Original Research Article

Association between Tpeak-Tend interval/ QT interval (Tp-e/QT ratio) and prognosis in patients with acute pulmonary embolism

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Abstract

Background: Risk stratification of patients with acute pulmonary embolism (PE) allows assessment of individual prognosis and guides therapeutic decision making. Several electrocardiographic (ECG) markers measuring the arrhythmogenic substrate(s) in ventricular myocardium are used to identify the high-risk patients with acute PE. However studies on Tp-e/QT ratio in patients with acute PE are lacking therefore the present study is aimed to evaluate the in hospital prognostic significance (death and in hospital adverse clinical events [ACE]) of Tp-e/QT ratio at admission in acute PE patients.

Materials and methods: This was a retrospective study that included adult patients who had been diagnosed with acute PE and were treated at our hospital between January 2012 and March 2016. After considering inclusion and exclusion criteria, data was collected from eligible patients. All ECG recordings were digitalized and evaluated by a computer based program. Tp-e and QT intervals were measured from all precordial leads and mean value is calculated. Statistical analysis was performed using SPSS 17.0. Receiver operator characteristic (ROC) curves were computed for the Tp-e/QT ratio to assess the optimal cutoff values for predicting mortality and ACE. Univariate logistic regression analysis for the predictors of in hospital events (death and in hospital ACE) in the study population was done. The statistical significance was considered for a p-value <0.05.

Results: A total of 48 patients were included in the study with mean age of 37.95 years (±13.86) and male: female ratio of 1.18:1. Patients with pulmonary embolism have mean Tp-e/QT ratio of 0.25 and the range of Tp-e/QT ratio was 0.18 to 0.29. In regression analysis, a Tp-e/QT ratio ≥0.26 increased the risk of death (P = 0.03) and a Tp-e/QT ratio ≥0.25 increased the risk of ACE (P = 0.01) significantly.

Conclusion: In acute Pulmonary Embolism, Tp-e/QT ratio is a simple and useful tool in predicting the patients at high risk of suffering adverse clinical events and death. Hence this ratio may serve as a prognostic marker in these patients.

Key words

Tpeak-Tend interval, QT interval, Tp-e/QT ratio, Pulmonary embolism, Prognosis.

Introduction

Acute pulmonary embolism (PE) is a significant cause of cardiovascular morbidity and mortality [1]. According to current recommendations risk stratification of patients with acute PE is mandatory to allow assessment of individual prognosis and to guide therapeutic decision making. As a result various combinations of clinical findings with imaging and laboratory tests have been proposed and tested in an attempt to improve the risk stratification. Electrocardiogram (ECG) is used less frequently in acute PE diagnosis due to the existence of newer diagnostic modalities such as echocardiography, computed tomography and angiography [2]. However the value of ECG has not declined as it is easily conducted, non-invasive and inexpensive.

Several ECG markers of ventricular repolarization have been reported to identify high-risk patients with acute PE [3]. The mechanism for the appearance of altered ventricular repolarization following the onset of acute PE is unknown but may involve, development of acute cor pulmonale [4], left ventricular underfilling, leading to reduced cardiac output and coronary perfusion [5] thus causing severe right ventricular (RV) ischemia, which may alter the pathway of electrical repolarization resulting in inverted T waves [6], neurohumoral activation, which leads to inotropic and chronotropic stimulation [7] thus altering myocardial repolarization. Therefore, myocardium of patients with acute PE is arrythmogenic.

Various studies have focused on electrophysiological characterization of arrhythmogenic substrate(s) in the myocardium. Research groups have focused on the QT interval as an index for quantitating this arrythmogenic risk and thus predicting fatal arrhythmias. Recently, the interval from the peak to the end of the T wave (Tpeak-Tend interval [Tp-e]) has been proposed for use in the prediction of malignant arrhythmias and sudden cardiac death (SCD) in some channelopathies [8]. Many studies have shown the predictive value of this interval in predicting mortality in patients with hypertrophic cardiomyopathy [9] and in patients undergoing primary percutaneous coronary intervention for myocardial infarction [10]. Previous studies [11] involving canine and rabbit left ventricular wedge models have indicated that Tp-e interval in an electrocardiogram measured across the wedge correlates well with the transmural dispersion of cellular repolarization (TDR) and may serve as an index of total dispersion of repolarization (transmural, apico-basal and global), thus more reliably predicting the arrythmogenic risk.

As body weight increases, there is a linear increase in the QT interval which is accompanied by a parallel increase in the Tp-e interval. Furthermore as heart rate (HR) increases from 60 to 100 bpm, the Tp-e interval decreases parallely with QT interval. Therefore the Tp-e/QT ratio may serve as an accurate index for dispersion of ventricular repolarisation, independent of dynamic changes in HR and body weight [12].

Contemporary research has suggested that the Tp-e/QT ratio is a more accurate predictor of ventricular arrhythmias than the QT interval, corrected QT (QTc) and Tp-e interval [13]. Little is known about this index in patients with acute PE. Therefore the present study aimed to evaluate the short-term or in hospital prognostic significance (both for death and in hospital adverse clinical events [ACE]) of Tp-e/QT ratio at admission in patients with acute PE.

Materials and methods

Study population

This was a retrospective study that included adult patients (Age >18 years) who had been diagnosed with acute PE and were treated at our hospital between January 2012 and March 2016. The study was approved by the ethical committee.

Patients were excluded from the study if

- ECG was unsuitable for analysis i.e. if the admission records indicated left bundle branch block, atrial flutter or atrial fibrillation,
- Active renal or hepatic diseases,
- Suffering from any infectious or inflammatory diseases,
- On anti-arrhythmic drugs,
- Known coronary artery disease.

Definition of In-hospital adverse clinical events

The adverse clinical events were defined as any of the following:

- Death,
- Hemodynamic instability needing catecholamine/ Ionotropic support, ventilatory support (non-invasive positive pressure ventilation or invasive positive pressure ventilation),
- Ventricular arrhythmias during hospital stay.

Measurement of Tp-e/QT

An “appropriate” ECG was defined as one that had at least ten analyzable leads for the required measurements. ECG measurements were done at admission using a supine, standard 12-lead ECG tracing at 25 mm/sec paper speed at 10 mm/mV amplitude. All ECG recordings were digitalised and evaluated in the computer. The Tp-e and QT intervals were calculated with a computer based program and calculator (**Figure - 1**). Tp-e and QT intervals were measured from all precordial leads and mean value is calculated. The end of the T wave was defined as the intersection of the tangent to the down slope of the T wave and the isoelectric line (when not followed by a U wave or if distinct from the following U wave). If a U wave followed the T wave (if not distinct), the T wave offset was measured as the nadir between the T and U waves. If the T wave amplitude was <1.5 mm in a particular lead, that lead was excluded from the analysis.

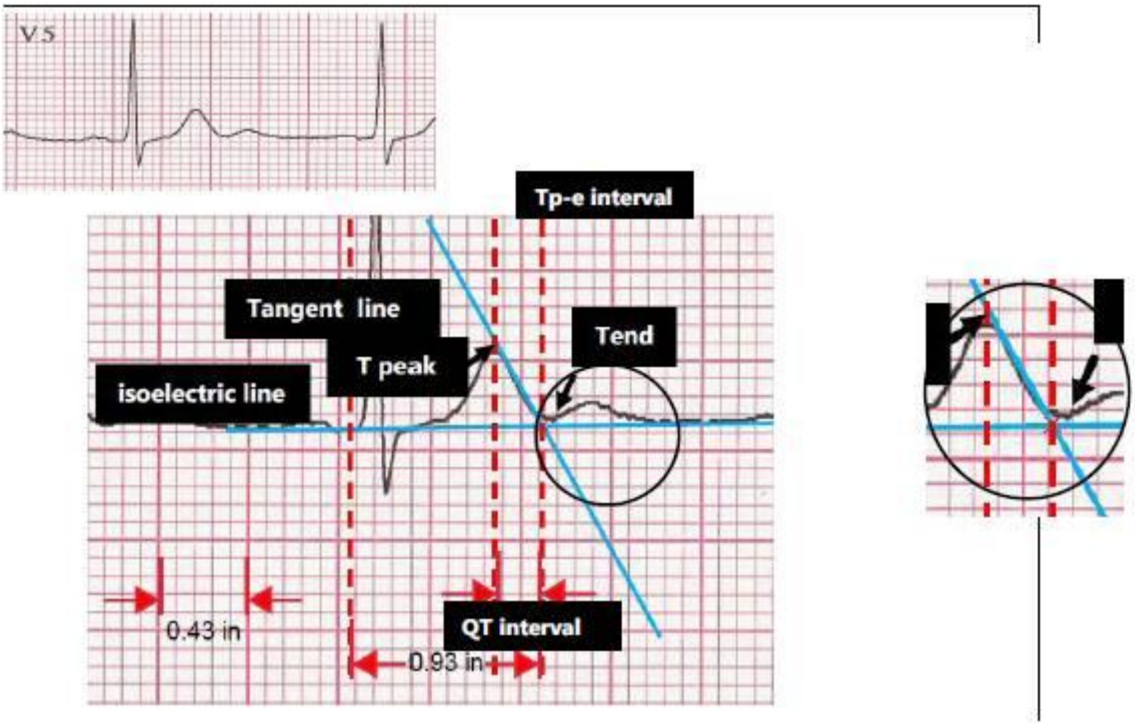
The QT interval was measured from the onset of the QRS complex (so-named for the Q, R, and S waves in an ECG) to the end of the T wave. All ECG measurements were performed by two independent investigators who were blinded to patient information.

To estimate intra-observer and inter-observer variability, twenty randomized ECGs were re-analyzed and the measurements were repeated by a second independent investigator who was blinded to the results obtained by the first investigators.

Statistical analysis

Statistical analysis was performed using SPSS 17.0 (IBM, Armonk, NY). Categorical and numerical variables were expressed in percentage and mean (± standard deviation [SD]) respectively. Numerical variables were tested with independent samples t-test and categorical variables were tested using Fisher’s exact test or chi-square test whichever was suitable. Receiver operator characteristic (ROC) curves were computed for the Tp-e/QT ratio to assess the optimal cutoff values to predict mortality and adverse clinical events. The optimal cutoff value was defined as the value yielding the maximal Youden index (Youden index = b[sensitivity]+[specificity] − 1). Univariate logistic regression analysis for the predictors of in hospital events (death and in hospital adverse clinical events [ACE]) in the study population was done. The statistical significance was considered for a p-value <0.05.

Figure – 1: Computer based method for calculating QT and Tp-e interval from digitalized ECG.



Results

A total of 66 patients were diagnosed as acute pulmonary embolism and treated during this period in our hospital. After considering the exclusion criteria 48 patients were included and 18 patients were excluded from the study. Of these 2 patients had no "appropriate ECG", 5 are known case of coronary heart disease. 1 had atrial fibrillation at presentation and 10 did not undergo confirmatory CT angiography.

The mean age of study population was 37.95 years (±13.86) and male: female ratio of 1.18:1. Baseline demographic and clinical characteristics of patients are depicted in **Table - 1**. Of 48 patients diagnosed as Acute Pulmonary Embolism, 32 Patients (66.67%) died in the Hospital and 39 Patients Suffered from Adverse Clinical event (81.25%) as showed in **Table - 2**.

Patients with pulmonary embolism have mean Tp-e/QT ratio of 0.25 and the range of Tp-e/QT ratios was 0.18 to 0.29. Electrocardiographic parameters are shown in **Table - 3**.

Table 1: Patient Demographics and Clinical Data. **(n=48)**

Age (n, %)	
≤40y	30 (62.5)
>40y	18 (37.5)
Sex (n, %)	
Male	26 (54.1)
Female	22 (45.8)
Co-morbidities (n,%)	
Hypertension	6 (12.5)
Diabetes Mellitus	8 (16.7)
Alcohol intake	12 (0.25)
Smoking	10 (0.21)

Table - 2: Patient Outcomes During Hospitalization.

Endpoints	**n (%)**
Death	32 (66.67)
Hemodynamic Instability	39 (81.25)
Ionotrope support	36 (75)
Ventilator support	5 (10.4)

The area under the ROC curve of Tp-e/QT ratio was 0.68 (95% CI: 0.63-0.74, P = 0.01) for death and 0.74 (95% CI: 0.66-0.85, P < 0.01) for adverse Clinical events. Tp-e/QT ratio ≥0.25 had a sensitivity of 78% and a specificity of 66% to predict ACE.

Table - 3: Electrocardiographic parameters in patients with acute PE.	
Mean QT (Sec)	371.1±22.3
Mean Tp-e (Sec)	85.7±6.1
Mean Tp-e/QT	0.25±0.03
Tp-e Maximum (Sec)	88.4±8.4
QT Maximum (Sec)	388.8±25.4

In univariate logistic regression analysis, a Tp-e/QT ratio ≥0.26 increased the risk of death (74.2% vs 31.6%; P = 0.03) and a Tp-e/QT ratio ≥0.25 increased the risk of adverse Clinical events (89.1% vs 35.3 %; P = 0.01) and a Tp-e/QT ratio ≥0.26 had a sensitivity of 71% and specificity of 67% to predict death in patients with acute PE. (**Figure - 2, 3**)

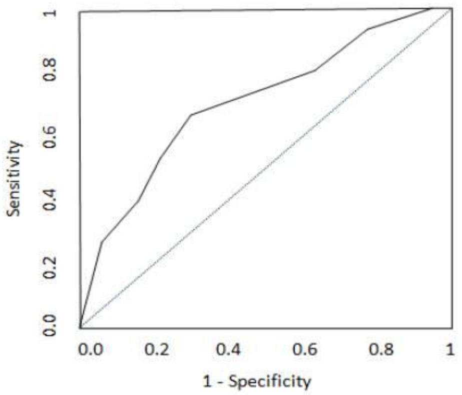


Figure 2: Receiver operating characteristic (ROC) curve of the Tp-e/QT ratio for death

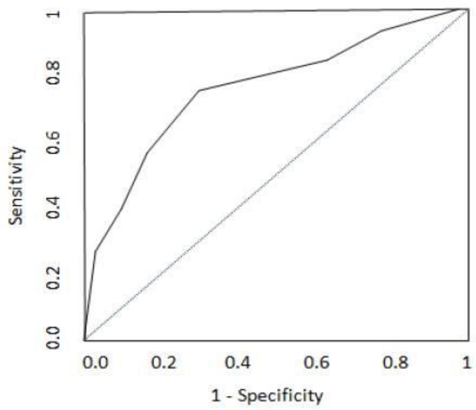


Figure 3: Receiver operating characteristic (ROC) curve of the Tp-e/QT ratio for adverse clinical events [ACE]

In univariate logistic regression analysis, only Tp-e/QT ratio was an independent predictor of mortality and ACE as shown in table 4. A Tp-e/QT ratio ≥0.26 increased the risk of death (74.2% vs 31.6%; P = 0.03) and a Tp-e/QT ratio ≥0.25 increased the risk of adverse Clinical events (89.1% vs 65.3 %; P = 0.01). Regression analyses for the predictors of mortality in the entire population were as per **Table - 4**.

Table - 4: Regression analyses for the predictors of mortality in the entire population.

Variable	**OR (95% CI)**	***P***
DM (n)	1.02 (1.41- 1.60)	0.67
Hypertension (n)	1.76 (0.85-3.65)	0.88
Age (n)	0.82 (0.12- 5.32)	0.83
Tp-e/QT ≥0.26	1.08 (1.01- 1.15)	0.01
Thrombolytic Therapy n (%)	2.42 (1.71- 3.28)	0.09

Discussion

This present study demonstrated that Tp-e/QT interval at admission have a prognostic value in patients with acute PE. Use of the Tp-e/QT ratio as an index for assessing risk in patients with acute PE may allow for future improvements in risk stratification and management leading to decreased mortality.

Vanni et al., reported that the commonly seen RV strain pattern (right bundle branch block, T negativity in precordial derivations, S1Q3T3) could predict short-term prognosis independent of blood pressure and echocardiographic abnormalities [14].

The most extensive study on this phenomenon was conducted by Kosuge, et al. [15], who found a relationship between the number of negative T waves seen in 12-lead ECG and the severity of acute PE, which confirmed via computed tomography, angiography and echocardiography. They also showed that the number of negative T waves during the course of hospitalization was the most significant predictor of death and hemodynamic instability.

In another study of 42 patients, Ding et al. showed an increase in QT and QTc dispersion in the first 24 hours in acute PE patients. Together with RV dysfunction, the authors reported increased QTc dispersion to be an indicator of poor prognosis [16].

Ryu, et al. examined various ECG patterns seen in acute PE patients [17]. They demonstrated that inverted T waves in V1–4 leads and sinus tachycardia could be used in risk stratification.

In recent study done by Icli, et al., showed the prognostic implications of Tp-e interval in acute PE patients [18]. Our study concludes that there is a direct association between prolonged Tp-e/QT ratio and increased fatal events.

Limitations

The primary limitation of this study is that it was retrospective, observational, and single-centred. This study was done on very limited number of patients. Even the indexes in patients with acute PE were only measured or calculated and no measurement of healthy subjects was performed. Thus no information exists for comparison of results between these groups, a baseline that would be a useful comparison to explore in future studies.

Conclusion

In acute pulmonary embolism, Tp-e/QT ratio is a simple and useful tool in predicting the patients at high risk of suffering adverse clinical events and death. Thus Tp-e/QT ratio may serve as a prognostic predictor in these patients and more studies should be carried to further evaluate its clinical value.

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