

Sudden Cardiac Death Prediction in Chagas Heart Disease Patients from ECG-derived Biomarkers of Ventricular Restitution

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Background: Chagas heart disease (ChHD) is strongly linked to sudden cardiac death (SCD). The Rassi score is currently the only used clinical score with a strong association with mortality, but it lacks specificity when identifying individuals at risk of SCD. Ventricular restitution dynamics, a key factor in SCD occurrence, are difficult to assess on a large scale due to invasiveness and cost. Therefore, this study aims to develop ECG-based indices for ventricular restitution and evaluate their correlation with SCD risk in ChHD patients.

Methods: We analyzed 24-hour ECG recordings from 145 ChHD patients, among whom 41 had the primary SCD endpoint within the follow-up period. We derived ECG restitution indices quantifying changes in QT and T-peak-to-end intervals (Tpe) with heart rate ($\Delta\alpha^{QT}$ and $\Delta\alpha^{Tpe}$), as well as changes in the overall T-wave morphology (*TMR*), or Tpe morphology (*TpeMR*). We then evaluated the association of these indices with SCD using survival analyses.

Results: Upon comparison between SCD and non-SCD groups, significant differences in clinical variables were found for Rassi score ($p < 0.001$), $\Delta\alpha^{Tpe}$ ($p=0.015$) and *TpeMR* ($p=0.033$). Univariate Cox analysis revealed that $\Delta\alpha^{Tpe} > 0.0269$ and *TpeMR* > 0.0254 outcomes were associated with SCD risk, with a hazard ratio of 2.57 (95% confidence interval [CI]: 1.34-4.91; $p = 0.004$) and 2.38 (95% CI: 1.25-4.50; $p = 0.007$), respectively. Multivariate Cox proportional hazard model was constructed by adjusting Rassi Points and, as a result, only $\Delta\alpha^{Tpe} > 0.0269$ showed a significant hazard ratio (2.22; $p = 0.016$).

Conclusions: This study demonstrates that ECG indices assessing late-phase ventricular repolarization restitution serve as robust and independent predictors of SCD in ChHD. The fact that *TMR* and $\Delta\alpha^{QT}$ weren't associated with SCD suggest that ChHD may have other effects on ventricular repolarization, manifested on the earlier part of the T-wave, which masks the arrhythmogenic substrate specifically linked to SCD.