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Impact Of Percutaneous Mitral Balloon Valvuloplasty on P Wave Dispersion In Patients With Rheumatic Mitral Stenosis

Romatizmal Mitral Stenozlu Hastalarda Perkütan Mitral Balon Valvüloplastinin P Dalga Dispersiyonu Üzerine Etkisi

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ABSTRACT

Introduction: P-wave dispersion (PWD) is a new electrocardiographic (ECG) index believed to reflect heterogenous atrial conduction with ECG leads of different orientation. Mitral stenosis (MS) is associated with increased P-wave dispersion, which are markers of atrial fibrillation risk. This study was conducted to assess the immediate effect of successful percutaneous mitral balloon valvuloplasty on these parameters.

Materials and Method: 70 patients with moderate or severe rheumatic MS (%98 fe¬males, aged 44±12 years) and 60 healthy vol¬unteers (%95,7 females, aged 45±11 years) as a control group were enrolled in this study. 12-lead ECGs were recorded for each patient 1 day before PMBV to evaluate baseline maximum, minimum P-wave duration, PWD and repeated within 72 hours.

Results: The maximum P-wave duration and PWD in MS patients were found to be significantly higher than the control group (p<0,001). Electrocardiographic parameters of maximum P-wave duration (142 (120-170) vs 130 (110-164), p< 0.001) and PWD (45 (30-69) vs 35 (16-57), p<0,001) decreased in the acute period of PMBV (p<0,001). On the other hand, the procedure had no significant effect on minimum P-wave duration (p=0,111).

Conclusion: Our study has shown that Pmax and PWD was significantly higher in patients with MS than in healthy control subjects and they decreased significantly after successful PMBV. Further prospective long term studies are needed to confirm the relation between atrial conduction velocities and development of AF in patients with MS.

Keywords: Mitral stenosis, Percutaneous mitral balloon valvuloplasty, P wave dispersion

ÖZET

Giriş: P dalga dispersiyonu, farklı elektrokardiyografi (EKG) leadlerinden heterojen atrial iletiyi yansıttığına inanılan yeni bir elektrokardiyografik indekstir. Mitral stenoz, atrial fibrilasyonun bir göstergesi olan artmış PWD ile ilişkilidir.Çalışmamız başarılı perkütan mitral balon valvüloplastinin bu parametreler üzerine olan etkisini incelemek için tasarlandı.

Hastalar ve Metod: Orta ve ciddi romatizmal mitral stenozu olan 70 hasta (%98 kadın, ortalama yaş 44±12) ve 60 sağlıklı kontrol grubu (%95,7 kadın, ortalama yaş 45±11) çalışmaya alındı. PMBV'den 1 gün önce ve yapıldıktan sonra 72 saat içinde 12 derivasyonlu EKG çekilerek maksimum ve minimum P dalga süresi, P dalga dispersiyonu hesaplandı.

Bulgular: Maksimum P dalga süresi ve PWD MS hastalarında kontrol grubuna göre anlamlı olarak fazla bulundu (p<0,001). Pmax (142 (120-170) vs 130 (110-164), p< 0.001) ve PWD (45 (30-69) vs 35 (16-57), p<0,001), PMBV sonrası akut dönemde azaldı (p<0,001). Diğer yandan işlemin minimum P dalga süresi üzerine anlamlı etkisi olmadı (p=0,111).

Sonuç: Çalışmamızda MS lu hastalarda P max ve PWD'nin sağlıklı kontrol grubuna göre anlamlı olarak fazla olduğunu ve başarılı PMBV sonrası anlamlı dercede azaldığını gösterdik. MS'lu hastalarda AF ile atrial ileti velositeleri arasındaki ilişkiyi doğrulamak için prospektif uzun dönem takipli çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: mitral stenoz, perkütan mitral balon valvüloplasti, P dalga dispersiyonu

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INTRODUCTION

In developing countries, rheumatic mitral stenosis (MS) is still a significant cause of morbidity and mortality. The combination of mitral valve disease and atrial inflammation, secondary to rheumatic carditis leads to left atrial (LA) dilation, fibrosis of atrial wall, and disorganization of atrial muscle bundles ; leading to electrical inhomogeneity, nonuniform conduction velocities and inhomogenous refractory periods (1). The resultant electrophysiologic and electromechanical abnormalities are associated with a higher risk of atrial fibrillation (AF) (2). P-wave dispersion (PWD) is a new electrocardiographic (ECG) index believed to reflect heterogenous atrial conduction with ECG leads of different orientation. Increased maximum P-wave duration (Pmax) on surface ECG has been reported to be associated with left atrial size and risk of developing AF (3). It has been defined as the difference between maximum and minimum P wave duration. Percutaneous mitral balloon valvuloplasty (PMBV) is the procedure of choice in patients who have clinically severe MS and favorable mitral valve morphology for this procedure. In previous studies it has been shown that PWD is increased in patients with MS and decrease both the short and long term (4,5). This study was conducted with an aim of studying the immediate effect of successful PMBV on PWD in patients with severe rheumatic MS, in normal sinus rhythm.

METHODS

We enrolled retrospectively 70 patients with moderate or severe rheumatic MS (%98 females, aged 44±12 years) who underwent successful PMBV in our clinic between 2009- 2017 and 60 healthy volunteers as a control group (%95,7 females, aged 45±11 years). The control group had normal physical examination, standard 12-lead ECG, negative stress test and normal echocardiographic examination. All patients were in sinus rhythm during evaluation. 12-lead ECGs were recorded for each patient 1 day before PMBV to evaluate baseline maximum, minimum P-wave duration, PWD and repeated within 72 hours. Transthoracic echocardiography (TTE) using Vivid S5 was performed for each patient. They also underwent transesophageal echocardiography (TEE) 1 day before the procedure in order to rule out left atrium or appendage thrombosis. All patients' mitral regurgitation grade was <2/4. Patients with significant valve disease other than secondary tricuspid regurgitation, left ventricular hypertrophy , left ventricular disfunction, coronary heart disease, atrial fibrillation, bundle branch block or evidence of any other intraventricular conduction defect, previous pacemaker implantation, electrolyte abnormalities, hyperthyroidism, hypertension, diabetes mellitus, renal failure, taking any chronotropic medication such as beta-blockers or digitalis were excluded from the study. Mitral valve anatomy was scored according to the Wilkins echo

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scoring system (6). All study subjects were informed and written consent was obtained. The indications for PMBV were; symptomatic patients with moderate or severe MS (MVA≤1,5 cm^2 by planimetry or mean transmitral diastolic gradient (MDG) ≥10 mmHg) with favorable valve morphology; symptomatic patients with unfavorable valve morphology but at high risk for surgery and asymptomatic patients with high thromboembolic risk and haemodynamic decompensation. Procedural success was defined as MVA >1.5 cm^2 without severe mitral regurgitation.

Echocardiography

All patients underwent TTE using Vivid 5 ultrasound system before PMBV and repeated within 72 hours. All measurements were made according to the guidelines of the American Society of Echocardiography (7). Cardiac dimensions and volumes were measured and left ventricular (LV) ejection fractions were calculated by the biplane Simpson's method.Mitral valve area (MVA) was measured by planimetry and pressure half-time methods (8). Continous wave Doppler was used to calculate the mitral gradient and the peak pressure gradient of TR by using the Bernoulli equation. Color flow Doppler was used to detect the presence of mitral regurgitation. Semiquantitative estimation of MR (mild, moderate, or severe) was made with color flow mapping in parasternal long axis and apical 4-chamber views. During echocardiographic evaluation a continuous one-lead ECG recording was provided. Data was recorded from the average of three cardiac cycles. Additionally; transesophageal echocardiographic examinations were performed 1 day before the procedure for evaluation of the mitral valve morphology and exclusion of the thrombosis.

Electrocardiography

At a rate of 25 mm/s 12-lead electrocardiogram in a supine position was recorded for each patient 1 day before and within 72 hours after PMBV. P-wave durations were measured manually by one investigator blinded to the clinical details of the patient, using digital calipers and magnifying lens (fivefold magnification) to define the electrocardiographic deflections. P-wave duration was measured from the onset to the offset of P wave. The longest P-wave duration measured on any of the 12 ECG leads was defined as the P maximum (Pmax) and the shortest P-wave duration on any lead was defined as the P minimum (Pmin). Subsequently, P-wave dispersion (PWD) was defined as the difference between maximum P-wave and minimum P-wave duration.

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Percutaneous mitral balloon valvuloplasty

An experienced cardiologist performed all PMBV procedures via an anterograde transvenous approach with a transseptal Brockenbrough needle, following the technique described by Inoue et al.(9) .Initial balloon size was selected according to body surface area .The final result was considered successful if the MVA >1.5 cm2 without severe mitral regurgitation (≤ 2/4 MR).

Statistical analysis

Statistical analysis was made using the computer software Statistical Package for Social Sciences (IBM SPSS Statistics for Windows, version 21.0. released 2012, IBM Corp., Armonk, New York, USA) and data were expressed as "mean (standard deviation; SD)" for variables with normal distribution, "n (%)" for categorical variables and "median (minimum-maximum)" for variables with abnormal distribution. Fischer's exact test analysis was performed for categorical variables. Fitness to normal distribution was analyzed with the Kolmogorov Smirnov test. Mann-Whitney U test was used for comparing quantitative variables with abnormal distribution while Student t-test was used for comparing the means between two groups with normal distribution. Pearson correlation tests were performed for correlations between ordinal variables or continuous variables with abnormal distribution. Paired sample t-test was used for related samples with normal distribution while Wilcoxon signed rank test was used for related samples with abnormal distribution. A p-value < 0.05 was considered statistically significant.

RESULTS

Demographic, clinical, and echocardiographic characteristics of the patient and control groups are presented in Table 1. All patients and controls had normal LV systolic function. The two groups were similar with respect to age, gender, LV ejection fraction, LV dimensions (p>0.05), but LA diameter, pulmonary artey pressure (PAPs) values were significantly higher in patients with MS. When we compared the two groups with regard to ECG parameters, baseline maximum P-wave duration and PWD in MS patients were found to be significantly higher than the control group (p<0,001) (Figure 1).

A comparison of changes in electrocardiographic and echocardiographic parameters between baseline and after PMBV is displayed in Table 2**.** Statistically significant improvement in left atrial diameter, mitral valve area (MVA), PAPs and max/mean mitral gradient were achieved in all patients after PMBV (p<0,001). Electrocardiographic parameters of maximum P-wave duration (142 (120-170) vs 130 (110-164), p< 0.001) and PWD (45 (30-69) vs 35 (16-57), p<0,001) decreased in the acute period of PMBV (p<0,001). On the other hand, the procedure had no significant effect on minimum P-wave duration (p=0,111) (Figure 2). Mean pre-PMBV MVA was 1.056±0.17 cm2 and significantly improved to 1,83±0,30 cm2 after PMBV (p<0.001). Median pre-PMBV mean gradient was 14 (4-33) mmHg, which significantly decreased to 5 (2-18) mmHg (p<0,001) within 72 hours after PMBV. Median PAPs 1 was 47,5 (30-120) mmHg and significantly decreased to 35 (20-120) mmHg (p:<0,001).

PWD was significantly correlated with severity of mitral stenosis [MVA (r= -0.8 p<0.0001), max gradient (r=0,74 p<0,0001), mean grad (r=0,77 p<0,0001), PAPs (r=0,79 p<0,0001), LA (r=0,76 p<0,0001)] (Figure 3).

DISCUSSION

In our study, we found that; Pmax and PWD were significantly longer in patients with clinically severe MS than in healthy control subjects and decreased within 72 hours after PMBV. However; echocardiographic parameters of MS were significantly correlated with PWD.

Rheumatic MS is an important health issue in developing countries (1). The combination of mitral valve disease and atrial inflammation secondary to rheumatic carditis causes increased atrial stretch and dilatation, fibrotic changes within the wall of the atrium and disorganization of the atrial muscle bundles (10). These structural changes may lead to electrical inhomogeneity, disparate conduction velocities, and inhomogenous refractory periods within the atrial myocardium reflecting on ECG as increased Pmax and PWD (3). Increased Pmax and PWD are well-known ECG markers of nonuniform and heterogeneous atrial conduction. Various studies have demonstrated their association with left atrial size and risk of developing AF (3,11,12). Dilaveris at al. (3) was the first to describe PWD as the difference between maximum and minimum P-wave duration.

Previous investigations have shown that PWD is increased in patients with rheumatic MS (4,5,13,14). Turhan et al. [4] showed the decrease in Pmax and PWD, in both the short and long term after PMBV. In accordance with those studies we found significantly higher PWD for patients with MS compared with control subjects and it was correlated with the echocardiographic parameters of MS significancy. We also found that Pmax and PWD significantly decreased within 72 hours after PMBV as previously described by other studies (13-15). Demirkan et al. (13) have shown in a study including 30 patients with moderate and severe MS, that there was statistically significant decrease in atrial electromechanical delay (AEMD) with P-max and PWD in the early period after PMBV (in 72 h). Also, in electrophysiological studies in patients undergoing PMBV, due

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to relief of atrial stretch after the procedure, immediate improvement in conduction abnormality was detected (16). The decline of PWD immediately after PMBV was not supported by Beig et al (17); they found statistically significant decrease in inter and intraatrial electromechanical delays and believed that surface ECG manifestations of delayed and heterogeneous atrial conduction may take time to resolve. This needs confirmation on follow-up.

All these findings suggest that PWD is increased in MS and mechanical dilation of the mitral valve with a balloon reduces susceptibility to AF even in the early period. Therefore, PWD can be used to classify patients with a high risk of AF during sinus rhythm.

LIMITATIONS

The main limitation of our study was that we measured the conduction times only with ECG but did not use echocardiographic and electrophysiological study to validate our results. Secondly, we don't have long term follow-up data. Hence, the relationship between these parameters and the development of AF is not clearly known. This study was carried out at a single center.Futher large-scale and long-term studies may be necessary to assess the clinical impact of Pmax and PWD on prevention of AF.

CONCLUSION

Our study has shown that Pmax and PWD was significantly higher in patients with MS than in healthy control subjects. In addition; they decreased significantly after successful PMBV. These simple ECG indices may predict the success of the procedure after PMBV and susceptibility to AF . Further prospective long term studies are needed to confirm the relation between atrial conduction velocities and development of AF in patients with MS.

CONFLICT OF INTEREST

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

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Table 1. The clinical, echocardiographic and electrocardiographic parameters of patients with mitral stenosis and control subjects

	Control	MS	p
Age (years)	44±12	45±11	0,570
Gender (F)	98%	95,7%	0,370
MVA	5 (4-6,2)	1,1 (0,7-1,6)	<0,001
Max grad	3 (2-6)	23,5 (8-46)	<0,001
Mean grad	1,50 (0,78-2,10)	14 (4-33)	<0,001
PAPs	15 (15-35)	48 (30-120)	<0,001
LA diameter (cm)	30 (23-38)	44 (34-69)	<0,001
LVEDD (cm)	44 (38-55)	45 (28-61)	0,266
LVESD (cm)	27 (22-39)	28 (19-43)	0,058
LVEF (%)	65 (50-65)	65 (50-67)	0,162
P-max (ms)	119±8	143±11	<0,001
P-min (ms)	95 (28-118)	98 (75-125)	0,187
PWD (ms)	25 (10-35)	45 (30-69)	<0,001

MVA, mitral valve area;PAPs, pulmonary artery systolic pressure; LA left atrium; LVEDD, left ventricle end diastolic diameter; LVESD,left ventricle end systolic diameter;LVEF, left ventricle ejection fraction; PWD,P wave dispersion

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Table 2. Baseline and after PMBV clinical, electrocardiographic and echocardiographic characteristics of patients

	Before PMBV	After PMBV	p
MVA	1,056±0,17	1,83±0,30	<0,001
Max grad	24,1±8,06	12,29±4,65	<0,001
Mean grad	14 (4-33)	5 (2-18)	<0,001
PAPs	47,5 (30-120)	35 (20-120)	<0,001
LA diameter (cm)	44 (34-69)	42 (31-54)	<0,001
LVEDD (cm)	45 (28-61)	46 (33-57)	0,272
LVESD (cm)	28 (19-43	28,5 (34-69)	0,87
LVEF (%)	65 (50-67)	65 (50-65)	0,383
P-max (ms)	142 (120-170)	130 (110-164)	<0,001
P-min (ms)	98 (75-125)	95 (80-125)	0,111
PWD (ms)	45 (30-69)	35 (16-57)	<0,001

MVA, mitral valve area;PAPs, pulmonary artery systolic pressure; LA left atrium; LVEDD, left ventricle end diastolic diameter; LVESD,left ventricle end systolic diameter;LVEF, left ventricle ejection fraction; PWD,P wave dispersion

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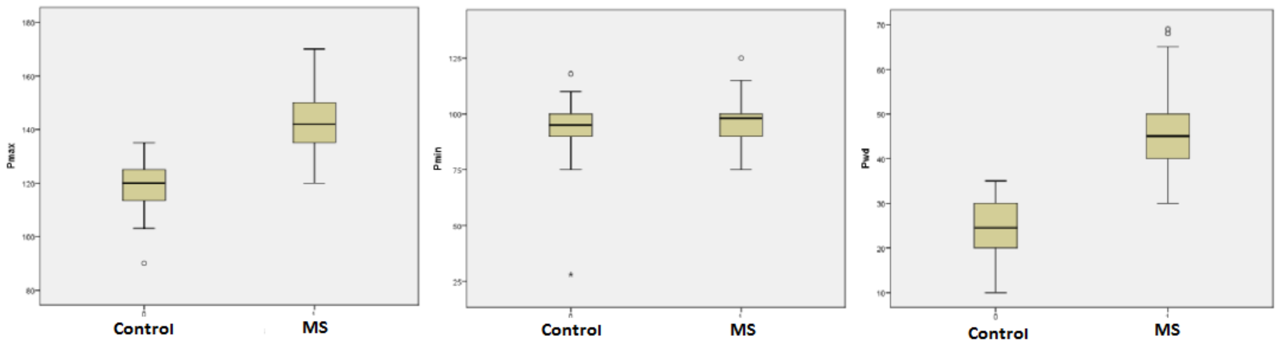

Figure 1: Box-plot representations for PWD, Pmax and P min between control and patients with mitral stenosis. MS:mitral stenosis.

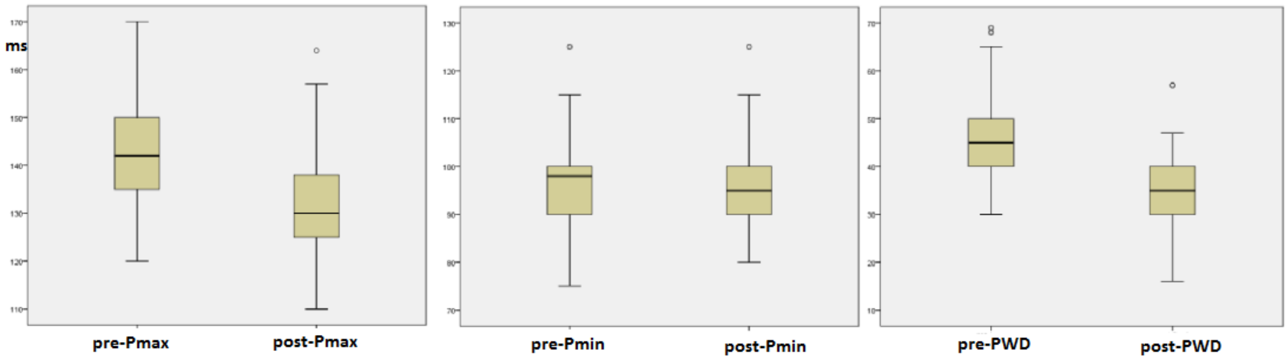

Figure 2: Box-plot representations for PWD, Pmax and Pmin between pre-PMBV and post-PMBV patients. PMBV: percutaneous mitral balloon valvuloplasty

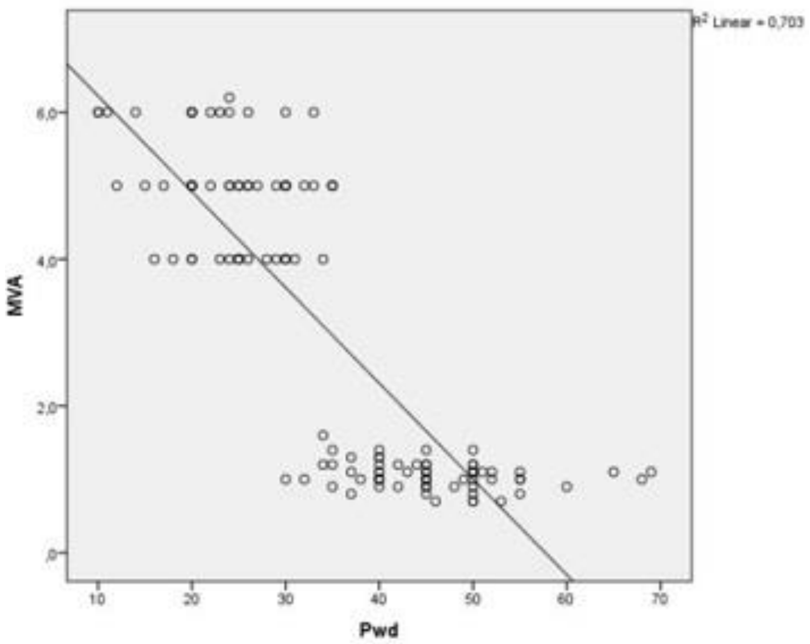

Figure 3: Correlation analysis of PWD with MVA. PWD:P wave dispersion, MVA: mitral valve area.