Tpeak-to-Tend/QT is an independent predictor of early ventricular arrhythmias and arrhythmic death in anterior ST elevation myocardial infarction patients

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Abstract

Background: The aim of our study was to analyse the markers of transmural dispersion of ventricular repolarization, especially Tpeak-to-Tend and Tpeak-to-Tend /QT ratio, in patients with anterior ST elevation myocardial infarction on admission and to evaluate their association with in-hospital life-threatening arrhythmias and mortality.

Methods and results: A total of 223 consecutive patients with anterior wall ST elevation myocardial infarction admitted to our Division of Cardiology between January 2010 and December 2012 were prospectively evaluated. A standard electrocardiogram was obtained on admission and then analysed. The primary end point was constituted by in-hospital ventricular arrhythmias and arrhythmic death. At univariate analysis heart rate (odds ratio = 1.03; 95% confidence intervals 1.006-1.05; p=0.001), maximal ST elevation (odds ratio =1.25; 95% confidence intervals 1.10–1.43; p=0.0001), QTc Bazett (odds ratio = 1.01; 95% confidence intervals 1.006–1.02; p=0.002), QT dispersion (odds ratio = 1.02; 95% confidence intervals 1.002–1.04; p=0.02) and both Tpeak-to-Tend and Tpeak-to-Tend/QT (odds ratio = 1.02; 95% confidence intervals 1.01–1.03; p<0.0001 and OR = 1.07; 95% confidence intervals 1.03–1.11; p<0.0001 respectively) were significantly associated with ventricular arrhythmias and arrhythmic mortality. Of note, Tpeak-to-Tend /QT remained a predictor of early ventricular arrhythmias and arrhythmic death (odds ratio = 1.02; 95% confidence intervals 1.003 – 1.10; p=0.03) independently from heart rate and maximal ST elevation. Receiver operating characteristic curve analysis showed that Tpeak-to-Tend /QT values <0.31 had a predictive negative value of 92% for the prediction of the composite outcome.

Conclusions: Tpeak-to-Tend /QT was an independent predictor of early ventricular arrhythmias and arrhythmic mortality in patients with anterior ST elevation myocardial infarction. Especially, Tpeak-to-Tend /QT <0.31 may identify a subgroup of ST elevation myocardial infarction patients with low risk of early arrhythmias and arrhythmic death.

Keywords

Tpeak-to-Tend, arrhythmias, ST elevation myocardial infarction, dispersion of ventricular repolarization

Introduction

ST-segment elevation myocardial infarction (STEMI) is a major cause of morbidity and mortality in contemporary populations. Several studies have focused on the arrhythmogenic substrates in the infarcted myocardium of these patients, such as prolonged QT intervals and T-wave alternans, in order to provide clinical markers for predicting
A prolonged QT interval has been shown to be closely associated with increased risk for SCD in organic diseases, including myocardial infarction. Recently, the interval from the peak to the end of the T-wave (Tpeak-Tend interval (TpTe)) has been proposed to predict the risk of malignant arrhythmia and SCD in some ion channel diseases. A prolongation of this interval might represent a period of potential vulnerability for re-entrant ventricular arrhythmias. In a recent work, higher TpTe values have been associated with SCD in the general population. However, little is known about the dispersion of ventricular repolarization and its relationship with life-threatening arrhythmias in patients with anterior STEMI. Therefore, the aim of this study was to assess TpTe and Tp-Te/QT ratio in patients with anterior STEMI and to analyse their association with in-hospital arrhythmias and mortality.

Material and methods

A total of 263 consecutive patients with anterior wall STEMI who were admitted to the Critical Care Unit of our Division of Cardiology in the University Hospital of Verona between January 2010 and December 2012 were evaluated. Patients fulfilling the following criteria were included in our study: (1) presentation within 12 hours from the onset of symptoms (typical chest pain lasting >30 minutes); (2) the amplitude of ST segments measured 60 ms after J point being ≥2 mm in at least two contiguous ECG leads. Exclusion criteria were: previous acute myocardial infarction; atrial fibrillation; left bundle branch block; poor ECG quality; pacemaker rhythm; lack of a timely ECG on admission. Sustained ventricular arrhythmias (ventricular tachycardias >30 seconds or ventricular fibrillation) and all-cause/arrhythmic deaths were evaluated during the whole hospital stay. The primary outcome was a composite end point of sustained ventricular arrhythmias and arrhythmic death. Ventricular arrhythmias occurring during the revascularization procedure were excluded from the analysis because they could be procedure-related.

A standard 12-lead ECG was performed on admission in all patients using a MAC 5000 digital ECG machine (GE Healthcare, Milwaukee, WI, USA) at the setting of 25 mm/mV. QT interval was measured from the onset of the QRS 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 analysed for each lead.

Leads with T-wave amplitude <1.5 mm were excluded from the analysis.

The QT intervals were adjusted for heart rate using Bazett and Fridericia's corrections and were evaluated in ECGs in which at least six leads were measurable. The QTd was measured as the difference between the maximum and the minimum QT intervals on the standard 12-lead ECG. The TpTe was assessed in leads unaffected by the infarction where ST-segment deviation was below 0.1 mV at the J-point to avoid problems in assessing QT and TpTe measurements. Therefore, TpTe was assessed in V4 or, if this lead was excluded for ST elevation or small T-wave amplitude, in V5 or V6 in descending order. The TpTe/QT ratio was calculated as the ratio of TpTe in that lead to the corresponding QT interval. Standard ECG parameters were also calculated: heart rate, PR interval, QRS duration, maximal ST elevation. All ECG measurements were independently analysed by two cardiologists blinded to clinical data. In case of disagreement, a third cardiologist was consulted.

Demographic data and clinical history were collected as well as door-to-balloon time, heart rate and blood pressure. Laboratory exams were required on admission and on a daily basis during the hospital stay. Left ventricular ejection fraction (LVEF) was evaluated by 2D transthoracic-echo-cardiography within the first 24 hours after admission to the Cardiologic Critical Care Unit.

Patients were addressed to primary PCI including balloon angioplasty and/or stent implantation in the infarct-related artery or medical therapy only, according to current guidelines and internal protocols. No patients were treated by fibrinolytic therapy.

Standard clinical care and treatment were applied for each patient with anterior wall STEMI. Continuous variables are expressed as mean ± SD and, if appropriate, were compared using the Student’s t-test. Categorical variables are expressed as numbers and percentages and, if appropriate, were compared with the Chi-square analysis. Multivariate analysis was performed using a logistic regression model including all factors that were significantly associated with arrhythmic events and arrhythmic death on univariate analysis.

A p value < 0.05 was deemed statistically significant. Statistical analysis was performed using SPSS 20.0.0 (IBM Inc., Armonk, New York, USA).

Results

A total of 263 consecutive patients were evaluated. Patients with previous acute myocardial infarction (n=12), atrial fibrillation (n=14), left bundle branch block (n=5), poor ECG quality (n=3), pacemaker rhythm (n=2), lack of a timely ECG on admission (n=4) were excluded from the analysis. A final population of 223 patients (171 males, 64 ± 16 years) was finally considered for our analysis.
Clinical and electrocardiographic characteristics are summarized in Table 1. Mean age was 64 ± 16 years and females represented 23% of the population. The mean QT interval and mean Tp/Te were 393 ± 44 ms and 127 ± 36 ms, respectively, and the LVEF was 43 ± 8%.

The overall occurrence of major arrhythmic events was 14.8% (33 patients) and all consisted of ventricular fibrillation except one (sustained ventricular tachycardia). Four episodes of ventricular fibrillation were excluded from the analysis as procedure-related arrhythmias. Patients with arrhythmic events showed higher heart rate (90 ± 23 vs. 81 ± 16 beats per minute; \( p = 0.006 \)), more pronounced ST segment elevation (6.3 ± 4.0 vs. 4.4 ± 2.3 mm; \( p = 0.001 \)), greater QT dispersion (55 ± 66 vs. 36 ± 20 ms; \( p = 0.002 \)) and greater Tp-Te/QT ratio (0.38 ± 0.10 vs. 0.31 ± 0.08; \( p = 0.02 \)). There were no differences in QRS duration (\( p = 0.2 \)), QT (\( p = 0.9 \)), LVEF (\( p = 0.9 \)) or cardiovascular risk factors between the two subgroups (Table 1).

Figure 1 shows the occurrence of arrhythmic events among different Tp-Te/QT quartiles. Most malignant arrhythmias occurred in patients with Tp-Te/QT >0.35 while only one arrhythmic episode occurred in patients with normal Tp-Te/QT.

Of note, main angiographic characteristics did not differ between arrhythmic group and the rest of the population (\( p > 0.1 \) for all); in addition, the mean symptoms-to-balloon delay was comparable (229 ± 146 min vs. 222 ± 168 minutes; \( p = 0.8 \)).

As an elevated collinearity was observed between QT, QTc, QT dispersion and TpTe values, only TpTe/QT was necessarily chosen for the multivariate model as the most predominant risk factor on the univariate analysis.
When the electrocardiographic characteristics were tested on the univariate analysis, many parameters were significantly associated with sustained ventricular arrhythmias and arrhythmic death, as shown in Table 3. In detail, heart rate (odds ratio (OR)=1.03; 95% confidence intervals (CI) 1.006–1.05; \(p=0.001\)), maximal ST elevation (OR=1.25; 95% CI 1.10–1.43; \(p=0.0001\)), QTc Bazett (OR=1.01; 95% CI 1.006–1.02; \(p=0.002\)), QT dispersion (OR=1.02; 95% CI 1.002–1.04; \(p=0.02\)) and both TpTe and TpTe/QT (OR=1.02; 95% CI 1.01–1.03; \(p<0.0001\) and OR=1.07; 95% CI 1.03–1.11; \(p<0.0001\) respectively) were significantly associated with the composite end point. Interestingly, TpTe/QT remained a predictor of early sustained ventricular arrhythmias and arrhythmic death (OR=1.04; 95% CI 1.003–1.10; \(p<0.0001\)). This model included also heart rate and maximal ST elevation, which, respectively, lost significance (\(p=0.1\) and \(p=0.07\)). Moreover, TpTe/QT remained the strongest predictor of arrhythmic events even if QTc Bazzet was included in the multivariate model. Arrhythmic events mostly occurred before the revascularization procedure (\(n=24, 73\%\)); all the remaining arrhythmic events after PCI occurred during the time the patients remained in the critical care unit. Patients remained in the critical care unit for 65±31 hours. The incidence of arrhythmic events was associated with a more prolonged critical care unit hospitalization (80±45 vs. 60±28 hours; \(p=0.03\)).

The overall mortality rate was 6.3% (14 patients); among these deaths, five (36%) were related to documented major arrhythmic events (in all cases ventricular fibrillation), which occurred during critical care unit stay and after PTCA procedures; in one of these cases the revascularization procedure was ineffective. Remaining deaths (nine; 64%) resulted from mechanical complications: six patients died from severe left ventricular failure with cardiogenic shock, two patients died from free wall rupture and cardiac tamponade and one patient died from ventricular septal rupture.

Predictors of arrhythmic death (Table 4) on the univariate analysis were the heart rate (OR=1.03; 95% CI 1.006–1.05;
Multivariate analysis

TpTe/QT remained the only variable independently associated with arrhythmic death. OR: odds ratio; HR: heart rate; bpm: beats per minute; CI: confidence intervals; TpTe: Tpeak-to-Tend; LVEF: left ventricular ejection fraction. As shown, TpTe/QT measurement showed a strong agreement between the observers. The intra-observer intraclass correlation coefficient was 0.92 (95% CI 0.87–0.95) and the inter-observer intraclass correlation coefficient was 0.88 (95% CI 0.84–0.94).

Discussion

The main findings of this prospective study on consecutive anterior STEMI patients are: (1) prolonged TpTe/QT index on admission is a strong independent predictor of early life-threatening arrhythmias and arrhythmic mortality; (2) the dispersion of ventricular repolarization is hugely increased in the acute phase of anterior STEMI; (3) TpTe/QT values <0.31 identify a subgroup of patients with a low risk of early ventricular arrhythmias and arrhythmic death; (4) the incidence of sustained ventricular arrhythmias is associated with more prolonged stay in critical care unit.

TpTe in precordial ECG leads has been suggested to provide an index of TDR.15 As a possible marker of TDR, TpTe should be measured in the precordial leads as the direction of these leads goes radially outward from the centre of the heart addressing the electrical field across the ventricular wall and resulting in a more representative assessment of the TDR itself. Conversely, the limb leads sample across the craniocaudal axis of the heart and they probably reflect the apico-basal and interventricular dispersion of repolarization. The TDR represents a vulnerable period for the occurrence of ventricular arrhythmias; indeed, during this period the epicardium has already repolarized and is excitable while M cells are still repolarizing and might be hypothetically affected by early after-depolarizations. In predisposing conditions, early after-depolarizations may result in re-entry phenomena leading to ventricular tachyarrhythmias. Since the steepness of the repolarization gradient rather than the total magnitude of dispersion is the major determinant of arrhythmogenicity, increased TDR is likely to be more arrhythmogenic because the dispersion of repolarization occurs over a brief distance, resulting in a steep repolarization gradient.16 Some studies confirmed these findings15,17 while contrary results emerged.

### Table 4. Univariate and multivariate regression model for predicting arrhythmic death.

<table>
<thead>
<tr>
<th></th>
<th>Univariate analysis</th>
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<th>Multivariate analysis</th>
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<tbody>
<tr>
<td></td>
<td>OR for arrhythmic death</td>
<td>P-value</td>
<td>OR for arrhythmic death</td>
<td>P-value</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>1.045 (95% CI 1.002–1.09)</td>
<td>0.04</td>
<td>1.03 (95% CI 0.98–1.08)</td>
<td>0.2</td>
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<tr>
<td>Max ST elevation (mm)</td>
<td>1.15 (95% CI 0.90–1.46)</td>
<td>0.3</td>
<td>0.96 (95% CI 0.68–1.34)</td>
<td>0.8</td>
</tr>
<tr>
<td>QT (ms)</td>
<td>0.98 (95% CI 0.95–1.003)</td>
<td>0.09</td>
<td></td>
<td></td>
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<tr>
<td>QTc Bazett (ms)</td>
<td>1.004 (95% CI 0.98–1.03)</td>
<td>0.7</td>
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<tr>
<td>QTc Fredericia (ms)</td>
<td>0.99 (95% CI 0.96–1.02)</td>
<td>0.6</td>
<td></td>
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</tr>
<tr>
<td>QT dispersion (ms)</td>
<td>0.99 (95% CI 0.95 – 1.04)</td>
<td>0.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tp-Te (ms)</td>
<td>1.02 (95% CI 1.00–1.04)</td>
<td>0.04</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tp-Te/QT</td>
<td><strong>1.10 (95% CI 1.03 –1.19)</strong></td>
<td><strong>0.008</strong></td>
<td><strong>1.09 (95% CI 1.01–1.19)</strong></td>
<td><strong>0.04</strong></td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>0.70 (95% CI 0.53–0.94)</td>
<td>0.02</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

OR: odds ratio; HR: heart rate; bpm: beats per minute; CI: confidence intervals; TpTe: Tpeak-to-Tend; LVEF: left ventricular ejection fraction. As shown, TpTe/QT remained the only variable independently associated with arrhythmic death.

Univariate analysis

p=0.01, TpTe/QT (OR=1.10; 95% CI 1.03–1.19; p=0.008) and the TpTe (OR=1.02; 95% CI 1.00–1.04; p=0.04). On the multivariate analysis only TpTe/QT was strongly associated to arrhythmic death (OR=1.09; 95% CI 1.005–1.19; p=0.04), while the heart rate did not show a significant result (p=0.2). Interestingly, those five patients who died from arrhythmic death exhibited very prolonged TpTe and TpTe/QT values, respectively 160±31 ms and 0.44±11. Thus, TpTe was significantly related to higher risk of composite end point and arrhythmic death only on the univariate analysis (Tables 3 and 4) but less strongly than TpTe/QT. Moreover, QTc (according Bazett and Fredericia) and QT dispersion were significantly related to higher risk of composite end point and arrhythmic death only on the univariate analysis (Tables 3 and 4) but less strongly than TpTe/QT.

Receiver operating characteristic (ROC) curve analysis was performed to assess the best cut-off points of TpTe/QT for the prediction of sustained ventricular arrhythmias and arrhythmic death (Figure 2(a)). The area under the ROC curve was 0.70 (95% CI 0.63–0.76); Tpeak-to-Tend/QT of 0.31 showed the best combined sensitivity and specificity (69.7% and 63.7%, respectively with a Youden’s Index of 0.33) along with positive predictive value of 5.3% and negative predictive value of 100%. TpTe/QT measurement showed a strong agreement between the observers. The intra-observer intraclass correlation coefficient for TpTe was 0.92 (95% CI 0.87–0.95) and the inter-observer intraclass correlation coefficient was 0.88 (95% CI 0.84–0.94).
European Heart Journal: Acute Cardiovascular Care

Prolongation of the TpTe interval has been associated with increased risk of ventricular arrhythmias in congenital as well as in acquired long-QT syndromes in hypertrophic cardiomyopathy with troponin I mutations and in patients with the Brugada syndrome. Moreover, Panikkath and co-workers have recently shown that prolonged TpTe interval is significantly associated with SCD in the general population and also in those patients with normal QT. They found that the majority of subjects (90.4%) who died of SCD exhibited a TpTe value >100 ms. TpTe has been also found to be associated with increased risk of ventricular arrhythmias in a sample of patients treated with cardiac resynchronization therapy.

This parameter has proven to have excellent reproducibility and repeatability after repeated measurements in a recent work. The global dispersion of ventricular repolarization between normal myocardial tissue and the infarcted tissue/ischaemic border zone is increased in the infarcted heart, resulting in a substrate for malignant arrhythmias.

The present study contributes to confirm the usefulness of TpTe/QT in a clinical setting poorly studied. Haarmark et al. have analysed the prognostic value of TpTe in 101 patients with first-time STEMI undergoing PCI after a long-term follow up of 22±7 months. They found that pre-PCI TpTe was significantly associated with subsequent life-threatening ventricular arrhythmias and arrhythmic mortality. The value of the area under the curve (AUC) is 0.70 (95% confidence intervals (CI) 0.63–0.76). (b) ROC curve for the relationship between TpTe/QT and arrhythmic death. The AUC is 0.84 (95% CI 0.74–0.89). Best cut-off value of TpTe/QT was 0.31 for both curve analyses.

### Table 5. Univariate regression model for predicting death and non-arrhythmic death.

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR for death</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (bpm)</td>
<td>1.021 (95% CI 0.99–1.05)</td>
<td>0.15</td>
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<tr>
<td>Max ST elevation (mm)</td>
<td>0.98 (95% CI 0.79–1.21)</td>
<td>0.82</td>
</tr>
<tr>
<td>QT (ms)</td>
<td>1.001 (95% CI 0.989–1.013)</td>
<td>0.83</td>
</tr>
<tr>
<td>QTc Bazett (ms)</td>
<td>1.009 (95% CI 0.997–1.022)</td>
<td>0.15</td>
</tr>
<tr>
<td>QTc Fredericia (ms)</td>
<td>1.008 (95% CI 0.994–1.022)</td>
<td>0.27</td>
</tr>
<tr>
<td>QT dispersion (ms)</td>
<td>0.99 (95% CI 0.98–1.02)</td>
<td>0.88</td>
</tr>
<tr>
<td>Tp-Te (ms)</td>
<td>1.008 (95% CI 0.995–1.023)</td>
<td>0.23</td>
</tr>
<tr>
<td>Tp-Te/QT</td>
<td>1.01 (95% CI 0.99–1.03)</td>
<td>0.15</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>0.80 (95% CI 0.72–0.90)</td>
<td>0.0001</td>
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</table>

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR for non-arrhythmic death</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (bpm)</td>
<td>1.004 (95% CI 0.97–1.04)</td>
<td>0.85</td>
</tr>
<tr>
<td>Max ST elevation (mm)</td>
<td>0.82 (95% CI 0.58–1.15)</td>
<td>0.25</td>
</tr>
<tr>
<td>QT (ms)</td>
<td>1.009 (95% CI 0.997–1.02)</td>
<td>0.15</td>
</tr>
<tr>
<td>QTc Bazett (ms)</td>
<td>1.012 (95% CI 0.996–1.028)</td>
<td>0.13</td>
</tr>
<tr>
<td>QTc Fredericia (ms)</td>
<td>1.014 (95% CI 0.998–1.030)</td>
<td>0.09</td>
</tr>
<tr>
<td>QT dispersion (ms)</td>
<td>1.002 (95% CI 0.98–1.02)</td>
<td>0.81</td>
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<tr>
<td>Tp-Te (ms)</td>
<td>0.99 (95% CI 0.98–1.02)</td>
<td>0.92</td>
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<tr>
<td>Tp-Te/QT</td>
<td>0.99 (95% CI 0.99–1.01)</td>
<td>0.64</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>0.87 (95% CI 0.79–0.95)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

OR: odds ratio; HR: heart rate; bpm: beats per minute; CI: confidence intervals; TpTe: Tpeak-to-Tend; LVEF: left ventricular ejection fraction.

Figure 2. (a) Receiver operating characteristic (ROC) curve for the relationship between TpTe/QT and the composite outcome constituted by life-threatening ventricular arrhythmias and arrhythmic mortality. The value of the area under the curve (AUC) is 0.70 (95% confidence intervals (CI) 0.63–0.76). (b) ROC curve for the relationship between TpTe/QT and arrhythmic death. The AUC is 0.84 (95% CI 0.74–0.89). Best cut-off value of TpTe/QT was 0.31 for both curve analyses.
all-cause mortality. In our study, we assessed TpTe on admission in consecutive 223 patients with anterior STEMI regardless of treatment and we evaluated in-hospital malignant arrhythmias and mortality. Age, sex and LVEF were similar in both populations; however, in our patients with anterior STEMI, we found higher TpTe values (127±36 ms) on admission than those reported by Haarmark et al. (mean TpTe: 104 ms, 95% CI 98–109 ms). This finding may be explained by a greater ischaemic injury and extent in our patient population composed of all anterior STEMI. Similar to the work of Haarmark et al., no correlations between TpTe and the site of culprit lesion were found. In the work of Zhao and co-workers, TpTe/QT values remained significantly higher TpTe values (127±36 ms) compared with normal reference values reported in literature. These findings suggest a greater dispersion of ventricular repolarization in the acute phase of anterior transmural myocardial infarction, which may predispose to higher risk of in-hospital sustained ventricular arrhythmias.

Greater TpTe values were found in patients with malignant arrhythmias compared with those without life-threatening arrhythmias, without statistical significance (respectively, 149±41 ms and 123±34 ms, p=0.2); TpTe/QT was significantly higher in patients with life-threatening arrhythmias compared with those without major arrhythmic events (0.38±0.10 and 0.31±0.08, p=0.02). Of note, we found that only TpTe/QT values remained significantly associated with in-hospital life-threatening arrhythmias and arrhythmic mortality on the multivariate analysis (respectively, OR=1.04; 95% CI 1.003–1.10; p=0.03 and OR=1.09; 95% CI 1.005–1.19; p=0.04), independently from heart rate and maximal ST elevation, which have been diffusely associated with prognosis and severity of myocardial infarction. TpTe/QT was the strongest parameter associated with ventricular arrhythmias and arrhythmic mortality on the univariate analysis (Table 3). As already reported by Gupta et al., TpTe/QT seems to represent a more sensitive index of arrhythogenesis as it provides an estimate of the repolarization dispersion relative to the total duration of repolarization avoiding possible confounding effects of heart rate variability and inter-individual variation of QT interval. The best cut-off value of TpTe/QT resulted in 0.31 both for the prediction of composite end point constituted by ventricular arrhythmias and arrhythmic death, and arrhythmic mortality only. This finding was very similar to the best cut-off value of TpTe (0.29) identified by Zhao and co-workers. Interestingly, the remarkable negative predictive value (92%) was able to predict with a great accuracy the absence of early life-threatening arrhythmias and arrhythmic death in patients with STEMI and TpTe/QT <0.31. Moreover, although a few patients experienced arrhythmic death in our patient population (n=5), the ROC curve analysis regarding the arrhythmic mortality showed two noticeable findings: (1) no patients with TpTe/QT < 0.31 experienced arrhythmic death (negative predictive value of 100%); (2) all five patients who died from early ventricular fibrillation did present TpTe/QT values higher than 0.31 (sensitivity of 100%). As discussed above, those five patients who died from arrhythmic death exhibited a marked prolongation of basal TpTe and TpTe/QT values (160±31 ms and 0.44±11, respectively). Although the positive predictive value was quite low, higher cut-off values of TpTe/QT were associated with a better predictive value. In fact, among patients with TpTe/QT >0.46 (n=19), eight of them had ventricular arrhythmias or arrhythmic death (positive predictive value of 42.1%). Therefore, the subgroup of patients with a very marked basal TpTe/QT (>0.46) was 3.4 times more likely to develop life-threatening arrhythmias and arrhythmic death compared with the rest of population (42.1% vs. 12.2%).

No relationship was found between the markers of repolarization dispersion and in-hospital all-cause mortality, suggesting that TpTe and TpTe/QT did not play a role in the prediction of non-arrhythmic deaths. On the contrary, we found that LVEF was able to significantly predict both in-hospital arrhythmic and non-arrhythmic death confirming that LVEF represents a prognostic predictor in the acute phase of anterior STEMI. Nevertheless, despite the relatively large sample size, the small event rate might represent a possible limitation for statistical analysis and our results should not be generalized.

In conclusion, TpTe/QT may represent a simple and useful marker predicting higher risk of in-hospital malignant arrhythmias in patients with anterior STEMI. This parameter may identify those patients with STEMI at higher risk for malignant arrhythmias probably requiring more urgent revascularization and closer and more prolonged monitoring in critical care unit. Especially, TpTe/QT values <0.31 seem to identify a subgroup of STEMI patients with a low risk of early life-threatening arrhythmias and arrhythmic mortality. However, further prospective, randomized and multi-centres studies are needed to confirm these results and to define optimal cut-offs of TpTe and TpTe/QT.

The single-centre design is a potential limitation of this study. The difficulty in locating the end of a T-wave when the T-wave morphology is flat or multiphasic might have impaired TpTe and QT measurements. However, readers were blinded towards the outcome and hence any such errors would be unrelated to clinical status. In addition, TpTe/QT measurements have shown a low variability in
both inter and intra observer assessment test, suggesting a good feasibility and reproducibility of this parameter. The sample size is moderately small and results of our study should be confirmed by larger prospective trials. Moreover, the small number of arrhythmic deaths also represents a possible limitation for statistical analysis.

Conflict of interest
None declared.

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