LETTER TO THE EDITOR

Further Insights into the Issue of Risk Stratification of Patients with Early Repolarization

Stavros Stavrakis, M.D., Ph.D., and Ralph Lazzara, M.D.

From the Department of Medicine, Cardiovascular Section and Heart Rhythm Institute, University of Oklahoma Health Sciences Center, Oklahoma City, OK

Ann Noninvasive Electrocardiol 2013;18(2):212–213

As we have pointed out in the discussion of our results, and reiterated by the authors in their letter, J-point elevation, which indicates transmural heterogeneity in ventricular repolarization, predisposes individuals to fatal arrhythmias during cardiac ischemic events, rather than being per se arrhythmogenic. The results of a large community based study support this hypothesis.²

According to our analysis, the presence of cardiomyopathy was not significantly associated with total mortality.¹ However, our data do not allow us to examine for the role of all potential triggers of early repolarization (ER)-related arrhythmogenesis. Although we controlled for known confounders, such as cardiomyopathy, we were not able to control for unknown confounding factors.

The association of ER with increased mortality (vs controls) in our patient population remained essentially unchanged, even after statistically adjusting for the presence of left ventricular hypertrophy ($P = 0.03$). Another way to control for the imbalance between the two groups is to exclude patients with left ventricular hypertrophy, as suggested by the authors. We opted to statistically adjust for left ventricular hypertrophy, because excluding patients would have reduced power.

To be consistent with the definition of ER used in major ER studies,^{2–4} we did not interpret leads V_1 – V_3 . Moreover, although ER and Brugada syndrome are part of the same spectrum of diseases, collectively called J-wave syndromes,⁵ there are major differences between these two entities, as indicated by the heterogeneous response to isoproterenol⁶ or ajmaline.⁷ Therefore, we believe that our decision to exclude leads V_1 – V_3 is justified.

We found that in our cohort, J-point elevation remained stable over time. Similar stability of J-point elevation over time was shown in a large community-based cohort study.² On the contrary, it was previously reported that in patients with ER-associated ventricular fibrillation, there is an often dramatic accentuation of J-point elevation before the onset of the arrhythmia.^{3,8} These findings reinforce the notion that in patients with idiopathic ventricular fibrillation, whose predominant arrhythmogenic mechanism is related to ER, the dynamic nature of J-point elevation may reflect a highly arrhythmogenic substrate, whereas in the general population with ER, this abnormality may not be sufficient to produce an arrhythmia, but rather has to interact with other factors (e.g., ischemia). Although examining whether

Address for correspondence: Stavros Stavrakis, M.D., Ph.D., University of Oklahoma Health Sciences Center, Heart Rhythm Institute, 1200 Everett Dr, TCH 6E103, Oklahoma City, OK 73104. Fax: +405-271-2619; E-mail: stavros-stavrakis@ouhsc.edu

*We thank Drs. Barra and Providencia for their interest in our study.*¹

dynamicity of J-wave patterns was associated to increased mortality risk would have been very informative, due to the retrospective nature of our data, we were not able to analyze ECGs before any arrhythmic events.

The hypothesis that increased use of antiplatelet agents or statins, which in turn prevent ischemic events may explain the protective effect of obesity in patients with ER is interesting and merits further investigation. Nonetheless, based on the available evidence, the reasons for obesity being protective in our population remain unclear.

African Americans probably have a more benign variant of ER, which despite their unfavorable cardiovascular profile, does not lead to increased vulnerability to ischemic ventricular fibrillation. This notion is supported by two recent population-based studies, which showed that, although ER is more prevalent in African Americans, it does not confer an increased risk of cardiovascular or arrhythmic death in this population.^{9,10}

Finally, we completely agree with the need for more aggressive cardiovascular primary prevention in patients with high-risk ER features, to prevent arrhythmogenic triggers, such as acute coronary syndromes.

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.
2. Tikkanen JT, Anttonen O, Junttila MJ, et al. Long-term outcome associated with early repolarization on electrocardiography. *N Engl J Med* 2009;361:2529–2537.
3. Haissaguerre M, Derval N, Sacher F, et al. Sudden cardiac arrest associated with early repolarization. *N Engl J Med* 2008;358:2016–2023.
4. Sinner MF, Reinhard W, Muller M, et al. Association of early repolarization pattern on ecg with risk of cardiac and all-cause mortality: A population-based prospective cohort study (monica/kora). *PLoS Med* 2010;7:e1000314. doi:10.1371/journal.pmed.1000314
5. Antzelevitch C, Yan GX. J wave syndromes. *Heart Rhythm* 2010;7:549–558.
6. Roten L, Derval N, Sacher F, et al. Heterogeneous response of j-wave syndromes to beta-adrenergic stimulation. *Heart Rhythm* 2012;9:1970–1976.
7. Roten L, Derval N, Sacher F, et al. Ajmaline attenuates electrocardiogram characteristics of inferolateral early repolarization. *Heart Rhythm* 2012;9:232–239.
8. Nam GB, Kim YH, Antzelevitch C. Augmentation of j waves and electrical storms in patients with early repolarization. *N Engl J Med* 2008;358:2078–2079.
9. Olson KA, Viera AJ, Soliman EZ, et al. Long-term prognosis associated with j-point elevation in a large middle-aged biracial cohort: The aric study. *Eur Heart J* 2011;32:3098–3106.
10. Perez MV, Uberoi A, Jain NA, et al. The prognostic value of early repolarization with st-segment elevation in african americans. *Heart Rhythm* 2012;9:558–565.