Journal of the American College of Cardiology
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Published by Elsevier Inc.

Vol. 61, No. 8, 2013
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2012.11.052

EDITORIAL COMMENT

Early Repolarization: A Benign Electrocardiographic Pattern or an Ominous Proarrhythmic Sign?*

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It is a relatively common experience for a clinical cardiologist to read electrocardiograms (ECGs) with ST-segment and J-point elevation and make a diagnosis of an early repolarization (ER) pattern (1,2). These alterations are predominantly observed in young active males and have long been considered of benign significance. Enhanced parasympathetic activity and increased cardiovascular fitness are the most common explanation for these ECG alterations (1–3).

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A growing number of recent reports (4–6), however, have associated J-wave elevation or pathological J wave (i.e., one of the typical ECG characteristics of the ER pattern) with an increased risk of cardiac sudden death and primary ventricular fibrillation. Haissaguerre et al. (4) were the first to describe an increased prevalence of J-point elevation in patients with idiopathic ventricular fibrillation. Cappato et al. (5) confirmed this observation in athlete victims of sudden cardiac death. In a recent paper, Tereshchenko et al. (7) reported that in patients with implantable cardioverter-defibrillators with structural heart disease, a transient elevation of the relative intracardiac J-point amplitude was detectable before the onset of polymorphic ventricular tachycardia/fibrillation. Unfortunately, there was no significant correlation between far-field electrogram J-wave amplitude and J-point elevation on surface ECG, thus leaving unsettled the predictive value of this QRS abnormality when only the surface ECG is considered (7).

These and other observations (5–8) have generated doubts about the benign interpretation of the ER pattern and have stimulated a lively debate on its clinical significance. The possibility that in the broad and variable definition of ER we include different types of patients, and probably different diseases, is the most likely explanation for these contrasting results (9). Indeed, we have only limited information on the clinical significance of ER in relation to the age of the patients, the presence or absence of structural heart disease, or the type and localization of these ECG abnormalities.

In this issue of the *Journal*, Walsh et al. (10) provided an important step in the understanding of the definition, natural history, and prospective association of cardiovascular risk factor with ER. The researchers collected data on 5,060 participants from the CARDIA (Coronary Artery Risk Development in Young Adults) cohort over 20 years and were able to analyze the prevalence of ER in asymptomatic individuals and identify predictors of ER maintenance over time. A definite ER pattern was present in 18.6% of participants at baseline but only in 4.9% after 20 years. Younger age, black race, male sex, longer exercise capacity, and QRS duration were among the most relevant parameters associated with the presence of ER. In the majority of participants, there was a spontaneous regression of ER pattern by middle age. Black race, lower body mass index, and longer QRS duration were independently associated with maintenance of ER over time. The researchers have to be commended for several aspects of the study: the large study population; the use of a precise and coded ECG definition of ER; and the description of the natural history of ER in relation to maintenance, regression, and development over time. Indeed, only 31 participants developed an ER pattern within the 20-year duration of the study and, of particular interest, only 21 deaths were attributable to cardiovascular disease during the entire follow-up period.

These results reassure the clinical cardiologists but need to be considered in a more general context. First of all, the study population consisted of young, healthy, physically active individuals rather than middle-aged men with possible but undetected structural heart disease. Second, the definition of ER coded in the study was based on the presence of a prominent J wave and upward concavity of the ST-segment elevation in V_3 to V_6 precordial leads. In contrast, there were few participants with >1.00 mm ST-segment elevation in any lead, including I, II, III, and aVF, and they were classified as "possible" phenotypes of ER with almost no progression to the definite ER pattern over time. The study therefore provided strong evidence that this young population with an up-sloping ST-segment elevation was indeed at low risk, leaving unaddressed the question whether a different ER pattern with J waves followed by horizontal ST-segment elevation should be viewed as potentially arrhythmogenic (8,9). The clinical relevance of the presentation pattern was also indicated by the results of a recent study that showed an inverse correlation between the slope of ST-segment elevation and mortality risk in a large black population (11).

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The small number of deaths observed during the follow-up period confirmed the favorable prognosis of these participants; on the other hand, any robust statistical analysis of the factors associated with mortality was prevented. An additional limitation of the study that deserves consideration was the high percentage of dropout at the 20-year follow-up visit. As indicated in the Online Table, black race and longer QRS duration, which were associated with maintenance of ER, were also associated with loss to follow-up, thus making possible an overestimation of the declining prevalence of ER and an underestimation of the number of deaths (10). Nevertheless, the study provided additional interesting pathophysiological insight that may justify the low cardiovascular death rate observed in these individuals. For example, the longer duration of QRS in participants with a persistent ER pattern was likely due to the slurring of the final part of QRS due to J-wave presence rather than an intraventricular conduction defect secondary to structural abnormalities; if present, participants with ER ECG alterations were characterized by a reduced left ventricular mass. A lower resting heart rate was also prevalent in these individuals, supporting the presence of a better cardiovascular fitting and a more physiological modulation of sinus node in this low-risk group (12).

This study provided additional and relevant support to the concept that J-wave and ST-segment elevation that characterize ER pattern could be categorized into 2 main types: type A, which is mainly detected in young, asymptomatic, physically active males, more often of black race, with a predominant ST-segment elevation in the precordial leads and type B, which includes middle-aged individuals with prominent J-wave and horizontal ST-segment elevation (8). In the latter group, J-wave amplitude could reflect an increased dispersion of ventricular repolarization (i.e., an electrophysiological alteration that may favor the occurrence of malignant ventricular arrhythmia under specific conditions such as acute myocardial ischemia or sympathetic activation) (12).

In the future, this hypothesis should be validated in appropriate registries and type B ER individuals should be evaluated in terms of risk prediction. It is unknown at the moment if use of the most common noninvasive methodologies such as heart rate variability, heart rate turbulence, or micro T-wave alternans analysis could be used to identify individuals at higher risk (12).

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Key Words: J waves ■ ST-segment elevation ■ sudden cardiac death.