DOI: 10.4149/BLL_2023_048

Bratisl Med J 2023; 124 (4)
313 – 319

CLINICAL STUDY

Major depressive disorder is an independent predictor of the electrocardiographic frontal QRS-T angle and TP-TE/QT ratio

Mucahid YILMAZ[1], Seda YILMAZ[2]

University of Health Sciences, Elazig Fethi Sekin City Hospital, Department of Cardiology, Elazig, Turkey.
mucahid.yilmaz@hotmail.com

ABSTRACT
OBJECTIVES: The relationship between ventricular arrhythmias and major depressive disorder (MDD) has been previously revealed. Recently, frontal QRS-T angle (fQRSTa) and Tp-Te/QT ratio proved to provide more accurate predictive data about ventricular arrhythmias than the measurement of QT, QTc, and QT dispersion. The aim of this study was to determine the effects of MDD on contemporary ventricular arrhythmia indicators.
PATIENTS AND METHODS: 57 newly diagnosed MDD patients and 65 healthy subjects were included in the study. Hamilton depression rating scale (HAM-D) and Hamilton Anxiety Rating Scale (HAM-A) were administered and ECG measurements were obtained. Ventricular arrhythmia predisposition was assessed by calculating the Tp-Te/QT ratio in addition to fQRSTa.
RESULTS: fQRSTa and Tp-Te/QT ratio values in the MDD group were significantly higher than the control group. Correlation analyses revealed that Tp-Te/QT ratio and fQRSTa significantly correlated with (HAM-D). It was found with linear regression analysis, MDD existence and its severities were independent predictors of fQRSTa and Tp-Te/QT ratio.
CONCLUSION: MDD predisposes to ventricular arrhythmia by causing increased fQRSTa and Tp-Te/QT ratio on ECG. Increased fQRSTa and Tp-Te/QT ratio may be useful indicators of dysregulation in the autonomic nervous system and increased risk of ventricular arrhythmias in MDD patients *(Tab. 6, Fig. 4, Ref. 38).* Text in PDF *www.elis.sk*
KEY WORDS: major depressive disorder, Hamilton depression rating scale, frontal QRS-T angle, Tp-Te/QT ratio.

Introduction

Major depressive disorder (MDD) is a psychiatric disorder that can be observed widely all over the world. While the incidence is 14.6 % in countries with high per capita annual income, it is reported as 11.1 % in low or moderate countries (1). Cardiac arrhythmia is caused by three main events: Myocardial electrical instability, often caused by coronary artery disease, an acute triggering event often associated with mental stress, and chronic-widespread and intense psychological stress often associated with depression and hopelessness (2). Dysregulated parasympathetic and/or sympathetic activity increases the risk of fatal ventricular arrhythmia. Increased ventricular repolarization heterogeneity (transmural dispersion of repolarization: TDR) with decreased heart rate variability and baroreceptor sensitivity are observed in the patients that have ventricular arrhythmia (3). Recently, dysregulation of the autonomic nervous system (ANS) is observed in MDD (4).

Increased ventricular repolarization heterogeneity indicates increased cardiac morbidity and mortality in parallel with ANS dysregulation and increased likelihood of ventricular arrhythmia (5). Until recently, it was accepted that Tp-Te interval was an indicator of total dispersion (transmural, apicobasal, and global) of ventricular repolarization, and an observed increase in Tp-Te interval could be a useful index for predicting ventricular tachyarrhythmia and cardiovascular mortality (6, 7). Moreover, in a recent study, it has been shown that an increase in Tp-Te interval and Tp-Te interval dispersion Tp-Te(d) values may lead to a predisposition to malignant ventricular arrhythmia (7). On the other hand, it has been shown that the Tp-Te/QT ratio is not affected by heart rate (HR) and therefore provides more accurate predictive data on ventricular arrhythmias than QT, QTc, QT dispersion and Tp-Te interval measurements (8).

The frontal QRS-T angle (fQRSTa), called the angle between the mean QRS and T wave axes, is a new method to use evaluation of the heterogeneity between myocardial depolarization and repolarization. ANS imbalance, myocardial ischemia, fibrosis, damaged or inhomogeneous regions in the myocardium may lead to wider fQRSTa (9). In recent studies, it has been suggested that the fQRS-T angle is more reliable due to the fact that it is less sensi-

[1]University of Health Sciences, Elaziğ Fethi Sekin City Hospital, Department of Cardiology, Elazig, Turkey, and [2]University of Health Sciences, Elazig Fethi Sekin City Hospital, Department of Psychiatry, Elazig, Turkey

Address for correspondence: Mucahid YILMAZ, University of Health Sciences, Elazig Fethi Sekin City Hospital, Department of Cardiology, Elazig, Turkey.
Phone: +905337719783

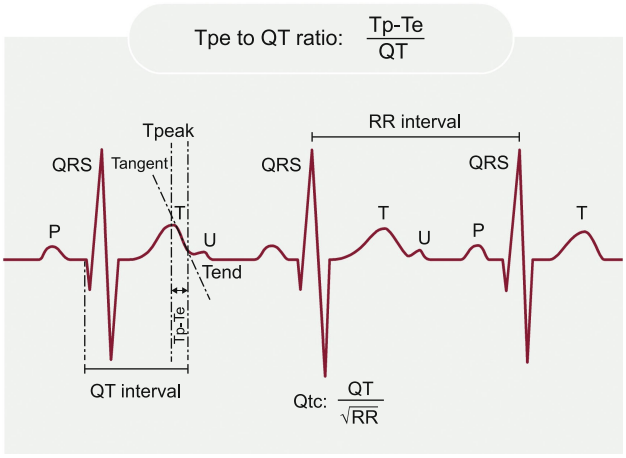

Fig. 1. Bazzett's formula and Tp–Te/QT ratio.

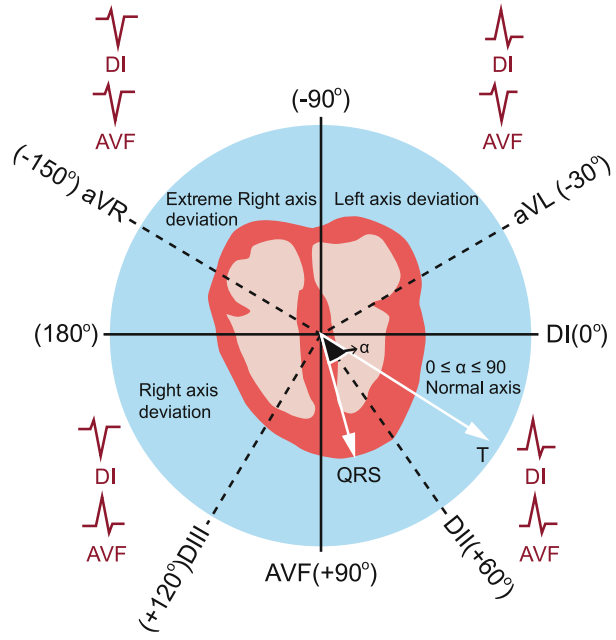

Fig. 2. Shematic presentation of frontal QRS-T angle.

tive to noise and definition problems compared to other traditional electrocardiographic myocardial repolarization parameters (10). Since the electrical activity of the heart during repolarization is represented by the direction of electrical direction of the T wave, measure of the T wave axis (Twa) provides an alternative measure of repolarization abnormality (11). The net direction of the electrical vectors which indicate atrial depolarization is represented by the P wave axis (Pwa). Electrical and/or structural pathological left atrial remodeling leads to an arrhythmogenic substrate which manifests as P wave axis deviation/abnormal P wave axis (aPwa) on surface electrocardiography (ECG) (11).

Despite the relation between MDD and ANS disorder has been identified, there is currently no well-defined electrocardiographic indicator that predicts a predisposition to ventricular arrhythmia in MDD. Therefore, fQRSTa, Tp-Te/QT ratio, P wave axis, and T wave axis were used to comprehensively examine whether the presence of MDD had an effect on ECG.

Material and methods

Population of the study

57 consecutive patients diagnosed with MDD for the first time and 65 healthy subjects with no known mental, systemic or cardiac disorders were enrolled in the study. Subjects who were using drugs that could affect the QT interval (such as flecainide, propafenon, hidroksiklorokin, quinidine, piperaquine, halofantrin, levofloxacin, azithromycin , anti-depressant agent, anti-psychotic agent), who had bundle branch block (left or right) on basal ECG, who had poor ECG quality and who had electrolyte imbalance in addition to professional athletes, BMI > 30 individuals and pregnant women were not included.

All patients were asked to complete questionnaires including Hamilton Depression Rating Scale (HAM-D) and Hamilton Anxiety Rating Scale (HAM-A) to measure the severity of depression. The required ethical approval was obtained from the Ethics Committee of T.C. Firat University.

Electrocardiographic measurements

For the analysis of ECG parameters, the recordings of the patients taken in the supine position on the device at a speed of 50 mm/sec were used. The voltage value of the ECG device was tuned to 10 mm/mV (GE HEALTHCARE MAC 2000, Turkey, Ankara,). After scanning all ECGs in the scanner, QT, RR and Tp-Te intervals were calculated with the help of MATLAB® (U.S.A., Massachusetts) program in the computer environment.

The isoelectric line between the beginning of the QRS wave and the end of the T wave was defined as the QT interval (12). The maximum slope intersection (tangent) method was used to determine the end of the T wave (13) (Fig. 1). The measurements were obtained from precordial derivations. QTmax values were defined as the longest distance on the precordial leads and QTc values were calculated by writing QT max to Bazett's formula as follows: QTc (ms)= QT interval /√RR interval (12) (Fig. 1). The Tp-Te interval was obtained by measuring the distance between the peak and the end of the T wave and was measured by taking the longest value among precordial leads (12,13) (Fig. 1). The Tp-Te (d) was obtained by subtracting the shortest Tp-Te interval from the longest one (13). When an U wave came after the T wave, the lowest point between the T and U waves was considered the end-point of the T wave (12) (Fig. 1). The lowest point of negative or biphasic T waves was accepted as the T peak (12). When a notched T wave existed, the end of the QT interval was determined with the help of the tangent line drawn down the second notch (13).

Since the ECG device presents the frontal QRS wave axis, T wave axis and P wave axis as automatic reports, the data were obtained from here. The absolute difference between the frontal QRS wave axis and the frontal T wave axis was identified as the frontal QRS-T angle (fQRSTa) (fQRSTa = frontal QRS wave axis

– frontal T wave axis) (Fig. 2). When this angle exceeded 180°, the current angle was subtracted from 360° and recalculated. Values were accepted as normal for the T wave axis between 15° and 75° and outside this range were considered abnormal (aTwa). P wave axis values between 0°–75° were accepted as normal and outside this range were considered abnormal (aPwa) (11) .

Statistical evaluation

SPSS 27 software (SPSS Inc., Chicago, IL, USA) was used for statistical evaluation. Comparison of categorical variables was performed with Chi-square test. Kolmogorov-Smirnov test was used to evaluate whether the continous variables were normally distributed. To analyze normally distributed continuous variables Student's t-test was used and Mann-Whitney U test was performed for analyzing continuous variables which were distributed non-normally. Median and 25th-75th percentiles were used to represent continuous variables that did not have a normal distribution. Mean and standard deviation were used for the presentation of normally distributed continuous variables. Correlation analysis between fQRSTa, TDR indices, HAM-D and HAM-A was performed with Pearson's correlation test. To determine which variables were independently associated with fQRSTa and Tp-Te/QT ratio, linear regression analysis was used. Beta coefficients and 95 % confidence intervals (CIs) were used for the presentation of results. For statistically significant values $p < 0.05$ were accepted.

Results

A total of consecutive 112 subjects who met the inclusion criteria (65 of whom were healthy with no known mental, systemic, or cardiac disorders, 57 of whom were newly diagnosed MDD patients) were included in the study. fQRSTa and TDR indices values (Tp-Te/QT ratio, Tp-Te/QTc ratio, Tp-Te interval, Tp-Te(d)) were found to be significantly increased in the MDD group when compared to the control group (Tab. 1, Fig. 3). It was observed that aPwa, aTwa, gender, and age parameters did not reach a statistically significant difference between the two groups (Tab. 1).

While it was determined by Pearson's correlation test that TDR indices were positively correlated with (HAM-D) and (HAM-A), no correlation could be detected between fQRSTa and (HAM-A) (Tab. 2, Fig. 4). However, it was detected a positive correlation between fQRSa and (HAM-D).

Four linear regression models were used to evaluate the independent effects of MDD presence and severity on electrocardiographic ventricular arrhythmia markers. When Model 1 was examined, it was observed that the linear regression model established was significant and the explanatory value of Tp-Te/QT ratio of the

Tab. 1. Intergroup comparison of demographic and electrocardiographic data.

	Control Group n = 65	MDD Group n = 57	p
Age (Year)	28.0(23.50–52.50)	38.0(25.0–45.50)	0.63#
Gender (Male/Female)(%)	19/46(29/71)	12/45 (21/79)	0.41
Tp-Te (ms)	66.0 (65.0–70.0)	80.0 (75.0–90.0)	<0.0001#
QTmax (ms)	347.03±23.66	376.49±26.91	<0.0001
QTc (ms)	391.88±25.66	424.82±30.06	<0.0001
Tp-Te/QT ratio	0.19±0.01	0.22±0.03	<0.0001
Tp-Te/QTc ratio	0.17±0.01	0.20±0.02	<0.0001
Tp-Te(d) (ms)	16.0 (10.0–20.0)	20.0 (20.0–35.0)	<0.0001#
HR	75.0 (71.5–80.5)	75.0 (69.0–82.0)	0.59#
Frontal QRS-T Angle	9.0 (5.0–11.0)	26.0 (16.0–42.0)	<0.0001#
Abnormal P axis	1/65 (%1.5)	5/57 (%8.8)	0.10
Abnormal T axis	0/65 (%0)	2/57 (%3.5)	0.21

Normality of the distribution was evaluated by the Kolmogorov-Smirnov test and the Mann-Whitney U test was applied to compare for continuous variables.

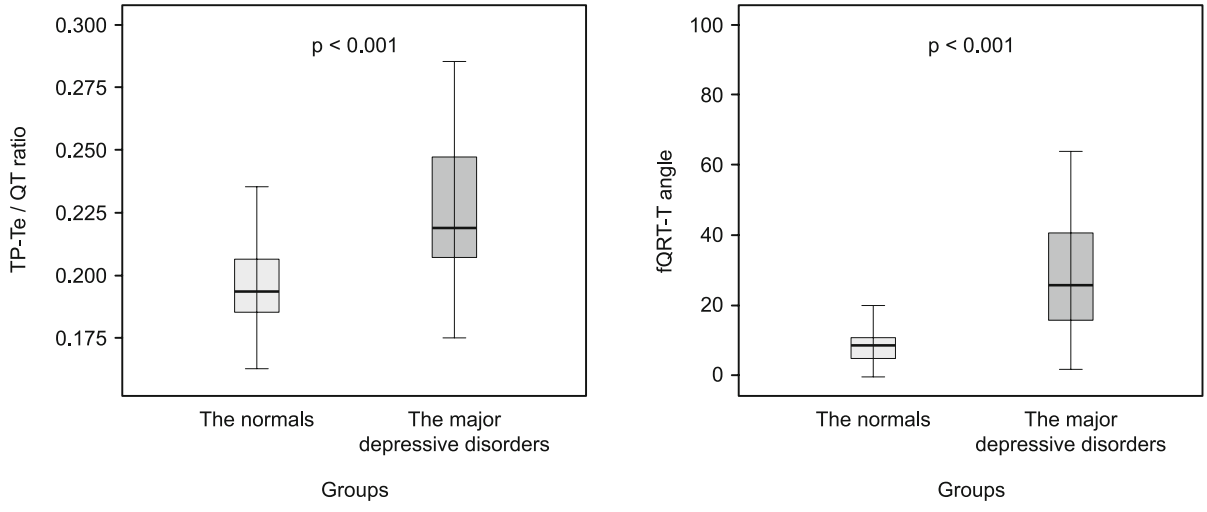

Fig. 3. Comparison of Tp-Te/QT Ratio and frontal QRS-T angle and frontal QRS-T angle between the two groups.

variables in the model was 31.0 % (Nagelke $R^2 = 0.310$; $p < 0.001$). In this model, those with MDD had a Tp-Te/QT ratio of 0.03 units higher than those without (Tab. 3). When Model 2 was examined, it was seen that the linear regression model established was significant and the fQRSTa explainability of the variables in the model was 36.4 % (Nagelke $R^2 = 0.364$; $p < 0.001$). According to this model, the fQRSTa value of those with MDD was found to be 19.517° higher than in those without (Tab. 4). Looking at Model 3, it was determined that the linear regression model established was significant and the explanatory value of Tp-Te/QT ratio of the variables in the model was 34.7 % (Nagelke $R^2 = 0.347$; $p < 0.001$). According to this model, it was determined that a 1-point increase in the HAM-D score increased the Tp-Te/QT Ratio value by 0.003 units (Tab. 5). Looking at Model 4, it was observed that the established linear regression model was significant and the fQRSTa explanatory power of the variables in the model was 18.6 %. (Nagelke $R^2 = 0.186$; $p = 0.028$). In this model, it was found that a 1-point increase in the HAM-D score increased the fQRSTa value by 1.866° (Tab. 6).

The results of these four regression models showed that the presence and severity of MDD are independent predictors for fQRSTa and Tp-Te/QT ratio (Tabs 3–6).

Tab. 2. Pearson correlation analysis between TDR parameters, HAM-D and HAM-A.

	HAM-D		HAM-A	
	r	p	r	p
Tp-Te (ms)	0.580	<0.0001	0.409	0.002
QTmax (ms)	0.257	0.05	0.189	0.160
QTc (ms)	0.403	0.002	0.427	0.001
Tp-Te/QT ratio	0.559	<0.0001	0.391	0.003
Tp-Te/QTc ratio	0.451	<0.0001	0.242	0.070
Tp-Te(d) (ms)	0.553	<0.0001	0.466	<0.0001
HR	0.100	0.45	0.163	0.23
frontal QRS-T angle	0.278	0.03	0.097	0.47

Discussion

The present study revealed that MDD patients diagnosed for the first time with no medication had significantly higher Tp-Te/QT ratio, Tp-Te/QTc ratio, Tp-Te interval, Tp-Te(d) and fQRST angle when compared to healthy subjects. This study revealed the positive correlation between TDR indices (Tp-Te/QT ratio, Tp-Te/QTc ratio, Tp-Te interval, Tp-Te(d)), fQRSTa and MDD severity. Statistical analysis revealed MDD existence and HAM-D score were indepent predictors for Tp-Te/QT ratio and fQRSTa. On the other hand, no difference was observed between the two groups in terms of aPwa, aTwa presence, gender and age.

Depression has a high risk of recurrence and chronicity and may cause comorbid disorders (14). MDD has been shown to

Tab. 3. Model-1. Linear Regression for Variables (Dependent Variable: Tp-Te/QT ratio).

	Unstandardized Coefficients		Standardized Coefficients	t	p
	B	Std. Error	Beta		
(Constant)	0.195	0.006	–	32.579	<0.001
Group	0.030	0.004	0.556	7.241	<0.001
Gender	0.000	0.005	–0.003	–0.042	0.966
Age	1.258E–7	0.000	0.000	0.001	0.999

Model $p < 0.001$; Nagelke $R^2 = 0.310$

Tab. 4. Model-2. Linear Regression for Variables (Dependent Variable: frontal QRS-T angle).

	Unstandardized Coefficients		Standardized Coefficients	t	p
	B	Std. Error	Beta		
(Constant)	11.846	3.556		3.331	0.001
Group	19.517	2.438	0.590	8.007	<0.001
Gender	–2.982	2.794	–0.079	–1.067	0.288
Age	–0.043	0.082	–0.039	–0.526	0.600

Model $p < 0.001$; Nagelke $R^2 = 0.364$

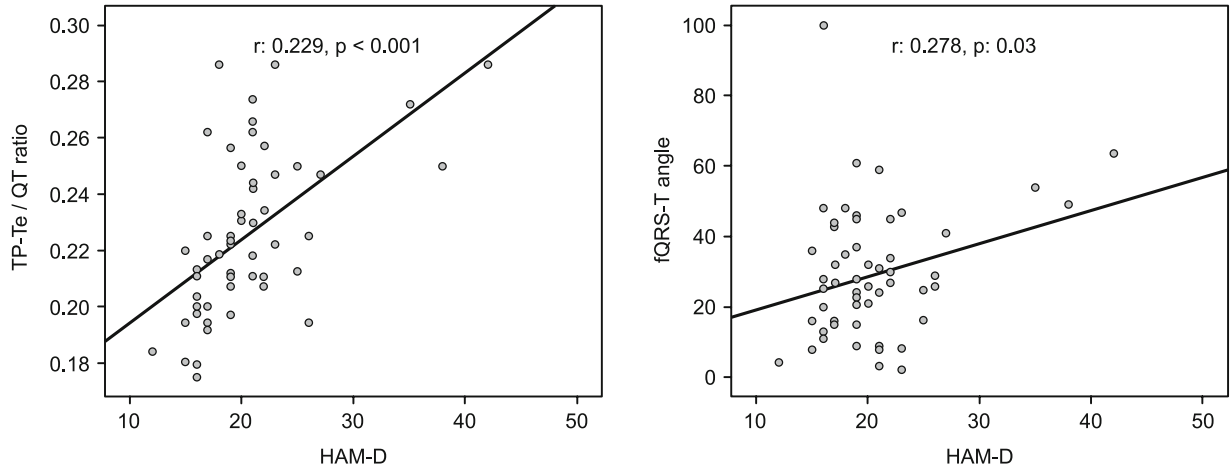

Fig. 4. Correlation analyses between Tp-Te/QT Ratio, frontal QRS-T angle and frontal QRS-T angle and Hamilton Depression Rating Scale (HAM-D).

Tab. 5. Model-3. Linear Regression for Variables (Dependent Variable: Tp-Te/QT Ratio).

	Unstandardized Coefficients		Standardized Coefficients	t	p
	B	Std. Error	Beta		
(Constant)	0.169	0.014	–	12.087	<0.001
Gender	0.010	0.008	0.145	1.245	0.219
Age	0.000	0.000	–0.140	–1.149	0.256
HDS	0.003	0.001	0.604	3.362	0.001
HAS	0.000	0.001	–0.014	–0.077	0.939

Model $p < 0.001$; Nagelke $R^2 = 0.347$

Tab. 6. Model-4. Linear Regression for Variables (Dependent Variable: fQRS-T angle).

	Unstandardized Coefficients		Standardized Coefficients	t	p
	B	Std. Error	Beta		
(Constant)	17.241	10.087		1.709	0.093
Gender	–10.553	5.723	–0.239	–1.844	0.071
Age	–0.131	0.183	–0.097	–0.713	0.479
HDS	1.866	0.686	0.546	2.722	0.009
HAS	–1.538	0.999	–0.324	–1.540	0.130

Model $p = 0.028$; Nagelke $R^2 = 0.186$

be a considerable risk factor for cardiovascular disease and cardiovascular mortality (15, 16). ANS imbalance is considered the main reason for this situation and it has been seen in the form of sympathetic/parasympathetic system impairment, or both (17, 18). Deterioration of ANS balance impacts cardiac electrophysiology adversely and may lead to sudden cardiac death via ventricular arrhythmias by increasing TDR (19–21). Therefore, ANS imbalance that can be observed in MDD patients may lower the ventricular extrasystole/tachycardia threshold, leading to malignant ventricular arrhythmias and sudden death (22, 23).

Ventricular arrhythmias are caused by electrical instability resulting from differences in repolarization phases between beats. For many years, non-invasive parameters of sudden cardiac death obtained from electrocardiograms (ECG) have been used for assessing the TDR parameters. These parameters have focused mostly on the QT distance (13). QT dispersion is a repolarization index that was the most widely used TDR parameter until recent years and is assumed to detect susceptibility to malignant ventricular arrhythmias (24). In fact, QT dispersion is considered a crude and close assessment of the overall heterogeneity of ventricular repolarization (25). It is also nearly impossible to detect the normal and abnormal ranges of QT dispersion. The most important reason for this is the wide range of values (10–71 milliseconds) that is considered normal, shown by various studies (26, 27). In addition, the ranges between values considered abnormal in some studies and those considered normal in other studies overlap. Some authors define the upper limit of QT dispersion in normal healthy individuals as 65 milliseconds (ms), while others agree that QT dispersion is a crude measure of TDR and that the upper limit reported for healthy individuals is unreliable. Hence, there is a consensus that only QT dispersion > 100 ms values are clinically important in demonstrating repolarization abnormality (28, 13).

Epicardial, midmyocardial and endocardial M cells are three types of myocytes with different electrophysiological properties. Among these three cell types, Midmyocardial M cells have the longest duration of repolarization. The repolarization of these cells extends to the endpoint of the T wave on the ECG. T peak is where the repolarization phase of epicardial cells ends. The Tp–Te interval is described as the distance in milliseconds (ms) from the peak to the endpoint of the T wave, which is considered a transmural dispertion of repolarization (TDR) index (8). Howbeit, recent studies have shown that alterations in HR affect the Tp-Te interval (8, 13, 29). On the other hand, since Tp-Te/QT ratio is not affected by alterations in HR, it has been accepted as a novel ECG indicator of ventricular TDR and has been recommended for use as a more reliable indicator of ventricular arrhythmia (29).

fQRSTa is a marker that indicates heterogeneous myocardial repolarization and electrically unstable myocardium. The QRS axis indicates the angle of myocardial depolarization, the T axis indicates the angle of repolarization. These axes are expected to be in a similar direction under normal circumstances (30, 31). In myocardial ischemia and fibrosis, damaged or inhomogeneous regions in the myocardium leading to wider fQRSTa are present (32). Variations in ANS may be another reason for the widened fQRSTa (33).

P-wave axis is the electrical vector that indicates atrial depolarization and P-wave axis deviation (aPwa) occurs as a result of electrical and/or structural abnormal left atrial remodeling. aPwa has a predictive role for atrial fibrillation and cardiovascular mortality (11, 34). Axis deviation in the T wave, which is an electrocardiographic indicator of ventricular repolarization, reflects abnormal ventricular repolarization and indicates subclinical myocardial electrical and/or structural pathology. A deviation observed in the T wave axis (aTwa), independently of other cardiovascular risk factors, is related with enhanced risk for malign ventricular arrhytmias and cardiovascular mortality (35). Situations in which autonomic activation is arrhythmic or antiarrhythmic and differ for arrhythmias of atrial and ventricular origin. While parasympathetic activity has an antiarrhythmic effect on ventricular fibrillation, sympathetic activity has a proarrhythmic effect on the ventricle. On the contrary, both parasympathetic and sympathetic activity causes a serious predisposition to atrial fibrillation (19). Therefore, regardless of mode of action, ANS disturbances/alterations can be shown as a strong cause of abnormal axis shift in P, QRS and T waves.

Today it has been known that ANS imbalance is among the most important causes of electrocardiographic ventricular repolarization heterogeneity (36). ANS imbalance has been reported in MDD patients (37). We observed increased electrocardiographic TDR parameters (Tp-Te/QT ratio, Tp-Te/QTc ratio, Tp-Te interval, Tp-Te(d)) and widened fQRSTa in MDD patients diagnosed for the first time with no medication. In addition, fQRSTa and Tp-Te/QT ratio were found to be correlated with HAM-D score in this study. Additionally, the results of linear regression analysis proved that MDD presence and its severity

have predictive values for Tp-Te/QT ratio and fQRSTa which indicate electrocardiographic ventricular repolarization heterogeneity and predisposition to ventricular arrhythmia. However, we found that Pwa and Twa did not deviate to abnormal degrees in MDD patients. The data obtained show that MDD could not deviate the depolarization and repolarization axes of the heart to abnormal degrees but the study suggests that MDD increases the risk of ventricular arrhythmias and cardiac adverse events by causing prolongation of the terminal period of myocyte repolarization and widening the electrical axis between these two electrical vectors. ANS disorder observed in MDD can be shown as the reason for all these findings. In light of this information, disorder in ANS balance can be considered as an important cause of increased electrocardiographic TDR observed in MDD patients. These results prove that the risk of ventricular arrhythmia in any individual increases in direct proportion to the presence and severity of MDD.

Finally, all ECG data obtained with this study, may provide important clues about the predisposition to the development of ventricular arrhythmia in MDD patients detected at the time of application, and since some antidepressants can increase the risk of malignant ventricular arrhythmias, it can also help clinicians in choosing antidepressants (38).

Conclusion

The study may feed into explaining why the prevalence of ventricular arrhythmias and the risk of cardiovascular mortality are higher in MDD patients by demonstrating increased heterogeneity of ventricular repolarization. Increased ventricular arrhythmias and sudden cardiac deaths observed in these individuals could be interpretted by increased fQRSTa and Tp-Te/QT ratio values. The findings obtained in this study suggest that the severity of the disease and ECG findings should be combined when choosing an antidepressant drug, which has the potential to increase ventricular repolarization heterogeneity in MDD patients.

References

1. Bromet E, Andrade LH, Hwang I, Sampson NA, Alonso J, de Girolamo G et al. Cross-national epidemiology of DSM-IV majör depressive episode. BMC Med 2011; 9: 90.

2. Brunckhorst CB, Holzmeister J, Scharf C, Binggeli C, Duru F. Stress, depression and cardiac arrhythmias. Ther Umsch 2003; 60 (11): 673–681.

3. Piccirillo G, Viola E, Bucca C, Santagada E, Raganato P, Tondo A et al. QT interval dispersion and autonomic modulation in subjects with anxiety. J Lab Clin Med. 1999; 133 (5): 461–468.

4. Tolentino JC, Schmidt SL. Association between depression severity and cardiac autonomic modulation**.** J Psychosom Res 2016; 85: 9–11.

5. Taylor CB. Depression, heart rate related variables and cardiovascular disease: Int J Psychophysiol 2010; 78: 80–88.

6. Kors JA, Ritsemavan Eck HJ, van Herpen G. The meaning of the Tp-Te interval and its diagnostic value. J Electrocardiol 2008; 41: 575–580.

7. Hevia JC, Antzelevitch C, Bárzaga FT, Sánchez MD, Balea FD, Molina RZ et al. Tpeak-Tend and Tpeak-Tend dispersion as risk factors for ventricular tachycardia/ventricular fibrillation in patients with the Brugada syndrome. J Am Coll Cardiol 2006; 47 (9): 1828–1834.

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. Borleff s CJ, Scherptong RW, Man SC, Van Welsenes GH, Bax JJ, van Erven L et al. Predicting ventricular arrhythmias in patients with ischemic heart disease: clinical application of the ECG derived QRS-T angle. Circ Arrhythm Electrophysiol 2009; 2: 548–554.

10. Zhang ZM, Rautaharju PM, Prineas RJ, Tereshchenko L, Soliman EZ et al. Electrocardiographic QRS-T angle and the risk of incident silent myocardial infarction in the Atherosclerosis Risk in Communities study. J Electrocardiol 2017; 50 (5): 661–666.

11. Moraes DN, Nascimento BR, Beaton AZ, Soliman EZ, Lima-Costa MF, Dos Reis RCP et al. Value of the Electrocardiographic (P Wave, T Wave, QRS) Axis as a Predictor of Mortality in 14 Years in a Population With a High Prevalence of Chagas Disease from the Bambuí Cohort Study of Aging. Am J Cardiol 2018; 121 (3): 364–369.

12. Yilmaz M, Kayançiçek H. Elevated LV Mass and LV Mass Index Sign on the Athlete's ECG: Athletes' Hearts are Prone to Ventricular Arrhythmia. J Clin Med 2018; 7 (6): 122.

13. Yilmaz M, Kayançiçek H, Gözel N, Bilen MN, Kurtoğlu E, Seçen Ö et al. Spotlights on some electrocardiographic paradigms: How should we evaluate normal reference values of Tp–Te interval, Tp–Te dispersion and Tp–Te/QT ratio? Advances in Clinical and Experimental Medicine 2020; 29 (9): 1091–1099.

14. Ten Have M, de Graaf R, van Dorsselaer S, Tuithof M, Kleinjan M, Penninx BWJH. Recurrence and chronicity of major depressive disorder and their risk indicators in a population cohort. Acta Psychiatr Scand 2018; 137: 503–515.

15. Barth J, Schumacher M, Herrmann-Lingen C. Depression as a risk factor for mortality in patients with coronary heart disease: A meta-analysis. Psychosom Med 2004; 66: 802–813.

16. Janszky I, Ahlbom A, Hallqvist J, Ahnve S. Hospitalization for depression is associated with an increased risk for myocardial infarction not explained by lifestyle, lipids, coagulation, and inflammation: The SHEEP Study. Biol Psychiatry 2007; 62: 25–32.

17. Kemp AH, Quintana DS, Gray MA, Felmingham KL, Brown K, Gatt JM. Impact of depression and antidepressant treatment on heart rate variability: A review and meta-analysis. Biol Psychiatry 2010; 67 (11): 1067–1074.

18. Koschke M, Boettger MK, Schulz S, Berger S, Terhaar J, Voss A et al. Autonomy of autonomic dysfunction in major depression. Psychosom Med 2009; 71: 852–860.

19. Shen MJ, Zipes DP. Role of the autonomic nervous system in modulating cardiac arrhythmias. Circ Res 2014; 114 (6): 1004–1021.

20. Rubart M, Zipes DP. Mechanisms of sudden cardiac death. J Clin Invest 2005; 115: 2305–2315.

21. Piccirillo G, Moscucci F, D'Alessandro G, Pascucci M, Rossi P, Han S et al. Myocardial repolarization dispersion and autonomic nerve activity in a canine experimental acute myocardial infarction model. Heart Rhythm 2014; 11 (1): 110–118.

22. Wellens HJJ, Schwartz PJ, Lindemans FW, Buxton AE, Goldberger JJ, Hohnloser SH et al. Risk stratification for sudden cardiac death: current status and challenges for the future. Eur Heart J 2014; 35 (25): 1642–1651.

23. Kliks BR, Burgess MJ, Abildskov JA. Influence of sympathetic tone on ventricular fibrillation threshold during experimental coronary occlusion. Am J Cardiol. 1975; 36: 45–49.

24. Al-Zaiti SS, Fallavollita JA, Canty Jr JM, Carey MG. Electrocardiographic predictors of sudden and non-sudden cardiac death in patients with ischemic cardiomyopathy. Heart & Lung: Journal of Acute and Critical Care 2014; 43: 527–533.

25. Ünal S, Yayla Ç, Açar B, Ertem AG, Akboğa MK, Gökaslan S et al. Tp–e interval and tp–e/qt ratio in patients with human immunodeficiency virus. Journal of infection and public health 2018; 11: 35–38.

26. Malik M, Batchvarov VN. Measurement, interpretation and clinical potential of qt dispersion. J Am Coll Cardiol 2000; 36: 1749–1766.

27. Punske BB, Lux RL, MacLEOD RS, Fuller MS, Ershler PR, Dustman TJ et al. Mechanisms of the spatial distribution of qt intervals on the epicardial and body surfaces. J Cardiovasc Electrophysiol. 1999; 10: 1605–1618.

28. Surawicz B. Will qt dispersion play a role in clinical decision making? J Cardiovasc Electrophysiol. 1996; 7: 777–784.

29. Yilmaz M, Kayançiçek H, Gözel N, Kurtoğlu E, Seçen Ö, Öner P et al. Is there a relationship between epicardial fat tissue thickness and Tp-Te/QT ratio in healthy individuals? Arch Med Sci Atheroscler Dis 2020; 5 (5): e127–e39.

30. Brown RA, Schlegel TT. Diagnostic utility of the spatial versus individual planar QRS-T angles in cardiac disease detection. J Electrocardiol 2011; 44: 404–409.

31. Oehler A, Feldman T, Henrikson CA, Tereshchenko LG. QRS-T angle: a review, Ann Noninvasiv Electrocardiol 2014; 19: 534–542.

32. Borleff s CJ, Scherptong RW, Man SC, Van Welsenes GH, Bax JJ, van Erven L et al. Predicting ventricular arrhythmias in patients with ischemic heart disease: clinical application of the ECG derived QRS-T angle. Circ Arrhythm Electrophysiol 2009; 2: 548–554.

33. Kuyumcu MS, Özbay MB, Özen Y, Yayla Ç. Evaluation of frontal plane QRS-T angle in patients with slow coronary flow. Scandinavian Cardiovascular Journal 2020; 54 (1): 20–25.

34. Rangel MO, O'Neal WT, Soliman EZ. Usefulness of the electrocardiographic P-wave axis as a predictor of atrial fibrillation. Am J Cardiol 2016; 117: 100–104.

35. Kors JA, de Bruyne MC, Hoes AW, Herpen GV, Hofman A, van Bemmel JH et al. T-axis as an indicator of risk of cardiac events in elderly people. Lancet. 1998; 352 (9128): 601–605.

36. Yazici M, Demircan S, Durna K, Şahin M. The role of adrenergic activity in slow coronary flow and its relationship to TIMI frame count. Angiology 2007; 58: 393–400.

37. Won E, Kim YK. Stress, the Autonomic Nervous System, and the Immune-kynurenine Pathway in the Etiology of Depression. Curr Neuropharmacol 2016; 14 (7): 665–673.

38. Qirjazi E, McArthur E, Nash DM, Dixon SN, Weir MA, Vasudev A et al. Risk of Ventricular Arrhythmia with Citalopram and Escitalopram: A Population-Based Study. PLoS One 2016; 11 (8): e0160768.

Received September 15, 2022.
Accepted November 14, 2022.