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EDITORIAL COMMENT

Ventricular Fibrillation Inducibility in the Early Repolarization Syndrome

We Still Haven't Found What We're Looking For*

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The early repolarization (ER) pattern is a frequent electrocardiographic (ECG) finding, seen in 1% to 30% of the general population (1–8). However, the long-established concept that ER is benign was recently challenged by several case-control studies, in which increased prevalence of ER was seen in survivors of cardiac arrest because of idiopathic ventricular fibrillation (VF) (9–11). Subsequent population studies further stressed the association between the ER pattern and increased risk of arrhythmic or cardiac mortality (3–5).

Besides the observed similarities in their underlying mechanism and some clinical manifestations (12), much current research around the ER pattern mimics the early years after Brugada syndrome (BrS) was first described (13). Considerable confusion has been created around the ECG features that define early repolarization syndrome (ERS) (14,15), similar to mixing of the diagnostic type 1 pattern with other non-diagnostic patterns in early BrS investigations. The classical definition (2,6) considered ER as the presence of ST-segment elevation, J-wave, and symmetrical tall T-wave, and it is not associated with increased risk of cardiac death (6). However, studies suggesting an increased risk for arrhythmic death focused on the J-wave notch or slur on the inferolateral leads, independent of ST-segment changes (3–5,9–11). Moreover, there is a discrepancy between the definition of the ER pattern using the American College of Cardiology/American Heart Association/Heart Rhythm Society recommendations for standardization and interpretation of the ECG (a normal variant, commonly characterized by J-point elevation and rapidly up-sloping or normal ST-segment) (16), and the Heart Rhythm Society/European Heart Rhythm Association/Asia Pacific Heart Rhythm Society Expert Consensus on Inherited Primary Arrhythmia Syndromes (≥1-mm elevation of the J-point in ≥2 contiguous inferior and/or lateral leads of a standard ECG) (17), which may account for conflicting data regarding ER's prognostic value. To avoid confusion, clinicians should use standard definitions to clearly differentiate classical, benign ER from the revised version associated with increased risk of sudden death.

Risk stratification has profound clinical relevance, particularly with such a prevalent ECG finding (up to 58% in marathon runners) (18), with a low lifetime risk of VF (only 1 in 3,000) (19). Unfortunately, identification of high-risk patients in the presence of ER remains extremely challenging. Criteria for distinguishing benign from malignant ER patterns remain rudimentary, and surface ECG is the only currently available tool. A horizontal or descending ST-segment elevation is associated with worse outcomes (compared with a rapidly ascending ST-segment elevation) following J-point elevation (20,21). The magnitude of the J-point elevation may also have prognostic significance: a slurred or notched J-point elevation ≥2 mm (0.2 mV) appears associated with a higher risk (3,21). Other findings, such as localization of the ER pattern in inferior or inferolateral (compared with lateral) leads (3) or extension of ER into a BrS pattern, may also represent a worse prognosis (22–24). Nevertheless, as in BrS, temporal variation in expression of ECG patterns must be considered. These ECG characteristics are clearly insufficient for risk stratification in patients with an ER pattern, and new methods are critically needed.

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In this issue of the *Journal*, Mahida et al. (25) present an intriguing electrophysiology study (EPS) of ventricular stimulation in 81 VF survivors diagnosed with ERS. The ER pattern definition required QRS slurring or S-wave notching, in addition to ≥1-mm elevation of the J-point in ≥2 contiguous inferior and/or lateral leads. Other structural diseases or inherited primary arrhythmia syndromes were excluded. They found that VF was infrequently (22%) inducible and not useful for predicting further implantable cardioverter-defibrillator shocks during 7.0 ± 4.9 years of follow-up. Despite this negative result, the authors should be praised for designing a comprehensive study and gathering a relatively large cohort of patients undergoing an EPS in an attempt to refine risk stratification in ERS.

Traditionally, VF induction during an EPS has been regarded cautiously, as it may appear in between 6% and 9% of individuals without a history of structural heart disease or arrhythmias (26–28). In 2 studies, the stimulation protocol was prematurely terminated if nonsustained polymorphic ventricular tachycardia was induced; a significantly higher rate was, therefore, expected (27,28). The low VF induction rate in cardiac arrest survivors diagnosed with ERS (with documented VF during the event) is rather surprising and banishes any hope of using EPS to diagnose ERS in asymptomatic patients with a "suspicious" ER pattern on ECG. It raises the question of whether the underlying mechanisms of ER are closely linked to BrS. By contrast, studies in BrS have shown increased probability of VF inducibility in symptomatic (up to 81%) (29) and asymptomatic patients with a type 1 ECG pattern (up to 40%) (30), although the role of EPS for risk stratification remains controversial. This study should prompt further research to clarify these discrepancies.

This paper brings the complexity of risk stratification of patients with ERS (even more for asymptomatic patients with an ER pattern) to the forefront. Further research is warranted to better understand of clinical entity and for development of better diagnostic and risk stratification tools.

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