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Subtle microstructural abnormalities in BrS, ERS, and IVF : An underlying cardiomyopathy?

Elijah Raphael Behr

Professor of Cardiovascular Medicine and Consultant Cardiologist and Electrophysiologist Director, Cardiovascular and Genomics Research Institute, St George's, University of London St George's University Hospitals NHS Foundation Trust, London Mayo Clinic Healthcare, London

Traditionally, arrhythmia syndromes associated with an apparently structurally normal heart have been thought of as primary electrical disorders, often due to hereditary channelopathies. Data from human pathology studies and epicardial mapping and ablation studies has suggested, however, that a subepicardial substrate of subtle microstructural abnormalities (fibrosis) is present in the right ventricular outflow tract of high-risk patients with Brugada syndrome (BrS). This observation has been extended to sudden cardiac arrest survivors with the early repolarisation pattern (ERP) evident in the inferolateral leads, the early repolarisation syndrome (ERS), and in BrS patients who also exhibit ERP (AKA global J wave syndrome). ERP-associated fibrosis tends to locate to the inferior right ventricular and inferolateral left ventricular subepicardial regions. Ablation of delayed and low amplitude signals associated with the type 1 Brugada ECG pattern and/or ERP, and amelioration of the ECG patterns themselves, leads to a reduction in ICD therapies in high-risk patients. Pathogenic SCN5A variants, associated with conduction delay and potentially myocardial fibrosis, have been identified in some patients with BrS and ERS. More recent epicardial ablation studies in patients with unexplained cardiac arrest and no sign of BrS or ERS (idiopathic VF), have also identified many with similar areas of abnormal signals. These regions appear to act as anchor points for VF drivers during body surface mapping of induced VF. Recent genetic studies have identified pathogenic variants in cardiomyopathy genes amongst patients with idiopathic VF. These findings have led to the proposal that the underlying pathology in BrS, and much of ERS and idiopathic VF, is a spectrum of subepicardial cardiomyopathy that can only be detected in vivo on the ECG and/or during mapping studies or at post-mortem by histopathology. Appreciating this paradigm will lead to a more personalised and granular approach to diagnosis and therapy.