Electrocardiography for Assessment of Hypertensive Heart Disease: A New Role for an Old Tool

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Left ventricular (LV) hypertrophy (LVH), detected either by electrocardiography (ECG) or echocardiography (ECHO), has long been recognized as a powerful predictor of serious cardiovascular (CV) sequelae.[1,2] A very large and highly consistent body of evidence indicates that LVH is not only an adaptation to increased hemodynamic load in hypertension, but is also independently associated with an enhanced risk for myocardial infarction, cardiac sudden death, congestive heart failure, and stroke in the general population, as well as in patients with systemic hypertension, coronary heart disease, chronic kidney disease, and atrial fibrillation.[1–5] Intriguingly, the cumulative incidence of cardiovascular events increases progressively with increasing LV mass (LVM), without evidence of any threshold separating the postulated "compensatory" from "pathological" LVH.[3] In other words, patients with LVM in the upper-normal range already have increased risk for CV events.[3]

Moreover, various studies suggest that LVH reversal is beneficial beyond blood pressure (BP) reduction and treatment by demonstrating that CV events occur in a higher proportion of individuals in whom LVH progresses rather than regresses.[6]

There are several determinants for the development of LVH. Hemodynamic factors such as BP, large artery structure and stiffness, and volume load are important. In addition, nonhemodynamic mechanisms such as trophic factors mediated by the sympathetic nervous system, the renin-angiotensin-aldosterone system, and other neurohormonal mediators play an important role in the development of LVH.[5,7]

ECHO is more sensitive than ECG in diagnosing LVH and may help in the more precise stratification of overall risk and in the determination of therapy for hypertensive patients.[7,8]

Furthermore, ECHO measurement of LV cavity size and of myocardial relative wall thickness allows the assessment of LV geometry.[7,8] The traditional classification of LV geometry in hypertensive heart disease comprised the condition of normal LVM and geometry and three abnormal LV geometric patterns: concentric LV remodeling, eccentric LVH, and concentric LVH.[5,7,8] These LV geometric patterns have been associated with different demographic and clinical characteristics including age, sex, metabolic factors, BP levels, LV systolic and diastolic function, hemodynamic profile, extracardiac target organ damage, and CV morbidity and mortality. In particular, it has been reported that concentric LVH, connoting severe pressure overload, is associated with worse outcome than eccentric LVH or concentric remodeling.[7,8] However, whether abnormal LV geometric patterns carry prognostic information beyond that provided by LV mass remains uncertain. More recently, the investigators of the Dallas Heart Study (DHS)[9] refined this classification of hypertensive LV geometric abnormalities by introducing the concept that LVH could exist in dilated or nondilated forms, adding concentric dilated and nondilated as well as eccentric dilated and nondilated subtypes.[9] The authors of the DHS suggested that eccentric LVH with no dilatation appeared to provide a lower risk for coronary artery disease and myocardial function impairment than in the remaining three groups of cardiac hypertrophy.[9] However, this cross-sectional study did not present results on outcome, and the subsequent prospective investigations yielded conflicting results regarding the prognostic role of these new subtypes of LV geometric abnormalities.[10,11]

Nevertheless, the correct indication for ECHO in hypertensive patients is still a matter of debate.[12] Indeed, advocating ECHO for the assessment of LVH in all hypertensive individuals would have enormous cost implications, as a result of the high number of patients. This imaging modality is more time-consuming than ECG and requires considerable skill to perform.

Even though more accurate and sophisticated modalities to diagnose LVH exist, such as ECHO, computerized tomography, magnetic resonance, and, more recently, three-dimensional ECHO, ECG remains the first-choice technique to diagnose LVH in patients with hypertension because it is widely available, easy to perform, specific, inexpensive, reproducible, and of established prognostic value.[13] ECG can also be used to detect patterns of ventricular overload or "strain" (known to indicate more severe risk), ischemia, conduction defects, and arrhythmias.[8,13] Current guidelines for the management of hypertension[8,14] strongly recommend ECG as the only examination to be performed in all hypertensive patients for detection of LVH.

Even if ECG assessment of LVH has been incorporated among standard tests in hypertension guidelines, a recent Italian survey showed that such a recommendation is largely ignored in current clinical practice. Indeed, in this survey, <40% of the study sample had

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undergone ECG during the 12-month period preceding ECHO examination.[15]

Moreover, in recent years, many studies have addressed the value of new ECG markers (fragmented QRS, ventricular activation time, P-wave analysis, P-wave dispersion, peak-to-end time interval of T wave) in detecting subclinical cardiac damage and predicting CV outcome, with promising results.[16,17]

Despite the limited sensitivity of ECG for LVH compared with ECHO, a recent analysis in a population of 40,444 hypertensive patients from 26 studies published in the past decade documented that ECG LVH is a frequent marker of hypertensive heart disease, being detected in 18% of the pooled population.[18]

In the current issue of the *Journal*, Cuspidi and coworkers[19] evaluated the combined prognostic impact of ECG and ECHO indices of LVH by analyzing the data obtained in the Pressioni Arteriose Monitorate E Loro Associazioni (PAMELA) study, a population study performed in a north region of Italy. They found that the association of ECG LVH with ECHO LVH significantly increased the risk of CV mortality independently of other risk factors known to predict mortality.[19] This was also true when ECG LVH was combined with some subtypes of ECHO LVH, such as concentric LVH and eccentric nondilated LVH. LVH as assessed by ECHO only showed borderline statistical significance.[19]

These findings seem to corroborate the concept that ECG and ECHO are complementary and not competing methods, each providing its own relevant information.[13,20]

Computer simulation studies[20] have shown that the increase in voltage and duration of the QRS complex of ECG do not have a straightforward relationship with LV mass. In other words, the so-called ECG LVH is not totally a reflection of increase in LV mass, but could be secondary to increased myocardial tension, disturbances of intraventricular electrical conduction, or neurohumoral and/or biochemical changes in the myocardium.[20] Moreover, some ECG criteria (such as LV strain, not assessed in the paper by Cuspidi and coworkers[19]) may reflect the subendocardial ischemia that is often associated with LVH.

However, there may be important diagnostic information hidden in this apparent discrepancy that needs to be fully explored.

The idea that ECG LVH could be a separate entity from imaging-based LVH is further supported by a genome-wide linkage analysis of ECG LVH and ECHO LVH in families with hypertension that showed stronger genetic signals for ECG LVH than ECHO LVH, and that the genetic determinants of each of these appear to be distinct.[21]

The findings by Cuspidi and coworkers are in agreement with previous data in the literature.[22–26] Sundstrom and coworkers[22] showed that the prognostic value of ECG LVH (diagnosed employing the Cornell product) is, to some extent, independent of ECHO-LV mass index in a population-based sample of 475 Swedish elderly men.

In the second Strong Heart Study, 2193 American Indians underwent both ECG and ECHO and were followed up over an average of 3 years. The presence of both ECHO LVH and ECG ST depression was associated with a 6.3-fold increased risk of CV death in this group of patients.[23] Similar results were obtained in another study in which ECG LVH was associated with incident ischemic stroke after adjustment for ECHO LVH.[24]

Moreover, an analysis of hypertensive patients from the Losartan Intervention For Endpoint Reduction in Hypertension (LIFE) study[25] showed that people with both forms of LVH tended to have greater evidence of cardiac disease and were more likely to be hospitalized for heart failure.

More recently, in a large prospective population-based investigation (the Oregon Sudden Unexpected Death Study), ECG LVH was significantly associated with sudden cardiac death. This association was only mildly attenuated when ECHO LVH was taken into account in multivariate analysis, and ECHO LVH was also independently associated with sudden cardiac death.[26]

The report by Cuspidi and coworkers provides a new piece of evidence in this scenario by adding the new finding that the additional prognostic value of ECG LVH is maintained even when ECHO LVH was classified in subtypes of geometric pattern, as defined by the updated classification proposed by DHS investigators.[9]

CONCLUSIONS

The study by Cuspidi and coworkers confirms that the traditional interpretation of standard ECG maintains an important role for CV risk stratification in hypertension and supports the notion that, in the assessment of hypertensive heart disease, ECG needs to be regarded as a much more important tool than previously thought, because its prognostic value seems to surpass its limited ability to detect LVH.

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