LETTER TO THE EDITOR

Risk Stratification of Patients with Early Repolarization . . . Still an Unresolved Matter!

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The study by Stavrakis S et al. "Development and Validation of a Prognostic Index for Risk Stratification of Patients with Early Repolarization"[1] proposes a risk stratification model for patients with early repolarization (defined as J-point elevation ≥0.1 mV in inferior/lateral leads). Their model, including the parameters *older age*, *lower body mass index*, *non-African American race*, *current use of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers or sulfonylureas*, *prolonged corrected QT*, and *higher ER amplitude*, revealed good calibration and discrimination for the prediction of all-cause mortality.

Their study deserves some additional considerations:

1. Their control group showed a higher mortality rate, suggesting a potential malignant role for ER. As the authors propose, J-point elevation may be a risk factor for fatal arrhythmias in the presence of additional proarrhythmic triggers such as acute myocardial ischemia. Transmural dispersion of ventricular repolarization associated with ER/J-wave patterns may not be arrhythmogenic by itself, but further increases in the net repolarizing current with subsequent loss of the epicardial action potential dome and a more profound dispersion of repolarization may lower the threshold for early afterdepolarizations and create an optimal electric substrate for phase-2 reentry capable of initiating ventricular fibrillation. The fact that older age was a strong predictor of mortality supports this notion, as cardiac ischemic events are an important cause of mortality in elderly individuals. Recently published studies have endorsed this theory.[2–5]
2. Proarrhythmic triggers like left ventricular dysfunction and/or chronic heart failure warranting treatment with angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (included in the model) can also be potential triggers for ER-associated arrhythmogenesis.[6] Additional triggers could include a prolonged corrected QT interval, a known risk factor for sudden cardiac death.
3. Left ventricular hypertrophy (LVH) was more frequent in patients with ER (vs controls), which could have influenced the higher mortality rate among them, as LVH is a strong and independent predictor of mortality. An analysis excluding patients with LVH would be useful.
4. Leads V1–V3 were not interpreted to avoid confusion with ECG patterns of Brugada syndrome (BrS) or right ventricular dysplasia. In ER, the ST segment elevation is attributed

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to shortening of ventricular action potential duration in epicardial regions resulting in a current similar to the subepicardial injury currents of the BrS. Differences between ER and the BrS concerning lead localization are important, but the ER ECG pattern has been shown to be readily convertible to the Brugada one in experimental models.[7] Therefore, excluding V1–V3 leads from interpretation may be arguable.

5. To avoid duplication of data, only the first ECG for each patient was used in the mortality analysis. Pérez-Riera AR and colleagues analyzed clinical-electrocardiographic distinction parameters between benign and malignant ER syndromes and suggested the latter were associated with dynamic and inconstant ST/T waves, with frequent dramatic changes in morphology.[8] Stavrakis S et al. could have evaluated whether dynamicity of J-wave patterns was associated to increased mortality risk, a phenomenon described for the BrS.
6. Obesity was also independently associated with a lower risk of mortality in patients with ER. If additional proarrhythmic triggers are needed for uncovering the malignant role of ER, this subject adds some controversy. Obese patients are more frequently admitted for acute coronary syndrome (ACS), although their mortality during hospitalization seems lower (the *obesity paradox*). We would therefore expect malignant ER patterns to associate with increased mortality in this population. Nevertheless, these patients are probably more often treated with antiplatelet agents or statins, which decrease their risk of ischemic events.
7. The apparent lack of an association between ER and mortality in African-American individuals remains controversial as well, as these patients have usually an increased cardiovascular risk profile and therefore would also be expected to suffer cardiac death more often in the context of myocardial ischemia and previous baseline ER.
8. Therapeutic implications of a prognostic score such as the one developed by Stavrakis S et al. may eventually extend to the need of more aggressive cardiovascular primary prevention in patients with high-risk ER patterns. Prevention of proarrhythmic triggers such as an ACS through comprehensive cardiovascular risk factor modification is probably more important than considerations regarding ICD implantation or antiarrhythmic therapy.

REFERENCES

1. Stavrakis S, Patel N, Te C, et al. Development and validation of a prognostic index for risk stratification of patients with early repolarization. Ann Noninvasive Electrocardiol 2012;17:361–371. doi: 10.1111/j.1542-474X.2012.00533.x.
2. Tikkanen JT, Wichmann V, Junttila MJ, et al. Association of early repolarization and sudden cardiac death during an acute coronary event. Circ Arrhythm Electrophysiol 2012;5:714–718.
3. Rudic B, Veltmann C, Kuntz E, et al. Early repolarization pattern is associated with ventricular fibrillation in patients with acute myocardial infarction. Heart Rhythm 2012;9:1295–1300.
4. Naruse Y, Tada H, Harimura Y. Early repolarization is an independent predictor of occurrences of ventricular fibrillation in the very early phase of acute myocardial infarction. Circ Arrhythm Electrophysiol 2012;5:506–513.
5. Patel RB, Ilkhanoff L, Ng J, et al. Clinical characteristics and prevalence of early repolarization associated with ventricular arrhythmias following acute ST-elevation myocardial infarction. Am J Cardiol 2012;110:615–620.
6. Pei J, Li N, Gao Y, et al. The J wave and fragmented QRS complexes in inferior leads associated with sudden cardiac death in patients with chronic heart failure. Europace 2012;14:1180–1187.
7. Yan GX, Antzelevitch C. Cellular basis for the Brugada syndrome and other mechanisms of arrhythmogenesis associated with ST segment elevation. Circulation 1999;100:1660–1666.
8. Pérez-Riera AR, Abreu LC, Yanowitz F, et al. "Benign" early repolarization versus malignant early abnormalities: Clinical-electrocardiographic distinction and genetic basis. Cardiol J 2012;19:337–346.