RESEARCH ARTICLE / *Araştırma Makalesi*

The Relatioship Between Basal T-Wave Peak-End Interval and Heart Rate Recovery Index Values in Patients with Stable Coronary Artery Disease

Stabil Koroner Arter Hastalığı Olan Hastalarda Bazal T-Dalgası Pik-Son İntervali ile Kalp Atış Hızı Düzelme İndeksi Arasındaki İlişki

Huseyin Oren

Cardiology Department, Ankara City Hospital, Ankara, TURKEY

Yazışma Adresi / *Correspondence:*
Huseyin Oren

Cardiology Department, Ankara City Hospital, Ankara, TURKEY
T: **:+90 532 574 36 30** E-mail **: husoren@hotmail.com**

Geliş Tarihi / Received : **08.10.2020** Kabul Tarihi / Accepted : **08.03.2021**

Orcid :

Huseyin Oren, https://orcid.org/0000-0002-0975-9457

(Sakarya Tıp Dergisi / ***Sakarya Med J*** **2021, 11(2):279-287) DOI: 10.31832/smj.807503**

Öz

Amaç Koroner arter hastalığı olan hastalarda otonom disfonksiyon kötü prognozun göstergesidir. Bu çalışmanın amacı, sol ventrikül ejeksiyon fraksiyonu (EF)>% 50 ve <% 50 olan stabil koroner arter hastalığı olan hastalarda başlangıç T-dalgası tepe-son intervali (Tp-e) ve kalp hızı geri kazanım indeksi (HRR-I) değerlerini karşılaştırmaktır.

Gereç ve Yöntemler Grup 1'de 2 aydan uzun süredir eforlu göğüs ağrısı olan 107 hasta ve koroner anjiyografide EF <% 50 olan sınıf 1-2 anjina, 3 damar hastalığı vardı. Grup 2'de koroner anjiyografide EF>% 50 olan, 3 damar hastalığı olan 76 hasta vardı. Başlangıçta her iki grubun başlangıç Tp-e ve kalp hızı değerleri ölçüldü ve transtorasik ekokardiyogramlar yapıldı. Daha sonra Grup 1 ve 2, Bruce protokolüne göre egzersiz testine tabi tutuldu ve egzersizin zirvesinde ve 1., 2. ve 3. dakikalarında kalp hızları ölçüldü.

Bulgular Bazal Tp-e açısından grup 1 [95,8 ± 6,8 msec] ve grup 2 [71,4 ± 5,1 msec] arasında istatistiksel olarak anlamlı fark vardı [P<0,0001]. cTp-e (düzeltilmiş T dalgası tepe-son aralığı) değerleri açısından grup 1 [108,1±7,9] ve grup 2 [79,3±7,7] arasında anlamlı fark vardı [P<0,0001]. 1. dakika iyileşme fazında HRR-I'e bakıldığında [14,4 ± 2,1 vs 20,1 ± 3,5], 2. dakika iyileşme fazında HRR-I'e bakıldığında [26,3 ± 2,2 vs 45,1 ± 2,4], 3. dakika iyileşme fazında HRR-I'e bakıldığında [42,6 ± 2,9 vs 64,1 ± 2,6], gruplar arasında istatistiksel olarak anlamlı bir fark vardı [P<0,00001].

Sonuç Stabil anjinası olan ve EF <% 50 olan hastalarda otonomik gecikme daha belirgindir, Tp-e aralığı değeri daha yüksek ve HRR-I değerleri daha düşüktür.

Anahtar Kelimeler Ateroskleroz; Elektrokardiyografi; Egzersiz testi; Kalp hızı; İndeks .

Abstract

Objective *Autonomic dysfunction is detected in patients with coronary artery disease and is indicative of poor prognosis. The aim of this study was to compare baseline T peak-end interval (Tp-e) and heart rate recovery index [HRR-I] values in patients with stable coronary artery disease who had a left ventricular ejection fraction [EF] > 50 % and < 50 %.*

Materials and Methods *In Group 1, there were 107 patients with exertional chest pain for more than 2 months and class 1-2 angina with EF < 50 %, had 3-vessel diseases on coronary angiography. In Group 2, there were 76 patients with EF > 50 %, had 3-vessel diseases on coronary angiography. Baseline Tp-e and heart rate values of both groups were measured and transthoracic echocardiograms were performed at the beginning. Both Group 1 and 2 were then subjected to exercise testing according to the Bruce protocol and heart rates were measured at the peak and 1st, 2nd, and 3rd minutes of exercise.*

Results *There was a statistically significant difference between group 1 [95.8 ± 6.8 msec] and group 2 [71.4 ± 5.1 msec] with regard to basal Tp-e [P<0.0001]. There was a significant difference between group 1 [108.1±7.9] and group 2 [79.3±7.7] in terms of corrected Tp-e(cTp-e) values [P<0.0001]. Looking at HRR-I at the 1st-minute recovery phase [14.4 ± 2.1 vs 20.1 ± 3.5], when looking at HRR-I at the 2nd-minute recovery phase [26.3 ± 2.2 vs 45.1 ± 2.4], when looking at HRR-I at the 3rd-minute recovery phase [42.6 ± 2.9 vs 64.1 ± 2.6], there was a statistically significant difference between the groups [P<0.00001].*

Conclusion *Autonomic delaying is more prominent, the Tp-e interval value was higher and HRR-I values were lower in patients with stable angina with EF < 50%.*

Keywords *Atherosclerosis; Electrocardiography; exercise test; heart rate; Index.*

INTRODUCTION

It is estimated that 40-50 % of all cardiovascular deaths are sudden cardiac death, 80 % of which are due to ventricular arrhythmia.[1] Sudden cardiac death is an unexpected condition due to ventricular arrhythmias[2] and most cardiac arrests are asymptomatic and fatal within 1 hour.[3]

Although malignant ventricular arrhythmias are held responsible for sudden cardiac death, the underlying cause of fatal ventricular arrhythmias is increased sympathetic activity or decreased vagal activity.[4] Despite all the studies, the electrophysiological mechanism underlying ventricular fibrillation has not been fully elucidated, yet an effective treatment strategy that prevents this has not yet been established.[5]

The tp-e interval is an electrocardiographic repolarization marker.6 The time between the peak and the end of the T wave [Tp-e interval] is an indication of the transmural spread of ventricular repolarization.[7] Tp-e / QT and Tp-e / QTc ratios can also be used as electrocardiographic indices of ventricular arrhythmogenesis.[8]

Topilski et al[9] found that QT, QTc, and T-peak to T-end intervals were strong predictors of torsades de pointes, with prolonged T-peak to T-end as the best single discriminator. Watanabe et al demonstrated that prolonged T-peak to T-end is associated with inducibility as well as spontaneous development of ventricular tachycardia in high-risk patients with organic heart disease.[10] The highest predictive value of prolonged Tp-e interval for arrhythmic events is seen in Brugada syndrome. The increased repolarization dispersion of prolonged Tp-e interval is a mechanism by which a reentrant mechanism occurs for arrhythmias.

The highest cut-off value for Tp-e in the general population, with an increased risk of arrhythmia, was 113.6 ms. The cut-off value for Tp-e in Brugada syndrome was 95.8 ms, 106.3 ms in heart failure, and 109.6 ms in ischemic heart diseases.[11]

Sympathetic activity increases during exercise, parasympathetic activity decreases; therefore, sudden cardiac deaths usually occur immediately after a heavy exercise. The best way to determine the delay in HRR is to perform a maximum exercise test [(220-age)x0.88] on the treadmill. There are various cutoff values in the literature to determine the delay in HRR at the first minute of exercise. In a study done by Lacasse et al.,[12] this value was <= 14 beats/min, while in many studies the cutoff value <= 12 beats/min was accepted.[13]

Tp-e and HRR-I values have not been evaluated in patients with stable angina so far. The aim of this study was to compare baseline Tp-e and heart rate recovery indices in patients with stable angina with an EF of > 50 % and < 50 % and to investigate the relationship between ventricular repolarization markers and HRR-I values in patients with stable coronary artery disease.

MATERIALS and METHODS

Study Population: In this study, 107 patients who applied to the cardiology outpatient clinic with typical chest pain more than 2 months duration and treadmill exercise test [+] and who had an EF < 50 % at echocardiography and had at least 50 % stenosis in each of the epicardial coronary arteries at coronary angiography were involved in Group 1. 76 patients who applied to the cardiology outpatient clinic with typical chest pain more than 2 months duration and treadmill exercise test [+] and who had an EF > 50 % at echocardiography and had at least 50 % stenosis in each of the epicardial coronary arteries at coronary angiography were involved in Group 2. The study was conducted between February 2019 and December 2019 at Ankara City Hospital. This study is a cross-sectional descriptive study performed at Ankara City Hospital.

Exclusion criteria from the study were: impaired liver or kidney function tests, having structural or severe valvular disease, blood electrolyte disturbance, anemia or impaired thyroid function tests, having a persistent pacemaker, dil-

atation of right and left ventricular cavities in the heart, diagnosis of chronic obstructive pulmonary disease and being on bronchodilator therapy, being unable to do pulmonary function tests and being diagnosed with cancer. Written informed consent was obtained from each individual included in the study. Smoking habits, demographic characteristics, and diseases of the individuals were questioned. In all subjects with stable angina, electrocardiography(ECG) and transthoracic echocardiograms were performed after 5 min of rest and after a complete physical examination including measuring blood pressure 3 times in a row.

Baseline Tp-e values of all patients with stable angina were measured and transthoracic echocardiograms were performed at the beginning. All patients were then subjected to treadmill exercise testing according to the Bruce protocol and heart rates at the peak, 1st, 2nd, and 3rd minutes of exercise were recorded. Heart rate recovery indices were then calculated by subtracting the heart rate at the 1st, 2nd, and 3rd minutes from the peak values of the exercise. Then, the patients who had positive exercise treadmill tests were taken to coronary angiography and the patients with at least 50 % stenosis in each epicardial coronary artery were included in the study. The patients were divided into two groups according to their EFs > 50 % or < 50 %.

Electrocardiography [ECG): The standard 12-lead ECG was taken using a standard ECG system with the patient lying on his back at a paper wave-length of 10 mm / mV and a rate of 25 mm / sec [CardiofaxV model 9320, Nihon Kohden, Tokyo, Japan]. Since the ECG was 10 sec long, each lead had 4-6 beats. ECGs were measured manually with the aid of a magnifying glass [TorQ, 150 mm Digital Caliper LCD] by the two cardiologists with no knowledge of the subjects. The T peak-end intervals were measured manually and with an accuracy of 0.01 mm.

The T peak-end interval was measured from the top of the T wave to the isoelectric line in V2-5 left leads. The values obtained were multiplied by 40 and the value of Tp-e in milliseconds was found. If the U wave is present, the end of the T wave is defined as the lowest point between the T and U waves. Arithmetic means of measurement are used for analysis.

Statistical Analysis

Continuous variables were defined as mean ± standard deviation. Categorical variables were defined as percentages. Student's t-test was used to compare continuous variables and the Chi-square test was used for categorical variables. To compare the values of two separate groups, the T-test was used for two independent means, and the Paired samples T-test was used for two dependent means to compare different values of the same group. Z test was used to compare ratios. Pearson correlation test was used to determine the correlation between the variables. $P < 0.05$ was considered statistically significant. Kolmogorov Smirnov test was performed to determine whether our data showed normal distribution and we found that in our study data showed normal distribution. Statistical analysis was performed using SPSS version 20.0 [IBM Co., Armonk, NY, USA].

Ethical Approval: All procedures performed in studies involving human participants were following the ethical standards of the National Health and Medical Research Council of Turkey and with the 1964 Helsinki declaration and its later comparable ethical standards. Ethical approval was obtained from the ethical committee of Ankara City Hospital (No: E1-20-1101, 30.09.2020). The informed patient consent was obtained from each subject.

RESULTS

Patients in Group 1 had been smoking for a mean of 17.5 ± 9.2 years, and patients in Group 2 had been smoking for 16.1 ± 8.5 years [$t = -1.047$ and $p = 0.29$]. There was no significant difference between Group 1 and Group 2 in terms of sociodemographic and baseline clinical characteristics [Tables 1 and 2].

Table 1: The Socio-demographic Properties and Basal Clinic Findings of The Group 1 (EF < % 50) and Group 2 (EF > % 50) patients.

Variable	Grup 1	Grup 2	T or Z value	P-value
Age	69.7±-3.6	68.2±7.9	T=-1.854	0.085
Males	80 %	78.8	Z=0.022	0.884
Females	20 %	21.2	Z=0.027	0.888
BMI, kg/m2	27.1±2.9	26.8±3.3	T=0.658	0.523
Basal heart rate, beat/min	76.6±3.7	73.9±7.9	T=-3.143	0.0023
Blood pressure, mmHg	122.6±11.5	119.4±10.6	T=1.569	0.136
LV mass, gram	178.2±22.1	175.5±19.5	T=0.677	0.537
Glucose, mg/dl	95.5±9.5	94.2±11.7	T=0.574	0.569
TSH, mU/l	2.2±0.56	2.31±0.4	T=0.893	0.374
Total cholesterol,mg/dl	231.7±43.7	226.6±39.7	T=-0. 883	0.421
Triglycerides, mg/dl	205.7±13.7	203.6±15.4	T=-0.972	0.336
LDL Cholesterol,mg/dl	136.4±22.6	132.8±22.6	T=0.856	0.428
Sodium, mEq/l	142.5±1.6	142.4±1.4	T=0.362	0.714
Calcium, mg/dl	9.6±0.3	9.7±0.5	T=1.095	0.473
Potassium, mEq/l	3.8±0.2	3.9±0.3	T=1.873	0.064
Magnesium, mg/dl	2.18±0.1	2.2±0.1	T=1.246	0.237
Creatinin, mg/dl	0.95±0.1	0.93±0.1	T=1.5428	0.124

Abbr: BMI; Body Mass Index, HR; Heart Rate, LV; Left Ventricle, TSH; Thyroid Stimulating Hormone, LDL; Low-Density Lipoprotein. Student's t-test and Z test were used for comparison of the variables in this table.

Table 2: The Socio-demographic Properties and Basal Clinic Findings of The Group 1 (EF < % 50) and Group 2 (EF >% 50) patients.

Variable	Grup 1	Grup 2	T or Z value	P-value
HDL Cholesterol, mg/dl	40.5± 3.9	41.5 ±4.0	T=1.7	0.0925
HT	70 %	71 %	Z=-0.15	0.884
DM	30 %	28.5 %	Z=0.22	0.835
Beta-blocker	56 %	54 %	Z=0.27	0.792
ACEI	58.3 %	59.2 %	Z=-0.12	0.974
ARB	18 %	17.6 %	Z=0.07	0.943
CCB	39 %	41 %	Z=-0.27	0.794
OAD	27 %	27.5 %	Z=-0.07	0.948
Statin	72 %	73.5 %	Z=-0.22	0.835

Abbr: HDL; High-Density Lipoprotein, HT; Hypertension, DM; Diabetes Mellitus, ACEI; Angiotensin-Converting Enzyme Inhibitor, ARB; Angiotensin Receptor Blocker, CCB; Calcium Channel Blocker, OAD; Oral Antidiabetic. Student's t-test and Z test were used for comparison of the variables in this table.

There was no statistically significant difference between the groups in terms of the drugs being currently used [Table 2].

There was a statistically significant difference between Group 1 [95.8 ± 6.8 msec] and Group 2 [71.4 ± 5.1 msec] [t = -26.4, P <0.0001] in terms of basal Tp-e. There were statistically significant difference between between baseline heart rates [76.6 ± 3.67 vs 73.9 ± 7.9] [t = -3.1, P <0.0023], between the first minute heart rates [119.2 ± 3.2 vs 116.2 ± 6.5] [t = -4.2, P = 0.0001], between the second minute heart rates [105.5 ± 3.3 vs 91.3 ± 6.9] [t = -18.5, P <0.0001],

between the 3rd minute heart rates [90.6 ± 3.3 vs 71.3 ± 6.9] [t=-25.2, p< 0.0001], between peak heart rates [132.3 ± 3.3 vs 136.3 ± 6.9] [t = 5.2, P <0.0001] [Table 3].

There were statistically significant differences between the groups when looking at HRR-I1 [14.4 ± 2.1 vs 20.1 ± 3.5] [t = 13.4, P <0.00001], when looking at HRR-I2 [26.3 ± 2.2 vs 45.1 ± 2.4] [t = -54.9, P <0.00001], when looking at HRR-I3 [42.6 ± 2.9 vs 64.1 ± 2.6] [t = -51.6, P <0.00001] [Table 3]

There was a moderately positive relationship between HRR-I1 and EF values in both Group 1 and Group 2 patients. There was a moderately negative relationship between Tp-e and EF, cTp-e and EF, and HRR-I1 and Tp-e in both Group 1 and Group 2 patients. There was no relationship between HRR-I2 and Tp-e, HRR-I3, and Tp-e in both groups.

Table 3: The Comparison of ECG Findings of The Group 1 (EF < % 50) and Group 2 (EF > % 50) patients.

Variable	Grup 1	Grup 2	T or Z value	P-value
Tp-e basal	95.8±6.8	71.4±5.1	-26.4	<0.0001
cTp-e basal	108.1±7.9	79.3±7.7	-24.5	<0.0001
Basal HR	76.6±3.7	73.9±7.9	-3.1	0.0023
Peak HR	132.3±3.3	136.3±6.9	5.2	<0.0001
1st min HR	119.2±3.2	116.2±6.5	-4.1	0.0001
2nd min HR	105.5±3.3	91.3±6.9	-18.5	<0.0001
3rd min HR	90.6±3.3	71.3±6.9	-25.2	<0.0001
HRR-I1	14.4±2.1	20.1±3.5	13.4	<0.00001
HRR-I2	26.3±2.2	45.1±2.4	-54.9	<0.00001
HRR-I3	42.6±2.9	64.1±2.6	-51.6	<0.00001

Abbrv: HR: Heart rate, HRR-I1: Heart rate recovery index at the 1st minute of the treadmill exercise testing, HRR-I2: Heart rate recovery index at the 2nd minute of the treadmill exercise testing, HRR-I3: Heart rate recovery index at the 3rd minute of the treadmill exercise testing. Student's t-test was used for comparison of the variables in this table.

Table 4: The relationship between various parameters in Group 1 (EF < % 50) and Group 2 (EF > % 50) patients.

Variables	R-value	P-value	The power of relationship		Variables	R-value	P-value	The power of relationship
EF >50					**EF<50**			
HRR-I1/EF	0.59	<0.00001	Moderately positive		HRR-I1/EF	0.38	0.000054	Moderately positive
HRR-I2/EF	-0.038	0.742	No relationship		HRR-I2/EF	0.13	0.182	No relationship
HRR-I3/EF	-0.103	0.386	Weakly negative		HRR-I3/EF	0.15	0.123	No relationship
Tp-e/EF	-0.67	<0.00001	Moderately negative		Tp-e-EF	-0.57	<0.00001	Moderately negative
cTp-e/EF	-0.59	<0.00001	Moderately negative		cTp-e-EF	-0.54	<0.00001	Moderately negative
HRR-I1/Tp-e	-0.57	<0.00001	Moderately negative		HRR1- Tp-e	-0.28	0.003	Moderately negative
HRR-I2/Tp-e	0.077	0.513	No relationship		HRR2- Tp-e	-0.086	0.387	No relationship
HRR-I3/Tp-e	0.09	0.465	No relationship		HRR3- Tp-e	-0.024	0.815	No relationship

Abbrv: HRR-I1: Heart rate recovery index at the 1st minute of the treadmill exercise testing, HRR-I2: Heart rate recovery index at the 2nd minute of the treadmill exercise testing, HRR-I3: Heart rate recovery index at the 3rd minute of the treadmill exercise testing, EF: Ejection fraction, Tp-e: T peak-end interval. Pearson correlation test was used to determine the correlation between the variables.

DISCUSSION

In group 1, HRR-I values were lower than in group 2. Also, in group 1, basal Tp-e and c Tp-e interval values were significantly higher than in group 2. And also, there were significant negative correlations in both groups in terms of HRR-I1 value and Tp-e interval values. Furthermore, there were significant positive correlations between HRR-I values and EF, and there were significant negative correlations between EF and Tp-e interval values.

Sudden cardiac death[SCD] is a death due to the cardiovascular cause, with or without a previously known heart disease. Sudden cardiac death accounts for 50 % of deaths due to coronary artery disease and 15-20 % of all deaths. 80% of these deaths are due to malignant ventricular arrhythmia.[14]

In normal individuals, during exercise testing, increased heart rate is caused by the withdrawal of vagal activity and increased sympathetic activity. A decrease in heart rate immediately after exercise is due to the reactivation of the parasympathetic nervous system. Although some studies have shown decreased HRR in patients with left ventricular systolic dysfunction[15] prognostic information about HRR in patients with heart failure has not been obtained yet. Patients with heart failure show decreased parasympathetic and increased sympathetic activity. Impaired vagal reactivation in patients with congestive heart failure may be due to decreased sensitivity to vagal stimulation. Vatner et al. demonstrated that cardiac muscarinic receptor density decreased in dogs with experimentally developed heart failure.[16]

Heart rate recovery index [HRR-I] is an indicator of autonomic nervous system function and is an independent prognostic risk factor for cardiovascular diseases. In one study, HRR-I was found to be impaired in heavy smokers.[17] In our study, we found that HRR-I at 1st min, 2nd min, and 3rd min of the exercise were significantly impaired in Group 1 compared to Group 2 [Table 3].

In our study, we found that HRR-I at 1st-min, 2-nd, and 3rd-min of the exercise was significantly impaired in Group 1 compared to Group 2 [Table 3]. This shows that HRR-I is reduced in patients with ischemic cardiomyopathy with EF < 50 %, parasympathetic activity is reduced, and the morbidity and mortality of these patients is higher than patients with stable coronary artery disease with EF > 50 %. In our study, a moderate positive correlation was found between HRR1 and EF in both Group 1 and Group 2 [Table 4]. In other words, as EF increases HRR1 increases, and as EFdecreases HRR1 decreases. The heart rate returned to normal immediately after exercise, due to the activation of vagal tone.

Myocardial repolarization markers such as the Tp-e interval, Tp-e / QT, Tp-e / QTc ratios can be used as a marker of malignant ventricular arrhythmia and thus as a predictor of sudden cardiac death.[8,18] Ventricular arrhythmias may be monomorphic or polymorphic VT or may be seen as ventricular fibrillation [VF]. Both are life-threatening and may result in sudden cardiac death. The prevalence of SCD is high and there are 4-5 million deaths worldwide each year. Therefore, safe markers are needed to detect patients at high risk for SCD. Relatively new ECG markers of ventricular repolarization, such as the interval from the peak to the end of the T wave [Tpeak-Tend] and the Tpeak-Tend/QT ratio have been recently proposed to predict ventricular arrhythmic events and SCD. These ECG markers were found to be important in congenital ion channel diseases such as Long QT and Brugada syndrome, myocardial infarction, cardiomyopathies, pulmonary embolism, hypertension, and other diseases such as Chagas disease.[11]

Tp-e interval is a predictor of arrhythmia in patients with Long QT syndrome,[19] in patients with Brugada syndrome,20 and patients with hypertrophic cardiomyopathy.[21] The Tp-e / QT ratio is a more sensitive indicator of arrhythmia risk as it eliminates variability in both Tp-e and QT.[8]

Arrhythmogenic right ventricular dysplasia, slow coronary flow, HIV infection, subclinical hypothyroidism, mitral valve prolapse, aortic stenosis, hypertrophic cardiomyopathy are the leading diseases associated with increased Tp-e interval and Tp-e / QT and Tp-e / QTc ratios.[18]

In our study, no significant difference was observed between the two groups in terms of demographic characteristics [Tables 1]. Again there was no significant difference between the groups in terms of the drugs being currently used [Table 2].

In the literature, no studies are investigating the relationship between Tp-e and cTp-e in patients with stable coronary artery disease. In our study, we found basal Tp-e and cTp-e values increased in Group 1 compared to Group 2 [Table 3]. Increased basal Tp-e and cTp-e values in patients with stable coronary artery disease with EF < 50 % indicate that Tp-e is increased in heart failure and ischemic heart diseases, thereby increasing the risk of developing malignant arrhythmias. In our study, a moderate negative relationship was found between EF and Tp-e and cTp-e in Group 1 patients with EF < 50 % [Table 4]. In other words, as EF decreases, Tp-e increases. In our study, a moderate negative relationship was found between EF and Tp-e and cTp-e in Group 2 patients with EF > 50 % [Table 4]. In other words, as EF increases, Tp-e decreases.

It has been considered more useful to predict cardiac arrhythmias than QTc and its dispersion in some clinical conditions.[22] Tp-e interval was proposed by Castro Hevia et al.[20] Using this marker, they found an increased risk for ventricular arrhythmias in patients with Brugada syndrome than healthy controls. It has been examined in other diseases demonstrating its usefulness to predict malignant arrhythmias and SCD. [23]

The interval between the peak and the end of the T wave [Tp-e interval] on 12-lead ECG is a measure of transmural dispersion of repolarization and may be related to malignant ventricular arrhythmias. In a study done by Tatlisu MA et al, Tp-e and cTp-e measured using the tail method were found to be predictors of both in-hospital and long-term mortality.[24]

Tp-e is the interval between the peak of the T wave and the end of the T wave. Commonly it is considered a reflection of the transmural cardiac repolarization expressed through surface 12 lead ECG. It has been proposed to indicate patients at an increased risk for ventricular arrhythmias.[25]

Savalieva et al[26] and Lubinski et al[27] also reported significant prolongation of Tp-e in patients with myocardial infarction associated with lethal arrhythmia as compared to patients with no lethal arrhythmias. Prolonged Tp-e is related not only to VT induction but also to spontaneous occurrence of VT in high risk patients.[10]

In a meta-analysis in which 33 studies and 155856 patients were evaluated, the cut-off value for the Tp-e interval was 103.3 ± 17.4 ms [range between 77.4 and 146.4 ms]. Almost all studies have found a positive correlation between increased Tp-e interval and increased risk of VT / VF or SCD. A meta-analysis showed that prolonged Tp-e interval increased the risk of VT / VF, SCD, cardiovascular or all-cause mortality by 1.14 times. The risk of VT / VF or SCD increases 5.6 times in Brugada syndrome, 1.52 times in hypertension, 1.07 times in heart failure, and 1.06 times in ischemic heart diseases. Prolonged Tp-e increases arrhythmias or mortality 1.59 times in the general population.11

Decreased HRR immediately after exercise is one of the predictors of mortality. HRR is an important indicator of mortality when calculated in patients with heart failure. Decreased HRR at 1st minute after peak exercise in heart failure patients is a serious indicator of exercise intolerance.[28]

In our study, we found a moderately negative relationship between HRR-I1 and Tp-e in both Group 1 and Group 2

[Table 4]. In other words, HRR1 decreases as Tp-e increases, HRR-I1 increases as Tp-e decreases.

CONCLUSION

As can be seen from these results, the recovery of vagal tonus is faster in Group 2 than Group 1. In patients with EF < 50 %, autonomic dysfunction is more prominent with higher Tp-e and cTp-e values than those with EF > 50 %. Again, in patients with EF < 50 %, HRR-I is lower than that in patients with EF > 50 %. In group 1, repolarization markers namely Tp-e and cTp-e interval were significantly higher than in group 2. This may explain why the malign ventricular arrhythmias are higher in patients with lower EF.

Conflict Of Interes

The authors declare that they have no conflict of interest.

Study Limitations

In our study, the number of cases is small, healthier data can be made with larger case studies. And also, we calculated Tp-e values manually by a digital caliper.

Ethical Approval

All procedures performed in studies involving human participants were following the ethical standards of the National Health and Medical Research Council of Turkey and with the 1964 Helsinki declaration and its later comparable ethical standards. Ethical approval was obtained from the ethical committee of Ankara City Hospital(No: E1-20-1101, 30.09.2020). The informed patient consent was obtained from each subject.

References

1. *Mehra R. Global public health problem of sudden cardiac death. J Electrocardiol. 2007;40(6 Suppl): S118–S122.*
2. *Fishman GI, Chugh SS, Dimarco JP, Albert CM, Anderson ME, Bonow RO, et al. Sudden cardiac death prediction and prevention: a report from a National Heart, Lung, and Blood Institute and Heart Rhythm Society Workshop. Circulation. 2010;122(22): 2335–2348.*
3. *Nichol G, Thomas E, Callaway CW, Hedges J, Powell JL, Aufderheide TP, et al. Regional variation in out-of-hospital cardiac arrest incidence and outcome. JAMA. 2008;300(12):1423–1431.*
4. *Sugishi M, Faminaro T. Cigarette smoking is a major risk for coronary spasm. Circulation.1993; 87: 76-79. PMID: 8419026. // Ng GA. Vagal modulation of cardiac ventricular arrhythmia. Exp Physiol. 2014; 99 (2): 295-9.*
5. *Ng GA. Vagal modulation of cardiac ventricular arrhythmia. Exp Physiol. 2014; 99 (2): 295-9..*
6. *Pérez-Riera AR, Barbosa-Barros R, Shenasa M. Electrocardiographic Markers of Sudden Cardiac Death (Including Left Ventricular Hypertrophy. Card Electrophysiol Clin. 2017;9(4):605-629.*
7. *Kors JA, Ritsema van, van Herpen G. The meaning of the Tp-Te interval and its diagnostic value. J Electrocardiol. 2008;41:575–580.*
8. *Gupta P, Patel C, Patel H, Narayanaswamy S, Malhotra B, Green JT, et al. T(p-e)/QT ratio as an index of arrhythmogenesis. J Electrocardiol. 2008;41:567–574.*
9. *Topilski I, Rogowski O, Rosso R, Justo D, Copperman Y, Glikson M, et al. The morphology of the QT interval predicts torsade de pointes during acquired bradyarrhythmias. J Am Coll Cardiol 2007;49:320-328*
10. *Watanabe N, Kobayashi Y, Tanno K, Miyoshi F, Asano T, Kawamura M, et al. Transmural dispersion of repolarization and ventricular tachyarrhythmias. Journal of Electrocardiology. 2004;37(3):191-200.*
11. *Tse G, Gong M, Wong WT, Georgopoulos S, Letsas KP, Vassiliou VS, et al. The Tpeak-Tend interval as an electrocardiographic risk marker of arrhythmic and mortality outcomes: A systematic review and meta-analysis. Heart Rhythm. 2017 Aug;14(8):1131-1137.*
12. *Lacasse M, Maltais F, Poirier P, Lacasse Y, Marquis K, Jobin J, et al. Post-exercise heart rate recovery and mortality in chronic obstructive pulmonary disease. Respir Med. 2005; 99 (7): 877-886.*
13. *Seshadri N, Gildea TR, McCarthy K, Pathier C, Kavuru MS, Lauer MS. Association of an abnormal exercise heart rate recovery with pulmonary function abnormalities. Chest 2004; 125 (4): 1286-1291,*
14. *Deo R, Albert CM. Epidemiology and Genetics of Sudden Cardiac Death. Circulation. 2012 Jan 31; 125 (4): 620-37.*
15. *Racine N, Blanchet M, Ducharme A, Boucher JM, Juneau M, White M, et al. Decreased heart rate recovery after exercise in patients with congestive heart failure: effect of β-blocker therapy. J Card Fail 2003; 9(4): 296-302.*
16. *Vatner DE, Lee DL, Schwarz KR, J P Longabaugh, A M Fujii, S F Vatner,et al. Impaired cardiac muscarinic receptor function in dogs with heart failure. J Clin Invest 1988; 81(6): 1836-42.*
17. *Erat M, Doğan M, Sunman H, Dinç Asarcıklı L, Efe TH, Bilgin M, et al. Evaluation of heart rate recovery index in heavy smokers. Anatol J Cardiol. 2016 Sep;16(9):667-72.*
18. *Taşolar H, Ballı M, Bayramoğlu A, Otlu YÖ, Cetin M, Altun B, et al. Effect of smoking on Tp-e interval, Tp-e/QT and Tp-e/QTc ratios as indices of ventricular arrhythmogenesis. Heart Lung Circ. 2014;23(9):827-32.*
19. *Yamaguchi M, Shimizu M, Ino H, Terai H, Uchiyama K, Oe K, et al. T-wave peak-to-end interval and QT dispersion in acquired long QT syndrome: A new index for arrhythmogenicity. Clin Sci (Lond) 2003; 105:671–676.*
20. *Castro Hevia J, Antzelevitch C, Tornes Barzaga F, Dorantes SM, Zayas MR, Quinones Perez MA, et al. TpeakTend and Tpeak-Tend dispersion as risk factors for ventricular tachycardia/ventricular fibrillation in patients with the Brugada syndrome. J Am Coll Cardiol 2006; 47:1828–1834.*
21. *Shimizu M, Ino H, Okeie K, Emoto Y, Yamaguchi M, Yasuda T, et al. T-peak to T-end interval may be a better predictor of high-risk patients with hypertrophic cardiomyopathy associated with cardiac troponin I mutation than QT dispersion. Clinical Cardiology 2002; 25:335–339.*
22. *Antzelevitch C, Shimizu W. Cellular mechanisms underlying the long QT syndrome. Curr Opin Cardiol. 2002;17:43–51.*
23. *Yaniel Castro-Torres, Raimundo Carmona-Puerta, Richard E Katholi. Ventricular repolarization markers for predicting malignant arrhythmias in clinical practice.World J Clin Cases. Aug 16, 2015; 3(8): 705-720.*
24. *Tatlisu MA, Özcan KS, Güngör B, Ekmekçi A, Çekirdekçi EI, Aruğarslan E, et al. Can the T-peak to T-end interval be a predictor of mortality in patients with ST-elevation myocardial infarction? Coron Artery Dis. 2014 Aug;25(5):399-404.*
25. *Xia Y, Liang Y, Kongstad O, Holm M, Olsson B, Yuan S. Tpeak-Tend interval as an index of global dispersion of ventricular repolarization: evaluations using monophasic action potential mapping of the epi- and endocardium in swine. J Interv Card Electrophysiol. 2005;14:79–87.*
26. *Savalieva I, Yag YP, Yi G, et al: Comparative reproducibility of QT, QT peak, and Tpeak-Tend intervals and dispersion in normal subjects with hypertrophic cardiomyopathy. Pacing Clin Electrophysiol. 1998;21: Pt II.*
27. *Lubinski A, Kornacewaichs-jach Z, Wnuk-Wojnar AM, Adamus J, Kempa M, Krolak T, et al. The termination of the T wave: A new electrocardiographic marker of risk of ventricular arrhythmias. Pacing Clin Electrophysiol. 2000;23 Pt II:1957-59.*
28. *Bilsel T, Terzi S, Akbulut T, Sayar N, Hobikoglu G, Yesilcimen K. Abnormal heart rate recovery immediately after cardiopulmonary exercise testing in heart failure patients. Int Heart J. 2006 May;47(3):431-40.*