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P-wave dispersion and its relationship with the severity of the disease in patients with stable coronary artery disease

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ABSTRACT

OBJECTIVE: P- wave dispersion (PD) is an indicator of inhomogeneous and discontinuous propagation of sinus impulses. In the present study we aimed to investigate the PD and its association with the severity of the disease. in patients with stable coronary artery disease.

METHODS: We prospectively analyzed 60 subjects with coronary artery disease (CAD) and 25 subjects with normal coronary angiograms (control group). The maximum and minimum P-wave duration and PD were measured from the 12-lead surface electrocardiograms. The CAD severity was assessed by the severity score (Gensini score) and the number of vessels involved (vessel score).

RESULTS: P max was longer in CAD group compared with the control group ($p<0.001$). PD was greater in the CAD group, compared with the control group ($p<0.001$). However, P min did not differ between the two groups. In bi-variate correlation, increased PD was correlated with presence of diabetes mellitus ($r=0.316$, $p=0.014$), smoking ($r=0.348$, $p=0.006$), left ventricular ejection fraction ($r=-0.372$, $p=0.003$), vessel score ($r=0.848$, $p=0.001$), and Gensini score ($r=0.825$, $p=0.001$). Multiple linear regression analysis showed that PD was independently associ¬ated with vessel score ((3=0.139, $p=0.002$) and Gensini score ((3=0.132, $p=0.007$).

CONCLUSION: PD was greater in patients with CAD than in controls and it was associated with CAD severity.

Key words: Coronary artery disease; gensini score; stable angina pectoris; P-wave dispersion.

P wave dispersion (PD) may be defined as the difference between the longest and shortest P wave duration recorded from different multiple surface electrocardiographic leads [1, 2]. Prolonged P wave duration and increased PD have been showed to be associated with an increased risk for atrial fibrillation (AF) which is characterized by inhomogeneous and discontinuous atrial conduction [3]. A

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growing evidence shows that people who are higher PD have higher risks for several cardiovascular-related conditions such as diabetes mellitus, obesity, hypertension, peripheral vascular disease, and myocardial infarction [4-7]. Furthermore, PD has been found to be to associated with an increase in carotid intima-media thickness and inflammatory markers such as C-reactive protein [8]. However, there are very few studies that have shown the relationship between stable coronary artery disease and P wave dispersion [9]. Therefore, in the present study we aimed to determine the association of PD with the severity of coronary artery disease (CAD) in patients with stable coronary artery disease.

MATERIALS AND METHODS

Study population

A total of 85 (30 women 55 men) consecutive patients routinely referred to coronary angiography for stable angina pectoris were included in the study after the following exclusions: any kind of rhythm abnormailities that could have interfered with P- wave analysis (AF, freguent atrial and ventriculer beats, pacemaker rhythm), acute coronary syndromes, valvular heart disease, serum electrolyte disturbances, abnormal thyroid function, pulmonary hypertension, cardiomyopathies, use of any antiarrhythmic drug, history of myocardial infarction, percutaneus coronary intervention, and cardiac surgery. Entry criteria included chest pain or other symptoms suggestive of myocardial ischemia whc clinically indicated coronary angiography. Detailed physical examination, electrocardiogram and echocardiogram were performed on all patients. The clinical risk factors for the patients such as age, gender, hypertension (HT), diabetes mellitus (DM), history of hyperlipidemia, and smoking status were noted.

Patients were divided into 4 groups based on their extent of angiographic coronary artery disease. Patients with normal coronary arteries were labeled as normal group (25 patients), 22 patients with signficant obstruction in 1 major epicardial artery were considered as having 1 vessel disease, 26 patients with significant obstruction in 2 major epicardial arteries were included in the 2 vessel disease group, finally 12 patients with significant obstruction in 3 major epicardial arteries were enrolled in the 3 vessel disease group. Hypertension was defined based on blood pressure 140/90 mm Hg or greater, and a history of antihypertensive drug use. DM was defined as fasting blood glucose≥126 mg/dl on two occasions or being on treatment. The local ethics committee approved the study protocol. All demographic and clinical data were collected prospectively.

Electrocardiography

A 12- lead surface electrocardiogram (ECG) was obtained from each patient while in supine position. Recordings were acquired at a paper speed of 50 mm/s, with 1 mV/cm standardization. Two in-vestigators without knowledge of the clinical status of the patients manually measured the maximum and minimum P-wave duration and PD. To improve accuracy we used calipers and magnifying lenses. ECG with measurable P- waves in over than 10-leads were included in the analysis. The onset of P-wave was defined as the junction between the end of the P-wave deflection and the ofset of the P-wave as the junction between the end of the P-wave deflection and the isoelectric line. We calculated P maximum (P max) and P minimum (P min) and their diferences were defined as PD.

Echocardiographic measurement

Echocardiographic measurements were performed by using a 2.5 mHz probe with Acuson Sequa echocardiographic device (Siemens, USA). LV dimensions were generally measured with 2D-guided M-mode from the parasternal projections, using a leading edge to leading edge convention. The left atrium and the left ventricle diameters, left ventricular ejection fraction (LVEF), and the presence of mitral insufficiency were evaluated.

Coronary Angiography

Coronary angiography was performed using the standard Judkins technique through femoral artery access. The angiographic characteristics, which included lesion location and percentage stenosis, of all coronary lesions in the index coronary angiogram

were obtained by throughly reviewing the angiogram. Angiographic analysis was carried out by two experienced cardiologists who were blinded to the study protocol. The severity of CAD severity was assessed by using the vessel and Gensini score. Vessel score was the number of vessels with a significant stenosis (>%50). Scores ranged from 0 to 3, depending on the number of vessels involved [10]. We also used Gensini scoring system [11]. According to this method we defined narrowing of the lumen of coronary arteries as 1 for 1-25% stenosis, 2 for 26-50% stenosis, 4 for 51-75% stenosis, 8 for 76-90% stenosis, 16 for 91-99% stenosis and 32 for total occlusion. Then the score is multiplied by a factor that shows the significance of the lesion's location. The multiplication factor for the left main system lesion is 5. It is 2.5 for proximal left anterior descending artery (LAD) and proximal circumflex artery (Cx) lesions, 1.5 for a mid-LAD lesion, and 1 for distal LAD, mid/distal CX and right coronary artery lesions. The multiplication factor for any other branch is 0.5.

Statistical analyses

SPSS-15.0 software (SPSS Inc., Chicago, IL) was used for all statistical analyses. Baseline demographic data are presented as mean ± SD for continuous variables and frequancies for discrete variables. Comparison of parametric values between the 2 groups was performed by means of an independent samples t-test. Categorical variables were assessed by using *chi*-square test. Correlation between P wave measurements and angiographic, clinical, and echocardiographic variables were assessed by Pearson correlation coefficient. To ascertain the independent contribution to PD multiple linear regression analysis was made. A two- tailed value of $p<0.05$ was considered statistically significant.

RESULTS

The clinical, echocardiographical and electrocardiographic characteristics of the cases in group 1 and group 2 are shown in Table 1. There was no difference in comparison of groups with regard to age, hypertension, diabetes and smoking. Male patients were more numerous in the CAD group. Pmax, PD and EF were also higher in the CAD group. We divided the study population into 4 subgroups according to vessel scores. P-wave measurements are given in Table

Table 1. Baseline clinical, echocardiographical and electrocardiographic characteristics of the study population

	CAD group (n=60)			Control group (n=25)			p
	n	%	Mean±SD	n	%	Mean±SD	
Age (years)			56.98±10.1			53.16±9.6	NS
Male gender	44	73.3		11	44		0.01
Hypertension	35	58.3		12	48		NS
Diabetes	25	41.6		11	44		NS
Smoking	27	45		8	32		NS
LAD (mm)			3.44±0.30			3.50±0.33	NS
LVESD (mm)			2.66±0.88			2.68±0.10	NS
LVEDD (mm)			5.24±0.23			5.18±0.26	NS
LVEF			55±5.49			58.8±3.74	0.002
Pmax (ms)			102.22±10.47			84.28±6.36	<0.001
Pmin (ms)			54.72±9.53			53.76±7.24	NS
PD (ms)			47.53±8.49			30.52±3.25	<0.001

CAD: coronary Artery Disease; LV: Left Ventricle; EDD: End-Diastolic Dimension; ESD: End-Systolic Dimension; EF: Ejection Fraction; LAD: Left Atrial Diameter; P max: P maximum; P min: P minimum; PD: P Dispersion; NS: Non-Significant.

Table 2. Comparison of P wave measurements of the groups according to vessel score

	Control (Group 1) (n=25)	Single vessel (Group 2) (n=22)	Double vessel (Group 3) (n=26)	Triple vessel (Group 4) (n=12)	P1	P2	P3
Pmax	84± 6	101±8	100±10	110±10	<0.001	NS	<0.013
Pmin	53±7	57±9	51±9	54±9	NS	NS	NS
PD	30±3	42±4	46±7	58±10	<0.001	0.039	0.001

P1: comparision of variables between group 1 and 2; P2: comparision of variables between group 2 and 3; P3: comparision of variables between group 2 and 4; P max: P maximum; P min: P minimum; PD: P Dispersion.

2. Although P max was significantly higher in Groups 2, 3 and 4, no difference was determined between Groups 1 and 2. PD was greater in all patient groups compared with the controls for all comparisons. The relationship between PD, and clinical, and echocardiographic characteristics in patients with CAD is shown in Table 3. In CAD group, PD was related to diabetes, smoking and EF (p=0.014, p=0.006, p=0.003) but not related to other clinical and echocardiographic characteristics (Table 3). Pmax and PD were related to vessel and Gensini scores in patients with CAD (Table 4). In multivariate logistic regression analysis, increased PD was found to be independently associated with vessel (β=4.139, p=0.002) and Gensini score (β=0.132, p=0.007).

Table 3. The relationship between P wave dispersion, and clinical and echocardiographic characteristics in patients with coronary artery disease

	r	p
Age	-0.004	0.974
Gender	0.052	0.695
Hypertension	0.017	0.895
Diabetes	0.316	0.014
Smoking	0.348	0.006
LAD	-0.068	0.605
LVS	-0.102	0.440
LVD	-0.016	0.901
Mild MR	0.071	0.591
LVEF	-0.372	0.003

LV: Left Ventricle; EDD: End-Diastolic Dimension; ESD: End-Systolic Dimension; EF: Ejection Fraction; LAD: Left Atrial Diameter; MR: Mitral Regurgitation

DISCUSSION

Our study showed, increased P wave duration and PD was related to the extent and severity of CAD in stable coronary artery disease patients. Similarly, increased PD has been observed to be associated with coronary artery disease severity [9].

AF is the most common cardiac rhythm abnor-

Table 4. The relationship between P wave measurements and Gensini and vessel scores in patients with coronary artery disease

	Vessel score	Gensini score
Pmax		
r	0.668	0.615
p	0.001	0.001
Pmin		
r	-0.080	-0.128
p	0.465	0.249
PD		
r	0.848	0.825
p	0.001	0.001

P max: P maximum; P min: P minimum; PD: P wave dispersion

mality and its incidence was 0.6% in the Coronary Artery Surgery Study (CASS) registry [12]. It was demonstrated that atrial fibrillation is a predictor of survival. Interatrial conduction delays have been shown to be implicated in initiating and maintaining AF [13-15].

Another mechanism for increased PD may be the increase in collagen fiber deposition in the cardiac interstitium. It was reported that PD was associated with inhomogeneus and discontinuous propogation of sinus impulses [16]. Electrocardiographic markers of abnormal atrial conduction, such as PD, P maximum, and P minumum, may be influenced by myocardial ischemia. Atrial fibrosis due to myocardial ischemia may prolong PD [17-20]. Previous studies have demonstrated that atrial ischemia is implicated in the pathogenesis of AF [21, 22].

Dilaveris et al. reported that myocardial ischemia prolongs PD in 95 patients with documented CAD and Özmen et al. confirmed this feature in patients with angioplasty induced myocardial ischemia [23,24]. PD has also been found to be associated with carotid atherosclerosis [8]. In addition, it has been shown that P-wave dispersion is increased in coronary slow- flow phenomenon [25].

Ischemia- induced inhomogeneous and discontinuous atrial conduction may be related to increased P maximum and PD [26]. Reduced blood flow due to coronary atherosclerosis may contribute to the development of tissue injury and fibrosis [27]. Another explanation for this is that ischemia causes renin angiotensin system activation [28, 29]. The regional fibrosis in the atrial wall, due to chronic ischemia could cause different atrial conductions leading to increased PD in surface ECGs.

Another pathophysiological explanation for increased P-wave duration and dispersion in CAD may be autonomic tone associated with CAD. Tükek et al.[30] reported that the autonomic tone changes may prolong PD. Increased serum catecholamine levels may cause atrial fibrosis and heterogeneus conduction properties.

It was reported that PD was significantly associated with LV diastolic dysfunction [31]. Ischemic left ventriculer dysfunction may increase left atrial pressure, and might another fundamental causes of increased P wave duration and PD in patients with CAD compared to control subjects [32]. Atrial strain, which is a sugnificant factor in the pathophysiology of AF together with ischemia- induced hetergeneous atrial conduction, may results an increase in P wave duration and PD. Yilmaz et al. [9] found no significant association between P min and coronary artery disease severity. Similarly, in our study there was no significant association between P min and Gensini and vessel scores.

There were some limitations in our study. The major limitation of our study is the small number of patients included in the study. For evaluation of ECG results we did not use the high-resolution computer software program. Previous studies have found a low error of the measurement of PD on paper printed ECGs, contrarily other studies reported that manual PD measurement on paper printed ECGs obtained at a standard signal size may effect the accuracy and reproducibility of the results [33,34].

In conclusion, our results suggest that there is a considerable association between increased PD and the severity of CAD.

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