

Heterogeneity of right ventricular refractory period: a novel prognostic predictor in type-1 Brugada

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Risk stratification in Brugada syndrome (BrS) is needed especially for the choice of an Implantable Cardiac Defibrillator (ICD). To date the predictive value of either clinical or conventional electrophysiological indexes in type 1 electrocardiographic pattern BrS is rather low.

We aimed to evaluate the eventual prognostic significance of refractoriness heterogeneity of right ventricular outflow tract, an emergent relevant pathophysiological substrate, at electrophysiological study (EPS) in patients with BrS.

From 5 centers 348 patients were retrospectively selected (age 44 ± 15 years, males 68%). Eighty-five (24%) patients had an ICD. EPS was proposed in patients with spontaneous type-1 ECG pattern regardless of symptoms, or in patients with drug-induced type-1 ECG pattern with symptoms (n = 174). The difference in the refractory period between the right ventricular outflow tract and the apex (Δ RP_{RVOT-apex}) at EPS was evaluated as a prognostic factor. The optimal Δ RP_{RVOT-apex} cutpoint for prognosis prediction was calculated through a P-spline hazard ratio analysis. Thus, Δ RP_{RVOT-apex} was compared through different statistical analyses to other other clinical or conventional electrophysiological prognostic indexes previously described in literature.

During a 36-month median follow-up (range 6-228) 3 SCD and 10 appropriate ICD shocks (aborted SCD, aSCD) occurred. Fifty patients (29%) had a positive EPS (induction of sustained ventricular tachycardia, VT, or ventricular fibrillation, VF, during the procedure). At multivariable logistic analysis, only Δ RP_{RVOT-apex} and late potentials remained independent predictors of a positive EPS. At Cox Proportional Hazard analysis, family history of SCD, history of syncope, VT/VF inducibility and a Δ RP_{RVOT-apex} >60 ms were all univariate predictors of SCD/aSCD. At bivariate analysis, a Δ RP_{RVOT-apex} >60 ms remained an independent predictor of SCD/aSCD even when adjusted the other univariate predictors. At C-Statistic analysis, the strongest predictive model was the one using Δ RP_{RVOT-apex} >60 ms as covariate with a C-statistics (95% CI) of 0.72 (0.51-0.93). At Kaplan-Meier curves, Δ RP_{RVOT-apex} >60 ms was confirmed a strong predictor of SCD/aSCD and another very interesting observation was possible: patients with positive EPS, but a Δ RP_{RVOT-apex} < 60 ms, had a similar risk to SCD/aSCD compared to patients with a negative EPS, while those with a positive EPS and a Δ RP_{RVOT-apex} > 60 ms were found to be at a higher risk of events.

Refractory period heterogeneity of the right ventricle defined as Δ RP_{RVOT-apex} > 60 ms at EPS is a strong and independent predictor of SCD/aSCD in patients with BrS, beyond VT/VF inducibility at EPS and common clinical predictors.

Abstract Figure.

