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TO STUDY THE EFFECT OF BMV ON P WAVE DISPERSION AND SHORT TERM PROGNOSTIC IMPACT OF P WAVE DISPERSION IN PREDICTION OF CLINICAL OUTCOME AFTER PERCUTANEOUS BALLOON MITRAL VALVULOPLASTY IN PATIENTS WITH MITRAL STENOSIS AND SINUS RHYTHM

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Abstract

Background: The aim of the present study was to study the effect of percutaneous balloon mitral valvuloplasty (PBMV) on P wave dispersion and to test the correlation between P-maximum and P-dispersion to right ventricular function and pulmonary artery pressure before and after PMBV. Also to study the impact of P-maximum and P-wave dispersion on the short term clinical outcome after successful PBMV in patients with mitral stenosis (MS) and sinus rhythm.

Methods: 75 patients undergoing PMBV were enrolled in this study. We evaluated P-maximum, P-minimum and P-wave dispersion before and one month and one year after PBMV. We studied the changes in pulmonary arterial pressure (PAP), left atrial (LA) dimension, mitral diastolic gradient, and mitral valve area, in addition to the changes in right ventricular function utilizing tissue Doppler assessment both before and after PMBV, in addition the role of the P-wave dispersion in prediction of late cardiac events.

Results: There were significant decrease in mean diastolic gradient, PAP, and LA size and significant improvement in right ventricular tissue Doppler indices after PMBV. Accompany these hemodynamic changes after PMBV. P-maximum and P-wave dispersion were found to be decreased ($P < 0.001$).

Conclusion: Successful PBMV was associated with a decrease in Pmax and PWD. These simple electrocardiographic indices may predict the success of the procedure immediately after PBMV. The P-maximum and P-wave dispersion changes were correlated with significant impairment of right dysfunction and the degree of pulmonary artery pressure.

Keywords: PBMV.PAP,LA

Introduction

P-wave duration (Pmax /Pmin) and P-wave dispersion (PWD) are electrocardiographic (ECG) indices that recently have received increasing attention and been examined in a broad range of clinical settings. The prolongation of intra- and inter-atrial conduction time, and inhomogeneous propagation of sinus impulses are well-known electrophysiologic characteristics of the atrium prone to fibrillate.[1,2] PWD has been associated with these characteristic changes in the atria and used for noninvasive surrogate detection of atrial electrophysiology.[1-4] It can be defined as the difference between Pmax and Pmin.

Rheumatic mitral stenosis (MS) is frequently seen in developing countries and causes significant morbidity and mortality.[5] Atrial fibrillation is the most common sustained arrhythmia encountered in patients with rheumatic MS. Limited studies are available in the literature on the relation between MS and P-wave indices.

First, Turhan et al.[6] evaluated the effect of PBMV on PWD in 29 patients with MS and concluded that PWD is significantly higher in patients with MS than in healthy control subjects, and it decreases significantly after PBMV both in the short and long term. Then, Guntekin et al.[7] followed 30 patients with mild to moderate MS with ECG and echocardiography and showed that Pmax and PWD increase progressively in accordance with the severity of MS.

The purpose of this study was to investigate for the first time if the immediate changes in these P-wave indices could confirm a successful PBMV procedure in patients with hemodynamically significant MS.

Aims and Objective

- The aim of the present study was to study the effect of PBMV on P wave dispersion and to test the correlation between P-maximum and P-dispersion to right ventricular function and pulmonary artery pressure before and after PMBV.
- Also to study the impact of P-maximum and P-wave dispersion on the short term clinical outcome after successful PBMV in patients with mitral stenosis (MS) and sinus rhythm.

Material and Methods

A total of 75 patients with mitral stenosis and fulfill the criteria needed for percutaneous mitral balloon

valvuloplasty were included in the study. Only persons 35 years of age or younger were included in the study to minimize the chance of the presence of associated coronary artery disease.

Inclusion criteria: 1) pure mitral stenosis of rheumatic origin; 2) nonexistent or mild mitral insufficiency; 3) absence of concomitant hemodynamically significant other valvular disease; 4) absence of any disease that could affect myocardial function (e.g. coronary artery disease, chronic lung disease, cardiomyopathies); 5) absence of atrioventricular conduction ab- normalities and atrial fibrillation.

None of them were taking type I or type III antiarrhythmic agents. Beta-blockers, digitalis which can affect atrial structural and electrophysiologic remodeling were withheld for at least 1 day before the procedure.

Study Site

Department of Cardiology, SMS Medical College and Associated Hospital, Jaipur, Rajasthan, India.

Study Duration

From May 2015 to December 2016

Methodology

Echocardiographic evaluation

The echocardiographic examination was performed at rest, with the patient at left lateral decubitus position. Transesophageal and transthoracic echocardiography were performed less than 24 hours before the procedure. Transthoracic echocardiography was repeated one day, one month and one year after PBMV. Mitral valve anatomy was scored on the basis of the Wilkins echo scoring system.[8]

Mitral valve area was calculated by planimetry or, in the absence of significant mitral regurgitation (MR), from pressure half-time.[9] Semiquantitative estimation of MR (mild, moderate, or severe) was made with color flow mapping in parasternal long axis and apical 4-chamber views. The mean transmitral diastolic mitral valve gradients (mMVG) were also calculated with Doppler ultrasound scanning studies. Systolic pulmonary artery pressure (sPAP) was calculated using the Bernoulli equation from tricuspid insufficiency flow in the parasternal short axis and apical 4-chamber views, and the highest tricuspid regurgitation velocity was taken as the study sample. All values were measured on three separate beats and then averaged for all parameters.

We defined the PBMV successful at the one month follow-up transthoracic echocardiography if a valve area increment ≥50% or a final valve area >1.5 cm2, with no more than moderate MR is achieved. Only successful PBMV cases were included in the study.

PBMV

It was performed under local anesthesia by the antegrade transseptal approach with a stepwise dilation technique using Inoue balloon catheter (Toray Industries, Inc., Tokyo, Japan). Left heart pressure measurements, that is left atrial (LA) and left ventricular diastolic pressures, were obtained before and after PBMV. The procedure was terminated once a satisfactory hemodynamic result was achieved.

ECG measurements

ECG was recorded for each patient 1 day before PBMV and repeated before discharge, and at the end of the first month and one year after discharge. All measurements of Pmax /Pmin were measured manually in all simultaneously recorded 12 leads of the surface ECG which was taken at a rate of 50 mm/sec with 1 mV/cm standardization. The mean Pmax /Pmin for at least 3 complexes were calculated in each lead and their average values were used for groups comparisons.

For greater accuracy, measurements were performed with magnifying lens, as described by previous investigators.[2,11] The onset of the P wave was defined as the point of first visible upward departure from baseline for positive waveforms, and as the point of first downward departure from baseline for negative waveforms. The return to the baseline was considered to be the end of the P wave. The Pmax measured in any of the 12 leads of the surface ECG was used as the longest atrial conduction time. The difference between the Pmax and the Pmin was calculated and defined as PWD.

Statistical Analysis

Continuous Data were expressed as the mean ± SD and categorical data as proportion. Groups were compared by the Student's t-test for the continuous variables, the $\chi 2$ test for qualitative variables. Baseline and follow-up echocardiographic and ECG parameters were compared by Repeated measure ANOVA. A P value<0.05 was considered significant. All statistical analyses were conducted with SPSS 17 (SPSS Inc., Chicago, IL), trial version.

Results

75 patients (34 men, 64 women; mean age 28.26 ± 5.78 years) were enrolled in this study. Among these patients, 75 (75%) experienced a successful PBMV according to our definition. The mean Wilkins echo score in all patients was 6.85 ± 0.91. The MVA was 0.79 ± 0.2 cm2 which increased to1.48 ± 0.26 cm2 after PBMV (Table 1). There was a trend for reduction in mean MVG and SPAP after successful PBMV. (Table 2).

Pmax and PWD were significantly decreased immediately after one day of procedure (P<0.001), at one month

(*P*<0.001) but at one year there was no change in Pmax and PWD as compared to that at 1 month(Table 2).

Table 1: General characteristics of the study subjects (N=100)

Age (mean ± SD); years		28.26 ± 5.78
Sex male N (%)		26(34.6%)
female		49 (65.3%)
ECHO score (mean ± SD)		6.85 ± 0.91
MVA (mean ± SD)		0.79 ± 0.197
LA size		43.83 ± 5.41
PASP		57.74 ± 28.76
TAPSE		19.17 ± 3.075
MR	absent	9 (9%)
	mild	31 (31%)
	trivial	35 (60%)

Table 2: P-wave indices before and after PBMV

Indices (msec)	Before BMV mean±SD	After 1 day mean±SD	After one month mean±SD	After one year mean±SD
P max	121.5 ± 9.958	98.4 ± 9.732* (<0.001)	85.33 ± 11.55* (<0.001)	85.13 ± 11.35 (<0.001)
P dispersion	71.47 ± 12.58	58.13 ± 11.6* (<0.001)	45.33 ± 11.23* (<0.001)	45.02 ± 11.19 (<0.001)

Table 3: Change in MVA after PBMV

Time point	MVA	P value (compared to before PBMV)	P value compared to previous time
Before PBMV	0.791 ± 0.1969	-	-
One day after PBMV	1.484 ± 0.2624	<0.001 (S)	<0.001 (S)
One month after PBMV	1.496 ± 0.2751	<0.001 (S)	1.000 (NS)
One year after PBMV	1.496 ± 0.2751	<0.001 (S)	-

Repeated Measures ANOVA --- F = 634.084 P < 0.001 (S)

Table 4: MTMG (mean transmitral gradient) before and after PBMV

Indices	Before BMV mean±SD	After 1 day mean±SD	After one month mean±SD	After one year mean±SD
MTMG	17.75 ± 6.284	5.893 ± 1.879*	5.387 ± 1.469	5.387 ± 1.469

Table 5: Change in PASP after PBMV

Time point	PASP	P value (compared to before PBMV)	P value compared to previous time
Before PBMV	57.74 ± 28.76	-	-
One day after PBMV	40.71 ± 16.21	<0.001 (S)	<0.001 (S)
One month after PBMV	32.14 ± 11.62	<0.001 (S)	<0.001 (S)
One year after PBMV	32.14 ± 11.62	<0.001 (S)	--

Repeated Measures ANOVA - F = 133.064; P <0.001 (S)

Table 6: Change in TAPSE after PBMV

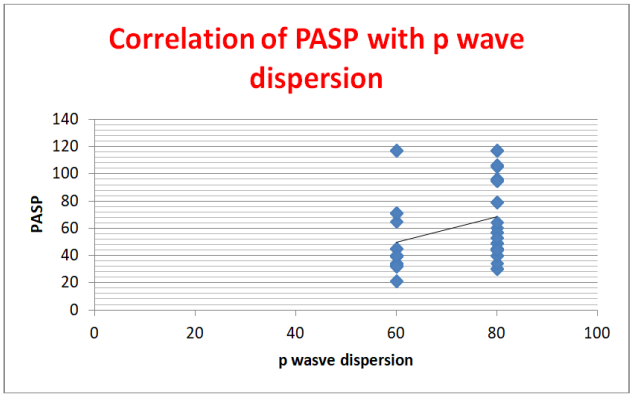
Time point	TAPSE	P value (compared to before PBMV)	P value compared to previous time
Before PBMV	14.17 ± 3.075	-	-
One day after PBMV	20.54 ± 1.795	<0.001 (S)	<0.001 (S)
One month after PBMV	21.13 ± 1.041	<0.001 (S)	<0.001 (S)
One year after PBMV	21.13 ± 1.041	<0.001 (S)	-

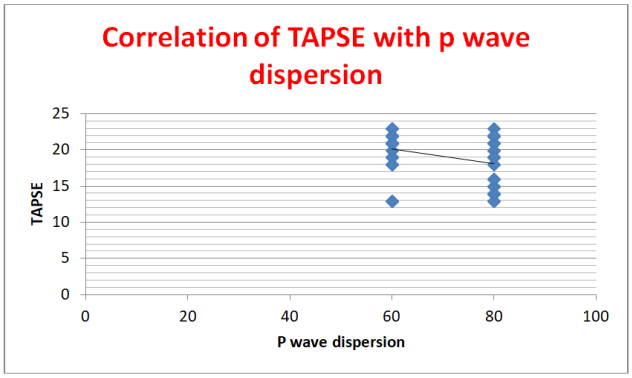
Repeated Measures ANOVA --- F 54.491; P < 0.001 (S)

Table 7: Correlation of P wave dispersion with different variables

Variable	r	P value
PASP	0.326	0.0044 (S)
TAPSE	-0.305	0.0078 (S)

The maximum P-wave duration and P-wave dispersion in patients with MS had a weak correlation with the degree of pulmonary artery pressure and tissue Doppler indices of right ventricular dysfunction.





Discussion

The major finding of this study was that in patients with severe MS only successful PBMV was associated with a decrease in Pmax and PWD. These simple ECG indices may predict the success of the procedure immediately after PBMV.

Dilaveris at al.[2] was the first to describe PWD as the difference between maximum and minimum P-wave duration measured on the standard 12-lead surface ECG and showed that it is a marker of inhomogeneous and discontinuous propagation of sinus impulses.[1,2] They also observed that increased PWD carries an increased risk for AF.[2] Furthermore, the correlation between inter-atrial and intra-atrial conduction abnormalities and the induction of AF has been well documented.[12,13]

However, there are only few studies [6,7,15-18] on the relation between MS and atrial conduction /refractoriness in the literature. Soylu et al.[16] studied hemodynamic and

electrophysiologic changes in 25 patients undergoing PBMV. They showed that relief of chronic atrial stretch results in an immediate increase in atrial effective refractory period (AERP) and decrease in AERP dispersion, which suggests the potential reversibility of the electrophysiological features of chronic atrial dilatation. Later on, Coronel et al.[17] determined AERP and activation times in 9 patient before and after PBMV and concluded that MS is associated with LA conduction delay, increased LA dispersion of conduction, and conduction asymmetry. These electrophysiologic changes were immediately reversed by PBMV.

There are only two studies which have explored the relation between MS and P-wave indices.

First, Turhan et al.[6] studied 29 patients who were undergoing PBMV and found that Pmax and PWD were significantly increased in patients with severe MS than in healthy control subjects and both decrease progressively after PMBV.

Later, Guntekin et al.[7] followed 30 patients with mild to moderate MS and observed that Pmax and PWD increase progressively in accordance with increasing severity of MS.

Rheumatic MS is an important health issue in the developing countries.[5] Increased LA pressure due to MS and the inflammation secondary to rheumatic carditis may produce atrial stretch and dilatation, fibrotic changes within the wall of the atrium and disorganization of the atrial muscle bundles.[18] These structural changes may lead to unequal conduction velocities and heterogeneous refractory periods through the atrial myocardium[5,18] reflecting on ECG as increased Pmax and PWD which lead to AF.[1,2]

In fact, AF is the most common sustained arrhythmia encountered in these patients which is poorly tolerated due to both loss of atrial contraction and associated rapid ventricular rate, and increases morbidity and mortality.[5] Timely and most importantly “effective” PBMV may help in preventing the progress of the above electrical and structural atrial remodeling and even reverse them, leading to a delay or even prevention in the initiation of AF.

Our findings complement previous studies on the immediate and short term electrophysiologic effects of relieving mitral valve obstruction reflected by simple ECG indices. The new finding of this study is that Pmax and PWD are reduced only if there is effective relief of mitral valve obstruction leading to decreased LA pressure .

Another finding in our study was that in patients with a successful PBMV the decreases in Pmax and PWD continued progressively till the end of the first month but not at one year follow-up.

Another finding in our study is The maximum P-wave duration and P-wave dispersion in patients with MS had a weak correlation with the degree of pulmonary artery pressure and tissue Doppler indices of right ventricular dysfunction.

Some investigators have reported increased sympathetic activity in patients with hemodynamically significant MS[19,20] which could lead to a significant increase in PWD.[21] Cheema et al.[22] verified significant prolongation of Pmax in healthy subjects during epinephrine infusion. Ashino et al.[19] demonstrated that PBMV results in early and long-lasting normalization of sympathetic nerve activity, possibly because of an improvement in arterial baroreflex sensitivity associated with increased cardiac index. We agree with Turhan et al.[6] that this might be the main reason for the immediate reduction in Pmax and PWD after successful PBMV.

The continued decrease in Pmax and PWD during follow-up may be due to remodeling and regression of the LA wall due to decreased intracavitary pressure leading to more homogeneous and continuous propagation of sinus impulses.

Clinical Implication

Chronic AF is associated with an increased risk of embolic events and negative impact on cardiac function and, therefore, an increased morbidity and mortality risk in patients with rheumatic MS. Therefore, the identification of patients who are susceptible to the development of AF will be of great value. Erbay *et al.* [27] have shown that four weeks of oral beta-blocker therapy in patients with moderate-to-severe rheumatic MS can significantly reduce the maximum P-wave duration and the P-wave dispersion. Prolongation of maximum P-wave duration and P-wave dispersion may help detect such patients and may be used as an indicator for early intervention in patients with mitral stenosis.

Limitations

Limitations in this study were: First, the sample size was relatively small, which highlights the need for larger studies. Second, the measurements performed manually on paper-printed ECGs using magnifying lens instead of computer assisted P-wave calculations may restrict the accuracy and reproducibility of the measurements. Although several studies have demonstrated a low error of the measurement of PWD on paper-printed ECGs,[12,21] others have questioned the accuracy and reproducibility of this method.[25,26] Third, large-scale and long-term studies may be necessary to assess the clinical impact of decrease in Pmax and PWD on prevention of AF.

Conclusion

Only successful PBMV was associated with a decrease in Pmax and PWD. These simple ECG indices may predict the success of the procedure immediately after PBMV. Patients without any decrease in Pmax and PWD after PBMV may potentially be at greater future risk and deserve closer follow-up.

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