

J Wave syndromes. Mechanistic insights into arrhythmogenesis and therapy

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Cardiac arrhythmias associated with Brugada syndrome (BrS) or an early repolarization (ER) pattern in the inferior or infero-lateral ECG leads are mechanistically linked to accentuation of transient outward current (I_{to})-mediated J waves. Although BrS and ER syndrome (ERS) differ with respect to magnitude and lead location of abnormal J waves, they are thought to represent a continuous spectrum of phenotypic expression termed J wave syndromes. ERS is divided into three subtypes with the most severe, Type 3, displaying an ER pattern globally in the inferior, lateral and right precordial leads. BrS has been linked to mutations in 18 different genes, whereas ERS has been associated with mutations in 7 different genes. In both ERS and BrS, ion channel gene mutations cause an outward shift in the balance of current, thus accentuating the action potential notch in ventricular epicardium and leading to the development of phase 2 reentry and polymorphic VT. These **repolarization defects** give rise to fractionated electrogram activity and high frequency late potentials in epicardial bipolar electrograms nearly identical to those recorded from the right ventricular outflow tract of patients with BrS. Hypothermia as well as ischemia potentiate the development of both ERS and BrS. Therapy in both congenital and acquired syndromes is geared toward producing an inward shift in the balance of current active during the early phases of the ventricular epicardial action potential. This is accomplished by inhibition of I_{to} using quinidine or augmentation of calcium channel current (I_{Ca}) together with inhibition of I_{to} using cilostazol or milrinone.