P wave dispersion in patients with erectile dysfunction

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Abstract: *Background and aims:* P wave dispersion (PWD) has been reported to be a non-invasive electrocardiographic predictor for atrial fibrillation. The aim of this study is to evaluate PWD between men with erectile dysfunction (ED) and healthy controls in order to investigate whether PWD was prolonged in patients with ED and related to severity of the disease. *Methods:* This study included a total of 72 men (42 patients with ED and 30 healthy controls). Demographic data and clinical features were recorded on admission. An electrocardiographic evaluation was obtained to measure PWD values for both patients and controls. *Results:* Maximum P wave duration was 108.5 ± 4.7 and 108.3 ± 4.3 in ED group and control group, respectively ($p = 0.748$). Minumum P wave duration was significantly higher in the control group than in the ED group. PWD was 48.1 ± 5.9 in the ED group. As a result, PWD was prolonged in patients with ED (48.1 ± 5.9 vs. 38.0 ± 3.9, $p < 0.05$). A significant negative correlation was observed between IIEF score and PWD values ($p < 0.05$, $r = -0.662$). *Conclusions:* Patients with ED exhibited prolonged PWD values compared with normal controls. In addition, PWD was found to be associated with severity of the disease.

Keywords: erectile dysfunction, P wave dispersion, autonomic nervous system, endothelial dysfunction, electrocardiography

Introduction

Erectile dysfunction (ED) is defined as the loss of ability to achieve or maintain a satisfactory erection long enough to engage in sexual intercorse. It is a world-spread problem, which mainly affects men older than 40 years old and its frequency increases in the older people [1]. As ED has many organic and non-organic factors, ED and cardiovascular diseases (CVDs) have common risk factors, such as hypertension, diabetes mellitus, dyslipidemia, obesity, metabolic syndrome, smoking, and sedanter lifestyle. In addition to these modifiable and unmodifiable risk factors, ED and CVD share two common pathophysiological mechanisms: autonomic nervous system (ANS) dysfunction and endothelial dysfunction [2, 3].

Deterioration of autonomic function can lead to cardiovascular events, which can increase morbidity and mortality. Moreover, it can lead to ED and the relationship between ED and ANS has been evaluated in previous studies. Another important mechanism underlying ED is endothelial dysfunction, which disrupts corpora cavernosal smooth muscle relaxation [4, 5].

Potential pathophysiological mechanisms including inflammation, oxidative stress, endothelial dysfunction, ANS dysfunction, hemodynamic, and vascular changes are the main causes and consequences of cardiovascular disorders and ED. Atrial fibrillation (most common sustained arrhythmia) is also associated with vascular dysfunction and its inflammation [6].

P wave dispersion (PWD) is a non-invasive electrocardiographic marker for atrial remodeling and a strong predictor of atrial arrhythmias and especially atrial fibrillation. P wave duration and dispersion have been reported to be influenced by the autonomic tone and reactive oxygen species. It has also been shown that a prolonged PWD was associated with coronary artery disease and prediction of atrial fibrillation in patients with acute coronary syndrome. This suggests that PWD could also be influenced by endothelial dysfunction [7–9].

P wave parameters in ED have not yet been investigated. In this study, we aimed to evaluate PWD in ED in order to evaluate cardiac autonomic dysfunction, endothelial dysfunction, and potential risk of developing atrial fibrillation in patients with ED.

Materials and Methods

The study population consisted of 42 patients with ED who were followed up at urology outpatient clinic. The control group consisted of 30 healthy controls.

The International Index of Erectile Function Questionnaire (IIEF-5) was used to evaluate the erectile status of patients. The questionnaire includes five questions and each question is scored between 1 and 5 points to find out a global sexual function score. According to the results, a total score of <22 was defined as ED [10]. Demographic data and clinical features were recorded on admission. Blood pressures were measured and blood samples were taken for hematological and biochemical parameters after an overnight 12-h fasting. Patients under 18 years and over 70 years of age were excluded. Patients with known CVD, congenital heart disease, metabolic-endocrine disease, renal disease, hypo–hyper thyroidism, diabetes mellitus, hypertension, acute–chronic respiratory diseases, neurological/psychiatric disorders, rheumatologic entities, gastrointestinal diseases, use of drugs that can cause ED or affect PWD, systemic infection, and electrocardiography (ECG) without clearly analyzable P wave were excluded from the study. The local ethics committee approved the study protocol.

Electrocardiography (ECG)

A 12-lead surface ECG during sinus rhythm was obtained from each participant in supine position following 10-min rest with 10 mm/mV amplitude and 25 mm/s paper speed. All of the ECG results were scanned and transferred to a personal computer for PWD calculation, as manual measurement has less accuracy compared with a computerized digital system. The point of first detectable atrial deflection from the isoelectric line was defined as the onset of the P wave. Return to the isoelectric line was defined as the end of the P wave. P wave duration was measured in all 12 leads on the surface ECG in order to evaluate maximum and minimum P wave duration (P max and P min, respectively). The difference calculated by substracting P min from P max was defined as PWD. All ECG measurements were performed by an independent cardiologist who was blinded to the subjects' clinical status.

Echocardiography

Transthoracic echocardiographic examinations were performed in all participants at the left lateral decubitus position to evaluate conventional parameters. All echocardiographic measurements were taken according to the guidelines of American Society of Echocardiography.

Statistical analysis

SPSS 22.0 (SPSS Inc., Chicago, IL, USA) program was used in analysis. The data were presented as mean ± standard deviation. The Kolmogorov–Smirnov test was used to examine if variables are normally distributed. Comparison between the two groups was performed with independent sample *t*-test and Mann–Whitney *U* test. Spearman's test was used for correlation analysis between IIEF score and PWD values. Intraobserver and interobserver agreements were assessed using the intraclass correlation analysis. The p value less than 0.05 was considered statistically significant.

Results

Forty-two patients with ED and 30 controls without ED were included in the study. The demographic and clinical characteristics of the patients and healthy controls are shown in *Table I*.

There were no significant differences between the patients and the controls in terms of age distribution. Body mass index and body surface area were similiar in the two groups. Furthermore, no significant differences were observed in systolic and diastolic blood pressures or in heart rates between the two groups.

Echocardiographic and electrocardiographic characteristics of the study groups were shown in *Table II*. Left ventricular ejection fraction, left ventricular end-diastolic diameter, left ventricular end-systolic diameter, left atrial (LA) diameter, interventricular septum, posterior wall thickness, and mitral inflow parameters were similiar in both groups.

Maximum P wave duration was 108.5 ± 4.7 and 108.3 ± 4.3 in ED group and control group, respectively ($p = 0.748$). Minumum P wave duration was significantly shorter in ED group as compared to that in the control group. PWD was 48.1 ± 5.9 in ED group and 38.0 ± 3.9 in the control group. As a result, PWD was prolonged in patients with ED ($p < 0.05$).

A significant negative correlation was observed between IIEF score and PWD values ($p < 0.05$, $r = -0.662$). In PWD measurements, intraobserver and interobserver agreement results showed a good reproducibility and small variability ($r = 0.95$, 95% CI = 0.878–0.98 and $r = 0.946$, 95% CI = 0.869–0.978, respectively).

Discussion

In this study, we found that patients with ED have longer PWD values than those with healthy controls. To the best of our knowledge, this is the first study to evaluate the impact of ED on P wave duration.

Table I Demographic, clinical, and echocardiographic variables of study group

	Control ($n = 30$)	Erectile dysfunction ($n = 42$)	p
Demographic and clinical variables			
Age (years)	38.0 ± 9.5	39.9 ± 6.7	0.333
BMI (kg/m^2)	26.9 ± 4.4	24.8 ± 4.4	0.053
Total cholesterol	182.7 ± 45.9	171.7 ± 31.6	0.500
TG	167.2 ± 68.7	174.9 ± 97.3	0.950
LDL	110.7 ± 35.3	114.8 ± 31.9	0.694
Glucose	87.8 ± 9.0	86.7 ± 9.4	0.485
Creatinin	0.8 ± 0.1	0.79 ± 0.1	0.895
Hb	15.3 ± 0.8	14.8 ± 1.4	0.062
SBP	118.8 ± 8.5	120.5 ± 10.8	0.488
DBP	73.8 ± 6.7	74.2 ± 3.2	0.958
HR	73.1 ± 8.6	76.5 ± 9.4	0.100
IIEF score	–	15.3 ± 2.9	–
Echocardiographic variables			
LVDD (cm)	46.8 ± 4.2	48.3 ± 3.6	0.153
LVSD (cm)	28.3 ± 3.9	28.9 ± 3.2	0.370
EF (%)	70.3 ± 5.8	69.8 ± 6.2	0.583
IVS	9.5 ± 0.9	9.7 ± 1.0	0.297
PW	9.4 ± 1.1	9.2 ± 1.2	0.420
Lad (cm)	34.1 ± 3.1	33.2 ± 2.2	0.145
E/A ratio	1.2 ± 0.3	1.1 ± 0.3	0.293

Data are presented as mean ± standard deviation values. TG: triglyceride; BMI: body mass index; LDL: low-density lipoprotein; Hb: hemoglobin; SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate; IIEF: International Index of Erectile Function Questionnaire; Lad: anterior–posterior left atrial diameter; EF: 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

Table II Electrocardiographic variables of study group

Electrocardiographic variables	Control ($n = 30$)	Erectile dysfunction ($n = 42$)	p
P maximum	108.3 ± 4.3	108.5 ± 4.7	0.748
P minimum	70.2 ± 3.3	60.5 ± 5.0	<0.050
PWD	38.0 ± 3.9	48.1 ± 5.9	<0.050

Data are presented as mean ± standard deviation values. PWD: P wave dispersion

It has been demonstrated that ED was associated with an increased risk of CVDs [11–13]. As ED and subclinical CVD have similiar risk factors, such as age, obesity, smoking, and hypertension. They also have common pathophysiological mechanisms including endothelial dysfunction and autonomic dysfunction [14, 15].

Endothelial dysfunction leads to insufficient relaxation of the vascular smooth muscle of the corpus cavernosum and it is one of the important mechanisms underlying ED. ED can be considered as an early manifestation of endothelial dysfunction and precursor or predictor of other forms of heart disease including atrial fibrillation. Endothelial impairment has been described in patients with atrial fibrillation previously [16, 17]. Especially any condition that impairs endothelial function could cause ED [18]. Lin et al. [19] investigated the association between atrial fibrillation and ED and they found that incidence of ED was significantly lower in patients without AF than those with AF. Yılmaz et al. demonstrated the relationship between ED and paroxysmal lone atrial fibrillation. They concluded that endothelial dysfunction as a consequence of atrial fibrillation could be the cause of ED in their study population [20].

Another important mechanism underlying ED is autonomic dysfunction, which plays a major role in cardiovascular mortality and morbidity [21–23]. An imbalance between parasympathetic and sympathetic system has been demonstrated in patients with ED. Decreased

parasympathetic activity and increased catecholaminergic state lead to ED [24, 25]. The normal functioning of the ANS is important for both cardiovascular system and erectile function. It has been demonstrated that the ANS has participated in the initiation of idiopathic atrial fibrillation [26]. Furthermore, it has been shown that autonomic remodeling leads to increased atrial sympathetic innervation in atrial fibrillation patients [27].

Kucukdurmaz et al. [28] reported that cardiac autonomic functions are impaired in patients with ED. Chen et al. [29] showed that patients with ED had significant cardiac sympathetic hyperactivity and cardiac vagal impairment. Autonomic impairment may change the atrial conduction velocity and affect the duration of the P wave [30]. The accuracy of PWD measurement, especially minumum P wave duration, could be influenced by the low resolution of standard 12-lead ECG due to vector differences between the leads. Due to this reason, we measured P wave duration using computerized digital system. In addition, it has been concluded that increased PWD is usually associated with increased maximum P wave duration. However, in this study, we found that minimum P wave was shorter and PWD was significantly longer in patients with ED as compared to those in the control group. It is revealed that increased sympathetic activity causes vasoconstriction and loss of erection. It has also been reported that increased sympathetic tone shortens PWD in normal subjects [31]. Similar to our results, Tukek at al. [32] demonstrated that shorter minimum P wave duration was associated with paroxysmal atrial fibrillation in patients with increased LA diameter. Dilaveris et al. [33] reported shorter P wave duration as an independent predictor of common atrial fibrillation. In an another study, shorter minimum P wave duration was found to be an important predictor of atrial fibrillation for patients undergoing coronary artery bypass grafting [34]. PWD is a valuable non-invasive method for predicting patients who have potential risk of developing atrial fibrillation. It has been reported that interatrial conduction delays are associated with initiating and maintaining atrial fibrillation [35, 36]. Furthermore, some authors reported increased PWD is associated with stable coronary artery disease, carotid atherosclerosis, and slow coronary phenomenon [9, 37, 38]. This suggests that another pathophysiological mechanism for increased PWD is endothelial dysfunction as well as autonomic imbalance. Endothelial dysfunction, oxidative stress, atherosclerosis, and autonomic dysfunction are the main causes and simultaneously consequences of atrial fibrillation.

Platek et al. [39] reported that ED was present in more than half of the study group in their cross-sectional, epidemiological study conducted in patients with a primary diagnosis of atrial fibrillation. We believed that impairment in autonomic cardiac function (increased conduction velocity from heightened sympathetic drive and shorter minimum P wave duration) with endothelial dysfunction could be the cause of prolonged PWD in patients with ED. Age, left atrial size, left ventricular ejection fraction, and left ventricular diastolic function parameters could be related to prolonged PWD in different patient groups. However, we did not found any difference between our study groups in terms of these parameters.

The limitations of this study are as follows:

1. This was a single-center study and a relatively small number of patients were included.
2. We did not evaluate the association between PWD and duration of ED. In addition, we could not make a correlation analysis between serum testosterone levels and electrocardiographic parameters in patients with ED and control subjects. We also did not investigate other evidence of autonomic dysfunction and examine its relationship with PWD to provide more mechanistic insight.
3. Furthermore, the psychosocial factors (e.g., anxiety, stress, enviromental factors during measurement, and mental state) of ED were not evaluated.
4. The results of this study cannot be applied to general population.

In conclusion, prolonged PWD may be associated with impaired autonomic and endothelial function in patients with ED. PWD analysis can be used as a non-invasive method to predict the risk of developing atrial fibrillation in ED patients. The findings of our analysis can guide for the further clinical practice. However, these findings must be confirmed by further large scale and prospective studies to support our hypothesis.

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