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Counterpoint Tpeak-Tend Interval as a Marker of Arrhythmic Risk

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We have read the commentary by Malik and coworkers¹ and the recent paper by Srinivasan and coworkers² and offer the following observations.

The study by Srinivasan and coworkers is the last in a long series of studies aiming to redefine the basis and significance of different aspects of the T wave, in this instance “Tpeak-Tend interval” is proposed to be a measure of dispersion of repolarization between the right and left ventricles and not that of apico-basal or global dispersion of repolarization, as previous studies had proposed.

The paper by Malik et al. does not give credence to this finding of Srinivasan et al. but further challenges the significance of Tpeak-Tend as a marker of risk, dismissing the relevance of the many previously reported careful studies associating Tpeak-Tend with arrhythmic risk on the basis of “sloppy measurements”. We take strong exception to this debunking of previous studies and maintain that Tpeak-Tend is an important risk stratifier.

Without faulting the methodology or interpretation employed by Srinivasan et al, we would simply point out that interventricular differences in repolarization have long been appreciated, have never before been associated with T peak-Tend and do not lend themselves to a steep repolarization gradient, long recognized as a key factor predisposing to arrhythmogenesis.

These new findings should be considered with some historical perspective. The Tpeak-Tend interval was introduced as a measure of ‘spatial’ dispersion of ventricular repolarization and as a potential ECG index for predicting arrhythmic risk over two decades ago.^{3–5}

The potential for Tpeak-Tend to serve a risk stratifier for the development of cardiac arrhythmias was initially proposed in 1998 on the basis of studies performed using

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arterially-perfused canine ventricular wedge preparations.³ In this experimental model, repolarization of epicardium (briefest action potential) coincides with the peak of the T wave and repolarization of the M cells (longest action potentials) with the end of the T wave, so that the interval between the peak and the end of the T wave provides a measure of transmural dispersion of repolarization (TDR). In these studies, Tpeak-Tend and TDR were shown to prolong when exposed to QT prolonging drugs, causing a dispersion of refractoriness across the ventricular wall and a vulnerable window which when captured by an early-afterdepolarization-induced extrasystole precipitates torsade de pointes (TdP) arrhythmias.

Although these relationships are relatively straight forward in isolated wedge preparations, they are understandably more complex in the whole heart *in vivo*, as demonstrated by Xia and coworkers⁶. While there is general consensus that Tpeak-Tend reflects dispersion of ventricular repolarization, debate continues as to whether the dispersion is transmural, global, or a combination of the two.^{4, 7, 8}

As we and others have previously argued⁵, because the precordial leads measure the electrical field across the ventricular wall, Tpeak-Tend is thought to be most representative of TDR in these leads. The precordial leads are unipolar leads placed on the chest and referenced to the Wilson central terminal. The direction of these lead axes is outward from the electrical “center” of the heart. In contrast, the bipolar limb leads, including leads I, II, and III, do not look across the ventricular wall and thus more likely reflect global dispersion, including apico-basal and interventricular dispersion of repolarization.

The proarrhythmic potential of increased TDR depends on the distance over which the dispersion occurs. A large increase in TDR is more likely to be arrhythmogenic because the dispersion occurs over a very short distance (the width of the ventricular wall), creating a steep gradient.^{9, 10} It has long been appreciated that the steepness of the repolarization gradient rather than the total magnitude of dispersion determines its arrhythmogenic potential. Interventricular dispersion of repolarization is less likely to lead to a steep gradient and thus less likely to be associated with arrhythmic risk.

Over the past two decades, Tpeak-Tend and Tpeak-Tend dispersion have been identified as indices prognostic of arrhythmic risk under a many pathophysiologic conditions, including long QT^{11–13}, short QT^{14, 15}, and Brugada syndromes (BrS)^{16, 17}, hypertrophic cardiomyopathy¹⁸, inducible and spontaneous ventricular tachycardia (VT) in patients with organic heart disease¹⁹, in patients with vasospastic angina²⁰ and in a study of 353 cases of sudden cardiac death.²¹ In many of these studies Tpeak-Tend was judged to be the “best predictor” of life-threatening ventricular arrhythmias.

In a review and meta-analysis of 33 studies involving 155,856 patients, Tse and coworkers reported that Tpeak-Tend prolongation (mean cutoff: 103.3±17.4 ms) is a significant predictor of arrhythmogenesis in BrS, followed by hypertension, heart failure and ischemic heart disease.²²

In conclusion, identifying patients at risk of developing life-threatening arrhythmias remains a major clinical challenge. Despite the ongoing debate regarding its genesis, the potential for

Tpeak-Tend and related ECG markers of repolarization abnormalities to aid in identifying patients at high-risk of arrhythmic SCD is unquestionable.

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