IMPROVING SUDDEN CARDIAC DEATH RISK STRATIFICATION IN PATIENTS WITH ISCHAEMIC CARDIOMYOPATHY: A COMBINED ELECTROCARDIOGRAM AND PLASMA BIOMARKER APPROACH


Introduction: Sudden cardiac death (SCD) risk prediction has substantial limitations. The Regional Restitution Instability Index (R2I2) is a promising new ECG-based biomarker of SCD. R2I2 uses the surface 12-lead ECG to quantify regional heterogeneity of electrical restitution, a property of ventricular myocardium implicated in arrhythmogenesis. We investigated the potential of a combined R2I2 and amino-terminal pro-B-type natriuretic peptide (NT-proBNP) SCD risk marker in an ischaemic cardiomyopathy cohort.

Methods: Blinded, prospective, observational study of 55 ischaemic cardiomyopathy patients (age: 67±9 years, ejection fraction: 31±10%) undergoing risk stratification for an implantable cardioverter defibrillator (ICD). R2I2 was calculated using a pre-defined technique: an electrophysiology study is performed and ECG surrogates for action potential duration (QRS-onset to T-peak) and diastolic interval (T-peak to QRS-onset) are used to measure heterogeneity of electrical restitution. Plasma samples obtained on the day of the ICD procedure were assayed for NT-proBNP. A pre-defined R2I2 cut-off (1.03) was combined with an optimal log NT-proBNP cut-off (2.65) to investigate the potential of a combined risk marker.

Results: During median follow up of 22 months, 15 patients experienced ventricular arrhythmia (VA)/SCD. R2I2 was significantly higher in patients experiencing VA/SCD than those not (mean±SEM: 1.12±0.05 vs 0.84±0.09, p=0.004). R2I2 was independent of age, gender, left ventricular ejection fraction, QRS duration and log NT-proBNP in prediction of endpoint (Cox model, p=0.002). Partitioning patients using a log NT-proBNP≥2.65 gave a significantly higher rate of VA/SCD in those with high versus low log NT-proBNP (38% vs. 6%, p=0.01). Patients with R2I2≥1.03 and log NT-proBNP≥2.65 had a hazard ratio for VA/SCD 17.2 times that of patients negative for both (Cox model, p=0.007). Kaplan Meier analysis (Figure 1) showed significant separation in rates of VA/SCD in patients stratified by R2I2≥1.03 and log NT-proBNP≥2.65 (log-rank, p<0.0001).

Conclusion: A combined R2I2+NT-proBNP risk marker identifies patients at particularly high risk of ventricular arrhythmia/SCD. These patients might benefit from careful treatment optimisation. R2I2+NT-proBNP might retain sufficient positive predictive value for application to lower risk cohorts.

Figure 1. Kaplan-Meier curves illustrating rates of VA/SCD in patients stratified using R2I2 and NT-proBNP.