correlates with the prognostic factors of atrial arrhythmia.

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MATERIALS AND METHODS

Study population

Forty patients with MVP (16 males/24 females, 33.04 ± 6.07 years), and 40 controls (18 males/22 females, 34.15 ± 4.19 years) were included in the study. The control group consisted of forty age- and

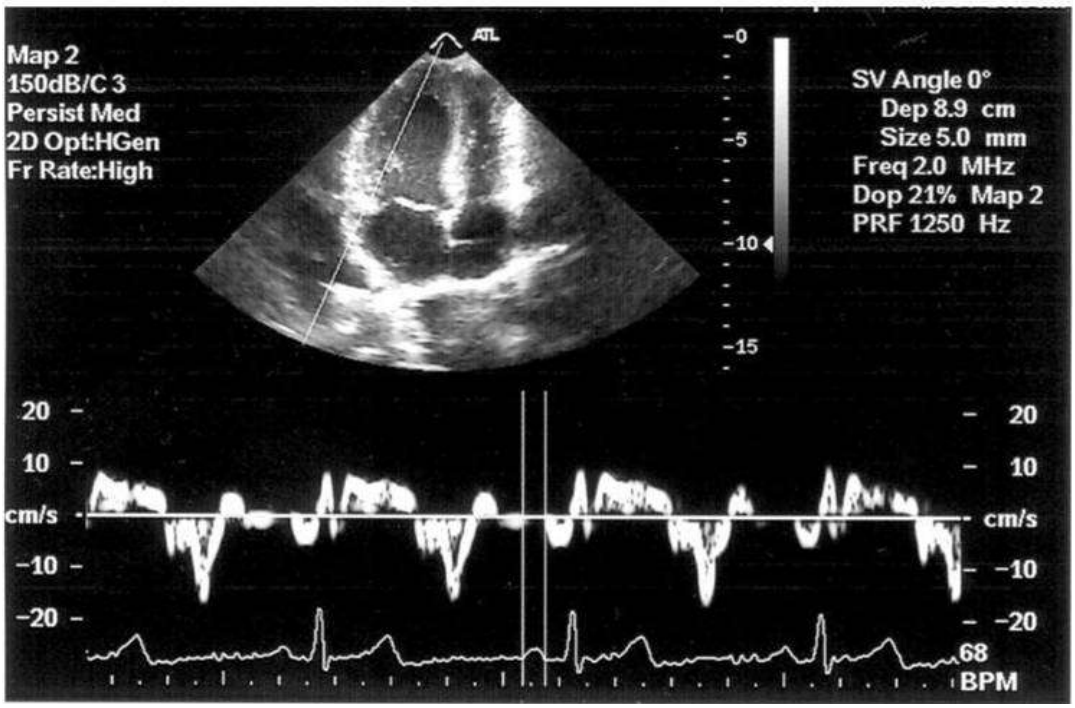

Figure 1. Measurement of the time interval from onset of the P wave on surface ECG to the beginning of A wave (PA) with tissue DOPPLER echocardiography.

sex-matched healthy subjects. All the patients were in sinus rhythm during the study period. The study was approved by the institutional ethics committee and all individuals gave informed consent for this study. The exclusion criteria were rheumatic heart disease, moderate to severe mitral regurgitation due to MVP, prosthetic valves, pericarditis, coronary artery disease, severe left ventricular (LV) dysfunction, patients with Marfan Syndrome, patients with MVP due to chordal rupture, congenital heart disease, renal or hepatic failure, malignancy, active inflammatory or infective disease, hematologic disorder, hypertension, diabetes mellitus, hyperlipidemia, smoking, thyroid dysfunction, electrolyte imbalance, left bundle or right bundle branch block and prior pacemaker implantation. All patients receiving medications known to affect the electrocardiographic parameters were excluded from the study.

Echocardiography

All participants underwent echocardiographic evaluation by using commercially available echocardiography equipped with 2.5-and 3.5-MHz transducer (ATL HDI–5000 Bothell, Washington, USA). All measurements were obtained by a single observer who was blinded to the clinical status of the patients. During echocardiography examination, a 1-lead ECG was recorded continuously. An average of 3 consecutive beats was analyzed for every parameter. M-mode and Doppler echocardiographic measurements were performed according to the criteria of American Society of Echocardiography (Schiller et al., 1989). Left atrial diameter, LV end-systolic and end-diastolic diameters, interventricular septum, and posterior wall thickness were measured in the parasternal long axis view by M-mode imaging. LV ejection fraction (EF) was estimated by Simpson's rule. The diagnosis of MVP was decided as the relative maximal superior systolic displacement of the mitral leaflet of at least 2 mm over the line connecting the annular hinge points measured on the parasternal long-axis view (Freed et al., 1999; Devereux et al., 2001). The thicknesses of anterior and posterior mitral leaflets during diastasis were measured by M mode imaging. Each leaflet was measured, and expressed according to the maximal thickness.

Atrial electromechanical delay

The assessment of AEMD was performed by TDI using the same echocardiography machine, adjusting the spectral pulsed Doppler signal filters with Nyquist limit of 15 to 20 cm/s and minimal optimal gain was used. In an apical 4-chamber view, the pulsed Doppler sample volume was subsequently placed at the level of LV lateral mitral, septal mitral and right ventricular (RV) tricuspid annuli. The time interval from the onset of the P wave on surface electrocardiogram (ECG) to the beginning of the late diastolic wave (A wave) on TDI, which is named as PA, was obtained from the lateral mitral (lateral PA), septal mitral (septal PA), and RV tricuspid annuli (tricuspid PA), respectively (Figure 1). The difference between lateral PA and tricuspid PA (lateral PA – tricuspid PA) was defined as inter-AEMD, and the difference between septal PA and tricuspid PA (septal PA – tricuspid PA) was defined as intra-AEMD (Ozer et al., 2005).

P-wave dispersion measurements on 12-lead ECG

12-lead surface ECGs of all subjects were obtained after a 20-min resting in the supine position at a paper speed of 50 mm/s and 20 mm/mV. The number of leads in which P-wave duration could be measured ranged from 8 to 12. In each lead, the mean values for the three complexes were calculated. The onset of the P-wave was defined as the point of first visible upward departure from baseline

Table 1. The comparison of clinical characteristics and laboratory and echocardiographic findings of the study population.

	MVP (n = 40)	Controls (n = 40)	p value
Age (years)	33.4 ± 6.1	34.2 ± 4.2	0.52
Males:females	16/24	18/22	0.82
Systolic BP (mmHg)	111.5 ± 9.7	113.5 ± 10.9	0.39
Diastolic BP (mmHg)	73.0 ± 7.9	74.3 ± 8.5	0.49
Heart rate (beats/min)	78.7 ± 9.6	75.3 ± 9.1	0.10
Septal thickness (mm)	9.1 ± 0.9	9.0 ± 0.8	0.34
PW thickness(mm)	8.6 ± 0.9	8.6 ± 0.7	0.79
AMLT(mm)	3.6 ± 0.9	2.8 ± 0.7	< 0.0001
PMLT (mm)	2.9 ± 0.7	2.2 ± 0.4	< 0.0001
The degree of leaflet of displacement into LA (mm)	3.5 ± 1.0	0.7 ± 0.3	< 0.0001
LA diameter (mm)	35.4 ± 3.0	31.9 ± 3.0	< 0.0001
LVEDD(mm)	45.4 ± 2.4	45.0 ± 2.3	0.42
LVESD(mm)	27.9 ± 2.2	27.2 ± 1.3	0.14
LV EF (%)	69.6 ± 1.5	69.5 ± 1.4	0.64

Abbreviations: MVP; mitral valve prolapse; BP, blood pressure; PW, posterior wall; AMLT: anterior mitral leaflet thickness; PMLT: posterior mitral leaflet thickness; LA: left atrial; LVEDD: left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; LV EF: left ventricular ejection fraction.

for positive waveforms, and as the point of first downward departure from the baseline for negative waveforms. The return to the baseline was considered to be the end of the P-wave. The longest atrial conduction time measured on any of the 12 leads was defined as Pmaximum (Pmax) and, the shortest time was defined as Pminimum (Pmin). The difference between Pmax and Pmin was calculated and defined as P wave dispersion (PWD) (PWD=Pmax–Pmin).

Statistical analysis

Statistical analysis was performed by SPSS software package (version 17.0, SPSS Inc, Chicago, Illinois, USA). All continuous variables were expressed as mean ± SD, and categorical variables were defined as percentages. For continuous variables unpaired student *t* test and for categorical changes Pearson Chi-square test were used. Correlations among inter-AEMD and other variables were evaluated by the Pearson correlation tests where appropriate. Statistical significance was accepted as p value less than 0.05.

RESULTS

Baseline clinical characteristics, laboratory and echocardiographic findings of the study population are given in Table 1. No significant difference was found between the patients with MVP and the controls with respect to age, sex, heart rate, systolic and diastolic blood pressures. LV end-diastolic and end-systolic diameters, LVEF, interventricular septum and LV posterior wall thicknesses were also similar between the groups. LA diameter was statistically higher in patients with MVP than in the controls (35.4 ± 3.0 vs 31.9 ± 3.0 mm, p<0.0001). The degree of displacement of the leaflets into LA were significantly higher in patients with MVP than controls (3.5 ± 1.0 vs 0.7 ± 0.3 mm p<0.0001). Anterior and posterior mitral leaflet thicknesses were also significantly higher in patients with MVP than in the controls (3.6 ± 0.9 vs 2.8 ± 0.7 mm, p<0.0001 and 2.9 ± 0.7 vs 2.2 ± 0.4 mm p<0.0001; p = 0.002; respectively). The electrocardiographic and electromechanical parameters of the study population are given in Table 2. PA lateral and PA septum durations were significantly higher in patients with MVP than in the controls (73.6 ± 13.2 vs 63.5 ± 9.4 ms, p<0.0001; 50.0 ± 9.8 vs 44.5 ± 8.5 ms, p = 0.008; respectively). However, PA tricuspid duration was similar between both groups (41.9 ± 9.2 vs 38.8 ± 8.4 ms, p=0.11). Inter-AEMD and intra-AEMD were significantly higher in patients with MVP than controls (31.6 ± 12.1 vs 24.7 ± 5.4 ms, p=0.001 and 8.1 ± 5.3 vs 5.7 ± 1.9 ms p=0.008; respectively). Pmax and PWD values were also significantly higher in patients with MVP than in the controls (99.7 ± 9.7 ms vs 92.2 ± 6.1 ms, p<0.0001; 41.3 ± 7.1 vs 34.7 ± 4.3 ms p<0.0001; respectively).

In correlation analysis, inter-AEMD was positively correlated with PWD (r=0.791, p<0.0001), LA diameter (r = 0.695, p<0.0001), anterior and posterior mitral leaflet thicknesses (r = 0.681, p<0.0001 and r = 0.602, p<0.0001; respectively) and the degree of displacement of the leaflet into LA (r = 0.772, p<0.0001). The positive correlation between inter-AEMD and LA diameter and PWD are given in Figure 2. LA diameter was also positively correlated with PWD (r = 0.730, p<0.0001).

DISCUSSION

Mitral valve prolapse is the most common diagnosed valvular heart disorder in the general population and

Table 2. The comparison of the electrocardiographic and electromechanical parameters of the study population.

	MVP (n = 40)	Controls (n = 40)	p value
P maximum (ms)	99.7 ± 9.7	92.2 ± 6.1	<0.0001
P minimum (ms)	58.4 ± 4.6	57.6 ± 3.4	0.35
PWD (ms)	41.3 ± 7.1	34.7 ± 4.3	<0.0001
Lateral PA (ms)	73.6 ± 13.2	63.5 ± 9.4	<0.0001
Septal PA (ms)	50.0 ± 9.8	44.5 ± 8.5	0.008
Tricuspid PA (ms)	41.9 ± 9.2	38.8 ± 8.4	0.11
PA lateral − PA tricuspid (ms)[1]	31.6 ± 12.1	24.7 ± 5.4	0.001
PA septal − PA tricuspid (ms)[2]	8.1 ± 5.3	5.7 ± 1.9	0.008

1= İnter-atrial electromechanical delay; 2= intra-atrial electromechanical delay.
Abbreviations: MVP; mitral valve prolapse; PWD; P-wave duration.

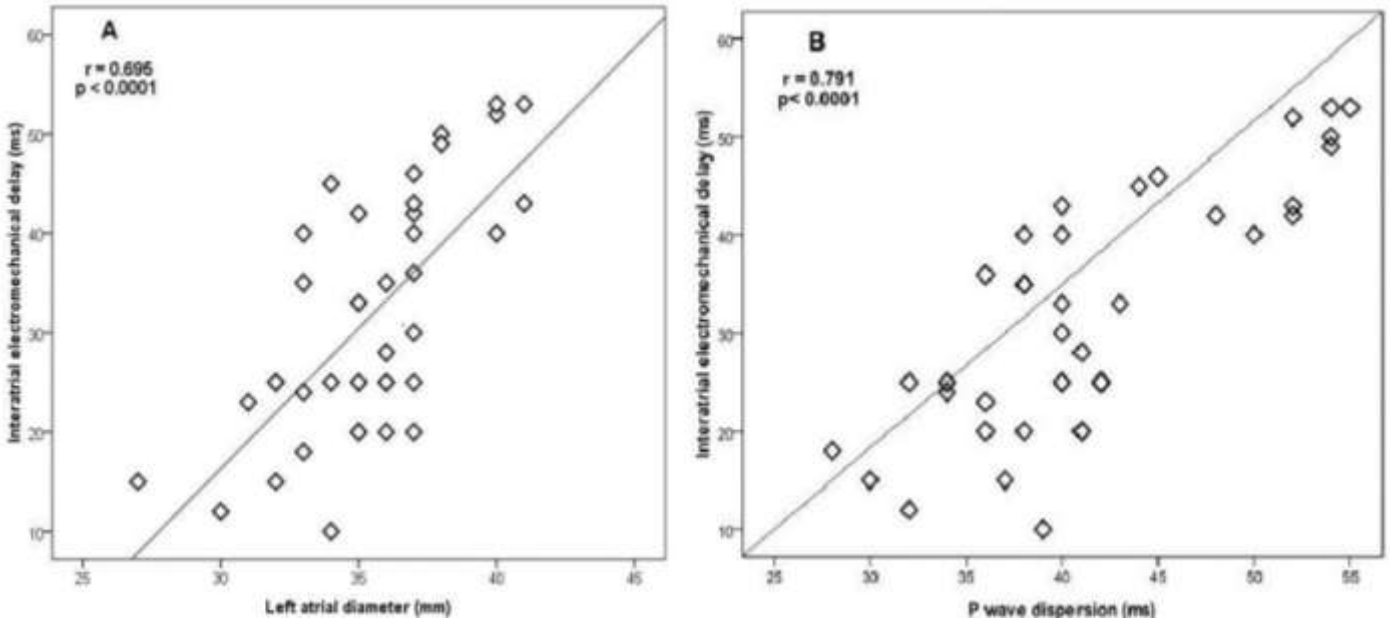

Figure 2. Positive correlation between interatrial electromechanical delay and left atrial diameter and between interatrial electromechanical delay and P-wave dispersion (B).

usually a benign condition (Freed et al., 1999; Devereux et al., 2001). Atrial arrhythmias such as atrial premature contractions, atrial couplets, atrial tachycardia, atrial flutter or AF have been reported to occur frequently in symptomatic patients with MVP ((Zuppiroli et al., 1994; Lévy, 1992; Baedeker, 1988). AF is the most important type of atrial arrhythmias encountered in clinical practice and is associated with a poor prognosis (Brand et al., 1985). Previous studies have reported that the frequency of AF in patients with MVP is as 8 to 28% (Berbarie and Roberts, 2006; Ohki et al., 2001; Grigioni et al., 2002; Avierinos et al., 2002). The prolongation of intraatrial and interatrial conduction times and the inhomogeneous propagation of sinus impulses are well-known electrophysiological characteristics of the atrium prone to fibrillate and have been evaluated using TDI (Ozer et al., 2005; Daubert et al., 2004; Dilaveris and Gialafos, 2001). Cui et al. (2008) have recently evaluated atrial electromechanical coupling by TDI in non-rheumatic paroxysmal AF subjects and have found it to be significantly longer than in the controls. Other studies have also shown that AEMD has been significantly longer in patients with paroxysmal AF, mitral annulus calcification and mitral stenosis than in the control groups (Ozer et al., 2005; Omi et al., 2005; Pekdemir et al., 2010). These studies have shown that prolonged AEMD seems to reflect atrial remodeling for an arrhythmogenic substrate. Based on this literature, prolonged AEMD

seems to be related with AF. Also, it is accepted that increased PWD indicates an atrial conduction disorder and is a useful predictive marker for the development of AF (Dilaveris and Gialafos, 2001; Aytemir et al., 2000). In our study, we demonstrated that both inter-AEMD and intra-AEMD and PWD were significantly longer in patients with MVP than in the controls. Moreover, we found that there was a strong positive correlation between increased PWD and prolonged AEMD and LA enlargement. Therefore, these findings may predict the increased risk of atrial rhythm disturbances in patients with MVP.

The exact mechanisms underlying atrial arrhythmias in patients with MVP are not well-known. However, different mechanisms may be responsible for this entity. Myxomatous changes observed in the valves of the patients with MVP may cause a displacement of the leaflet into LA together with an increased elasticity which may be responsible for an abnormal tension on the papillary muscle. Such an action of excessive mechanical forces in patients with MVP can result in a heterogeneity of refractoriness and abnormal repolarization, which eventually causes not only mechanical but also electrophysiological alterations (Zouridakis et al., 2001; Sanfilippo et al., 1992). Gornick et al. (1986) have shown that papillary muscle traction can be responsible for the significant regional repolarization changes in the ventricule in a canine heart model. In our study, we found that mitral leaflet thickening and the amount of displacement of the leaflet into LA were significantly higher in patients with MVP than in the controls. Moreover, we found that there was a positive correlation between inter-AEMD and mitral leaflet thickening and the degree of displacement of the leaflet into LA. We speculated that these changes in the mitral valves may result in inhomogeneous and discontinuous propagation of sinus impulses through the atrial wall. Another possible mechanism for the development of atrial arrhythmias in patients with MVP may be autonomic dysfunction. Several studies have shown an increased adrenergic activity in patients with MVP and there is evidence that sympathetic stimulation can cause increased dispersion through regional shortening or prolongation of the refractory period (Puddu et al., 1983; Pasternac et al., 1982). However, further studies are needed to clarify the exact mechanisms.

Study limitations

The main limitations of our study are the small sample size and the cross-sectional design of the study, in which we couldn't follow up the patients prospectively for future arrhythmic events. Therefore, we do not know whether prolongation of AEMD and increase of PWD predict atrial arrhythmias in patients with MVP. Finally, Pmax and Pmin measurements were obtained manually using magnifying lens instead of a more reliable computer-assisted P-wave calculating system (Dilaveris et al., 1999).

Conclusion

We found that both interatrial and intraatrial AEMD were prolonged in patients with MVP and they were significantly correlated with PWD, mitral leaflet thickening, the degree of displacement of the leaflet into LA and LA diameter parameters. We concluded that this prolongation might predict the increased risk of atrial arrhythmias and especially AF in patients with MVP.

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