Electrocardiographic Strain Pattern and Cardiovascular Prognosis in Hypertension

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There is sound evidence that the presence of typical left-ventricular strain pattern on standard electrocardiograms, ST segment depression and asymmetrical T-wave inversion on left precordial leads, is not only a marker of increased left-ventricular mass and concentric left-ventricular hypertrophy, but also a strong predictor of an unfavorable cardiovascular prognosis.

Although the exact physiopathologic mechanisms underlying the relationship between strain pattern and the occurrence of cardiovascular events are still unclear, they are probably multifactorial, involving not only the increased left-ventricular mass per se (with its higher risk of life-threatening ventricular arrhythmias and development of heart failure, and silent myocardial ischemia, particularly in the subendocardial layers due to low coronary flow reserve), but also other untoward factors associated with strain pattern, such as high blood pressure (BP) levels, the presence of diabetes and atherosclerotic vascular diseases, older age, and male gender.

In this issue of the Journal, Verdecchia et al provide further insight into this subject. For 3 years, they followed 496 hypertensive patients with electrocardiographic left-ventricular hypertrophy (ECG-LVH), defined by the Pe-rugia score, which is a multifactorial criterion that requires positivity in at least one of three different criteria: a modified Cornell voltage (≥2.4 mV in men, and ≥2.0 mV in women), the presence of typical strain pattern, or a Romhilt-Estes score ≥5 points. They demonstrated that the regression of ECG-LVH was associated with a 58% lower risk of developing a composite endpoint of fatal and nonfatal cardiovascular events after adjustment for other predictors of untoward outcome (age, gender, and diabetes). Moreover, they showed that the absence of in-treatment regression of the strain pattern was associated with a 53% lower risk of future cardiovascular morbidity and mortality. Also, this protective effect was independent of in-treatment Cornell voltage reduction, which was not significantly associated with cardiovascular prognosis.

The study has several strengths, mainly its prospective multicenter design and the novelty and clinical relevance of its findings.

However, the study also has some limitations that the authors correctly acknowledge. First, it has a relatively small number of patients and events analyzed because of a high dropout rate, mainly in the first year of follow-up. In consequence, the study was probably underpowered, for example, to show the prognostic value of Cornell voltage, if it existed. Second, some potentially important prognostic variables in cardiovascular outcome, such as BP level, lipid profile, and smoking status, were not adjusted for in the final multivariate models. The absence of adjustment for in-treatment BP reduction seems particularly important, as it is expected that individuals who regressed from ECG-LVH and its strain component were those with greater BP reductions during the study. The authors argued, during the review process, that the inclusion of nonsignificant variables in the final multivariate survival models would not provide further reduction of the likelihood ratio of the models, i.e., would not improve their predictive performance. On the contrary, such an inclusion would increase the dispersion of the models’ variability at the expense of subtracting predictive value from the significant variables. This is correct from a statistical point of view. Otherwise, a relevant clinical question, of whether the beneficial effect of strain regression on cardiovascular outcome is also independent or not of BP reductions during treatment, could not be answered.

Therefore, additional large, prospective studies are necessary, taking into consideration other potential confounders of the associations of evolutive changes of electrocardiographic voltage and strain with cardiovascular prognosis, especially reductions of BP and left-ventricular mass during treatment. In particular, it is important to establish whether regression of the strain pattern is really an independent cardiovascular protective factor in hypertension, and hence should be considered an intermediate objective of antihypertensive treat-
ment above and beyond BP control, or whether the presence of a strain pattern constitutes a composite surrogate risk marker, reflecting abnormal ventricular repolarization secondary to several unfavorable conditions, such as increased left-ventricular mass and hypertrophy, myocardial ischemia and patchy fibrosis, high BP levels, and hyperglycemia, each one determining a worse cardiovascular outcome. Until this knowledge is available, hypertensive patients presenting the typical electrocardiographic strain pattern, either at baseline or developing during treatment, should be considered at very high risk for future cardiovascular morbidity and mortality, and should be more aggressively investigated and treated.

References


