A Novel Strategy Based On Dynamic Analysis Of Cardiac Repolarization Predicts Mortality In Patients With Implantable Cardioverter-Defibrillators

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INTRODUCTION

We wish to identify patients at risk for sudden cardiac death (SCD). Prior studies have proposed that, in illness, organs uncouple signaling pathways, and entropy of their actions increases. Entropy is fundamentally different from variability analyses, and has not been explored in this field. We hypothesized that the QT entropy in normal sinus rhythm (NSR) predicts mortality in heart failure patients.

METHODS

QT intervals were collected from 5-min ECGs of 573 consecutive patients in NSR and receiving optimal medical therapy at time of ICD implantation. H&P, labs, biomarkers, and imaging data were also collected. SCD was defined as ICD shocks for ventricular tachyarrhythmias (VT/VF) or deaths from VT/VF not corrected by the ICD, and served as the primary endpoint.

The coefficient of sample entropy (CoSEn) was used to measure entropy of the QT interval time series. Unlike traditional HRV measures, entropy quantifies the degree to which fluctuation patterns of repolarization repeat, and can provide insight into coupling between signaling processes not available otherwise.

RESULTS

Over 51±28 months, 205 patients (36%) experienced SCD (N=97) or died from other causes (N=108). Baseline QT entropy of the SCD (-3.0±0.65) and total mortality (-3.0±0.63) groups was significantly higher than those alive (-3.3±0.56; p<0.0000001). In contrast, there were no significant changes in time and frequency domain analyses (i.e., SDNN, HF, LF, QTVi).

In multivariate analysis, QT entropy was the strongest predictor (p<0.001) after taking age, gender, risk factors, NYHA class, duration of follow-up, medications, labs, biomarkers, ejection fraction, and all HRV metrics into account. In a Cox proportional hazards model with all clinical parameters, the 5th quintile of QT entropy added predictive value for SCD [HR=3.8 (95% CI:1.7-8.2)] and total mortality [HR=2.7 (1.7-4.4)].

CONCLUSIONS

Higher entropy of cardiac repolarization is strongly associated with SCD and total mortality risk. This finding is consistent with modern views of dynamical changes in physiology. Compared to linear ECG metrics, entropy expands on simpler concepts of variability and provides additional prognostic insight into the dynamic heterogeneity of ventricular repolarization.