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Computer simulation of ECG manifestations of left ventricular electrical remodeling☆

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Abstract An increased QRS voltage is considered to be specific for the electrocardiogram (ECG) diagnosis of left ventricular hypertrophy (LVH). However, the QRS-complex patterns in patients with LVH cover a broader spectrum: increased QRS voltage, prolonged QRS duration, left axis deviation, and left anterior fascicular block– and left bundle branch block–like patterns, as well as pseudo-normal QRS patterns. The classical interpretation of the QRS patterns in LVH relates these changes to increased left ventricular mass (LVM) per se, while tending to neglect the modified active and passive electrical properties of the myocardium. However, it has been well documented that both active and passive electrical properties in LVH are altered. Using computer simulations, we have shown that an increased LVM is not the only determinant of QRS complex changes in LVH, as these changes could also be produced without changing the left ventricular mass, implying that these QRS patterns can be present in patients before their LVM exceeds the arbitrary upper normal limits. Our results link the experimental evidence on electrical remodeling with clinical interpretation of ECG changes in patients with LVH and stress the necessity of a complex interpretation of the QRS patterns considering both spatial and nonspatial determinants in terms of the spatial angle theory. We assume that hypertrophic electrical remodeling in combination with changes in left ventricular size and shape explains the variety of ECG patterns as well as the discrepancies between ECG and left ventricular mass.

Keywords: Left ventricular hypertrophy; Electrocardiography; Electrical remodeling; QRS complex; Modelling

Introduction

The electrocardiogram (ECG) diagnosis of left ventricular hypertrophy (LVH) is based mainly on an increased amplitude of the QRS complex in specific leads. The underlying assumption is that the increased LV mass further enhances the normal electrical dominance of the left ventricle and augments the electrical forces directed to the left, downward, and posteriorly.

However, the augmentation of QRS amplitude in patients with LVH is not proportional in all directions. As is presented in the American Heart Association (AHA) recommendations,[1] the recommended criteria vary considerably, and the increased QRS amplitude can be seen either in limb leads, or precordial leads, or in their combinations. Recommended criteria also include prolonged QRS duration and left axis deviation.[2,3] Frequent findings in patients with LVH are also left bundle branch block (LBBB) and left anterior fascicular block (LAFB), and the AHA recommendations also address these combinations. In addition, the ECG criteria for LVH (ECG-LVH criteria) suffer from low sensitivity, which means that a number of ECG findings in patients with LVH are within normal limits. Thus, the QRS complex patterns in patients with LVH cover a broad spectrum: increased QRS voltage, prolonged QRS duration, left axis deviation, and LAFB- and LBBB-like patterns, as well as pseudo-normal QRS patterns.[4,5]

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Although there is a continuous effort to improve the diagnostic performance of the ECG-LVH criteria, to obtain the best agreement between ECG and a reference method (currently, echocardiography; more recently, magnetic resonance imaging), the sensitivity and specificity of ECG criteria vary considerably between studies if left ventricular dimensions/mass are taken as the reference.[6]

The classical interpretation explicitly relates the increased QRS amplitude to the increased left ventricular dimensions/mass per se, while tending to neglect the modified electrical properties of the hypertrophied myocardium, including changes at cellular, subcellular, and molecular levels. It has been well documented that both active and passive electrical properties in LVH are altered. Paradoxically, there is limited evidence on the effect of impaired conduction/electrical remodeling on the QRS complex morphology (eg, in Refs.[7,8]). In our previous studies, we have used computer models to simulate the effect of anatomy and decreased conductivity,[9,10] as well as of reduced intracellular coupling on the QRS morphology.[11] In this article, we summarize these results and demonstrate a possible effect of electrical remodeling on the QRS patterns observed in patients with LVH, using 2 different computer models, referred to as Model 1[12,13] and Model 2.[14] The 2 models differ in the principle they are based on, and each of the models thus enables to study the changes in simulated LVH from different aspects, such as changes in left ventricular dimensions, conduction velocity, or intercellular coupling.

Increased QRS voltage

The classical theoretical concept is based on the solid angle theory[15]: the increased size of the activation front moving across the thickened wall subtends a larger solid angle and results in higher body surface voltage. Citing from the AHA recommendations[1]: "The most commonly used diagnostic criteria for LVH are based on measurements of QRS voltage… These changes have been correlated with direct or indirect assessments of ventricular size or mass to establish electrocardiographic criteria for the diagnosis of hypertrophy."

As has been repeatedly shown in numerous studies, the incidence of increased QRS voltage in patients with LVH is relatively low; even in the classical work of Sokolow and Lyon[16] it is only 38%. The incidence varies considerably and is reflected in a wide range of sensitivities and specificities, and although the ECG-LVH criteria are considered highly specific, the specificity also varies considerably.[4]

In simulations using Model 1, the simulations of anatomical types of LVH (concentric hypertrophy, eccentric hypertrophy, dilatation) without changes in conduction velocity have shown that QRS amplitude was not proportional to the increase in left ventricular mass (LVM), wall thickness, or changes in intraventricular diameter.[9] There was a good positive correlation between QRSmax and LVM ($r=0.907$), a relatively good positive correlation with wall thickness ($r=0.768$), and a poor negative correlation with LV diameter ($r=-0.170$). The good positive correlation between QRSmax and LVM seemingly confirms the classical theoretical concept. However, it is not consistent with the documented low sensitivity of ECG-LVH criteria.

Because the solid angle theory considers not only spatial determinants of the resultant voltage (the extent of activation front and the distance of the activation front from the recording electrode), but also the nonspatial determinants, we have simulated also the effect of slowed conduction velocity on the resultant QRS voltage. The simulated slowing of conduction velocity was consistent with published data on electrical remodeling in LVH in animals and humans,[17-22] and we have shown that the conduction velocity slowing in the left ventricle by 30% in the Purkinje fiber net and by 50% in the working myocardium resulted in an increase in QRS amplitude in all simulated cases including the reference heart.[9]

In this simulation study,[9] we also showed that anatomical types of hypertrophy and conduction slowing have different effect on ECG-LVH criteria. The Sokolow-Lyon index was influenced by both the concentric and the eccentric hypertrophy, but the maximum increase in this criterion was observed after the slowing of conduction velocity in the left ventricle. On the other hand, the Cornell voltage and Cornell voltage-duration product were more affected by the slowing of the conduction velocity than the anatomical types of hypertrophy (Fig. 1).

Interestingly, the Cornell voltage-duration product showed minor relation to the LVM and/or type of hypertrophy but was remarkably influenced by conduction

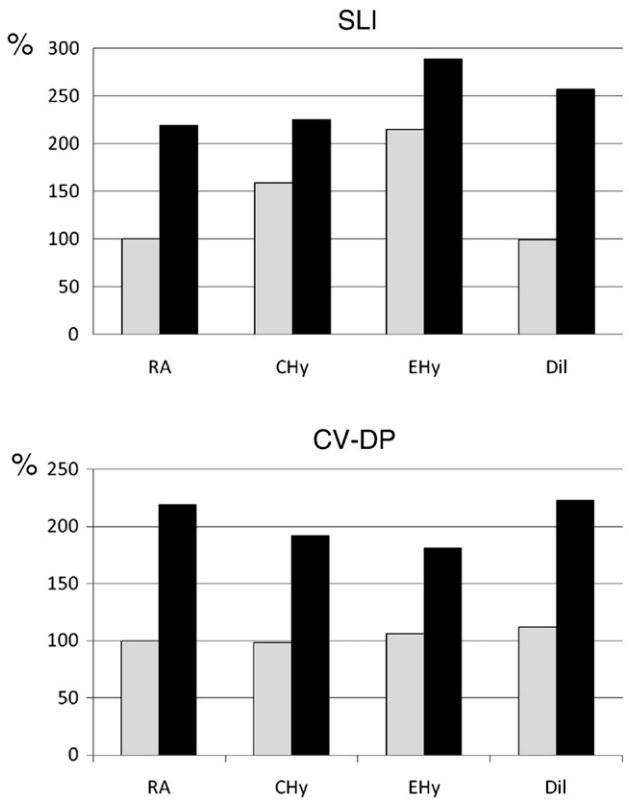

Fig. 1. The values of Sokolow-Lyon index (SLI) and Cornell voltage-duration product (CV-DP) as percent of the reference values. RA indicates reference heart with reference (normal) anatomy; CHy, concentric hypertrophy; EHy, eccentric hypertrophy; Dil, dilatation. Gray columns: Reference (normal) conduction velocity; black columns: slowed conduction velocity. (Adapted from Bacharova et al.[9]).