LETTER TO THE EDITOR

Response of Robyns to the Tse's letter to editor

Dear Editor,

We would like to thank Gary Tse and Bryan P. Yan for their interest in our research regarding the index of electrophysiological balance (iCEB), a novel marker of arrhythmic risk (Lu, Yan, & Gallacher, 2013; Robyns et al., 2016). We illustrated that QT/QRS is a simple surrogate for cardiac wavelength that otherwise can only be measured from invasive recordings. Cardiac wavelength plays an important role in arrhythmogenesis, and therefore, an ECG surrogate of wavelength is an interesting tool with potential large interest for clinical practice. We showed that iCEB is reduced in conditions with increased propensity for nontorsadogenic ventricular fibrillation (patients with Brugada syndrome and flecainide use) and that iCEB is increased in conditions with increased risk for torsadogenic ventricular fibrillation (long QT syndrome and sotalol use). In their letter to the editor, Tse and Yan highlight their description of novel markers in a recent issue of *Europace* and present two additional novel risk markers (Tse & Yan, 2017, 2016).

The similarity between iCEB and these novel markers is that they are based on inclusion of both a repolarization and a depolarization parameter. The first two markers (TpTe/QRS and TpTe/(QT × QRS)) include TpTe instead of QT, based on the fact that TpTe is probably a better marker for increased risk of sudden death compared to the QT interval (Tse & Yan, 2017). The markers they propose in their letter to the editor include the addition of QRS dispersion in their formula. Again, based on the fact that QRS dispersion is a marker of conduction velocity dispersion which might be a better marker

for increased risk compared to QRS (Yamada et al., 2004). We do agree that these are interesting markers to evaluate; however, our main antagonism is that, compared to iCEB, it is not based on any pathophysiological background such as cardiac wavelength. Indeed, TpTe is related to transmural or global dispersion of repolarization (Izumi et al., 2012; Yan & Antzelevitch, 1998). Replacing QT by TpTe therefore moves away from the idea to measure cardiac wavelength from the surface ECG. Furthermore, as Tse and Yan correctly underline, none of these parameters have been clinically evaluated. Therefore, we tested in our described cohort of patients with long QT syndrome and Brugada syndrome and individuals started on either flecainide or sotalol whether the parameters including TpTe show any signal. Similar to iCEB, the two parameters proposed by Tse are decreased in Brugada syndrome and increased in long QT syndrome (Table 1). However, the overlap between controls and patients with BrS is larger with TpTe/QRS compared to iCEB (post hoc *p*-value only .12 for TpTe/QRS compared to <.001 for iCEB). In individuals started on flecainide or sotalol on the other hand, there is no significant difference in the parameters proposed by Tse in contrast to iCEB (Table 2).

To conclude, in our population of patients with arrhythmogenic heart disease, the parameters proposed by Tse including TpTe are similarly altered as iCEB, while they do not show any signal in patients started on drugs with potential pro-arrhythmic effect. Further evaluation of these parameters in large patient cohorts with endpoints of sudden death is required to establish their role in risk stratification.

TABLE 1 Markers in Brugada syndrome and long QT syndrome

	Controls	BrS	LQTS	<i>p</i> -Value
iCEB (QT/QRS)	4.24 ± 0.50	3.52 ± 0.43	5.22 ± 0.93	<.001
TpTe/QRS	0.83 ± 0.17	0.71 ± 0.13	1.16 ± 0.32	<.001
TpTe/(QT × QRS)	0.0022 ± 0.00044	0.0018 ± 0.00031	0.0026 ± 0.00063	<.001

iCEB, index of electrophysiological balance.

TABLE 2 Markers in patients started on flecainide and sotalol

	Flecainide			Sotalol		
	Before	After	<i>p</i> -Value	Before	After	<i>p</i> -Value
iCEB (QT/QRS)	4.36 ± 0.60	4.16 ± 0.59	.033	4.14 ± 0.65	4.37 ± 0.77	.011
TpTe/QRS	0.86 ± 0.15	0.87 ± 0.26	.72	0.80 ± 0.17	0.83 ± 0.23	.55
TpTe/(QT × QRS)	0.0022 ± 0.00035	0.0021 ± 0.00071	.64	0.0020 ± 0.00044	0.0019 ± 0.00054	.58

iCEB, index of electrophysiological balance.

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