Torsadogenic Drug-Induced Increased Short-term Variability of JT-area

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It is well recognized that QT prolongation alone is inadequate for assessment of drug-induced cardiac toxicity. Increased beat-to-beat variability of repolarization (BVR) has been suggested to indicate increased susceptibility to drug-induced arrhythmia. The goal of this study is to characterize BVR in patients before and after administration of sotalol, a torsadogenic antiarrhythmic drug, in the search for new biomarkers of proarrhythmic risk. Two electrocardiogram (ECG) datasets, consisting of individuals with (group I, n=16) and without (group II, n=17) history of drug-induced torsades de pointes, were employed. Identification of peaks and limits for individual P, QRS and T waves was performed via quadratic spline wavelet transform of the ECG signal. QT interval was measured as the interval between the onset of QRS wave and the end of the T wave. JT-area (total T wave area) was computed as the area between the curve and the baseline from J-point to the end point of the T wave. BVR was evaluated by short-term variability (STV, the mean orthogonal distance from each point in the Poincaré plot to the diagonal) of QT interval and JT area. We found that in both groups, sotalol injection resulted in significant increase in STV of JT-area (from 3.1 ± 2.3 to 4.8 ± 2.6 mVms in group I, p=0.008; from 3.5 ± 1.6 to 4.5 ± 2.3 mVms in group II, p=0.009), while no significant change occurred in STV of QT interval (from 16.3 ± 18.0 to 17.6 ± 17.9 in group I, p=0.7; from 12.2 ± 9.6 to 16.4 ± 19.0 ms in group II, p=0.4). In conclusion, STV of JT-area, as an indicator of BVR, has the potential to be a biomarker for drug toxicity. Further evaluation is needed in order to establish its predictive value.