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Research Article

Evaluation of Ventricular Repolarization in Patients with Erectile Dysfunction

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Abstract

Objectives: Erectile dysfunction (ED) is defined as the inability to initiate or maintain sexual intercourse for at least 6 months due to organic and psychogenic causes. Organic causes include autonomic nervous system dysfunction and endothelial dysfunction. These disorders in patients with ED may also cause heart diseases such as coronary artery disease or arrhythmia. T-wave peak-to-end interval (Tp-e interval) and Tp-e/QT ratio are relatively new markers of ventricular arrhythmogenesis and repolarization heterogeneity. In the present observational study, we investigated the changes in ventricular repolarization in patients with ED by performing 12-lead electrocardiography (ECG).

Methods: This study included 40 healthy men and 40 ED patients (Age range: 44.7±5.8 vs 43.9±6.3).The QT and corrected QT (QTc) intervals, Tp-e interval and Tp-e/QT ratio of the patients were measured by 12-lead ECG.

Results: QTc intervals, Tp-e interval and Tp-e/QT ratio were significantly increased in the ED group.

Conclusion: These results suggest that ED is associated with impaired ventricular repolarization parameters and that possible autonomic nervous system dysregulation and endothelial dysfunction lead to this condition.

Keywords: Arrhythmias, cardiovascular diseases, erectile dysfunction, myocardial repolarization

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Erectile dysfunction (ED) is a penile erectile deficiency leading to an inability to initiate or maintain anerection for at least 6 months.[1] It is classified as organic, psychogenic and mixed types according to their etiology. One of the organic causes is neurological and associated with deterioration of the autonomic nervous system (ANS).[2] Another organic cause in ED etiology is vasculogenic. Studies indicate that endothelial dysfunction, subclinical inflammation and androgen insufficiency lead to ED development with a complex relationship.[3] As atherosclerosis affects all vascular beds, the earliest symptom development is expected in the artery with the narrowest vessel lumen. The penile artery with an arterial lumen of 1-2 mm has an earlier symptom than the proximal left descending coronary artery with larger lumen diameters (3-4 mm). Vasodilation, which is essential for erection, may lead to earlier symptom development in small arteries such as the penile artery than in others.[4] Therefore, men without coronary artery disease (CAD) are at increased risk of CAD, ischemic stroke, and peripheral artery disease within 2 to 5 years after ED is diagnosed.

ED may be a predictor of the development of vascular diseases and a precursor of preventable cardiovascular events (CE).[5] A prospective study on patients with ED showed subclinical obstructive CAD in 19% of the patients.[6] Again, the association of ED with subclinical CAD and microvascular angina indicates the role of endothelial dysfunction in the mutual physiopathogenesis.[7, 8] There are many studies evaluating fatal and non-fatal CEs (myocardial infarction,

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ischemic stroke) and total mortality in the general population and high-risk patients.[9–12] A meta-analysis including 14 prospective studies (92.757 patients; mean follow-up period 6.1 years) demonstrated that ED, independent of the traditional risk factors, increased the risk of total CE by 44%, cardiovascular mortality risk by 19%, acute myocardial infarction risk by 62%, cerebrovascular event risk by 39% and all-cause mortality risk by 25%.[13, 14]

The parasympathetic nervous system has an effect on cardiac arrhythmia.[15, 16] Clinical conditions such as increased heart rate and ED may be due to a decrease in parasympathetic activity. Low parasympathetic activity may be a risk factor for cardiovascular disease.[17] Evaluation of T-wave in the electrocardiogram (ECG) is one of the most important components of ventricular repolarization. In the absence of structural heart disease, ventricular repolarization abnormalities are associated with cardiac arrhythmias. Studies have demonstrated ventricular repolarization markers such as QT and corrected QT (QTc) intervals, T-wave-peak-to-end-interval (Tp-e interval) and Tp-e/QT ratio to predict life-threatening cardiac arrhythmias.[18] Some studies have found an association between increased Tp-e interval andTp-e/QTc ratio and increased risk of fatal ventricular arrhythmias.[19–21]

Some studies examined the association between cardiac arrhythmias and ED and established a link between atrial fibrillation and ED.[22–24] Moreover, some investigated the role of ED in predicting the prognosis of cardiac arrhythmias in patients with a permanent pacemaker and found a significant relationship.[25] However, changes in ventricular repolarization parameters in ED patients have not been clearly investigated. The present study hypothesized that the increased Tp-e interval and Tp-e/QT ratio indicating ventricular repolarization abnormalities in ED patients and aimed to compare the changes in the Tp-e interval and Tp-e/QTc ratio in ED patients with those of healthy subjects.

Methods

Study Design

This is a cross-sectional study.

Study Population

This study included 40 male patients (mean age 43.9 ± 6.3 years) with ED and without any known cardiovascular disease, and 40 healthy males (mean age 44.7 + 5.8 years). The patients applied to the urology clinic between June 2016 and July 2017 were evaluated by an experienced specialist in the urology clinic. Those who were diagnosed with ED and referred to the cardiology clinic were selected for the study. The patients were evaluated with the Sexual Health Inventory for Men (SHM) or IIEF-5, abbreviated version of the International Index of Erectile Function (IIEF), a validated five-item questionnaire assessing erectile function, orgasmic function, desire and satisfaction after sexual intercourse. Patients with smoking habits, hypertension, diabetes mellitus, heart failure, coronary artery disease, moderate or severe valvular heart disease, hyperthyroidism or hypothyroidism, atrial fibrillation, right or left bundle branch block, atrioventricular block, chronic kidney or chronic lung disease and who are on medication for these conditions were not included in the study. All patients underwent 12-lead resting ECG. They were all in sinus rhythm. Glucose, sodium, potassium, magnesium, and calcium values were studied. The study protocol was approved by the institutional ethics committee, and informed consent was obtained from each patient.

Electrocardiographic and Echocardiographic Examinations

The 12-lead ECG (10 mm/mV and 25 mm/s; Cardiofax V; Nihon Kohden Corp., Tokyo, Japan) was taken while the patients were in the supine position at rest. Obtained electrocardiograms were transferred to a computer via a browser and analyzed with x400% using the Adobe Photoshop CS2 program (Adobe Systems Inc., San Jose, California, USA). Tp-e and QT intervals were measured and calculated. Two separate personnel repeated each measurement at least twice andaveraged the data. Measurements of the QT and R-R intervals were obtained from leads V2 and V5. The QT interval was defined as the time interval between the onset of QRS and the point at which the T-wave returns to the isoelectric line.

The R-R interval was measured as the average of three consecutive beat complexes. The Bazzet formula was used to calculate the QTc interval and the heart rate.Those with a U wave in the ECG were excluded from the study. The interval at the end of the electrocardiographic T-wave peak corresponding to the transmural dispersion of the repolarization was measured as Tp-e.

Echocardiographic examination was performed to the patients at rest, in a 45-degree left lateral decubitus position. M-mode, two-dimensional and color flow Doppler recordings were performed using echocardiography device (General Electric Vivid S5, Milwaukee, WI, USA). 2.5-3.5 MHz transducers were used. Two-dimensional imaging was performed with parasternal short and long axes, apical four-chamber and two-chamber. The examination was performed simultaneously while the patients were on ECG monitoring. We repeated all measurements at least three times and averaged the data. Standard M-mode measurements were made in accordance with the suggestions of

Table 1. Basic laboratory and echocardiographic values of patients

	Healthy Group	ED Group	p
Age (mean, years)	44.7±5.8	43.9±6.3	0.547
BMI (kg/m^2)	28.6±3.3	28.5±3.2	0.908
Glucose (mg/dl)	96.5±9.1	96.7±8.7	0.919
Sodium (mg/dl)	140.1±1.9	140.1±1.9	0.982
Potassium (mg/dl)	4.4±0.3	4.4±0.3	0.724
Calcium (mg/dl)	9.4±0.2	9.5±0.2	0.674
Magnesium (mg/dl)	2.2±0.3	2.2±0.3	0.853
TSH	1.5±0.7	1.5±0.7	0.884
IVS (mm)	9.4±2.2	9.7±1.7	0.544
PW (mm)	8.5±1.9	8.9±1.6	0.328
LA (mm)	34.6±3.1	35.1±2.5	0.484
LVSD (mm)	30.2±3.8	30.3±3.9	0.977
LVDD (mm)	44.9±2.8	45.6±4.0	0.374
LVMI	86.4±99.19	80.15±91.18	0.280
Ejection fraction (%)	61.9±3.2	62.8±4.5	0.297

ED: Erectile dysfunction; BMI: Body mass index; TSH: Thyroid stimulating hormone; IVS: Interventricular septum; PW: Posterior wall; LA: left atrium; LVSD: Left ventricle systolic diameter; LVDD: Left ventricle diastolic diameter; LVMI: Left ventricular mass index.

the American Society of Echocardiography.Besides, left ventricular posterior wall thickness, interventricular septum, left ventricular diastolic and systolic diameters were all measured. Again, at the recommendation of the American Society of Echocardiography, we examined and evaluated the left ventricular regional wall motion according to the 17-segment model. Left ventricular ejection fraction (EF) was calculated using the "modified Simpson" method in apical two- and four-chamber views.[26] EF >50%, normal left ventricular end-diastolic and end-systolic diameters, and lack of major regional contraction deficits was defined as a normal left ventricular systolic function. Mitral valve, aortic and tricuspid valve structure and functions were evaluated in the apical four-chamber view as well as using color Doppler echocardiography. In addition, the flow rate was also assessed by pulse- or continuous-wave Doppler.

Statistical Analysis

All statistical analyses were performed using SPSS software (SPSS 18.0 for Windows Inc., Chicago, IL, USA). Categorical variables are expressed as n (%), and continuous variables are expressed as mean±standard deviation. Eligibility of data for normal distribution was evaluated using Kolmogorov–Smirnov test. Relative differences between ED and non-ED patients for each electrocardiographic parameter were evaluated using a paired-sample t-test. Differences between the categorical variables were compared using chi-square test. P<0.05 was considered statistically significant.

Table 2. Electrocardiographic data

	Healthy Group	ED Group	p
Lead V2			
QT (ms)	346±23	351±19.7	0.919
QTc (ms)	394.9±32	391±22.4	0.032
Tp-e (ms)	88±5.8	96.4±8.8	0.039
Tp-e/QTc	0.25±0.02	0.27±0.02	0.030
Lead V5			
QT (ms)	348.6±25.8	355.7±18.5	0.246
QTc (ms)	397.6±32	395.2±22.7	0.018
Tp-e (ms)	86.3±11.8	92.4±5.5	0.001
Tp-e/QTc	0.24±0.02	0.26±0.01	0.228
Mean heart rate	73±8.3	74±8.1	0.502

ED: Erectile dysfunction; QTc: Corrected QT; Tp-e: T wave peak-to-end interval.

Results

The study included 80 patients (40 healthy people and 40 people with ED). Table 1 demonstrates the basic clinical features of the participants. There was no significant difference between the groups regarding EF, left atrial diameter, ventricular systolic and diastolic diameters, interventricular septal and posterior wall thickness obtained from echocardiographic analyses and serum sodium, potassium, magnesium, calcium, glucose, creatinine, low- and high-density lipoproteins levels.

Electrocardiographic parameters are shown in Table 2. QTc (394.9±32 vs. 391±22.4 millisecond [ms]), Tp-e interval (88±5.8 vs. 96.4±8.8 ms) and Tp-e/QTc (0.25±0.02 vs. 0.27±0.02) values were significantly higher in the ED group compared with that of the control group.

Discussion

To the best of our knowledge, our study is the first study showing that ventricular repolarization parameters are impaired in ED.

Several studies report the presence of sympathetic instability or hyperfunction, sympathetic hypofunction and/or parasympathetic dysfunction in this patient group.[27] Mcvary et al.[28] reported a significant relationship between increased sympathetic tonus and ED and lower urinary tract symptoms in their study aimed to assess the autonomic activity.

The complex autonomic innervation of the heart plays an important role in regulating cardiovascular functions. For example, an increase in sympathetic tonus may serve a function in shortening the QT interval and in sinus tachycardia. In contrast,increased parasympathetic tonus may be involved in sinus bradycardia, atrioventricular block and T-wave abnormalities.[29]

The impact of ANS on the heart can be evaluated by heart rate variability (HRV). Decreased HRV is an indicator of increased cardiovascular disease and mortality.[30] Of the ventricular repolarization parameters, QT and QTc prolongation are closely related to increased risk of sudden cardiac death without structural heart diseases.[31] It was also reported that the Tp-e interval is an electrocardiographic parameter used to assess ventricular repolarization.[32] The increase in Tp-e interval and Tp-e/QT ratio can be used to predict ventricular arrhythmia and cardiovascular mortality.[33] Furthermore, a meta-analysis showed that prolongation of the Tp-e interval is associated with an increased risk of ventricular tachycardia/ventricular fibrillation or sudden cardiac death, and can be used for risk classification in different diseases and the general population.[34] Based on these findings, the Tp-e interval and Tp-e/QT ratio can be used since they demonstrate changes in ventricular repolarization in ED patients.

As we know, the first study evaluating ventricular repolarization changes in ED is ours. Our study showed a significantly higher Tp-e interval and Tp-e/QT ratio in patients with ED compared to that of the healthy subjects.Therefore, the risk of ventricular arrhythmia may be increased in ED patients. Both conditions appear to be caused by ANS and endothelial dysfunction in their etiologies.

Limitations of the Study

Our study has some limitations to be mentioned. The number of patients involved in the study was limited. Due to the variability of the T-wave, there was difficulty in assessing the end of the T-wave in the ECG. We could not obtain data on autonomic imbalance such as HRV and heart rate turbulence, as there were no ambulatory ECG Holter recordings.

Conclusion

The present study is the first study demonstrating the relationship between ED and ventricular repolarization parameters such as Tp-e, QT, QTc and Tp-e/QTc.Considering the prognostic significance of the Tp-e interval and the Tp-e/QT ratio, we have shown another reason for closely monitoring patients with ED in terms of adverse cardiovascular outcomes. In conclusion, further studies are needed to evaluate the relationship between increased Tp-e interval and Tp-e/QT ratio in patients with ED.

Disclosures

Ethics Committee Approval: The Ethics Committee of Gaziosmanpaşa University provided the ethics committee approval for this study (30.04.2019-KAEK-112).

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