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Clinical Importance of P Wave Dispersion in Mitral Valve Prolapse

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ABSTRACT

Objective: Mitral valve prolapse (MVP) is a widespread valvulopathy present in 2–6% of the population, affecting more than 170 million people globally. The objective of this study was to assess P wave dispersion (PWD) in patients with MVP to identify the presence of cardiovascular autonomic dysfunction and the potential risk of developing atrial arrhythmias in these patients.

Materials and Methods: The study included 40 healthy control participants (Group 1), 41 patients with non-classic MVP (Group 2), and 36 patients with classic MVP (Group 3). Demographic and clinical characteristics were documented upon admission. An electrocardiographic assessment was conducted to quantify PWD values for both patients and the control group.

Results: The minimum P wave duration was lower in classic MVP patients than in controls and non-classic MVP patients (63±3.6 vs. 70±2.0, p<0.001; 63±3.6 vs. 63±3.6, p<0.001, respectively). P wave dispersion was higher in classic MVP patients than in non-classic MVP patients (47.3±3.2 vs. 39.0±2.3, p=0.001). A significant positive correlation was detected between PWD and maximum P wave duration (P_{max}), minimum P wave duration (P_{min}), maximal leaflet displacement, maximal leaflet thickness, and left atrial diameter (LAD) (r=0.723, p<0.001; r=-0.771, p<0.001; r=0.557, p<0.001; r=0.770, p<0.001; r=0.517, p<0.001, respectively). Maximum leaflet thickness and maximum leaflet displacement were independent predictors of increased PWD in linear regression analysis (β=1.456, p<0.001, β=-0.851, p<0.001).

Conclusion: Patients with classic MVP exhibited prolonged PWD values compared with non-classic MVP patients and normal controls.

Keywords: Autonomic dysfunction, mitral valve prolapse, P wave dispersion.

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INTRODUCTION

Mitral valve prolapse (MVP) is a relatively common heart valve disorder, affecting 2–6% of the population and impacting over 170 million individuals worldwide.[1,2] Patients with MVP frequently experience supraventricular and ventricular tachyarrhythmias. Numerous studies have explored the underlying pathophysiology of increased arrhythmogenesis in these patients, yet the precise etiology of arrhythmia in MVP remains elusive.[3] The prognosis for individuals with MVP largely

depends on the presence and severity of mitral regurgitation (MR). However, findings indicate that individuals with MVP are highly susceptible to abnormal heart rhythms and have an increased risk of mortality, irrespective of the severity of MR or left ventricular systolic dysfunction.[4] Clinically, patients with classic MVP often present with more frequent morbidity conditions, such as rhythm disturbances, and are more susceptible to major complications such as stroke, death, and the need for surgical intervention.[5] Differentiating patients as having classic or non-classic MVP may assist clinicians in determining the prognosis for MVP patients.

P wave dispersion (PWD) is an electrocardiographic (ECG) measure that can be assessed non-invasively and is used to evaluate atrial remodeling. Additionally, it acts as a reliable marker for atrial arrhythmias, particularly atrial fibrillation (AF). Impaired autonomic function has been shown to influence the duration and dispersion of P waves.[6] This dysfunction is closely associated with the development of dysrhythmias and sudden cardiac death (SCD).[7]

To ascertain the clinical significance of MVP on the function of the cardiac autonomic system, we assessed the duration of the P wave and PWD in MVP patients and compared the results with those of a control group.

KEY MESSAGES

- P wave dispersion can be helpful for determining cardiac autonomic dysfunction in the mitral valve prolapse population.
- Patients with mitral valve prolapse exhibiting classic echocardiographic characteristics are more prone to major complications such as rhythm disturbances, stroke, death, and the need for surgical intervention compared to those with non-classic forms.
- Differentiating patients into classic and non-classic forms may assist clinicians in determining the prognosis for individuals with mitral valve prolapse.

MATERIALS AND METHODS

The study population comprised 40 control participants and 77 patients with mitral valve prolapse who were followed up at the cardiology outpatient clinic between December 2018 and January 2024. Upon admission, demographic data and clinical characteristics were documented. Hematological and biochemical parameters were assessed by measuring blood pressure and obtaining fasting blood samples. Exclusion criteria included patients under 18 years of age and those over 70 years of age. Patients with a history of cardiovascular disease (CVD), congenital heart disease, metabolic-endocrine disorders, acute or chronic renal failure, thyroid dysfunction, diabetes mellitus types 1 and 2, hypertension, acute or chronic respiratory diseases, neurological or psychiatric disorders, rheumatologic conditions, gastrointestinal diseases, those taking medications that could impair endothelial function or affect P wave dispersion, those with a systemic infection, or those with an electrocardiogram (ECG) that had indistinctly analyzable P waves were excluded from the study. The study protocol was approved by the Ethics Committee of Alanya Alaaddin Keykubat University School of Medicine (Number: 3-19/26/10/2018).

Electrocardiography

Each participant was positioned in a supine posture and underwent a 12-lead ECG while in sinus rhythm. Prior to the ECG, participants rested for 10 minutes. The electrocardiogram was recorded at a magnitude of 10 mm/mV and a recording speed of 25 mm/s. P wave dispersion was calculated manually on the ECG paper by a cardiologist using a magnifying glass and ruler. The start of the P wave was determined by the initial observable atrial deviation from the isoelectric axis. The return to the isoelectric line marked the end of the P wave. The duration of the P wave was assessed on all ECGs to determine the maximum (P_{max}) and minimum (P_{min}) durations. The difference obtained by subtracting the minimum value of the P wave from the maximum value was defined as PWD. The electrocardiogram results were analyzed by an unbiased clinician who was not aware of the patients' clinical status.

Echocardiography

All participants underwent transthoracic echocardiographic examinations while positioned on their left lateral side to assess standard parameters. Echocardiographic measurements were obtained according to the guidelines set by the American Society of Echocardiography. The diagnosis of MVP was confirmed using cross-sectional echocardiography, which demonstrated a clear protrusion of the anterior and/or posterior leaflet of the mitral valve above the mitral annulus plane. This displacement was observed in both the parasternal longitudinal perspective and the tip of the four-chamber view.

Based on prior clinical and predictive research, patients with MVP were categorized into two groups: non-classic and classic MVP. Classic MVP is characterized by a displacement of the mitral leaflets by at least 2 mm during systole, and a peak thickness of at least 5 mm during diastole. Non-classic MVP was characterized by a displacement of less than 2 mm and a maximum thickness of less than 5 mm.[8] These criteria were considered in making the MVP diagnosis. The severity of MR was evaluated using the method recommended by the current guidelines.

Table 1. Demographic, clinical, echocardiographic, and electrocardiographic variables of study groups

	Study population (n=117)	Group 1 (Controls, n=40)	Group 2 (Non-classic MVP, n=41)	Group 3 (Classic MVP, n=36)	p
Demographic and clinical characteristics					
Age, years	29 (4)	29.5 (5.25)	30 (4)	28 (4)	0.896
BMI, kg/m^2	24 (3)	24 (3)	23 (3)	23.5 (3)	0.175
SBP, mmHg	115 (10)	120 (5)	115 (10)	110 (10)	0.167
DBP, mmHg	70 (10)	70 (7.75)	70 (10)	70 (11.25)	0.933
Creatinine, mg/dL	0.8 (0.2)	0.8 (0.2)	0.8 (0.3)	0.8 (0.125)	0.709
HR, /min	74 (10)	76 (10.25)	73 (10)	74 (7)	0.639
Hemoglobin, (g/dL)	13 (2)	13.5 (1)	13 (2)	13 (2)	0.495
Echocardiographic parameters					
LVDD, mm	44 (2)	43.5 (3)	44 (2)	44 (2)	0.653
LVSD, mm	28 (3)	27 (2)	30 (3)[a]	30 (3.25)[a]	<0.001
LVEF, %	66 (7.3)	62.9 (6.8)	67.5 (5.1)[a]	66.7 (7)[a]	<0.001
IVS, mm	9.4 (0.9)	9.2 (0.8)	9.5 (1)	9.6 (0.72)	0.279
PW, mm	9.3 (8)	9.4 (0.8)	9.3 (1)	9.4 (0.8)	0.158
LAD, mm	35 (3)	33 (3)	34 (3)[a]	36.5 (4)[a,b]	<0.001
E/A	1.2 (0.2)	1.2 (0.22)	1.2 (0.2)	1.1 (0.2)	0.347
Maximal leaflet displacement, mm	3.2 (2.5)	1.2 (0.4)	3.4 (0.8)[a]	3.85 (0.75)[a]	<0.001
Maximal leaflet thickness, mm	3.4 (3.7)	1.2 (0.4)	3.5 (0.8)[a]	5.9 (1.1)[a,b]	<0.001
Presence of mitral regurgitation, n (%)	46 (39.3)	6 (15)	10 (24.4)	30 (83.3)[a,b]	<0.001
Electrocardiographic parameters					
P_{max}, ms	109 (5)	108 (4.25)	107 (4)	112 (3)[a,b]	<0.001
P_{min}, ms	64 (4)	71.5 (3.25)	68 (1)[a]	64 (3.25)[a,b]	<0.001
PWD, ms	40 (8)	37 (3)	40 (4)[a]	47 (3)[a,b]	<0.001

a: Significant difference vs. Group 1; b: Significant difference vs. Group 2. Data are presented as median (interquartile range). BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; HR: Heart rate; LAD: Anterior-posterior left atrial diameter; LVEF: Left ventricular ejection fraction; LVDD: Left ventricular diastolic diameter; LVSD: Left ventricular systolic diameter; IVS: Interventricular septum; PW: Posterior wall; E/A: Early to late atrial mitral doppler peak flow velocity; P_{max}: Maximum P wave duration; P_{min}: Minimum P wave duration; PWD: P wave dispersion.

Statistical Analysis

Data analysis was conducted using IBM Corp's SPSS for Windows, version 23.0. Categorical variables were represented by their frequencies (n) and percentages (%), while continuous variables were represented by their median and interquartile range (IQR). The data were evaluated for normal distribution using the Kolmogorov-Smirnov test. The Kruskal-Wallis test was employed to compare independent continuous variables. The Bonferroni adjustment was used as a post-hoc analysis for groups that showed a statistically significant difference according to the Kruskal-Wallis test. Categorical variables were compared using the Chi-square test, followed by a post-hoc Bonferroni adjustment. The association between continuous variables was assessed using Pearson's correlation test. A p-value below 0.05 was considered statistically significant. Linear regression analysis with the enter method was conducted to examine the independent variables significantly correlated with P wave dispersion. Minimum and maximum P wave durations were not included in the regression analysis due to significant collinearity with P wave dispersion. A natural logarithmic transformation was applied to non-normally distributed variables before regression analysis.

RESULTS

The study included 40 healthy control subjects (Group 1), 41 non-classic MVP patients (Group 2), and 36 classic MVP patients (Group 3). There were no noticeable disparities among the groups in terms of initial demographic and clinical characteristics (Table 1). The groups had similar values for left ventricular end-diastolic diameter (LVDD), interventricular

Table 2. Pearson's correlations of P wave dispersion to other parameters

Pearson's correlations	Pearson's r	p
Age	0.095	0.311
BMI	-0.156	0.094
Creatinine	0.089	0.338
Hemoglobin	-0.073	0.435
SBP	0.002	0.981
DBP	-0.029	0.759
HR	-0.044	0.641
LVDD	0.166	0.073
LVSD	0.214	0.020
LVEF	0.128	0.168
IVS	0.042	0.649
PW	0.013	0.893
E/A	-0.063	0.500
P_{max}	0.723	<0.001
P_{min}	-0.771	<0.001
Maximal leaflet displacement	0.557	<0.001
Maximal leaflet thickness	0.770	<0.001
LAD	0.517	<0.001

BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; HR: Heart rate; LAD: Anterior-posterior left atrial diameter; LVEF: Left ventricular ejection fraction; LVDD: Left ventricular diastolic diameter; LVSD: Left ventricular systolic diameter; IVS: Interventricular septum; PW: Posterior wall; E/A: Early to late atrial mitral doppler peak flow velocity; P_{max}: Maximum P wave duration; P_{min}: Minimum P wave duration; PWD: P wave dispersion.

septum thickness, posterior wall thickness, and mitral inflow parameters (E/A waves). Left ventricular ejection fraction [62.9 (6.8), 67.5 (5.1), 66.7 (7), p<0.001, respectively], left ventricular systolic diameter [27 (2), 30 (3), 30 (3.25), p<0.001, respectively], and left atrial diameter (LAD) [33 (3) vs. 34 (3) vs. 36.5 (4) mm, p<0.001, respectively] were statistically larger in non-classic and classic MVP patients than in the control group. Those with classic mitral valve prolapse had a significantly shorter minimum period of the P wave compared to both control subjects and those with non-classic MVP [71.5 (3.25) vs. 68 (1) vs. 64 (3.25) ms, p<0.001, respectively]. The maximum duration of the P wave was found to be similar among MVP patients (both classic and non-classic) and healthy individuals. P wave dispersion was significantly higher in classic MVP patients compared to those with non-classic MVP [37 (3) vs. 40 (4) vs. 47 (3) ms, p<0.001, respectively].

There was a statistically significant correlation between PWD and P_{max}, P_{min}, maximal leaflet displacement, maximal leaflet thickness, and LAD (r=0.723, p<0.001; r=-0.771, p<0.001; r=0.557, p<0.001; r=0.770, p<0.001; r=0.517, p<0.001, respectively) (Table 2).

Maximum leaflet thickness and maximum leaflet displacement were independent predictors of increased PWD in linear regression analysis (β=1.456, p<0.001, β=-0.851, p<0.001) (Table 3).

DISCUSSION

Our study revealed that MVP patients exhibit longer PWD values. Patients diagnosed with MVP commonly experience palpitations, although it remains unclear which cases are specifically linked to arrhythmias. There is limited research focused on supraventricular arrhythmias in MVP. Erkal et al.[9] discovered that values of PWD and atrial electromechanical delay might be used to predict the presence of supraventricular arrhythmias in MVP patients. Autonomic dysfunction plays a significant role in the development of cardiac arrhythmias,

Table 3. Linear regression analysis to identify the best predictor of P wave dispersion

Coefficients					
Model	**Unstandardized coefficients**		**Standardized coefficients**	**t**	**Significance**
	B	**Std. Error**	**Beta**		
(Constant)	3.169	0.549		5.776	<0.001
Left ventricular end-systolic diameter	-0.125	0.112	-0.075	-1.113	0.268
Left atrial diameter	0.182	0.137	0.105	1.335	0.184
Maximal leaflet thickness	0.286	0.040	1.456	7.242	<0.001
Maximal leaflet displacement	-0.205	0.045	-0.851	-4.531	<0.001

Natural logarithmic transformation was applied to non-normally distributed variables.

contributing to both the occurrence and severity of cardiovascular diseases.[10] It has been demonstrated that autonomic dysfunction is prevalent in MVP patients through various clinical and biochemical tests.[11] In individuals with severe MR and MVP, the presence of acute or chronic ventricular volume overload is a significant factor, especially when combined with myocardial fibrosis.[12] To assess the heightened risk of arrhythmias, our study deliberately excluded patients with severe mitral regurgitation.

Autonomic dysfunction can alter the speed of electrical signals in the atria and affect the duration of the P wave. Additionally, it has been observed that elevated PWD is typically associated with a prolongation of the maximum P wave duration. However, our investigation revealed that patients with MVP exhibited a shorter minimum P wave duration and a significantly longer PWD. Similarly, shorter P wave durations and longer PWD were also found in pediatric MVP patients compared to children without MVP.[13] Further research indicated that a reduced minimum P wave duration is a significant predictor of atrial fibrillation in patients undergoing coronary artery bypass surgery.[14]

P wave dispersion is an effective and non-invasive method for identifying patients at high risk of developing atrial fibrillation. It reflects the presence of irregular and discontinuous electrical activity in the atria.[15] Calik et al.[16] discovered that longer inter/intra-atrial conduction time is a more reliable predictor of the frequency of atrial fibrillation episodes compared to dimensions of the left atrium, such as diameter and volume. Tison et al.[17] conducted a study to identify MVP patients susceptible to arrhythmias and cardiac fibrosis based on electrocardiograms. Their findings showed that, by excluding individuals with moderate to severe MR, the most significant ECG parameters for predicting late gadolinium enhancement (LGE) in cardiac magnetic resonance imaging (MRI) were the P wave and PR interval.

Patients diagnosed with MVP and experiencing left atrial enlargement are at a higher risk of developing atrial arrhythmias.[18,19] It is crucial to make early predictions about the likelihood of developing supraventricular arrhythmias, such as atrial fibrillation, in patients with MVP. Our hypothesis suggests that the increased PWD in patients with MVP may be due to impaired cardiovascular autonomic functions. This impairment is characterized by a higher conduction velocity resulting from increased activity of the sympathetic system and a shorter minimum PWD. Age, ejection fraction of the left ventricle, and characteristics of left ventricular diastolic function are similar across the study groups. The size of the left atrium was found to be larger in MVP patients.

The study was limited by its single-site nature and relatively small sample size. The patients were not subjected to 24-hour Holter monitoring to evaluate arrhythmias. We did not evaluate the link between PWD and the duration of MVP. Additionally, we did not investigate other signs of autonomic dysfunction or examine its association with PWD to obtain a more comprehensive comprehension of the underlying mechanisms. The results of this study are not generalizable to the wider population.

CONCLUSION

Analysis of PWD can be used as a non-invasive method to predict the probability of atrial arrhythmias in individuals with MVP. The findings of our investigation can provide direction for future clinical treatment. However, further comprehensive and future investigations are necessary to support our claim.

Ethics Committee Approval: The Alanya Alaaddin Keykubat University Clinical Research Ethics Committee granted approval for this study (date: 26.10.2018, number: 3-19).

Author Contributions: Concept – CRÖ; Design – CRÖ, CK; Supervision – CRÖ, CK, AÇ; Resource – CRÖ, CK, AÇ; Materials – CRÖ, CK, AÇ; Data Collection and/or Processing – CRÖ, CK, AÇ; Analysis and/or Interpretation – CRÖ, CK, AÇ; Literature Search – CRÖ, CK, AÇ; Writing – CRÖ, CK, AÇ; Critical Reviews – CRÖ, CK, AÇ.

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