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Editorial

12-Leads Conventional Electrocardiographic Repolarization Indices Associated to Prognosis in Acute Myocardial Infarction

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There is no doubt that there have been major advances in the diagnostic and therapeutic management of cardiovascular diseases. However, ischemic heart disease (IHD) continues to be the leading cause of mortality and morbidity worldwide. IHD affects nearly 16 million persons aged 20 years and older in the USA. Nearly 4 million cases of acute myocardial infarction (AMI) occur annually in the world. These numbers will likely increase over the next decade due to advancing age [1,2]. The prevalence of patients who have survived an episode of AMI is estimated at 15 million, these patients are at high risk to develop additional episodes of acute coronary syndromes. Malignant ventricular arrhythmias are the more prevailing cause of sudden cardiac death in patients with IHD [3]. It is estimated that up to 20% of patients with AMI develop these ventricular arrhythmias [4]. Therefore, there is an increasing necessity to develop adequate tools for risk assessment for SCD in this set of patients with IHD. Several ECG indices have been proposed for risk stratification and prognosis in patients with AMI [5,6].

Several clinical studies have focused on the electrophysiological characterization of arrhythmogenic substrates in the myocardium of AMI patients to try to predict malignant arrhythmias and sudden cardiac death (SCD) [7-9]. Some researchers have focused on the QRS complex, QT interval, and T-wave alternans as an index for predicting fatal ventricular arrhythmias [8]. The interval from the peak to the end the T wave (Tpeak-Tend interval) has been also proposed for the prediction of malignant arrhythmias and SCD in some entities [9]. Previous experimental animal studies have indicated that the Tpeak-Tend interval in the electrocardiogram measured across the wedge correlates well with the transmural dispersion of cellular repolarization and, may serve as an index of total dispersion of transmural global repolarization [10]. The Tpeak-Tend/QT ratio is another good index of ventricular repolarization that remains constant despite differences in body mass index or dynamic changes in heart rate. It provides a valuable consistency and permits longitudinal comparison of results. It has a better sensitivity for arrhythmogenesis compared to the lone utilization of either the Tpeak-Tend or QT intervals [11].

In this context, Shu J., *et al*. [12] demonstrated that the Tpeak-Tend/QT ratio was associated with malignant ventricular arrhythmias in patients with AMI. They demonstrated in 120 patients with ST segment elevation AMI that the Tpeak-Tend/QT ratio was significantly elevated in those who suffered malignant ventricular arrhythmias as compared with those who did not experience these events (0.32 ± 0.07 vs 0.26 ± 0.05, $P < 0.001$). Zhao X., *et al.* [13] investigated the utility of the Tpeak-Tend/QT ratio as a marker of prognosis in 338 patients with STEMI undergoing primary percutaneous coronary intervention (PCI). The Tpeak- Tend/QT ratio was correlated with both short- and long-term outcomes. The optimal cutoff value for outcome prediction was a Tpeak-Tend/QT ratio of 0.29. A total of 115 (34.0%) patients exhibited a Tpeak-Tend/QT ratio ≥ 0.29. These patients showed elevated rates of both in-hospital death (21.9% vs 2.3%; $P < 0.001$) and main adverse cardiac events (48.1% vs 15.3%; $P < 0.005$). After discharge, the Tpeak-Tend/QT ratios ≥ 0.29 remained an independent predictor of all-cause mortality (35.5% vs 5.2%, $P < 0.001$) and cardiac death (32.3% vs 2.6%, $P < 0.001$). Therefore, the authors

concluded that the Tpeak-Tend/QT ratio may serve as a prognostic predictor of adverse outcomes after successful primary PCI treatment in ST segment elevation AMI patients [13]. In this physio-pathological context, Yan GX., *et al.* [14] demonstrated that Phase 2-reentry produced by the heterogeneous loss of the transient outward potassium current acted as trigger to initiate ventricular fibrillation during early acute myocardial ischemia. They observed that phase 2-reentry can generate a closely coupled premature ventricular complex (R on T) leading to VF under conditions of ST-segment elevation unrelated to ischemia [14].

Wang X., *et al.* [15] investigated the relationship between ST segment resolution post- revascularization and Tpeak-Tend related ECG parameters in 374 patients with the first ST segment elevation AMI undergoing PCI. These ECG parameters were measured in infarction- related and non-infarction-related ECG leads. They prospectively evaluated the ST-segment resolution defined as ≥ 50% reduction as the complete ST resolution group, and those patients with less than 50% as the incomplete ST resolution group. In addition, the Tpeak-Tend interval, and the ratio of Tpeak-Tend/QT interval were also measured, calculated and analyzed with major advanced cardiovascular events. The authors observed that the corrected Tpeak- Tend interval ($P < 0.001$) and the Tpeak-Tend/QT ratio ($P < 0.001$) were significantly increased by myocardial infarction and partly recovered post-PCI. Patients with incomplete ST resolution showed more increased corrected Tpeak-Tend interval ($P < 0.001$) and Tpeak- Tend/QT ratio ($P < 0.001$) than those patients in the complete ST resolution group post-PCI. In multivariate analysis and receiver operating characteristic curves analysis, the Tpeak-Tend/QT ratio was an independent and strongest predictor for ST segment resolution. These ECG parameters showed prognostic value for major advanced cardiovascular events in Kaplan-Meier survival analysis. Increased corrected Tpeak-Tend interval and Tpeak-Tend/QT ratio post-PCI predicted less ST segment resolution. The latter ECG parameter was the strongest predictor for ST segment resolution. The extent of ST segment elevation could represent the transmural potential gradients of phase 2 reentry. Increased Tpeak-Tend interval could facilitate early and delayed after-depolarization-induced triggered activity developing malignant ventricular arrhythmias [14].

The Tpeak-Tend/QT ratio yields a relatively constant normal range between 0.17 and 0.23 [16]. It seems that increases in the Tpeak-Tend/QT ratio represent a higher dispersion of repolarization developing ventricular arrhythmias. Nevertheless, three different studies did not demonstrate differences in the Tpeak-Tend/QT ratio between high and low risk patient groups [17-19]. However, a systematic review and meta-analysis performed by Tse G., *et al*. found otherwise [20]. They analyzed whether Tpeak-Tend interval and Tpeak-Tend/QT ratio can distinguish patients with AMI who are at high risk of arrhythmic or mortality events from those free from these events. A total of 1967 AMI patients with a mean age of 68 years were followed for a mean follow-up period of 15 ± 12 months. The authors found that the Tpeak- Tend/QT ratios were significantly higher in high risk patients compared to the low risk group (mean difference: 0.06, standard error 0.02, $P < 0.01$; $I^2 = 88\%$). The pooled meta-analysis demonstrated that a higher Tpeak-Tend/QT ratio is associated with approximately 3.16 times higher risk of lethal ventricular arrhythmias or mortality (95% CI: 1.13 to 8.82; $P < 0.05$) [20].

In conclusion, there is convincing evidence showing that the Tpeak-Tend interval and, the Tpeak-Tend/QT ratio are significant predictors of ventricular arrhythmias and mortality in AMI. These easily obtainable ECG repolarization indices should be utilized in clinical practice to improve risk stratification and prognosis in AMI patients. Further studies will be critical for a better comprehension of risk stratification associated to ischemic myocardial events.

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