Concordant Increase of Post-pacing Action Potential Duration and Contractility Predicts Occurrence of Ventricular Arrhythmia in Brugada Syndrome Model

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Introduction: Mechano-electrical coupling from integration of action potential duration (APD) and contractility plays an important role in arrhythmogenesis but not clear in Brugada syndrome. We investigate whether distinctive mechano-electrical coupling may contribute to the genesis of ventricular arrhythmias (VAs) in Brugada syndrome.

Methods: Conventional microelectrodes were used to record the electrical and mechanical activity simultaneously in right ventricular outflow tract rabbit tissue preparations before and after receiving transient outward current enhancer (NS 5806, 10 μM), a ATP sensitive potassium channel opener (Pinacidil, 2 μM), and a sodium channel blocker (Pilsocanide, 5 μM) for Brugada model construction. Events of VAs were recorded under rapid electrical pacing (cycle lengths from 1000 to 100ms) with or without NCX inhibitor (KB-R7943, 10 μM).

Result: There were 13 (12.4%) episodes of triggered ventricular tachycardias (VTs) (Group 1) and 92 (87.6%) of non-inducible VTs (Group 2) in Brugada model rabbits. The first occurrence of post-pacing APD in group 1 had increasing APD90 (APD90, 48.4±8.3% versus 11.6±2.0%, P = 0.001) and contractility (348.2±56.7% versus 178.2±14.8%, P < 0.001) than group 2 (Table 1). Triggered VT was common (75%) in those with ∆APD90 >15% and ∆Contractility >270%, but not detectable in ∆APD90 <15% and ∆Contractility <270% (Figure). A cut-off value of product of “∆Contractility and ∆APD90” above 1.29x104 (%%) would predict 100% genesis of VTs. In those with pacing-induced VTs, KB-R7943 significantly reduced the occurrence of VT from 100.0% to 23.1% (P <0.001). After multivariate analysis, the “ΔContractility x ΔAPD90” (OR: 35.77, P = 0.039) and “ΔContractility/ΔAPD90” between 2-7 (OR: 186.93, P = 0.033) were independent predictors of triggered VAs (Table 2).

Conclusion: Concordant increase of post-pacing APD and contractility results in the occurrence of VAs in the triggered Brugada model. NCX inhibition may be a potential therapeutic strategy for Brugada syndrome.