Atrial Electrical and Electromechanical Characteristics in Patients with Rheumatic Mitral Stenosis

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ABSTRACT

Introduction: AF in patients with mitral stenosis (MS) causes significant morbidity and mortality. PMBV, which is a treatment of choice for patients with MS, is a highly successful procedure that provides significant improvement in symptoms and echocardiographic parameters. In this study we aimed to demonstrate the probable effects of PMBV on novel echocardiographic and electrocardiographic parameters that can predict the development of AF in 1-year period in patients with MS.

Patients and Methods: Twenty-eight patients with moderate or severe rheumatic MS (mean age 37.6 ± 7.4 years; 14 (50%) males) were enrolled this study. All patients who were eligible for this procedure underwent comprehensive echocardiographic examinations with evaluation of ACT measured using tissue Doppler imaging (TDI) before PMBW and repeated at the end of the 1 year after successful PMBV. In addition, 12-lead ECGs were recorded for each patient 1 day before PMBV for the evaluation of baseline maximum and minimum P-wave duration and P-wave dispersion (PWD); this was repeated at the end of the 1 year after successful PMBV.

Results: ACT (148.1 ± 20.5 vs 121.3 ± 20.5 p< 0.001), P-max (151.7 ± 15.8 vs 137.3 ± 15.6 p< 0.001) and PWD (84.7 ± 18.8 vs 71.1 ± 18.5 p< 0.001) were found to be significantly decreased after PMBV. A strong positive correlation was detected between ACT, P-max, PWD, LAVi ve PAPs before and after PMBV. In addition, there was a strong correlation between Δ values that were measured by subtracting the baseline measurements from the post-PMBV measurements. Accordingly, ΔACT was correlated with ΔP-max ve ΔPWD (r= 0.5 p= 0.007 and r= 0.55 p= 0.002, respectively). ΔACT, ΔP-max and ΔPWD correlated significantly with only ΔLAVi and ΔPAP in echocardiographic parameters.

Conclusion: This study demonstrated that atrial conduction properties that have also been evaluated with ECG and TDI studies significantly correlate with other echocardiographic parameters in patients with MS. In addition, significant improvement occurred in these parameters at the end of the 1 year after PMBV. Further prospective investigations may provide useful data for the detection of the relation between atrial electromechanical characteristics and development of AF in patients with MS.

Key Words: Rheumatic mitral stenosis; atrial fibrillation; atrial conduction tine P-wave dispersion; percutaneous mitral balloon valvuloplasty

Mitral Darlığı Olan Hastalarda Atriyal Elektiriksel ve Elektromekanik Özellikler

ÖZET

Giriş: Mitral darlığı olan hastalarda atriyal fibrilasyon (AF) önemli bir mortalite ve morbidite nedenidir ve bu hastalarda perkütan mitral balon valvüloplasti (PMBV) semptomlarda ve ekokardiyografik parametrelerde önemli düzelme sağlayan başarılı bir girişimdir. Bu çalışmada mitral darlıklı hastalarda PMBV'nin AF gelişimini predikte edebilen yeni ekokardiyografik ve elektrokardiyografik parametreler üzerindeki bir yıllık dönemdeki etkisinin gösterilmesi amaçlanmıştır.

Hastalar ve Yöntem: Orta ve ileri mitral darlığı olan 28 hasta (ortalama yaş 37.6 ± 7.4, %50'si erkek) çalışmaya dahil edilmiştir. PMBV girişimine aday olan hastaların işlem öncesi ve sonrasındaki birinci yılda atriyal ileti zamanı (ACT) açısından ayrıntılı ekokardiyografik incelemeleri doku Doppler yöntemiyle yapılmıştır. Ayrıca her hastanın işlemden bir gün önce ve birinci yılda maksimum ve minimum P dalga süreleri (Pmax ve Pmin) ve P dalga dispersiyonu (PWD) elektrokardiyografi ile değerlendirilmiştir.

Bulgular: PMBV işleminden sonra ACT (148.1 ± 20.5 vs. 121.3 ± 20.5, p< 0.001), Pmax (151.7 ± 15.8 vs. 137.3 ± 15.6, p< 0.001), PWD (84.7 ± 18.8 vs. 71.1 ± 18.5, p< 0.001) değerleri istatistiksel anlamlı olarak düşmüştür. İşlem öncesi ve sonrası ACT, Pmax, PWD, LAVi ve PAPs parametreleri arasında güçlü pozitif korelasyon tespit edilmiştir. Ayrıca işlem sonrası ve öncesi değerlerin çıkarılmasıyla hesaplanan Δ değerleri arasında güçlü korelasyon tespit edilmiştir. Buna göre; ΔACT'nin ΔPmax ve ΔPWD (r= 0.5, p= 0.007 ve r= 0.55, p= 0.002, sırasıyla) değerleriyle korele olduğu tespit edildi ve ΔACT, ΔPmax ve ΔPWD, ekokardiyografik parametrelerden sadece ΔLAVi ve ΔPAP ile anlamlı olarak korele idi.

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Sonuç: Bu çalışma mitral darlıklı hastalarda EKG ve TDI yöntemleriyle değerlendirilen atriyal ileti özelliklerinin diğer ekokardiyografik parametrelerle önemli derecede korele olduğunu göstermiştir. Ayrıca işlem sonrası birinci yılda bu parametrelerde önemli düzeyde düzelme meydana gelmiştir. Yapılacak prospektif özellikte daha fazla çalışma atriyal elektromekanistik özellikler ve AF gelişimi arasındaki ilişki açısından daha fazla bilgi sağlayabilir.

Anahtar Kelimeler: Romatizmal mitral darlık; atriyal fibrilasyon; atriyal ileti zamanı; P dalga dispersiyonu; perkütan mitral balon valvüloplasti

INTRODUCTION

Rheumatic mitral stenosis (MS) still remains a considerable heart valve disease in developing countries. Predisposition to atrial fibrillation (AF) in MS is associated with the effects of pressure and volume overload on the left atrial (LA) wall, and AF causes thromboembolic complications with an increased morbidity and mortality rate. LA enlargement is a well-known parameter of atria that are prone to undergo fibrillation. The prolongation of atrial conduction times (ACT) and atrial electromechanical delay (AEMD) that have been measured using echocardiographic tissue Doppler imaging (TDI) are other characteristics resulting in increased AF risk. In addition, some of the electrocardiographic markers [maximum P-wave duration (P-max) and P-wave dispersion (PWD)] predict the onset and persistence of AF. It has been reported that percutaneous mitral balloon valvuloplasty (PMBV) could effectively decrease PWD and AEMD in patients with MS in the early period after PMBV. In this study we aimed to examine the relationship of ACT and PWD with echocardiographic parameters in patients with MS and assess the probable effects of PMBW on PWD and ACT in 1-year period.

PATIENTS and METHODS

Patient Selection

In our clinic, from March 2010 to February 2013, 28 patients with MS in sinus rhythm (14 men, mean age 37.6 ± 7.4 years) who were New York Heart Association Class ≥ II and were eligible for PMBV were enrolled in this study. Patients who had moderate or severe mitral and aortic regurgitation, moderate or severe tricuspid stenosis or regurgitation, previous history of documented paroxysmal AF, left ventricular systolic dysfunction, coronary artery disease, hypertension, diabetes mellitus, hyperthyroidism, pericardial effusion, chronic obstructive pulmonary disease, bundle branch block, atrioventricular conduction abnormalities or ventricular pre-excitation were excluded from the study.

Twenty-eight patients who were eligible for this procedure underwent comprehensive echocardiographic examinations with evaluation of ACT measured using TDI before PMBW and repeated at the end of the 1 year after successful PMBV. In addition, 12-lead ECGs were recorded for each patient 1 day before PMBV for evaluation baseline maximum and minimum P-wave duration and PWD and repeated at the end of the 1 year after successful PMBV.

Echocardiography

All echocardiographic examinations were performed with the GE Vivid 7 system (GE Vingmed Ultrasound AS, Horten, Norway) using 3.5-MHz transducer with the patients resting in the left lateral decubitus position. Blood pressure and a continuous one-lead ECG recording were monitored during the echocardiographic examination. The data analysis was performed offline using Echo PAC (GE Vingmed Ultrasound AS). Cardiac dimensions and volumes were measured according to the ESC guidelines and left ventricular (LV) ejection fractions were calculated by the biplane Simpson's method[1]. The biplane area-length method was used to calculate the LA volume (LA volume = 0.85 × [(LA area in 4-chamber view) × (LA area in 2-chamber view)]/LA length) and LA volume was indexed by dividing the LA volume by body surface area[2]. In the apical four-chamber view, the sample volume was placed at the level of mitral valve coaptation point. Transmitral valve gradient was calculated as the mean of gradients obtained from three consecutive beats using continuous wave Doppler echocardiography. The mitral valve area (MVA) was calculated using the planimetric method in the short-axis view, and MVA was accepted as the mean of three measurements indifferent beats. The colour Doppler jet area (expressed as a percentage of LA area) was used for evaluation of severity of MR. Pulmonary artery systolic pressure (PAPs) was calculated from tricuspid regurgitant jet velocity (V) using the Bernoulli equation ($4V^2$) with adding the estimated right atrial pressure[3]. In addition, transesophageal echocardiographic examinations were performed 1 week before the procedure for evaluation the favourable mitral valve morphology scored according to the Wilkins echo scoring system for PMBV.

Atrial Conduction Time

The LV lateral mitral annulus was evaluated using TDI methods, and the myocardial velocity curves were constructed from digitised images in the apical four-chamber view for the assessment of ACT. ACT was measured from the onset of P-wave on ECG to the beginning of late diastolic wave was calculated from lateral mitral annulus (see, Figure 1). Values were averaged over three consecutive beats and ACT were corrected for heart rate by dividing with the square root of the R-R interval[4].

Electrocardiographic Measurements

All patients underwent a 12-lead ECG recording using the commercial recorder (Cardioline Delta 60 Plus, Remco, SpA, Italy) at a paper speed of 50 mm/s and a gain setting

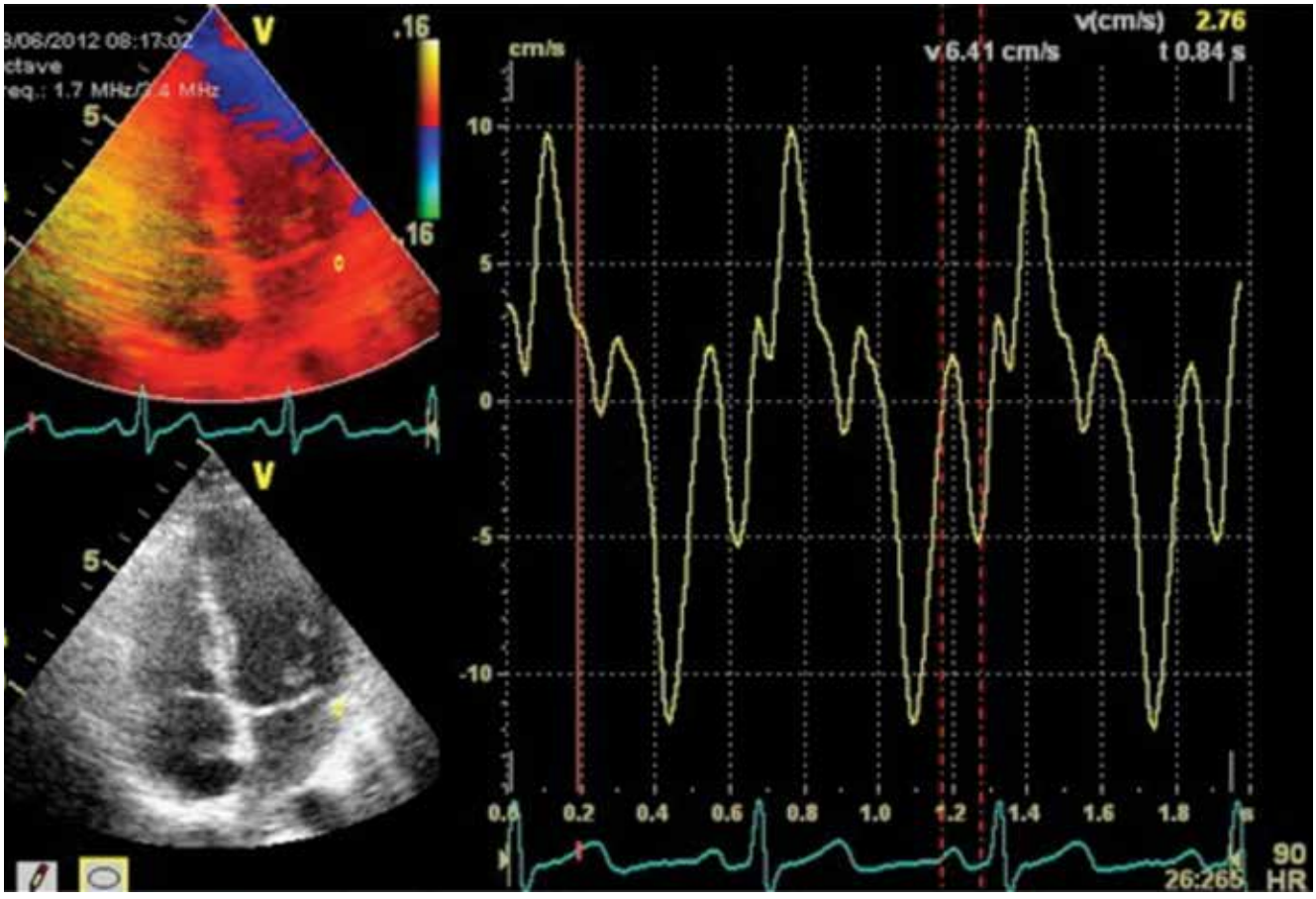

Figure 1. Measurement of the total atrial conduction time A simultaneously acquired registration of surface electrocardiogram lead II (blue tracing) was displayed underneath the tissue Doppler tracing. ACT was assessed by measuring the time interval between the onset of the P-wave in lead II and the peak A'-wave on the tissue Doppler tracing.

of 20-mm/mV. The ECG intervals for each study patient were measured manually by a cardiologist who was blinded to the clinical status of the patients. P-wave analysis was obtained with calipers and magnifying lens to improve accuracy. The onset of the P-wave was defined as the initial deflection of the P-wave crossing the isoelectric line and the end point was defined as the final deflection of the P-wave crossing the isoelectric line. P waves that could be accurately measured in ≥ 10 leads were included in the analysis. The onset and the end of the P-wave could not be markedly demonstrated were excluded. The difference between the maximum P-wave duration (P-max) and the minimum P-wave duration (P-min) was defined as PWD. Values were corrected for heart rate by dividing with the square root of the R-R interval[4].

Percutaneous Mitral Balloon Valvuloplasty

Percutaneous mitral balloon valvuloplasty is considered for symptomatic patients with moderate or severe MS with favourable valve morphology in the absence of or moderate to severe mitral insufficiency or LA thrombus. In addition, PMBV is considered for asymptomatic patients with moderate or severe MS who have PAPs ≥ 50 mmHg at rest or 60 mmHg with exercise) and valve morphology favourable for PMBV. The PMBV was performed as described previously[5]. PMBV procedures were performed by an anterograde transvenous approach using the Inoue balloon catheter (Toray Industries, Inc., Houston, Texas). Standard haemodynamic right and left heart pressure measurements were evaluated before and after PMBV. Oxygen saturation of pulmonary artery, aorta and superior and inferior vena cava were also evaluated during the procedure. The result of PMBV procedure was considered satisfactory if the MVA was > 1.5 cm^2 without > 2+ mitral insufficiency and left-to-right shunt.

Statistical Analysis

Continuous variables were presented as mean ± standard deviation and categorical variables were presented as percentage. Chi-square test and unpaired t-test were used for comparing categorical and continuous variables between two groups. The correlation between basal and 12^{th} month echocardiographic variables with P-wave variables was evaluated with the Pearson correlation test. Comparison between the continuous variables basal and 12^{th} month

measurements in the patient group were made with the Paired t-test. A P-value of < 0.05 was considered to be statistically significant. Statistical analyses were performed using SPSS, version 15.0 for Windows.

RESULTS

Twenty-eight patients with moderate or severe rheumatic MS (the mean age of the patients was 37.6 ± 7.4 years and 14 (50%) were male) were enrolled this study. Baseline clinical features and echocardiographic and electrocardiographic parameters of the patients with MS are displayed in Table 1.

The heart rate, NYHA Class, transmitral mean gradient, LA volume index (LAVi) and PAPs were significantly decreased after PMBV procedure for all study patients and also statistically significant improvement occurred in MVA. ACT (148.1 ± 20.5 vs 121.3 ± 20.5 p < 0.001), P-max (151.7 ± 15.8 vs 137.3 ± 15.6 p< 0.001), PWD (84.7 ± 18.8 vs 71.1 ± 18.5 p < 0.001) were found to be significantly decreased after PMBV; however, there was no statistical difference regarding P-min value (66.1 ± 12.3 vs 67.1 ± 11.9 p= 0.195) (Table 1).

A strong positive correlation was detected between ACT, P-max, PWD, LAVi and PAPs before and after PMBV (Table 2). In addition, there was a strong correlation between Δ values that were measured by subtracting the baseline measurements from the post-PMBV measurements. Accordingly, ΔACT was correlated with ΔP-max and ΔPWD (r= 0.5 p= 0.007 and r= 0.55 p= 0.002, respectively). ΔACT, ΔP-max and ΔPWD correlated significantly with only ΔLAVİ and ΔPAP in echocardiographic parameters. [ΔACT-ΔLAVi (r= 0.54 p= 0.003), ΔACT-ΔPAPs (r= 0.6 p= 0.001), ΔP-max-ΔLAVi (r= 0.47 p= 0.012), ΔP-max-ΔPAPs (r= 0.43 p= 0.023), ΔPWD-ΔLAVi (r= 0.5 p= 0.007) and ΔPWD-ΔPAPs (r= 0.45 p= 0.016)].

DISCUSSION

This study has demonstrated that ACT and P-wave duration significantly correlate with other echocardiographic parameters and together in patients with MS and also significant improvement occurred in these parameters at the end of the 1 year after PMBV.

Rheumatic MS still remains a major health problem in developing countries and causes significant morbidity and mortality[6]. A common arrhythmic complication encountered in patients with MS is AF.

The combination of mitral valve disease that result in pressure and volume overload on LA and atrial inflammation caused by rheumatic involvement result in atrial enlargement, interstitial fibrosis within the atrial wall and disorganisation of the muscle bundles of LA. These structural changes in LA cause inhomogeneous electrical properties, abnormal conduction velocities and local dispersion of refractoriness within the atrial myocardium. Consequently, the changes in LA hemodynamics with fibrosis of atrial wall correlate with vulnerability to AF[7]. Prospective data from the large population based studies have

Table 1. Baseline and after PMBV clinical and echocardiographic properties of patients

	Before PMBV	After PMBV	p
Age (year)	37.6 ± 7.4	-	-
Gender (F/M)	14/14	-	-
BSA	1.69 ± 0.18	-	-
NYHA class (I/II/III/IV)	0/10/14/4	25/3/0/0	< 0.05
Heart rate	74.5 ± 4.6	70.2 ± 5.9	0.007
Sist blood P	123.5 ± 14	122.3 ± 14.3	0.776
Dias blood P	70.4 ± 7.5	69.6 ± 7.1	0.703
End diastolic diameter	4.8 ± 0.6	4.8 ± 0.6	0.774
End systolic diameter	2.9 ± 0.4	2.9 ± 0.6	0.924
EF	69.6 ± 3.7	71 ± 4.4	0.064
LAVi	61.65 ± 10.5	55.5 ± 10	**< 0.001**
MVA	1.02 ± 0.2	2.1 ± 0.20	**< 0.001**
Max gradient	24.8 ± 6.4	12.7 ± 2.9	**< 0.001**
Mean gradient	15 ± 5.6	6.6 ± 1.7	**< 0.001**
Mitral regurgitation (1/2)	27/1	21/7	**0.031**
PAPs (mmHg)	51.5 ± 11.4	37.7 ± 7.1	**< 0.001**
Atrial conduction time	148.1 ± 20.5	121.3 ± 20.5	**< 0.001**
P-max	151.7 ± 15.8	137.3 ± 15.6	< 0.001
P-min	66.1 ± 12.3	67.1 ± 11.9	0.195
P-wave dispersion	84.7 ± 18.8	71.1 ± 18.5	**< 0.001**

PMBV: Percutaneus mitralballoon valvuloplasty, NYHA class: New York Heart Association Class, PAPs: Pulmonary artery systolic pressure, LAVi: LA volume index.

Table 2. Correlation analysis of ACT and P-max with MVA, Max Grad, Mean Grad, LAVi and PAPs parameters

	ACT		P-max		PWD	
Before PMBV	**r**	**p**	**r**	**p**	**r**	**p**
MVA	-0.23	0.15	-2.8	0.16	-2.8	0.15
Max Grad	0.1	0.78	0.14	0.47	0.1	0.67
Mean Grad	0.1	0.74	0.16	0.42	0.1	0.74
LAVi	0.54	0.003	0.52	0.005	0.47	0.01
PAPs	0.6	0.001	0.6	0.001	0.32	0.1
ACT	-	-	0.66	< 0.001	0.51	0.005
After PMBV						
MVA	-0.42	0.03	-0.1	0.87	-0.3	0.14
Max Grad	0.12	0.54	0.1	0.81	0.12	0.68
Mean Grad	0.22	0.26	0.32	0.10	0.38	0.05
LAVi	0.61	0.001	0.57	0.002	0.50	0.007
PAPs	0.52	0.005	0.58	0.001	0.27	0.16
ACT	-	-	0.58	0.001	0.57	0.001

MVA: Mitral valve area, ACT: Atrial conduction times, PMBV: Percutaneus mitralballoon valvuloplasty, NYHA class: New York Heart Association Class, PAPs: Pulmonary artery systolic pressure, LAVi: LA volume index.

also shown that M-mode anteroposterior LA diameter is related to the development of AF[8,9]. The anteroposterior LA diameter > 5 cm in sinus rhythm was associated with approximately four times the risk of developing AF in the Cardiovascular Health Study. The effect of LA volume on the prediction of AF has superiority over the LA diameter[10-12].

In recent studies, the novel echocardiographic and electrocardiographic parameters that predict the structural changes in the left atria and correspondingly the occurrence of AF have been reported. These are PWD that is an electrocardiographic parameter and AEMD and ACT that are measured by TDI study[13-17]. In addition, in various contributing factors to develop AF such as obstructive sleep apnoea, diastolic dysfunction, dilated cardiomyopathy and hypertension the prolongation of AEMD during sinus rhythm has been reported[12,18-21]. Therefore, increase in AEMD is an electrophysiological marker that predisposes a patient to develop AF. Prolongation of P-wave duration and increased PWD were correlated with increased AF risk[13,22]. It has been reported that PWD was higher in patients with rheumatic MS than in the healthy control group[23-25].

Ozer et al. investigated AEMD in patients with MS by using this TDI method. Their findings suggested that patients with mild-to-moderate MS had longer AEMD than healthy control subjects[26]. In that study the correlation between AEMD and LA size and also between AEMD and electrocardiographic AF markers (P-max and PWD) have been well documented. Güntekin et al. have also shown that P-max and P-min were longer and PWD was higher in patients with MS than in control subjects. They have also reported that progressive increase in P-wave duration and PWD are related to MS progression. Correspondingly Rezaian et al. found a significant prolongation of P-max in patients with MS compared to control subjects ($p< 0.001$) and significant correlation between P-max and LA size ($r= 0.505$, $p< 0.001$), transmitral valve gradient ($r= 0.371$, $p= 0.01$) with no significant correlation with MVA ($r= -0.379$, $p= 0.007$[27]. But the correlation between PWD and echocardiographic parameters was not detected in this study.

PMBV is considered for patients who have symptomatic, moderate or severe MS who have indications favourable for this procedure. The procedure of PMBV has a low complication rate with significant effects in symptoms and haemodynamic changes. A successful PMBV had a beneficial effects on the improvement in MVA and transmitral gradient that resulted in decrease in LA volume and LAVi. It has been estimated that PMBV decreases the incidence of AF in patients with MS, although there are not data from comparative studies. Eid Fawzy et al. investigate the effect of PMBV on the occurrence of AF in 382 patients who underwent successful PMBV. Their study demonstrated that the incidence of AF (8.9%) was lower in patients with severe MS who underwent PMBV in comparison with reported series (29%) of similar patients without any intervention. They have also shown the AF predictors such as larger LA, age and smaller MVA[28]. Turhan et al. demonstrated the decrease in maximum P-wave duration and PWD on the first day and at the end of the first month after PMBV[29]. However, they could not demonstrated that the decrease in maximum P-wave duration and PWD have no relation with improvement in MVA, LA size, LA pressure, PAPs and mean mitral gradient after the procedure. It is reasonable to suggest that the decrease in sympathetic activity after the successful PMBV procedure that was associated with the increase in cardiac index causes the decrease in PWD and P-max after PMBV. Demirkan et al.

have shown in a study including 30 patients who were eligible for PMBV that there was statistically significant decrease in AEMD with P-max and PWD that were calculated using the ECG recording in the early period after PMBV (in 72 h) analogically pre-PMBV period[30].

CONCLUSION

This study has demonstrated that atrial conduction properties that have also been evaluated with ECG and TDI studies significantly correlate with other echocardiographic parameters in patients with MS. In addition, significant improvement occurred in these parameters at the end of the 1 year after PMBV. Further prospective investigations may provide useful data for the detection of the relation between atrial electromechanical characteristics and development of AF in patients with MS.

CONFLICT of INTEREST

The authors reported no conflict of interest related to this article.

AUTHORSHIP CONTRIBUTIONS

Concept/Design: AG, CD

Analysis/Interpretation: AG, MB, UA

Data Acquisition: SP, YG, SE

Writting: YG, AG, EA

Critical Revision: KT, TK, İB, SB

Final Approval: All of authors

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