Critical Value of the Electrocardiogram in LVH: From Predictive Index to Therapeutic Reassessment

To the Editor:

Although QRS voltages for left ventricular hypertrophy (LVH) are widely recognized as an independent factor for coronary artery disease (CAD), little information is available on reversion of ST-T alterations in hypertensive subjects with electrocardiographic (ECG) criteria for LVH.

Two recent articles in *Hypertension* by Fagard et al.1 and Schneider et al.2 presented the regression of QRS voltages in treated hypertensive subjects without evidence of improvement on ventricular repolarization abnormalities. The first study, the Systolic Hypertension in Europe (Syst-Eur) Trial based on nitrrendipine therapy to which enalapril or thiazide could be added, showed that serial 1 mV increase in QRS voltage predicts cardiovascular morbidity and mortality, whereas a 1 mV regression was associated with lower cardiovascular events, without mention of the ST-T alterations. In the second study, the Cardiovascular Irbesartan Project, the reduction of QRS voltage at 6- and 18-month periods was more significant with irbesartan as compared with atenolol, but no precise information was given on the ST-T changes (see Tables 2 and 4 in the article). It is, therefore, uncertain whether all of these therapeutic measures failed to improve the ventricular repolarization abnormalities or if the investigators failed to report them. This is a critical point because QRS voltage may decrease with the lowering of blood pressure irrespective of derangement of coronary blood supply relative to LV mass. In fact, ST-T changes may precede, occur simultaneously with, or appear after the increase in QRS voltages,3 whereas the T wave inversion may carry an elevated risk for ischemic heart disease, whether in conjunction with ST depression or increased QRS voltages.4

Such “minor” alterations, often discarded as clinically meaningless and receiving little attention, provide some explanation for the increasing number of CAD reported in hypertensive subjects despite improved BP control.5 In this context, we have recently documented how these ST-T alterations in hypertensive subjects with LVH or CAD can be improved or reversed in a significant number of subjects within the first 6 months of treatment, when closer attention is given to each ECG abnormality.6

In general, these uncompleted reports on ST-T changes in hypertensive subjects with ECG-LVH1,2 probably result from the use of single QRS voltages criteria, as in the Syst-Eur trial or by the misconception that only “classical” LV strain pattern in V5, V6 is important. It should be remembered that the earliest ECG criteria by Sokolow-Lyon (1949)7 or DW Romhilt and EH Estes Jr (1968)8 included both QRS voltage with any ST segment shifts opposite to mean QRS and diphasic or inverted T wave, and that the classical LV strain pattern was included as ECG score for the increasing number of CAD reported in hypertensive patients.13,14 It is thus surprising that after several reports from the Framingham Heart Study9–11 on the predictive value of ECG-LVH (QRS voltage, ST segment shift, flat or inverted T waves), the prognostic significance of ECG-LVH is universally related to the increased QRS voltages. Other reports, such as LIFE study patients,12 included typical LV strain but on ECG recorded at a 1-year interval. In this context, a policy of obtaining ECG recordings on a more regular basis (ie, yearly in the absence of ST-T changes, but every 3 months if ST-T minor changes appear) can certainly contribute to an improved ECG diagnosis of subclinical heart disease in hypertensive patients and, more importantly, to a critical reassessment of the therapeutic measures in these patients with LVH.

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Response:
Antonio Delgado-Almeida raises the point that in contrast to QRS voltages, ST-T alterations are underreported in clinical trials on subjects with arterial hypertension. In this sense, he criticizes our recent report on the cardiac effects of antihypertensive treatment with either irbesartan or atenolol as failing to report on ST-T alterations.1 However, we did report on the presence of repolarization abnormalities at baseline and after
treatment in Tables 2 and 4 of our article, respectively. Furthermore, repolarization abnormalities were defined exactly as in the report from the Framingham study (ST depression or a strain pattern of ST depression in association with inverted or biphasic T waves, Reference 2 of our article), which was the first to show that changes in these repolarization abnormalities have prognostic implications, similar to changes in QRS voltage criteria.

In our study, we found that irbesartan leads to improvements in voltage criteria but we did not find changes in repolarization abnormalities in either the irbesartan or the atenolol treatment group. It should be noted, however, that our results are limited by the fact that we investigated patients with only mild left ventricular hypertrophy and that results may be different in patients with higher left ventricular mass or more severe repolarization abnormalities. We agree that changes in QRS voltage and in repolarization abnormalities do not need to go in parallel. Whereas QRS voltage reflects anatomic left ventricular mass to some degree, ST-T abnormalities are associated not only with left ventricular hypertrophy but also with many other factors, such as coronary heart disease, drug effects, and electrolyte disturbances.

In addition, Antonio Delgado-Almeida makes the point that the lack of awareness for ST-T alterations provides some explanation for the increasing number of patients with coronary artery disease in hypertensive patients, referring to the seventh report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7). We do not think, however, that JNC 7 can be used as a reference here, as in this report it was shown that coronary artery disease rates have dropped and this was at least partly explained by the fact that we investigated patients with only mild left ventricular hypertrophy and that results may be different in patients with higher left ventricular mass or more severe repolarization abnormalities.

Whereas QRS voltage reflects anatomic left ventricular mass to some degree, ST-T abnormalities are associated not only with left ventricular hypertrophy but also with many other factors, such as coronary heart disease, drug effects, and electrolyte disturbances.

Response: Prognostic Significance of Serial Electrocardiographic Repolarization Changes

Dr Delgado-Almeida is right in stating that the Syst-Eur investigators only considered the electrocardiographic QRS voltages in the Syst-Eur trial and that ST-T alterations have not been assessed. This is not because the Syst-Eur investigators are not convinced of the importance of ST-T alterations and consider them as clinically meaningless. It should be realized, however, that the Syst-Eur trial was a randomized placebo-controlled outcome trial in which the emphasis was on hard end points, that is, stroke morbidity and mortality as the primary end point and cardiovascular events as secondary end points. A number of other measurements and side-projects were included in the protocol but kept as simple as possible to not jeopardize the main aim of the trial and to safeguard compliance in this large long-term trial in which 198 centers and many investigators were involved. Local investigators were therefore asked to make only a few simple ECG measurements, which are considered to be representative for the electrocardiographic left ventricular mass, ie, the voltages of the R waves in leads aVL and V5, and of the S wave in lead V6, and these measurements were checked on the approximately 28 000 original ECG tracings at the coordinating office. We do not dispute the fact that ST-T alterations may be changed by antihypertensive therapy, but such changes and their prognostic implications were not assessed in the Syst-Eur trial. However, we would like to draw the attention of Dr Delgado-Almeida to a publication from the Framingham Heart Study, in which the prognostic significance of serial ECG voltage changes and of serial repolarization changes was considered in 524 men and women with ECG evidence of left ventricular hypertrophy, irrespective of blood pressure. Voltage changes and repolarization changes were analyzed separately, and each of them was found to be predictive of cardiovascular risk. A decrease in voltage and an improvement of repolarization changes reduced the risk by approximately 50%, whereas a voltage increase and worsening of repolarization were associated with a 2-fold hazard for cardiovascular disease. The Framingham investigators did not, however, assess whether the prognostic significance of serial changes in repolarization were independent of the voltage changes, or whether the changes in voltage and in repolarization ran parallel in the study participants. In addition, the causes of the ECG changes were not reported.

In summary, serial ST-T changes were not analyzed in the Syst-Eur trial, but data from the Framingham Heart Study indicate that such changes do carry prognostic information, but it is not known if this information is independent of changes in voltage.

Robert H. Fagard on behalf of the Syst-Eur investigators

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