Association between ventricular premature contraction burden and ventricular repolarization duration

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SUMMARY

OBJECTIVE: Premature ventricular contraction is generally known as benign in the absence of structural heart disease; however, premature ventricular contraction-induced left ventricular systolic dysfunction or ventricular arrhythmias are defined in some cases. Ventricular repolarization duration differs between myocardial cells, which causes myocardial electrical heterogeneity and is thought to be responsible for ventricular arrhythmias. In our study, we aimed to evaluate the association of ventricular repolarization parameters including Tp-Te interval, Tp-Te/QT ratio, and QRS-T angle with premature ventricular contraction frequency in patients with premature ventricular contraction burden.

METHODS: A total of 80 subjects who were admitted to our cardiology department and underwent 24-h electrocardiography Holter monitoring were included. Patients were divided into two groups: group 1 is defined as premature ventricular contraction burden that had frequent premature ventricular contraction ≥1% in 24-h Holter monitoring, and group 2 is defined as rare premature ventricular contraction <1% in 24-h Holter monitoring.

RESULTS: Tp-Te interval and Tp-Te/QT ratio are statistically significantly prolonged in the premature ventricular contraction burden group than in the control group (85.3 ± 13.9 vs. 65.7 ± 11.9, p<0.001; 0.19 ± 0.03 vs. 0.15 ± 0.02, p<0.001, respectively). QRS-T angle was statistically significantly abnormal in the premature ventricular contraction burden group (p=0.024).

CONCLUSION: Increased Tp-Te interval and widened QRS-T angle are associated with ventricular arrhythmias and might be used for the prediction of premature ventricular contraction burden in patients with premature ventricular contraction in electrocardiography in the absence of 24-h Holter monitoring.

KEYWORDS: Arrhythmias, cardiac. Ventricular premature complexes. Tachycardia, ventricular.

INTRODUCTION

Premature ventricular contraction (PVC) can be detected in structurally normal hearts with a prevalence of 1–4% in the general population[1]. A previous study found the prevalence of PVC as 40–75% in healthy populations by 24–48 h electrocardiography (ECG) Holter monitoring[2]. PVC is generally known as benign in the absence of structural heart disease; however, PVC induces deterioration of the left ventricular systolic functions in some cases. Also, frequent PVC might worsen the existing cardiomyopathies. There is no consensus in the literature about the cutoff amount of PVC, which has a high risk for cardiomyopathy or ventricular arrhythmias[3,4].

Myocardial cells are divided into three groups: epicardium, midmyocardium, and endocardium cells, which have different durations of action potentials. The action potential of the epicardium is shorter than the endocardium. The midmyocardium has the longest action potential[5]. As a result of these different action potential durations, heterogeneity of electrical conduction occurs in the myocardium. Transmural dispersion of heterogeneous electrical activity is shown as a responsible mechanism of arrhythmogenesis[6]. T_{peak} to T_{end} (Tp-Te) interval is the indicator of transmural dispersion of repolarization. Previous studies showed that a prolonged Tp-Te interval is associated with a high risk of ventricular tachycardia (VT)[7]. A previous study evaluated the Tp-Te interval during ventricular pacing in an electrophysiological study and showed that the Tp-Te interval is prolonged by ventricular premature beats[8]. In recent years, the Tp-Te/QT ratio has been used as a more sensitive marker than the Tp-Te interval for the assessment of transmural dispersion of repolarization[9]. The Tp-Te/QT ratio is superior to the Tp-Te interval due to its independence from heart rate[10]. Previous studies showed that increased Tp-Te/QT ratio is associated with an increased risk of VT in Brugada syndrome, short QT, and long syndromes[11,12].

In recent years, the QRS-T angle has gained importance for the prediction of cardiac poor prognosis. QRS-T angle is an ECG parameter and is defined as the difference between ventricular depolarization and repolarization. Previous studies showed that widened QRS-T angle increased arrhythmia-associated mortality in patients with ischemic cardiomyopathy[13].

In our study, we aimed to evaluate the association of ECG parameters including Tp-Te interval, corrected QT (QTc), Tp-Te/QT ratio, and QRS-T angle with PVC frequency in patients who underwent 24-h ECG Holter monitoring.

METHODS

A total of 80 subjects who were admitted to our cardiology department with palpitation, syncope, dyspnea, or any other cardiac complaint and underwent 24-h ECG Holter monitoring between January 2018 and October 2019 were included. A 24-h ECG Holter monitoring was performed on all patients, irrespective of having PVC on baseline ECG, and analyzed by the same operator. Patients were divided into two groups: group 1 was defined as PVC burden, which had frequent PVC≥1% in 24-h Holter monitoring, and group 2 was defined as rare PVC<1% in 24-h Holter monitoring. Patients with low ejection fraction, structural heart disease, moderate-to-severe degree heart valve disease, coronary artery disease with the sign of ischemia, thyroid disorders, and anemia were excluded from the study. The patient's medical history and medications were questioned.

A 12-lead ECG was performed at a speed of 25 mm/s. V5 derivation was chosen for the analysis of Tp-Te, QT, and Tp-Te/QT measurements in all patients. Tp-Te ratio was calculated from the baseline ECG as the interval of the peak to the end of the T wave. QT interval was defined as the duration from the beginning of the QRS complex to the end of the T wave. The QTc interval was calculated according to the patient's heart rate with Bazett's formula. Tp-Te interval is divided by the QTc interval for the measurement of the Tp-Te/QT ratio. The frontal QRS-T angle is calculated as the difference between the QRS axis and the T-wave axis. According to previous studies, we chose the normal range of QRS-T angle as -39 to 71o[14]. Patients were divided into two groups according to QRS-T angle: the normal group (QRS-T angle is between -39 and 71o) and the abnormal group (QRS-T angle is out of this range). The single operator analyzed the ECG parameters.

A 2D echocardiography was performed on all patients for the detection of any heart valve disease or structural heart disease. The ejection fraction (EF) was measured by the modified Simpson method.

The study was approved by the local Ethical Committee.

Statistical analysis

Statistical analysis was performed using the SPSS (version 20.0, SPSS Inc., Chicago, IL, USA) software package. Continuous variables were expressed as the mean±standard deviation (mean±SD), and categorical variables were expressed as a percentage (%). The Kolmogorov-Smirnov test was used to evaluate the distribution of variables. The Student's t-test was used to evaluate continuous variables showing normal distribution, and the Mann-Whitney U test was used to evaluate variables that did not show normal distribution. For categorical variables, the chi-square test was used. Multivariable logistic regression using the enter method was used to assess independent predictors for regression. A p<0.05 was considered statistically significant.

RESULTS

A total of 37 patients had PVC burden (PVC≥1%) and 43 patients had rare PVC<1% in 24-h ECG Holter monitoring. The mean age of the study population was 49.4±14.6, and 50% of them were male. In total, 20% of them had a history of coronary artery disease, and 41.3% of them were taking antiarrhythmic treatment (81.8% of them are beta-blockers). Baseline characteristics of the study population are shown in Table 1.

Demographic features regarding diabetes mellitus (DM), hypertension (HT), smoking status, coronary artery disease, and EF were similar between the two groups (Table 2). Patients with PVC burden were significantly older than the other group (53±17.5 vs. 46.2±11, p=0.046). Tp-Te interval, Tp-Te/QT, and Tp-Te/QTc interval were statistically significantly prolonged in patients with frequent PVC than control group (86.6±13.3 vs. 65.4±12.8, p<0.001; 0.22±0.04 vs. 0.15±0.03, p<0.001; 0.2±0.03 vs. 0.15±0.03, p<0.001, respectively). QT and QTc intervals were similar between the two groups (387±29.3 vs. 375.4±32.8, p=0.098; 428.5±29.2 vs. 429.1±23.5, p=0.928,

Table 1. Demographic features.

	Mean±SD
Age	49.4±14.6
Male (%)	40 (50)
DM (%)	7 (8.8)
HT (%)	18 (22.5)
Smoking (%)	21 (26.3)
CAD (%)	16 (20)
Antiarrhythmic medication	33 (41.3)
PVC>1%	37 (46.3)
Nonsustained VT	4 (5)
EF (%)	60.3±2.3
Number/percentage of PVC	5268.2±9384.7/4.9±8.6

DM: diabetes mellitus; HT: hypertension; CAD: coronary artery disease; PVC: premature ventricular contraction; VT: ventricular tachycardia; EF: ejection fraction.

respectively). QRS-T angle was statistically significantly wider in the group with PVC burden (p=0.024). A comparison of ECG parameters between the two groups is shown in Table 2.

Pearson's correlation analysis showed a significant correlation between Tp-Te and PVC frequency. Also, Tp-Te/QT and Tp-Te/QTc ratios were significantly correlated with PVC frequency. The correlation of ECG parameters with PVC frequency is shown in Table 3. Multivariate analysis of ECG parameters showed that Tp-Te interval and QRS-T angle are the independent predictors of an excessive amount of PVC in 24-h ECG Holter monitoring (p<0.001 and p=0.04, respectively).

Table 2. Comparison of the basic demographic features and electrocardiography parameters.

Parameters	Group 1 (PVC>1%) (n=37)	Group 2 (PVC≤1%) (n=43)	p-value
Age (year)	53±17.5	46.2±11	**0.046**
Male, n (%)	22 (59.5)	18 (41.9)	0.178
HT (%)	9 (24.3)	9 (20.9)	0.792
DM (%)	3 (8.1)	4 (9.3)	1.0
Smoking (%)	10 (27)	11 (25.6)	1.0
CAD (%)	8 (21.6)	8 (18.6)	0.785
Nonsustained VT	3 (8.1)	1 (2.3)	0.253
EF (%)	60.4±2	60.2±2.6	0.673
HR (beat/min)	75.5±15.3	79.9±15.8	0.213
Tp-Te interval	86.6±13.3	65.4±12.8	**<0.001**
QT interval	387±29.3	375.4±32.8	0.098
QTc interval	428.5±29.2	429.1±23.5	0.928
Tp-Te/QT	0.22±0.04	0.15±0.03	**<0.001**
Tp-Te/QTc	0.2±0.03	0.15±0.03	**<0.001**
Abnormal QRS-T angle (%)	11 (29.7)	4 (9.3)	**0.024**

PVC: premature ventricular contraction; HT: hypertension; DM: diabetes mellitus; CAD: coronary artery disease; VT: ventricular tachycardia; EF: ejection fraction; HR: heart rate. Bold value indicates the significance of p<0.05.

Table 3. Correlation of electrocardiography parameters with premature ventricular contraction frequency.

	PVC (n)		PVC (%)	
	r	P	R	p
Heart beat/24 h	0.070	0.535	-0.008	0.945
Tp-Te interval	**0.372**	**0.001**	**0.384**	**<0.001**
QT interval	0.77	0.495	0.108	0.341
QTc interval	0.163	0.148	0.158	0.161
Tp-Te/QT ratio	**0.323**	**0.003**	**0.323**	**0.003**
Tp-Te/QTc ratio	**0.311**	**0.005**	**0.326**	**0.003**

PVC: premature ventricular contraction. Bold value indicates the significance of p<0.05.

DISCUSSION

The main finding of our study is the increased Tp-Te interval, Tp-Te/QT, Tp-Te/QTc ratio, and abnormal QRS-T angle in patients with frequent PVC in 24-h ECG Holter monitoring. As compared to QTc interval and heart rate, there was no statistically significant difference between the groups. The Tp-Te interval and abnormal QRS-T angle are the independent predictors of an excessive amount of PVC in 24-h ECG Holter monitoring.

The myocardium has three types of cells: epicardium cells, midmyocardium cells, and endocardium cells, which have different action potential durations[15]. Midmyocardium cells have the longest action potential duration. Different action potential durations are thought to be responsible for ventricular arrhythmias. QT, QTc, Tp-Te interval, and Tp-Te/QT ratio are the indicators of transmural dispersion of ventricular repolarisation[9]. A previous study showed that ventricular extra stimuli increase QTc interval, which may indicate the increased action potential duration in midmyocardium cells during the electrophysiological study[8]. It is shown that PVC causes increased transmural dispersion of repolarization as a result of increased midmyocardium action potential duration in patients with long QT syndrome[16]. In our study, the QTc interval was not different between the PVC burden and the rare PVC group. Several studies showed that an increased Tp-Te interval and Tp-Te/QTc ratio are linked with ventricular arrhythmias in Brugada syndrome, long QT syndrome, and hypertrophic cardiomyopathy[11,12]. Nugraheni et al.[17] showed that the Tp-Te/QT ratio is associated with an increased risk of VT in patients with idiopathic outflow tract PVC. Comparably with previous studies, we found an association between Tp-Te, Tp-Te/QT, and PVC burden. The relationship between ventricular repolarization parameters and sudden cardiac death has been known for many years[18]. However, there are controversial findings about the association between coronary artery severity and ventricular repolarization parameters. Bektaş et al.[19] evaluated 172 participants with coronary artery disease and found that Tp-Te and Tp-Te/QTc were higher in the group that had high Syntax score levels. On the contrary, Cosgun et al.[20] found that Tp-Te and Tp-Te/QTc are similar between high and low Syntax score groups.

QRS-T angle is defined as the angle between the QRS axis and T-wave axis[13,14]. Widened QRS-T angle predicts abnormal depolarization and repolarization, in situations with abnormal electrical activation including ischemia, bundle branch block, and left ventricular hypertrophy[21]. There is a limitation in the use of spatial QRS-T angle in clinical practice as a result of difficulties in the calculation. Frontal QRS-T angle is more

widely used than spatial QRS-T angle because of its availability in most ECG devices, so it is easily evaluated by most clinicians[22]. In our study, we defined an abnormal QRS-T angle as being out of the range of -39 to 71º, in the light of findings in previous studies[14]. We found that an abnormally widened QRS-T angle is significantly associated with PVC burden in 24-h ECG Holter monitoring.

Most of the PVCs are considered benign and not associated with ventricular arrhythmias in the absence of structural heart disease[23]. PVC frequency is important to predict ventricular arrhythmias. Multiple Risk Factor Intervention Trial showed that more than one PVC in 2-min ECG is associated with increased sudden cardiac death 7.5-year follow-up[24]. Although asymptomatic PVC is known as a benign arrhythmia, it may induce premature ventricular complex-induced cardiomyopathy. As asymptomatic patients are unaware of their conditions and arrhythmias, they have a higher risk of prolonged exposure to frequent PVC, which might be progressed to cardiomyopathy[25]. Ventricular repolarization parameters can be used to predict the PVC burden for high-risk patients. However, patients with detected PVC in ECG should be advised to undergo 24-h Holter monitoring for the assessment of PVC frequency, morphology, and distribution pattern in a day.

CONCLUSION

Increased Tp-Te interval and abnormal QRS-T angle might be used for the prediction of high PVC burden risk from baseline ECG in patients with PVC in ECG in the absence of 24-h Holter monitoring.

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AUTHORS' CONTRIBUTIONS

NS: Conceptualization, Data curation, Formal Analysis, Supervision, Validation, Writing – review & editing. **BY:** Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Visualization, Writing – original draft.

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