LETTER TO THE EDITOR

T-Wave Alternans, ST-Segment Depression, Left Ventricular Hypertrophy, and Mortality Risk in Patients with Ischemic Cardiomyopathy: Some Possible Confounding Factors

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The study by Friedman et al.,¹ published in the July 2013 issue of the *Journal*, is interesting, and of practical importance for clinicians caring for patients with ischemic cardiomyopathy (ICM). The authors thought of combining the response to T-wave alternans (TWA) testing via invasive right atrial pacing, and ST-segment depression (-ST) in the resting electrocardiogram (ECG) in the assessment of mortality risk in 317 patients with ICM, left ventricular ejection fraction (LVEF) $\leq 40\%$, and documented nonsustained ventricular tachycardia, who had undergone invasive electrophysiology evaluation, in anticipation of a possible implantation of an implantable cardioverter defibrillator (ICD). The essence of their motivation was that, although ECG left ventricular hypertrophy (LVH) by the Cornell product (CP) method predicts a mortality increase in patients with ICM, the patients without CP LVH are also at high risk, and whether TWA and -ST depression in combination, will improve the risk assessment of such patients. The authors concluded from their multivariate models analysis that both positive TWA (HR 2.52) and -ST (HR 2.87) were independent predictors of mortality in patients without CP LVH, and that patients without CP LVH, negative TWA, and no -ST, had a 5.6% 3-year all-cause mortality, in comparison with the 20% mortality of the overall cohort, suggesting that such patients are unlikely to benefit from ICD implantation.

There are three possible confounding factors that, if taken into consideration in the data analyses, may lead to even higher HR for the independent mortality predictive value of TWA and -ST, and their combined performance: (1) It is known that the amplitude of the ECG QRS complexes decreases from the baseline, in patients with edematous states, in general,² and patients with heart failure (including those with ICM) during their decompensated phases³⁻⁵; indeed in such edematous patients, ECG LVH is "concealed," during phases of decompensation.⁶ Accordingly, and if such patients exist among the 317 patients with ICM, it would be informative to both analyze the subgroups of patients who at the time of their assessment were and were not in a decompensated phase of their ICM, or use for the characterization (positive or negative) for -ST and CP LVH a previous ECG with higher amplitude QRS complexes. In fact, even the magnitude of the TWA may be influenced by an edematous state, although in the present study there is no way with data at hand to evaluate TWA based on an ECG during a well-compensated phase of the illness. (2) It is common knowledge that patients with ECG LVH (including the ones diagnosed by CP LVH criteria) have tall T waves, and generous ST-elevations in the precordial ECGs (including lead V₃), and it is these leads that overwhelmingly show the highest TWA magnitude in TWA testing (this is of significance, even

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DOI:10.1111/anec.12126

when one employs the spectral method of TWA analysis, since the characterization of a test result as positive or negative is based on a specific cutoff magnitude value in μV). Accordingly it would be of interest to reanalyze the spectral TWA magnitude values after correcting them by the amplitude of the corresponding T wave(s), or even better, by the "area under the curve" of the JT interval(s).⁷ (3) One wonders whether the conclusions of the study apply equally to patients with left bundle branch block (LBBB) (3.4%–24.1% of the patients, in the four subgroups in their Table 1) or increased QRS duration ($\uparrow\text{QRSd}$) (? percentages in the four subgroups, using any conventional $\uparrow\text{QRSd}$ partition value, e.g., 110 or 120 ms) in the patients without such ECG features, due to the concern about the validity of applying CP LVH criteria, and nondifferentiation of -ST due to LVH (left ventricular strain), or -ST due to LBBB or a $\uparrow\text{QRSd}$, in such patients. A reanalysis with the exclusion of patients with LBBB and $\uparrow\text{QRSd}$ may provide an answer. The authors have proposed a very useful predictive mortality index for patients with ICM, and their contribution may be enhanced by providing a response to the above inquiries, about these three possible confounding factors in their analyses. The authors should be congratulated for their work,

and particularly for their stepwise risk stratification method involving sequential testing, first via an ECG and then via TWA testing, in evaluating patients for ICD implantation, instead of only be guided by the cut point of ≤ 30 in the LVEF.

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