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Novel conduction-repolarization indices for the stratification of arrhythmic risk

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Sudden cardiac death (SCD) affects approximately 800,000 individuals per annum globally.[1] It is most frequently due to cardiac tachy-arrhythmias, which include mono-morphic or polymorphic ventricular tachycardia (VT), torsade de pointes and ventricular fibrillation (VF). Risk stratification for SCD remains a challenging problem in clinical practice. Patients with structural heart disease or cardiac ion channelopathies have an increased risk of SCD, their risks are not the same. Consequently, several indices have been devised for this purpose, mainly focusing on ventricular repolarization, which is reflected by the QT interval on the electrocardiogram.[2] These include QT interval corrected for heart rate (QT_c), QT dispersion (QT_d), interval from the peak to the end of the T wave ($T_{peak} - T_{end}$, reflecting increased transmural dispersion of repolarization, TDR), and ($T_{peak} - T_{end}$)/QT ratio.[3]

There are two major problems with these indices. Firstly, TDR has been shown to be a poor predictor of arrhythmogenicity in pre-clinical models even in disorders of repolarization, such as long QT and short QT syndromes. Secondly, none of the above indices takes into account the role of abnormal conduction in ventricular arrhythmogenesis. It may be reasonable to assume that abnormal conduction plays a minor role in disorders primarily affecting repolarization. However, it is not appropriate to do so in structural heart diseases such as heart failure or Brugada syndrome. In these conditions, reduced conduction velocities (CVs) are observed,[4] which manifest as prolonged QRS durations on the ECG.[5,6] Reduced CV increases the risk of reentrant arrhythmias by shortening the excitation wavelength λ given by CV × effective refractory period, as demonstrated in pre-clinical experiments. However, a major disadvantage of λ is that it must be determined invasively by electrophysiological studies in humans.

In view of this, there is a need for arrhythmic risk markers that take into account both conduction and repolarization. Recently, the index of Cardiac Electrophysiological Balance, iCEB, given by QT/QRS, was proposed.[7] This ratio can easily be derived from the electrocardiogram and is a good approximate of λ.

Previous work has shown that $T_{peak} - T_{end}$ and ($T_{peak} - T_{end}$)/QT are superior to the QT interval in predicting arrhythmic risk.[2] Thus, I recently proposed two novel indices, ($T_{peak} - T_{end}$)/QRS and ($T_{peak} - T_{end}$)/(QT × QRS), that might be able to better predict arrhythmic risk in Brugada syndrome.[8,9] There is no reason why these cannot not be applied in other clinical conditions where conduction is abnormal, such as heart failure. The advantage of ($T_{peak} - T_{end}$)/QRS is that it can be easily calculated and therefore sufficiently convenient for clinical use. ($T_{peak} - T_{end}$)/(QT × QRS) is potentially more accurate for risk stratification for research purposes, but is too cumbersome to use by the bedside. Both indices are derived from electrophysiological findings that both conduction and repolarization abnormalities are important in arrhythmogenesis. The validity of these indices will require further study, but may ultimately provide superior predictive values than ventricular repolarization markers such as QT_c, QT_d, $T_{peak} - T_{end}$ or ($T_{peak} - T_{end}$)/QT ratio. Animal models are useful for studying arrhythmogenic mechanisms and provide a platform for assessing the efficacy of pharmacological therapy.[10–16] Measurement of the magnetic field in the heart has been useful for characterizing cardiac structural abnormalities.[17–19] It can be used to diagnose and predict the risk of cardiac arrhythmias in clinical practice by magnetocardiography, which may provide helpful clinical markers for risk stratification in the future.[20]

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