

**(Tpeak-Tend)/QRS and (Tpeak-Tend)/(QT x QRS): novel markers for predicting  
arrhythmic risk in Brugada syndrome**

Gary Tse BA Hons MBBS MA PhD <sup>1</sup>

<sup>1</sup> School of Biomedical Sciences, Li Ka Shing Faculty of Medicine, University of Hong Kong

Corresponding author:

Dr Gary Tse

School of Biomedical Sciences

Li Ka Shing Faculty of Medicine

University of Hong Kong

Hong Kong

Email: [gary.tse@doctors.org.uk](mailto:gary.tse@doctors.org.uk)

Telephone: +852 39177548

Fax: +852 2817 0857

Keywords: QT dispersion; transmural dispersion of repolarization; wavelength; depolarization; conduction; repolarization; QT/QRS; Tpeak-Tend/QRS; Tpeak-Tend/(QRS x QT); Brugada syndrome

I read the recent paper by Zumhagen and colleagues with great interest, who demonstrated that the interval from the peak to the end of the electrocardiographic T wave ( $T_{\text{peak}} - T_{\text{end}}$ ) and  $(T_{\text{peak}} - T_{\text{end}})/QT$  ratio, were strongly risk markers for Brugada patients with life-threatening ventricular arrhythmias<sup>1</sup>. These ratios reflect the transmural dispersion of repolarization (TDR), increases in which can lead to unidirectional conduction block and reentry<sup>2</sup>.

Nevertheless,  $T_{\text{peak}} - T_{\text{end}}$ ,  $(T_{\text{peak}} - T_{\text{end}})/QT$  ratio and TDR do not take into account the contribution of cellular depolarization or action potential conduction, which is abnormal in Brugada syndrome<sup>3</sup>. The latter finding is in keeping with prolonged QRS duration on the electrocardiogram that suggests intra-ventricular conduction delay<sup>4</sup>. Pre-clinical experiments suggest that excitation wavelength,  $\lambda$ , given by conduction velocity x effective refractory period), may be a better predictor of arrhythmogenicity, because it combines both depolarization and repolarization parameters. However, a major disadvantage of  $\lambda$  is that it must be determined invasively. A recent study proposed calculating the ratio of the time taken of repolarization to that of depolarization, i.e.  $QT/QRS$  (index of Cardiac Electrophysiological Balance, iCEB)<sup>5</sup>. The advantage of this index is that it can be easily determined from the electrocardiogram and can be used by the bedside to approximate  $\lambda$ .

Given that  $T_{\text{peak}}-T_{\text{end}}$  interval is a better predictor of arrhythmic risk than QT interval, it follows that it should replace QT interval in the calculation of iCEB. Thus, I propose two novel markers,  $(T_{\text{peak}}-T_{\text{end}})/QRS$  and  $T_{\text{peak}}-T_{\text{end}} / (QT \times QRS)$  for stratification of arrhythmic risk.  $(T_{\text{peak}}-T_{\text{end}})/QRS$  can easily be calculated by the bedside or in the clinic, whereas  $(T_{\text{peak}}-T_{\text{end}})/(QT \times QRS)$  is potentially more accurate for use in epidemiological studies. Both indices are firmly based on physiological principles that  $\lambda$  is critical in the determination of arrhythmic tendency. Their validity will require further investigation, and may ultimately provide better predictive values than  $T_{\text{peak}}-T_{\text{end}}$  or  $(T_{\text{peak}} - T_{\text{end}})/QT$  ratio.

## Acknowledgements

GT was supported by a BBSRC Doctoral Training Award at the University of Cambridge.

## References

- [1] Zumhagen S, Zeidler EM, Stallmeyer B, Ernsting M, Eckardt L, Schulze-Bahr E. Tpeak-Tend interval and Tpeak-Tend/QT ratio in patients with Brugada syndrome. *Europace* 2016.
- [2] Tse G, Wong STT, V., Lee YT, Lin HY, Yeo JM. Cardiac dynamics: alternans and arrhythmogenesis. *J Arrhythm* 2016.
- [3] Tse G, Wong ST, Tse V, Yeo JM. Depolarization vs. repolarization: what is the mechanism of ventricular arrhythmogenesis underlying sodium channel haploinsufficiency in mouse hearts? *Acta Physiol (Oxf)* 2016.
- [4] Ohkubo K, Watanabe I, Okumura Y, Ashino S, Kofune M, Nagashima K, et al. Prolonged QRS duration in lead V2 and risk of life-threatening ventricular Arrhythmia in patients with Brugada syndrome. *Int Heart J* 2011; **52**: 98-102.
- [5] Lu HR, Yan G-X, Gallacher DJ. A new biomarker – index of Cardiac Electrophysiological Balance (iCEB) – plays an important role in drug-induced cardiac arrhythmias: beyond QT-prolongation and Torsades de Pointes (TdPs). *J Pharmacol Toxicol Methods* 2013; **68**: 250-259.