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ST-segment elevation and the Tpeak-Tend/QT ratio predict the occurrence of malignant arrhythmia events in patients with vasospastic angina

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ABSTRACT

Background: ST-segment elevation (STE) and an increased Tpeak-Tend interval (Tp-e) have prognostic value for malignant arrhythmia events (MAEs) in patients with ST-segment elevation myocardial infarction (STEMI) and Brugada syndrome. Whether STE could predict MAEs and has an electrophysiological relationship with Tp-e in electrocardiogram (ECG) of vasospastic angina (VA) patients needs to be elucidated.

Methods: Sixty-five patients with VA and 23 patients with VA complicated by MAEs were enrolled. The relationship of ECG parameters and MAEs (defined as ventricular tachycardia/ventricular fibrillation (VT/VF), syncope, and aborted sudden death) was analyzed by *t*-test, regression and receiver operating characteristic (ROC) curve analyses.

Results: Patients with MAEs showed greater STE ($P < 0.001$) and corrected QT dispersion (cQTd) ($P = 0.021$), a longer corrected Tp-e interval (cTp-e) ($P < 0.001$), and a larger Tp-e/QT ratio ($P < 0.001$) than those in non-MAE groups. Univariate analysis revealed that cQTd (odds ratio (OR) = 1.065; $P = 0.020$), cTp-e (OR = 1.159; $P = 0.001$), Tp-e/QT (OR = 1.344, $P = 0.002$), and STE (OR = 5.655, $P < 0.001$) were significantly associated with MAEs. In the multivariate analysis, Tp-e/QT and STE remained predictors of MAEs. ROC curve analysis showed that the areas under curve (AUCs) for Tp-e/QT (AUC = 0.944) and STE (AUC = 0.974) were not significantly different ($P > 0.05$), but both were significantly different than AUCs for cQTd (AUC = 0.724) and cTp-e (AUC = 0.841) (all $P < 0.05$). STE was well fitted with the Tp-e/QT ratio in a multivariable linear regression model.

Conclusions: STE and increased Tp-e/QT ratio had related electrophysiological properties and were independent prognostic indicators of MAEs in patients with VA.

Introduction

A considerable proportion of patients with vasospastic angina (VA) show characteristic ST-segment elevation (STE) on electrocardiograms (ECGs) and suffer from malignant arrhythmia events (MAEs), such as sudden cardiac death (SCD), syncope and other life-threatening ventricular arrhythmias, during spontaneous coronary spasm. MAEs were thought to be caused by electrophysiological abnormalities of ventricular repolarization [1,2]. In cellular models, the extent of STE represents a potential gradient for phase-2 reentry, and phase-2 reentry is the primary mechanism underlying arrhythmogenesis in Brugada syndrome (Brs) and ST-segment elevation myocardial infarction (STEMI) patients [3]. However, there have not been reports on whether STE predicts the occurrence of MAEs. STE -related diseases, such as Brs and STEMI, are characterized by increased Tpeak-Tend (Tp-e) intervals (defined as the interval from the peak to the end of the T wave) from ECG leads [4–6]. The mechanism for the genesis and utility of the Tp-e interval remains controversial. However, an increased Tp-e interval, accompanied by STE in precordial lead ECGs, was considered a risk factor for malignant ventricular arrhythmia in patients with Brs [4–6]. Therefore, we hypothesized that STE and prolonged Tp-e interval observed in ECGs were mechanistically related, as in Brs, and had similar prognostic value in patients with VA. Therefore, this study aimed to elucidate the electrophysiological relationship of STE and the Tp-e interval and their prognostic values for MAEs in VA patients.

Methods

Study population

A consecutive series of 88 patients suffering from episodic ischemic STE in People's Hospital of Zhengzhou University from 2010 to 2015

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were included in the present study. Sixty-five patients with VA (No-MAE group, 48 men and 17 women) and 23 patients with VA complicated by MAEs (MAE group, 16 men and 7 women) were enrolled in this study. The Judkins technique was used to perform coronary angiography. None of the patients revealed any significant coronary artery stenosis (defined as <50% by coronary angiography). All patients exhibited myocardial ischemic STE associated with spontaneous episodes of chest pain on a 12-lead ECG. Twenty patients in the MAE group had a definite history of MAEs (defined as ventricular tachycardia/ventricular fibrillation (VT/VF), syncope, and aborted sudden death) induced by STE following coronary spasm.

Both groups had normal results on physical examination and no history of cardiac disease, chronic obstructive lung disease, renal disease, or endocrine disorders. None of the patients had abnormalities in resting 12-lead ECGs, 2-dimensional echocardiograms, or Doppler echocardiograms. No patient was receiving antiarrhythmic agents or other types of therapy that could affect the ECG parameters.

Measurement of ECG parameters

The ECGs were recorded with a standard digital recorder with 12 simultaneous leads at a paper speed of 25 mm/s. STE and MAEs were detected and recorded by ECG when symptom onset and MAEs were correlated with STE. After onset, ECG parameters were recorded and measured when the elevated ST-segment and reversed T waves were back to normal.

The single ECG lead showing the maximum STE was considered. In anterior and non-anterior leads showing STE, the greatest STE from a single lead was measured from base to point 40 ms after the J point. The QT interval was measured from the onset of the QRS complex to the end of the T-wave, defined as a return to the T-P baseline. If U waves were present, the QT interval was measured to the nadir of the curve between the T and U waves. Three consecutive cycles were analyzed for each lead. In case of complete fusion of the T and U waves, no determination of the T wave end was attempted, and the corresponding lead was excluded from the measurement. Data from leads showing a T-wave amplitude <1.5 mm were excluded from the analysis. The QTc was obtained using Bazett's Formula, and the maximum values from all leads were applied in the analysis. The QT dispersion was defined as the difference between the maximum and minimum QT interval from the 12 leads [2]. The Tp-e interval was measured from each lead and obtained from the difference between the QT interval and QTpeak interval, and the QTpeak interval was measured from the beginning of the QRS complex to the peak of the T-wave from leads showing STE and those not showing STE. In the case of negative or biphasic T waves, QTpeak was measured to the nadir of the T-wave. If STE and T waves on ECGs were fused into a monophasic curve, the case was excluded from the study. The corrected Tp-e interval (Tp-ec) was obtained using Bazett's Formula. The reported value for the Tp-e interval was the maximum obtained by two observers for all leads. The measurement of each parameter was obtained by averaging three consecutive beats. Two independent experts obtained the measurements, and in the case of a difference of 20 ms in each measurement, the third expert was recruited. The interobserver Pearson correlation coefficients for QTc dispersion, Tp-ec and Tp-e/QT were 0.953, 0.975 and 0.991, respectively.

Statistics

Continuous variables are expressed as the mean ± SD and, if appropriate, were compared using a dependent-samples Student's *t*-test. Categorical variables are expressed as numbers and percentages and, if appropriate, were compared with the Chi-square analysis. To examine the prognostic value of ECG parameters and determine cut-off values, analyses of receiver operating characteristic (ROC) curves were performed according to standard procedures. Multivariate analysis was performed using a binary logistic regression model including related factors that were significantly associated with MAEs on univariate analysis. STE was associated with Tp-e parameters using multiple linear regression. A P value <0.05 was deemed statistically significant. Statistical analysis was performed using SPSS 20.0.0 (IBM Inc., Armonk, New York, USA). The area under the ROC curve (AUC) comparison was performed by MedCalc 15.2.2 (MedCalc Software, Ostend, Belgium).

Results

Baseline clinical characteristics of study patients with and without MAE

The clinical characteristics and risk factors for coronary artery disease of the patients included in the study are presented in Table 1. Sixty-five patients were classified as having VA without MAEs (non-MAE group: 48 men and 17 women; mean age 53 years, range 35 to 71), and 23 were classified as having VA with MAEs (MAE group: 16 men and 7 women; mean age 55 years, range 33 to 77). There were no differences in age, sex, hypertension, smoking, diabetes or vasospastic culprit coronary lesions between the two groups (all P > 0.05).

Comparison of electrocardiographic parameters between patients with and without MAE

At the onset of coronary spasms (onset phase in Table 2), the ST-segment showed a greater elevation in the MAE group than in the non-MAE group (0.72 ± 0.23 VS 0.41 ± 0.10; P < 0.001). There were no differences in QTc intervals (P = 0.081) between the MAE and non-MAE groups. Patients in the MAE group showed greater QTc dispersion (49.55 ± 15.4 vs. 39.98 ± 7.4; P = 0.017), a longer Tp-ec interval (162.07 ± 24.8 vs. 127.69 ± 12.9; P < 0.001), and a higher Tp-e/QT ratio (0.355 ± 0.05 vs. 0.297 ± 0.03; P < 0.001) than those in the non-MAE group.

Univariate and multivariate regression model for predicting MAE

A multiple collinearity diagnosis was implemented for STE, QT dispersion, the Tp-ec interval and the Tp-e/QT ratio. The maximum value of the variance inflation factor (VIF) was 3.1 and that of the condition index was 32.9, which indicated the existence of certain collinearity among these ECG parameters. Then, the ECG parameters were tested in a univariate analysis, and many parameters were significantly associated with MAEs, as shown in Table 3. Because related risk factors and physiological indices were not significantly different, only QT dispersion, the Tp-ec interval, the Tp-e/QT ratio and STE were included in the model. In detail, QTc dispersion (odds ratio (OR) = 1.065; 95% confidence intervals (CI) 1.025–1.107; P = 0.020), Tp-ec (OR = 1.158; 95% CI 1.068–1.254; P = 0.001), Tp-e/QT (OR = 1.344; 95% CI 1.127–1.618; P = 0.002), and STE (OR = 5.655; 95% CI 1.830–17.539; P < 0.004) were significantly associated with MAEs. A likelihood ratio multivariable binary logistic regression analysis was then performed. Only STE remained a predictor of MAEs in this model, and the OR and CI were

Table 1
Baseline clinical characteristics of study patients with and without MAE.

	Non-MAE (65)	MAEs (23)	P value
Age (years)	52.8 ± 11.5	54.8 ± 10.6	0.230
Sex (male/female)	48/17	16/7	0.692
Hypertension	23	9	0.748
Smoking	29	13	0.326
Diabetes	8	3	0.927
Site of spasm			
LAD	27	8	
LCX	6	2	0.828
RCA	32	13	

Data are presented as the mean ± SD or number of cases unless otherwise indicated.
LAD = left anterior descending artery; MAE = malignant arrhythmia events; RCA = right coronary artery; LCX = left circumflex artery.

Table 2
Comparison of electrocardiographic parameters between patients with and without MAEs.

	Non-MAE group	MAE group	P value
STE (mV) -onset	0.41 ± 0.10	0.72 ± 0.23	<0.001
cQT Bazett (ms) -onset	438.60 ± 33.3	454.10 ± 56.0	0.061
cQTd (ms) -onset	38.35 ± 8.0	45.83 ± 18.9	0.021
cTp-e (ms) -onset	128.07 ± 11.9	152.70 ± 27.7	<0.001
Tp-e/QT -onset	0.300 ± 0.03	0.356 ± 0.05	<0.001

MAE = malignant arrhythmia events; cQT = corrected QT interval; cTp-e = corrected Tpeak-Tend interval; Tp-e/QT = ratio of Tpeak-Tend interval to QT interval.

consistent with those in the univariate analysis. After STE was removed from the analysis, only the Tp-e/QT ratio remained a significant predictor in the model among the three parameters. The elimination of the Tp-e/QT ratio and STE resulted in only the Tp-ec interval being significant in the logistic regression model including the Tp-ec interval and QTc dispersion. Both the OR and CI were constant in the models. (Table 3).

ROC curve and cut-off value of ECG parameter for predicting MAE

ROC curve analysis was performed to assess the sensitivity, specificity and best cut-off values for different ECG parameters for the prediction of MAEs (Table 4). The AUCs were 0.724 (95% CI 0.576–0.873) for QTc dispersion, 0.841 (95% CI 0.720–0.963) for Tp-ec, 0.944 (95% CI 0.823–0.972) for Tp-e/QT and 0.974 (95% CI 0.830–0.987) for STE. Comparisons of AUCs with a Z test using MedCalc showed that the AUCs for STE and Tp-e/QT were significantly different from those for QTc dispersion and Tp-ec, respectively (all $P < 0.05$). The AUC for STE was not significantly different from that for Tp-e/QT (all $P > 0.05$). The cut-off value of 44.2 ms for QTc dispersion showed the best combined sensitivity and specificity (68.0% and 37%, respectively). The best cut-off value, with the best combination of sensitivity and specificity, was found for Tp-ec ≥ 142 ms (84.0% and 84.2%), Tp-e/QT ≥ 0.317 ms (84.0% and 89.5%) and STE ≥ 0.45 mV (93.1%, 71.4%), respectively. The results of the comparison between the AUCs for ECG parameters indicated that both STE and Tp-e/QT were independent predictors of VA patients likely to experience MAEs. Correlation analyses showed that the correlation coefficient for STE and Tp-e/QT was 0.763 (95% CI, 0.576–0.862, $P < 0.001$) and that for STE and Tp-ec was 0.658 (95% CI, 0.527–0.754, $P < 0.001$). Multiple linear regression was performed with STE as the dependent variable and other ECG parameters as the independent variables. The best regression equation was [STE] = −3.194 + 26.202[Tp-e/QT], which meant only Tp-e/QT was included in the final equation.

Discussion

This study showed that ECG parameters such as STE, cQTd, the cTp-e interval and the Tp-e/QT ratio could predict the occurrence of MAEs in VA patients. This was the first investigation of the prognostic value of STE in relation to MAEs. Furthermore, the results of the regression analysis and ROC analysis of ECG parameters indicated that STE and the Tp-e/QT ratio were independent predictors of VA patients likely to develop MAEs, and an increased Tp-e/QT ratio could predict the extent of STE, which meant there was a significant correlation between these parameters.

In Brs, the resultant transmural voltage gradients induced by the depression or loss of the action potential (AP) dome occurring in the ventricular epicardium causes an STE, which predisposed the ventricle to the development of phase 2 reentrant extrasystoles, which can precipitate VT/VF [7]. Farsighted investigation have showed that arrhythmias occurred frequently during VA and correlated well with the degree of ST-segment elevation and change of R wave, but the possible mechanisms was not involved [8,9]. During acute ischemia, some studies using cardiac wedge preparations indicated two distinctly different mechanisms, 1) loss of the epicardial AP dome and 2) a markedly delayed transmural conduction, underlie the transmural dispersion of repolarization (TDR), which leads to STE and cause a potential gradient of phase 2 reentry. [10,11] The extent of STE could represent the potential gradients of phase 2 reentry, which manifest as a closely coupled R-on-T extrasystole on the ECG. The extrasystole, in turn, is capable of initiating MAEs, such as VT/VF and sudden death. Thus, in this study, STE was a simple and intuitive parameter for predicting MAEs in VA patients. Meanwhile, VA was a good model for investigating ischemic effects on ECG parameters because, in addition to transient ischemia, there are no chronic or secular ischemic factors related to the effect on ECG parameters if a spasmodic coronary artery has no significant atherosclerotic stenosis. Therefore, in this study, we conclude that greater STE predicts a higher incidence of MAEs in VA patients, which coincides with the conclusion in previous investigations [8,9].

The $T_{p\text{-}e}$ interval was a useful risk stratification tool in different diseases, such as Brugada syndrome, hypertension, heart failure and

Table 3
Univariate and multivariate regression model for predicting MAEs.

	OR for MAEs	P value	OR for MAEs	P value
	Univariate analysis		Multivariate analysis	
cQTd (ms)	1.065 (95% CI, 1.025–1.107)	0.020		
cTp-e (ms)	1.159 (95% CI, 1.068–1.254)	0.001	1.159 (95% CI, 1.068–1.254)[a]	0.001
Tp-e/QT	1.344 (95% CI, 1.127–1.618)	0.002	1.344 (95% CI, 1.127–1.618)[b]	0.002
STE (mV)	5.655 (95% CI, 1.830–17.539)	<0.001	5.665 (95% CI, 1.830–17.539)	<0.001

MAE = malignant arrhythmia events; OR = odds ratio; cQT = corrected QT interval; cTp-e = corrected Tpeak-Tend interval; Tp-e/QT = ratio of Tpeak-Tend interval to QT interval.
[a] Elimination of Tp-e/QT ratio and STE;
[b] Elimination of STE.

Table 4
ROC curve and cut-off values for electrocardiographic parameters for predicting MAEs.

	AUC	P value	Cut-off value (sensitivity, specificity)
cQTd (ms)	0.724 (95% CI, 0.576–0.873)[a,b]	0.012	44.2 (68.0%, 37%)
cTp-e(ms)	0.841 (95% CI, 0.720–0.963)[a,b]	<0.001	142 ms (84.0%, 84.2%)
Tp-e/QT	0.944 (95% CI, 0.823–0.972)	<0.001	0.317 (84.0%, 89.5%)
STE (mV)	0.974 (95% CI, 0.830–0.987)	<0.001	0.45 mV (93.1%, 71.4%)

AUC = Area under ROC curve; MAE = malignant arrhythmia events; cQT = corrected QT interval; ROC = receiver operating characteristic; cTp-e = corrected Tpeak-Tend interval; Tp-e/QT = ratio of Tpeak-Tend interval to QT interval.
[a] vs STE $P < 0.01$.
[b] vs Tp-e/QT $P < 0.01$.

ischemic heart disease. The OR value was similar between our studies and the meta-analysis in ischemic heart disease [12]. But Tp-e/QT seemed to represent a more sensitive index of arrhythmogenesis as it provided an estimate of the repolarization dispersion relative to the total duration of repolarization, avoiding possible confounding effects of heart rate variability and interindividual variation of QT interval, so Tp-e/QT was the strongest parameter associated with MAEs among QT dispersion, Tp-e interval and the Tp-e/QT ratio [13]. Although the mechanism for the genesis and the utility of the Tp-e interval remains controversial, our previous study speculated that TDR may play a significant role in the characteristics of the Tp-e interval in pathophysiological conditions, including VA [13]. An increased Tp-e interval caused by coronary spasms provides a mechanistic cause for the prolongation of TDR and was correlated with MAEs in our study. Similar to the results for VA patients, in Brs patients, the Tp-e interval is significantly increased, leading to an increase in the Tp-e/QT ratio from right precordial leads and a coved configuration of the STE, and this was considered a risk factor for arrhythmic events [4,14].

Transmural voltage gradients cause a STE, reflecting a partial potential gradient of phase 2 reentry, while the Tp-e interval represents an index of TDR that can be used in predicting arrhythmogenesis. STE was related to the Tp-e interval. However, no study has explained this relationship. What is the relationship between the Tp-e interval and STE in acute ischemia? We describe this relationship with the following scheme (Fig. 1, modified from Ref. [15], with permission of Copyright © 2014 Elsevier Inc.) [15]. Endocardial (Endo) and epicardial (Epi) transmembrane APs and ECGs were simultaneously recorded from top to bottom. Fig. 1A illustrates that an apparent STE (the difference of Endo AP plateau [or R wave in this paper] and delayed Epi AP plateau) and an inverted T wave were induced by ischemia-induced transmural conduction slowing of Epi conduction. Simultaneous ECG recordings showed that the Tp-e interval (the difference between the end of the Endo AP and the end of delayed Epi AP) was increased significantly in ischemic conditions compared with that in control conditions after 25 min of ischemia in ventricular wedges. If STE was considered a marked prolongation of the R wave on the ECG because of delayed Epi transmural conduction, the extent of STE can determined by the decreased extent and amplitude of delayed conduction, which also determine the duration of the Tp-e interval. Fig. 1B shows that an all-or-none repolarization at the end of phase 1 of the AP was induced by the ischemia-induced loss of the Epi AP dome after 12 min of ischemia. This produced the voltage gradients at the AP plateau level between the Endo and Epi regions and then induced non-isoelectric STE, while the potential difference in the isoelectric line between Epi and Endo APs determined the TDR or the duration of Tp-e interval. Therefore, ischemia induced the potential gradients of the transmural phase 2 plateau of the AP, which induced the elevation of the ECG ST-segment and the difference in the augmentation of AP duration; the latter induced the increased Tp-e interval. If the Epi AP disappeared, the ECG showed a monophasic curve, similar to the shape of an Endo AP. Meanwhile, if R wave was the difference of Epi and Endo AP of depolarization phase 0, the amplitude of R wave increased during VA crises, because of delayed conduction of Epi AP or decreased amplitude of depolarization phase 0 of Epi AP in above cellular model. These mechanisms agreed with the results for the relationship among STE, R wave change and the investigated ECG parameters in this and previous investigation [8,9].

In our previous study, we hypothesized that Tp-e dispersion reflected the global dispersion of repolarization (GDR) and that the Tp-e interval in ischemic-related leads mainly reflected TDR in the acute ischemic state. The relationship of STE and Tp-e explained by the above scheme increases the possibility that the Tp-e interval reflects TDR in the ischemic state. Even if the results of these studies only

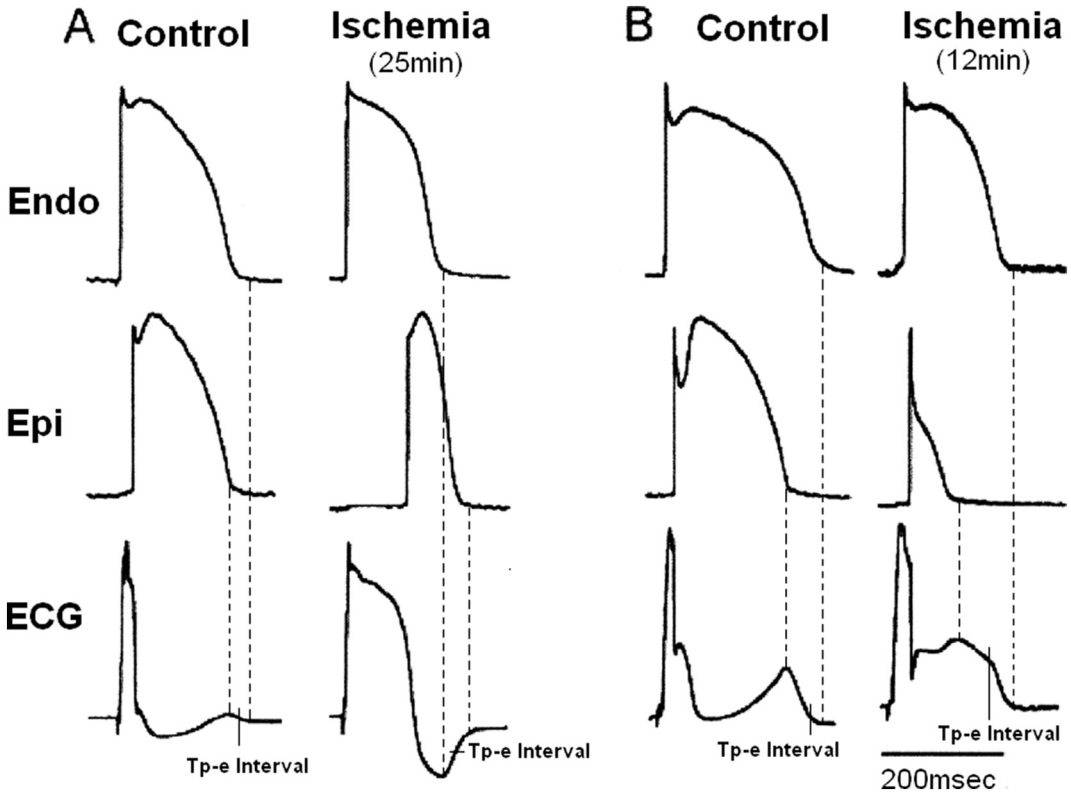

Fig. 1. Scheme of electrophysiological effects of ischemia in the ventricular wedge model. Results were from 2 different preparations. (A) Recordings obtained under control conditions and after 25 min of ischemia. Tp-e was increased significantly in the ischemic condition compared with control. (B) Recordings obtained under control conditions and after 12 min of ischemia. Tp-e was also increased significantly in the ischemic condition compared with control. BCL = 800 ms (modified from Ref. [15], with permission).

originated from clinical data investigation, they provided new perspectives for the genesis of STE and increased Tp-e intervals in pathophysiological conditions and offers important tools for predicting MAEs.

Some studies have reported poor inter- and intra-observer reproducibility of manual measurements of the ECG parameters[10]. This shortfall applies to the measurement of the ST-segment and Tp-e in patients with VA. In addition, there has been some confusion as to how to measure these parameters with different configurations of the T wave, especially for STE, to assess T wave markers. Recent experimental studies have clarified this, and we applied these methods in our measurements [16]. However, we eliminated some cases where it was difficult to definitively identify the peak of the T wave, such as for monophasic-curve T waves, which are more suitable for predicting MAEs than T waves with other shapes. Another limitation was that clinical results were deduced on the basis of cellular electrophysiological mechanisms in this study. We should be cautious of results extrapolated only according to theory and inference with regard to the conclusions of this study, but inferences for the functional meaning and utility of the Tp-e interval were constructive and beneficial in assessing pathophysiologic conditions. A larger series and further investigations, both in vitro and in vivo, with electrophysiological recordings of VA could help confirm these results.

Conclusions

Both STE and Tp-e were predictors of MAEs, and an increased Tp-e interval could predict the extent of STE in patients with VA. STE and increased Tp-e had related electrophysiological properties in representing TDR in patients with VA.

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Declarations of interest

None.

References

[1] Yasue H, Takizawa A, Nagao M, Nishida S, Horie M, Kubota J, et al. Long-term prognosis for patients with variant angina and influential factors. Circulation 1988;78:1–9.
[2] Parchure N, Batchvarov V, Malik M, Camm AJ, Kaski JC. Increased QT dispersion in patients with Prinzmetal's variant angina and cardiac arrest. Cardiovasc Res 2001;50:379–85.
[3] Yan GX, Joshi A, Guo D, Hlaing T, Martin J, Xu X, et al. Phase 2 reentry as a trigger to initiate ventricular fibrillation during early acute myocardial ischemia. Circulation 2004;110:1036–41.
[4] Castro Hevia J, Antzelevitch C, Tornes Barzaga F, Dorantes Sanchez M, Dorticos Balea F, Zayas Molina R, 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;47:1828–34.
[5] Kanters JK, Haarmark C, Vedel-Larsen E, Andersen MP, Graff C, Struijk JJ, et al. T(peak)T(end) interval in long QT syndrome. J Electrocardiol 2008;41:603–8.
[6] Haarmark C, Hansen PR, Vedel-Larsen E, Pedersen SH, Graff C, Andersen MP, et al. The prognostic value of the Tpeak-Tend interval in patients undergoing primary percutaneous coronary intervention for ST-segment elevation myocardial infarction. J Electrocardiol 2009;42:555–60.
[7] Morita H, Zipes DP, Wu J. Brugada syndrome: insights of ST elevation, arrhythmogenicity, and risk stratification from experimental observations. Heart Rhythm 2009;6:S34–43.
[8] Kerin NZ, Rubenfire M, Naini M, Wajszczuk WJ, Pamatmat A, Cascade PN. Arrhythmias in variant angina pectoris. Relationship of arrhythmias to ST-segment elevation and R-wave changes. Circulation 1979;60:1343–50.
[9] Bayes de Luna A, Carreras F, Cladellas M, Oca F, Sagues F, Garcia Moll M. Holter ECG study of the electrocardiographic phenomena in Prinzmetal angina attacks with emphasis on the study of ventricular arrhythmias. J Electrocardiol 1985;18:267–75.
[10] Antzelevitch C. Genetic, molecular and cellular mechanisms underlying the J wave syndromes. Circ J 2012;76:1054–65.
[11] Di Diego JM, Antzelevitch C. Cellular basis for ST-segment changes observed during ischemia. J Electrocardiol 2003(36 Suppl):1–5.
[12] Tse G, Gong M, Wong WT, Georgopoulos S, Letsas KP, Vassiliou VS, et al. The T_{peak} - T_{end} interval as an electrocardiographic risk marker of arrhythmic and mortality outcomes: a systematic review and meta-analysis. Heart Rhythm 2017;14:1131–7.
[13] Xianpei W, Sha W, Chuanyu G, Juanjuan Y, Chong C, Yongen S, et al. Tpeak-Tend dispersion as a predictor for malignant arrhythmia events in patients with vasospastic angina. Int J Cardiol 2017;249:61–5.
[14] 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;41:567–74.
[15] Di Diego JM, Antzelevitch C. Acute myocardial ischemia: cellular mechanisms underlying ST segment elevation. J Electrocardiol 2014;47:486–90.
[16] Rivard L, Roux A, Nault I, Champagne J, Roux JF, Tadros R, et al. Predictors of ventricular arrhythmias and sudden death in a Quebec cohort with Brugada syndrome. Can J Cardiol 2016;32:1355.e1–7.