Electrocardiographic criteria for Left Ventricular Hypertrophy diagnosis

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Several criteria for LVH have been proposed in the literature. LVH can be diagnosed on ECG with good specificity. When the myocardium is hypertrophied, there is a larger mass of myocardium for electrical activation to pass through; thus, the voltage of the QRS complexes representing ventricular depolarization, is increased. In other words increased R wave amplitude in the left-sided ECG leads (I, aVL and V4-6) and increased S wave depth in the right-sided leads (III, aVR, V1-3). Voltage criteria alone are not diagnostic of LVH.

Likewise, when the myocardium is abnormally thickened, and electrical activity takes longer to traverse throughout the whole heart, the duration of the QRS complex may be widened. This is referred to as "LVH with QRS widening."

Finally, repolarization may be affected via similar mechanisms that can result in abnormal ST segments or T waves. This is referred to as "LVH with strain" or "LVH with repolarization abnormality." At times, these repolarization abnormalities can mimic ischemic ST changes, and distinguishing them from those during a myocardial infarction is important, though often difficult. The typical pattern with LVH includes deviation of the ST segment in the opposite direction of the QRS complex (discordance), and a typical T wave inversion pattern is present, as seen in the image here:

Criteria of LVH classification

1. Criteria based on increase of amplitude/ voltage of the QRS complexes;
2. Criteria based on the discrete increase in QRS complex duration at the expense of a delay in the time of appearance of R-wave apex: ventricular activation time(VAT), "R peak time" in the leads that are opposite to the LV (I, aVL, V5-V6), initial time of ventricular activation time (VAT) Observation: The last guidelines of American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; American College of Cardiology Foundation; Heart Rhythm Society (Hancock et al., 2009). Prolongation of initial ventricular depolarization on the ECG, R-wave peak time or delayed intrinsicoid deflection (DID), can indicate LVH. This marker is associated with increased SCD risk independent of echocardiographic LVH, ECG-LVH, and reduced LVEF ejection fraction. This association remained significant in multivariate analysis

after adjusting for increased LV mass as well as severely reduced LV systolic function. Further, in patients with narrow QRS, the R-wave peak time was associated with SCA risk independent of LVH voltage criteria. Prolongation of the early phase of ventricular depolarization, represented by the R-wave peak time, therefore appears to be a form of electrical remodeling that is independently predictive of SCA (Darouian et al., 2016).

3. The time-voltage area of each Q, R, and S wave in all 12 leads Criteria based on $^{QRS}/_{ST\text{-}T}$ angle broadening: ST segment depression and T wave inversion in the left precordial leads and in the limb leads in which major QRS deflections are upright;
4. Tendency to SÂQRS deviation to the left, backward and upward;
5. Association: Ex Point score systems
6. Indirect criteria.

LVH criteria based on increase of amplitude or voltage of the QRS complexes

The ECG diagnosis of LVH frequently use the QRS voltage criteria. Theoretically, the QRS voltage increases proportionally with left ventricular mass (LVM). However, ECG criteria for LVH have low sensitivity (Reichek & Devereux, 1981). Voltage criteria must be accompanied by non-voltage criteria to be considered diagnostic of LVH.

One important issue in developing and applying diagnostic criteria for LVH based on QRS voltage is that QRS voltages are influenced by a variety of factors other than LV size or mass. The ECG diagnosis of LVH is based on the assumption that QRS voltage increases with LV mass. However, most of patients with echocardiographically detected LVH do not have increased QRS voltage. Low QRS voltage does not necessarily contradict a diagnosis of LVH but may be an indication for electrical uncoupling. Gap junctions in normal adult human working ventricular myocardium occupy an area of 0.0051 micron2/micron3 myocyte volume. This surface area is reduced in ventricular myocardium from hearts subject to chronic hypertrophy and ischemia, despite a normal number of intercellular abutments, and this alteration may contribute to abnormal impulse propagation in these hearts (Peters, Green, Poole-Wilson, & Severs, 1993). The reduction in Cx43 expression in spontaneously hypertensive rats is associated with decreased QRS voltage (Bacharova, Plandorova, Klimas, Krenek, & Kyselovic, 2008). Experimental models have shown that reduced expression of connexin 43 (Cx43) leads to a decrease in QRS voltage (Danik et al., 2004), Apparently, the reduced intercellular conductivity

caused by a lower content in Cx43 can more than counterbalance the expected effect of increased LVM.

The diagnostic value of this "relative voltage deficit" needs to be demonstrated in clinical studies (Bacharova et al., 2011). These factors include age, gender, race, and body habitus. Their effects may contribute to the limited accuracy of the ECG criteria. Day-to-day variability and variability resulting from variations in the sites of electrode placement also impact QRS voltages and, hence, the diagnostic value of ECG voltage criteria.

Age Apart from the wide variation in the normal limits of QRS voltage in infants and children of various ages, there are important differences between adults of various ages, with QRS voltages tending to decline with increasing age. In general, the commonly used QRS voltage criteria apply to adults older than 35 years (MacFarlane & Lawrie, 1988). Standards for the 16- to 35-year age group are not as well-established, and the diagnosis of LVH based on voltage alone has a low accuracy in this age group. The diagnosis of LVH in highly trained athletes is especially problematic. The age-dependent performance of ECG criteria was examined for LVH prediction. During 2009, 570 middle-aged (54±7 years, 45% men) and 507 elderly (75±6 years, 45% men) inhabitants of the Ikaria Island (Icaria is considered one of the world's five "Blue Zones"– places where the population regularly lives to an advanced age (one in three make it to their 90s). This is due to healthy diets and lifestyles.) were studied. Seven ECG criteria were calculated (Sokolow-Lyon voltage and product, sex-specific Cornell voltage and product, Gubner-Ungerleider voltage, Lewis voltage and Framingham), whereas LVH was defined as LV mass indexed for body surface area (BSA) at least 125 g/m in men and at least 110 g/m in women or LV mass indexed for height ≥49 g/m in men and ≥45 g/m in women. The Framingham criteria had in hierarchical order the highest, although insignificant, sensitivity among the elderly individuals, either when LVH was indexed for BSA or for height (18.4 and 16.7%, respectively). Cornell voltage and product criteria had hierarchically the highest sensitivity among middle-aged participants, either when LVH was indexed for BSA (19.0 and 23.8%, respectively) or for height (17.2 and 20.3%, respectively). In the multi adjusted analysis applied in elderly participants, Cornell voltage, its product and Framingham criteria were associated with echocardiographic detection of LVH (indexed for BSA); however, when LVH was indexed for height, the Sokolow-Lyon and Framingham criteria were associated with LVH detection. In contrast, among middle-aged individuals, the Cornell product was the only ECG criterion that was associated with LVH detection (irrespective of indexation). Age should be taken into consideration in

selection of appropriate ECG criteria for LVH detection. Indexation of LV mass differentiates the diagnostic ability of ECG criteria, especially in older patients (Tsiachris et al., 2011).

ECG parameters for diagnosing LVH in children

Parameter	Description
SV3R	S-wave amplitude in V3R
SV1	S-wave amplitude in V1
RV6	R-wave amplitude in V6
RV7	R-wave amplitude in V7
TV6	Inverted T-wave in V6
TV7	Inverted T-wave in V7
SV1 + RV6	Sokolow-Lyon voltage
(SV1 + RV6) x QRSd	Sokolow-Lyon voltage-duration product
(SV1 + RV6) area	Sokolow-Lyon voltage-time integral
SV3R + RV7	Additional Sokolow-Lyon voltage
(SV3R + RV7) x QRSd	Additional Sokolow-Lyon voltage-duration product
(SV3R + RV7) area	Additional Sokolow-Lyon voltage-time integral
12-lead sum	Sum of top-top deflections of all leads
12-lead sum x QRSd	12-lead sum voltage-duration product
12-lead sum area	12-lead sum voltage-time integral

Gender Adult women have a slightly lower upper limit of QRS voltage than men do, although SV3 is the only measurement with a large difference (Simonson, 1961). The difference persists after adjustment for body size and cardiac mass. Some criteria have been shown to improve their performance with gender adjustment, but the adjustment is not the same for all criteria (Casale, Devereux, Alonso, Campo, & Kligfield, 1987). The sensitivity of the ECG for echocardiographic LVH is marginally lower in women than in men, possibly because of attenuation of QRS voltage by the greater spatial separation of myocardium from precordial electrodes because of breast tissue in women, consequently precordial QRS voltage is lower in women than in men (Levy et al., 1987). Similarly, mastectomy results in increased QRS amplitude (LaMonte & Freiman, 1965). Diminished

ECG sensitivity in women might also be, in part, a result of less voltage generated by the female heart, which contains approximately 25% less wall mass than the male heart.23 The findings of this study suggest that the voltage threshold for defining LVH should be lower in women than in men. Recent sex-specific strategies for the ECG diagnosis of LVH have reported increased sensitivity (Casale et al., 1987; Casale et al., 1985). The number of cardiomyocytes is similar in men and women at birth. Cardiomyocytes do not replicate during the first years of life and heart size increases concurrently with the increase of body size in both genders. From puberty on, the growth rate of the heart is higher in men than in women, implying that men and women have specific cardiac growth curves. This may explain why women develop LVH less frequently than men, despite having a similar number of adult cardiomyocytes (De Simone et al., 2011; de Simone, Devereux, Daniels, & Meyer, 1995).

Race Normal values of QRS voltages vary by race. African Americans have a higher upper normal limit of QRS voltage than do Euro-Americans, whereas Hispanic Americans have lower limits. In patients with mild or moderate hypertension, the Sokolow-Lyon criterion has a higher sensitivity and lower specificity in African-Americans than in Euro-Americans, whereas the Cornell voltage criterion shows lower sensitivity and higher specificity in African-Americans than in Euro-Americans (Rao, Thapar, & Harp, 1984; P. M. Rautaharju, Zhou, & Calhoun, 1994; Vitelli et al., 1998).

Body Habitus Obesity is associated with increased left ventricular mass by echocardiographic measurement but not with increased QRS voltage. This may be attributed to the insulating effect of adipose tissue and the greater distance from heart to the chest wall electrodes. The effect of obesity differs among the various ECG criteria. In a study of patients with mild or moderate hypertension, the Cornell voltage-duration product was more often in the LVH range in obese patients than in the nonobese, whereas the Sokolow-Lyon criterion was less often in the LVH range in obese patients (Abergel, Tase, Menard, & Chatellier, 1996; Nath, Alpert, Terry, & Kelly, 1988; Okin et al., 2000; Okin, Roman, Devereux, & Kligfield, 1996).

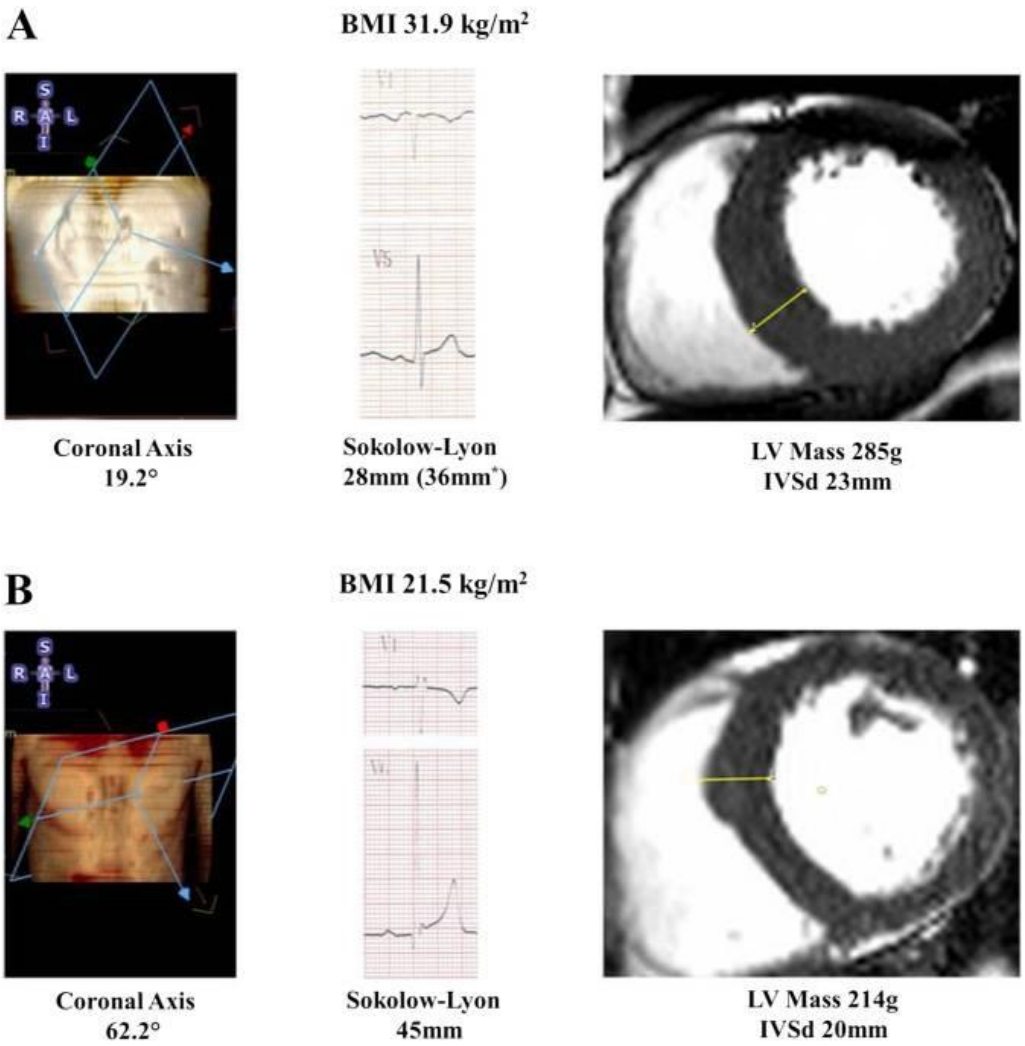
Muiesan et al aim to investigate the prevalence and the prognostic significance for fatal and nonfatal cerebrovascular and cardiovascular events of different ECG criteria for LVH in normal weight, overweight and obese patients in an adult Italian population. A total of 18330 adults hypertensive patients were analyzed from the Moli-sani cohort. Obesity was defined using the ATPIII criteria. ECG-LVH was defined according to 2013 ESC-ESH guidelines. The age and sex adjusted prevalence of ECG-LVH did not differ from normal

weight patients to class 1-3 obesity patients, when Cornell-voltage criterion was used. In overweight and obese patients, as compared with normal weight patients, a progressively lower prevalence of ECG-LVH was observed when the Sokolow-Lyon index was used, whereas a higher prevalence was shown by using the aVL R-wave voltage (>11 and >5.7 mm) and the Cornell-voltage-QRS duration product. The incidence of cardiovascular events was significantly greater in patients with ECG LVH diagnosis by the Cornell voltage and the Cornell product. After adjusting for different confounders (age, sex, cigarette, hypertension, hypercholesterolemia, diabetes, income, education, occupational class and physical activity) and for BMI categories, only the Cornell product remained significantly associated with a higher incidence of cardiovascular events. The predictive significance of different LVH criteria was assessed across BMI categories; after adjusting for confounders, no LVH criteria were significantly associated with an increased risk of cardiovascular events in obese patients; Cornell-product LVH remained an independent predictor of events in normal weight and overweight individuals. These results confirm that ECG LVH prevalence may differ according to the criteria used across BMI categories in a low cardiovascular risk cohort. The use of different LVH criteria according to BMI categories may improve cardiovascular risk stratification in a general population independently of several confounding factors (Muiesan et al., 2017).

A) LVH criteria on precordial leads

1. Sokolow-Lyon voltage index or **Sokolow-Lyon Criteria:** Add the S wave in V1 plus the R wave in V5 or V6. If the sum is greater than 35 mm, LVH is present. In other words S of V_1 + R of V_5-$V_6 \geq$35 mm or 3.5 mV in adults older than 30, 40 mm or 4.0 mV between 20 and 30 years (Sokolow-Rapaport) and >60 mm between 16 and 20 years and >65 mm between 11 and 16 years. Modified Sokolow and Lyon index: S wave of V_2 + R of V_5 or $V_6 \geq$35 mm. Investigations have repeatedly demonstrated poor performance of the Sokolow-Lyon's criteria. However, they have been the most widely used LVH criteria for the past six decades and their impact has been more substantial than any other criteria in clinical and epidemiological electrocardiography. The publication of Sokolow and Lyon clearly deserves to be considered a landmark in electrocardiographic literature (P. Rautaharju, 2001). Currently, the Sokolow-Lyon voltage index is possibly the most widely used criterion for ECG-LVH (Yamabe et al., 2016). Adjusting the Sokolow–Lyon index for BMI (overweight +4 mm, obesity +8 mm) improves the diagnostic accuracy

for detecting LVH. As the ECG, worldwide, remains the most widely used screening tool for LVH, implementing these findings should translate into significant clinical benefit (**Rider OJ, Ntusi N, Bull SC, et al.Improvements in ECG accuracy for diagnosis of left ventricular hypertrophy in obesity. Heart. 2016 Oct 1;102(19):1566-72**.), Figure



The effect of obesity and leftward axis deviation on electrocardiogram (ECG) voltage criteria. (A) Clear left ventricular hypertrophy (LVH) in obesity with leftward axis and negative Sokolow–Lyon criteria for LVH, which becomes positive only when adjusted for body mass index (BMI) (by +8 mm) and (B) clear LVH in a normal weight participant with normal left ventricular (LV) anatomical axis and positive Sokolow–Lyon criteria for LVH. IVSd, Intraventricular Septum in Diastole.

2. R wave of greater voltage + S wave deeper than any precordial lead ≥45 mm or 4.5 mV.
3. R wave of V_5 or V_6 ≥26 mm (2.6 mV).
4. S wave of V_1 ≥23 mm.
5. S wave of V_2 ≥ of 29 mm or greater.
6. If any S wave of V_1, V_2 or V_3 ≥30 mm.
7. If any R wave of V_4, V_5 or ≥27 mm.
8. R wave of V6 > than R wave of V_5 when both have an increased voltage.

B) LVH criteria on limb leads

1. Limb-lead QRS-sum defined as the sum of R+S-waves (or Q if deeper than S) in all six limb-leads (Ostman-Smith, Wettrell, & Riesenfeld, 1999);
2. S wave of aVR ≥15 mm;
3. Q or S aVR > 19mm (Schack, Rosenman, & Katz, 1950);
4. R wave of I ≥14;
5. R wave of aVL ≥11 (1.1 mV). R wave voltage in aVL >1.1 mV correlates well with LV mass index (**Bacharova 2010**). Reduced intercellular coupling, which is a part of the hypertrophic remodeling of myocardium, would result in a decrease in QRS amplitude of the 12-lead ECG except for the increase of R-wave amplitude in aVL, (This finding could contribute to the explanation of the "discrepancies" between the QRS voltage and increased LVM),
6. R wave of aVF ≥20 mm (2.0 mV) or 20mm (Goldberger, 1949). The augmented unipolar limb leads aVR, aVL, and aVF, introduced by Goldberger in 1942, are an integral part of the 12-lead ECG (Goldberger, 1942a, 1942b);
7. Any R + S in limb leads ≥20 mm (Romhilt & Estes, 1968);
8. Lewis index (LI): **(R I–S I)+(S III–R III**) >17 mm (Lewis, 1914);
9. Gubner-Ungerleider index = (RI+SIII>2.5 mV) R of I + S of III ≥25 mm (2.2 mV) (Gubner & Ungerleider, 1943); Sensitivity: 6.0; Specificity: 95% (Morrison, Clark, & Macfarlane, 2007);
10. White-Bock index W-B = (R1 + RIII) -- (RIII+ S1) >17 mm.

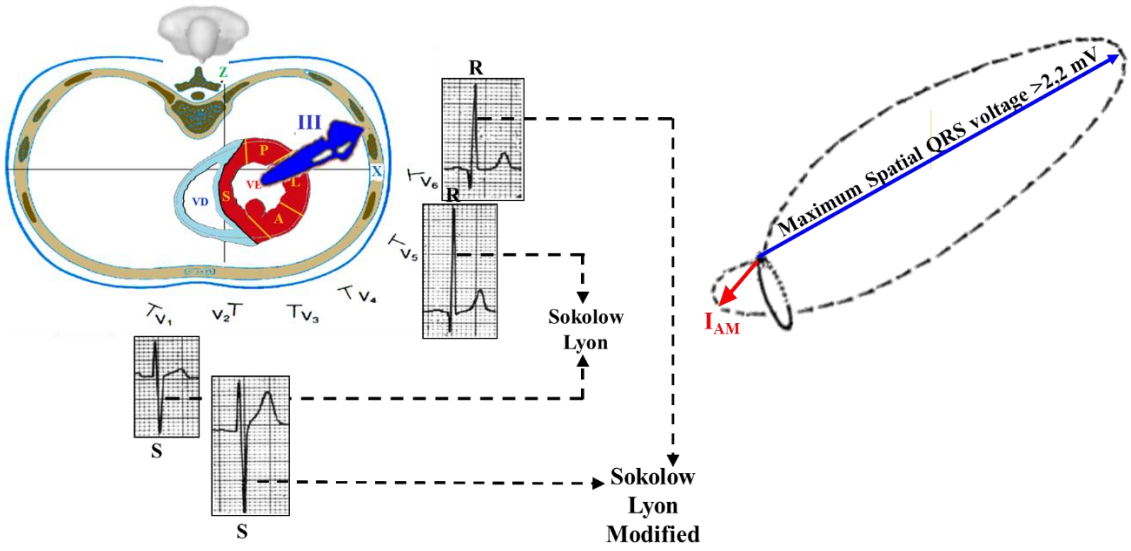
C) LVH criteria using both planes

1. Cornell index (CI)/criteria or Casale criteria: CI = R aVL + S V3 > than 28 mm in men or > 20 mm in women indicates LVH. In other words **Cornell criteria:** Add the R wave in aVL and the S wave in V3. If the sum is greater than 28 millimeters in males or greater than 20 mm in females, LVH is present.
2. **Modified Cornell Criteria:** Examine the R wave in aVL. If the R wave is greater than 12 mm in amplitude, LVH is present.

3. Six chest-lead QRS-sum, 12-lead QRS-sum (Siegel & Roberts, 1982).

4. The amplitude of the deepest S wave (S_D) in any single lead and adding it to the S wave amplitude of lead V_4 (SV_4). **(Peguero JG, Lo Presti S, Perez J, Issa O, Brenes JC, Tolentino A. Electrocardiographic Criteria for the Diagnosis of Left Ventricular Hypertrophy. J Am Coll Cardiol. 2017;69(13):1694-1703)**.

Sokolow index and Sokolow index modified for LVH (Sokolow & Lyon, 1949, 2001)



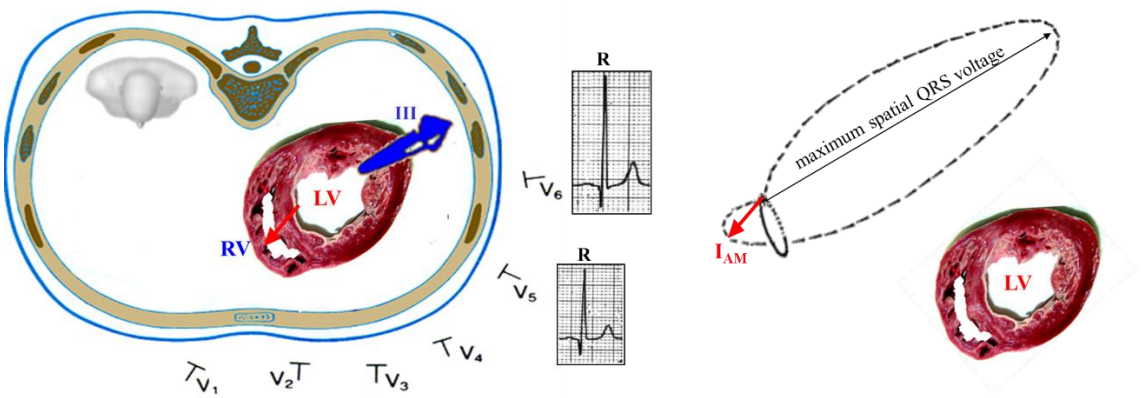
S wave of V1 + R of V5 ≥ 35 mm or 3.5 mV in adults older than 30, > 40 mm or 4.0 mV between 20 and 30 years (Sokolow-Rapaport), > 60 mm between 16 and 20 years and > than 65 mm between 11 and 16 years. Sensitivity: 25%. Specificity: 95%.

Modified index: S wave of V2 + R of V5 or V6 ≥35 mm. This index uses a close lead (V2) and a distant one (V6). This is the reason why it has the same value as the Sokolow-Lyon index, which uses a distant lead (V1) and a close one (V5).

Modified Sokolow-Lyon Voltages in athletes < 16 years, as reported by Garson et al. (Garson, 2002) and Rijnbeek et al. (Rijnbeek et al., 2008).

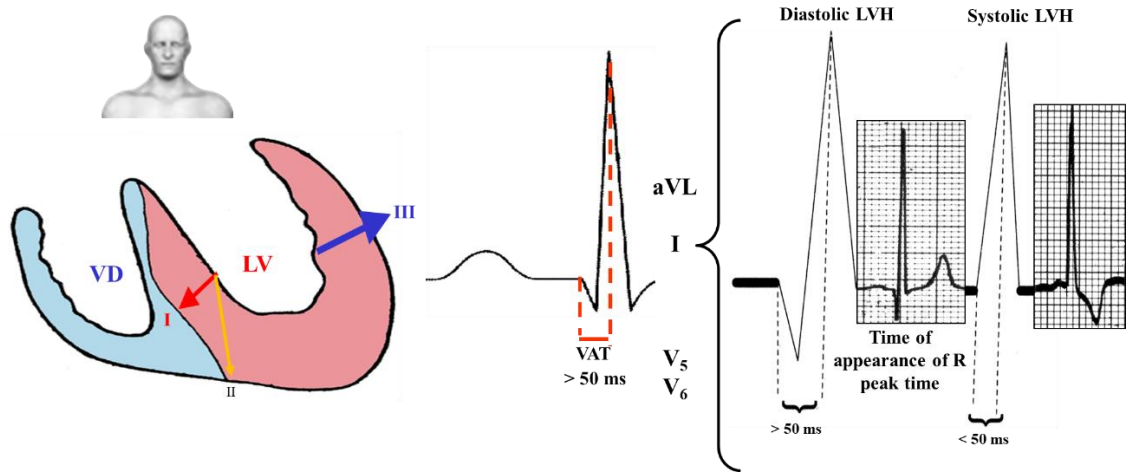
R wave voltage in V6 taller than R wave voltage in V5 when both are increased: RV6>RV5

The presence of this sign suggests LV dilatation, i.e. diastolic, eccentric or volumetric LVH (S. K. D. Talbot, 1979)**.**



Additionally, left ventricular volumes were estimated in 59 patients, who were investigated by single plane ventriculography and coronary arteriography. The relation of the left ventricular end-diastolic volumes to the QRS voltage of the 12-lead ECGs and Frank VCGs was examined. It was found that the maximum spatial QRS voltage and the R wave voltage of leads V5 and V6 in patients without LVH were inversely correlated with end-diastolic volume. This inverse relation of QRS voltage and left ventricular volume may explain the loss of QRS voltage with dilatation of the heart. In patients with left ventricular hypertrophy, QRS voltage is usually positively correlated with the degree of LVH (S. Talbot, Kilpatrick, Jonathan, & Raphael, 1977).

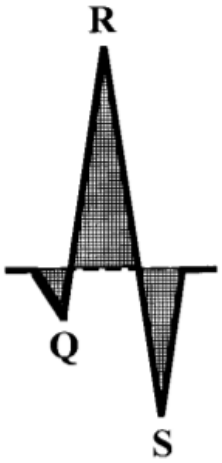
II. Ventricular Activation Time (VAT), "R-wave peak time" or intrinsicoid deflection, or left lateral leads I, aVL, V5-V6



Left Ventricular Activation Time (VAT): it is the time from QRS complex onset to peak of R wave on left leads (time of appearance of R peak). The normal value of VAT is <0.05 sec or 50 ms in V5 or V6 (Perez-Riera, de Abreu, Barbosa-Barros, Nikus, & Baranchuk, 2016). This parameter is prolonged in diastolic, volumetric, or eccentric LVH. VAT is shorter in systolic or concentric LVH than in diastolic LVH (Buchner et al., 2009). The prolongation of VAT is associated with diastolic dysfunction in patients with newly diagnosed untreated hypertension (Boles et al., 2010).

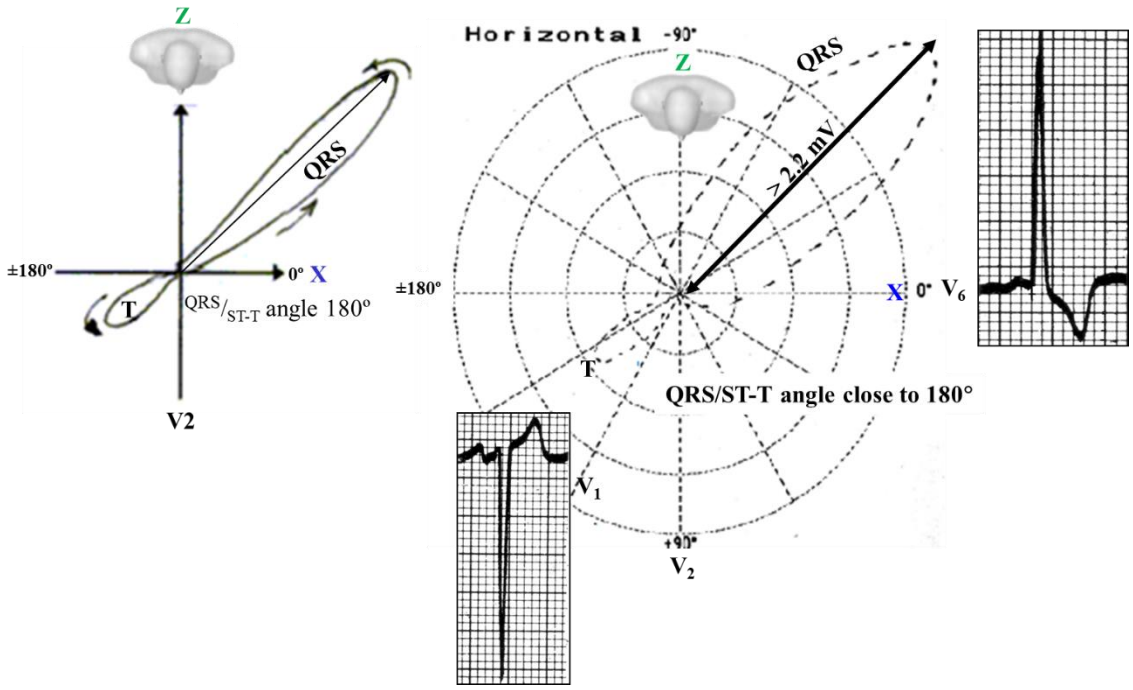
III. The time-voltage area of each Q, R, and S wave in all 12 leads

The time-voltage area of each Q, R, and S wave in all 12 leads is measured by the Marquette MUSE system, and the measurements are accessed using custom software. This measurement process is graphically illustrated in Fig xx. Two new time-voltage area criteria are derived from the individual 12-lead QRS complex measurements: Sokolow-Lyon area and the 12-lead sum area. Sokolow-Lyon area is calculated as the sum of the area of the S wave in lead V1 and the area of the R wave in lead V5 or V6, whichever was greater. The 12-lead sum area is calculated as the sum of Q, R, and S wave areas in all 12 leads in a manner parallel to the calculation of the 12-lead sum of QRS voltage (Odom et al., 1986; Siegel & Roberts, 1982).



A typical QRS complex illustrating measurement of the time-voltage area of each QRS complex used to derive time-voltage area criteria for LVH. The computer measures the area inscribed by each individual Q, R, and S wave as denoted by the shaded areas.

IV. Criteria based on QRS/T angle prolongation: Systolic, concentric Cabrera type or LVH Strain pattern



$^{QRS}/_{ST\text{-}T}$ angle >100º and a T wave upright in V2 and more negative than -01 mV in V6. ST segment depression with upward convexity and T wave inversion in the left precordial leads. repolarization changes secondary to LVH cause marked changes in the ST segment and T waves in addition to changes in the QRS amplitude and width. Although in many patients the pattern is typical (ST elevation in V1-V3 with ST depression and T wave inversion or biphasic T waves in leads I, aVL, V4-V6), in some patients the pattern is atypical and ST deviation can be detected in other leads. The magnitude of ST deviation

can change over time and not always reflect acute ischemia. Integration of clinical assessment along with serial ECGs, including comparison to previous ECGs, when the patient was asymptomatic, often assist in reaching the diagnosis. At times the diagnosis is difficult and in such cases with ongoing symptoms despite initial medical therapy, emergent coronary angiography is recommended by the STEMI guidelines. It is recommended that the appropriate professional organizations (ESC, ACC/AHA) consider these problems at their next revision of STEMI Guidelines, and consider a special section of these guidelines relating to the problems of diagnosis in hypertensive individuals (Birnbaum & Alam, 2014).

LV strain pattern is a dynamic process with many evolving components, not all of which change simultaneously. The advent of two-dimensional echocardiography moved this field forward enormously. The addition of CMRI has added a major tool in our understanding of the functional anatomy of the heart and our understanding of the pathophysiology of the LV strain pattern in both health and in the presence of LV remodeling (Myerson, Bellenger, & Pennell, 2002). The complexity of strain led many to lump all of the strain pattern components under the nomenclature of ST-T abnormalities associated with LVH and repolarization abnormalities and the cited avoidance of the terminology (Hancock et al., 2009). Voltage is so much simpler to measure and digitize directly. For example, the LV strain pattern consists not only of the R-ST segment but also the classically asymmetric T wave, itself. Both of these key components can vary in shape and relationship to the isoelectric baseline. The strain pattern does not simply appear as a fully developed form but evolves as do many other J-ST-T changes. Depression of the RS-T segment with preservation of upright T occurs first. Next, T wave amplitude decreases followed by inversion of the T wave with downsloping R-ST segment. The R-ST segment then takes on a concave shape transitioning to an asymmetric inverted T wave (Katz, 1946; Katz & Weinstein, 1947). This evolutionary sequence of events may convey much more information about the nature of electrical ventricular remodeling than voltage alone. In addition to the idea that LV strain pattern reflects an electrical abnormality associated with LV repolarization, there might also be electromechanical abnormalities associated with prolonged depolarization as well as diastolic events that are associated with local, regional or global pathophysiological processes. The morphology of LV strain pattern and its duration may be closely related to prolong the QRS duration and morphology. This relationship may be due to non-specific intraventricular conduction delay or more specific RBBB or LBBB, each of

which has its own characteristic repolarization changes in the R-ST segment and T wave. This relationship between prolonged depolarization and repolarization may allow differentiation among multiple ongoing processes (Bacharova, Szathmary, & Mateasik, 2013). These processes include increase in LV mass, presence of ischemia, acid-base disturbance or electrolyte abnormality. Moreover, attempts to improve our understanding of this concept of strain may not consider the spatial and physiological milieu, an entirely new source of variability in the strain pattern.

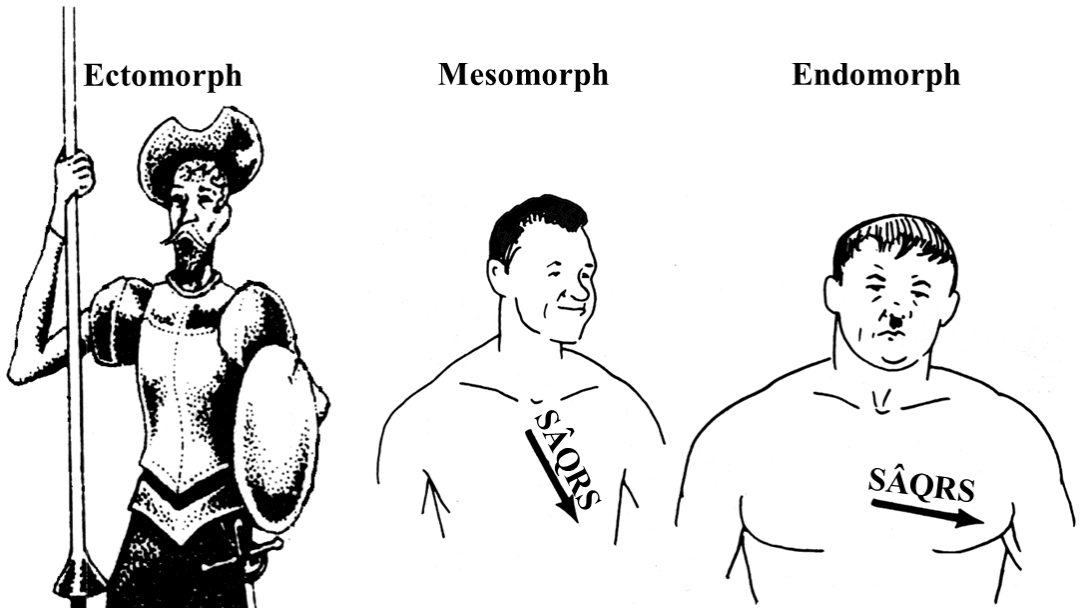
Variables influencing ECG ventricular gradient and LV strain pattern

1. Anatomic
   - Spatial (body mass index(BMI), chest wall configuration)
   - Left ventricular mass and influence of the RV
   - Size and orientation of the heart
2. Biochemical a. Sympathetic, parasympathetic neurohormonal effects
   - Centrally mediated neurogenic inputs, influences of reflex inputs
   - Metabolic, acid-base balance
   - Major and minor cationic and anion influences
3. Depolarization variables a. QRS duration
   - QRS morphology
4. Repolarization variables
   - R-ST-T duration
   - R-ST-T morphology

V. Tendency to SÂQRS deviation to the left, backward and upward

In adults SÂQRS beyond -30° is considered left axis deviation (LAD). Axes between 0° and – 30° may be observed in endomorphs and pregnant women.

Electrical axis according to biotype and the causes for axis deviation in LVH.



In LVH, SÂQRS may be deviated to the left as a consequence of:

1) Levorotation of the heart in its longitudinal axis
2) Deviation to the left of basal vector **IV**

LVH in young people and children, usually presents non-deviated SÂQRS in the frontal plane.

LVH associated to Left Anterior Fascicular Block (LAFB), extremely deviates SÂQRS to the left beyond - 45°.

SÂQRS in LVH in the Frontal Plane

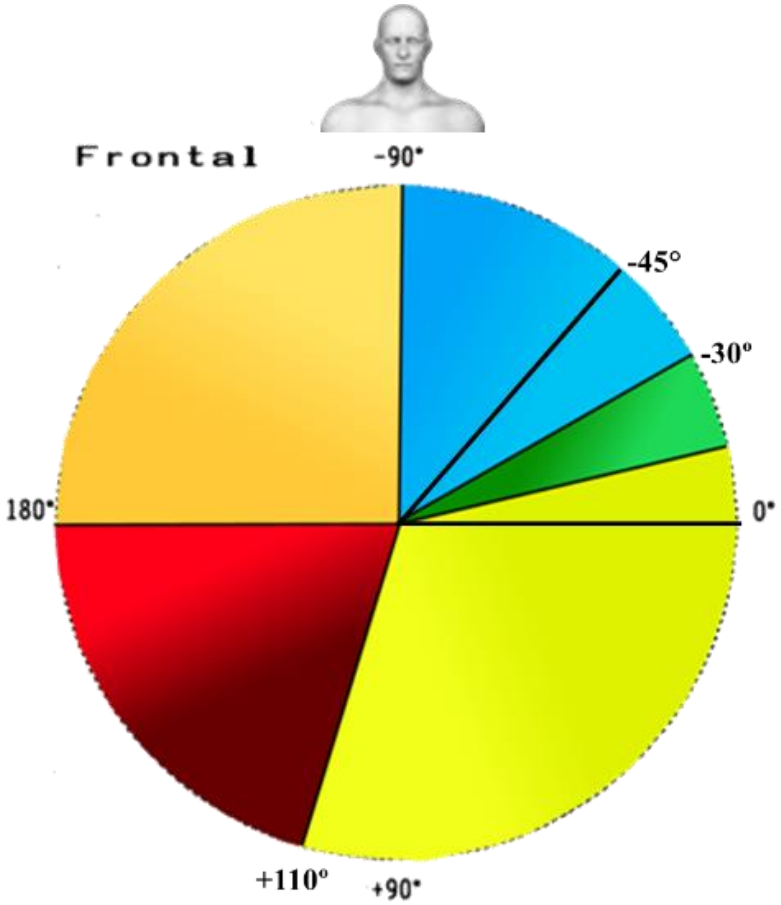
I. Normal QRS axis between -30º and +110º

II. Minimal left axis QRS deviation or normal. Note: Axes between 0° and –30° may be observed in endomorphs and pregnant women. When the axis is between 0 and -30°, it is sometimes referred to as a physiological (as opposed to pathological) left axis deviation. Axis of QRS in LVH in the frontal plane is considered with left axis deviation when ≥30º**.** (Romhilt & Estes, 1968).

III. Extreme left axis QRS deviation between -30º and -90º. It is observed in LAFB, LVH + LAFB, inferior MI. Between -45º and -90º is criteria of LAFB.

IV. Right axis QRS deviation. QRS axis between ±110º and ±180º. It is observed in RVH, LPFB, lateral MI asthenic biotype.

V. Extreme right axis QRS deviation or right shoulder axis. Negative QRS complexes in lead I and negative QRS complexes in lead aVF.



Main causes of extreme left axis deviation in the Frontal Plane

1) Left anterior fascicular block of the His bundle: LAFB;
2) Right End Conduction Delay by the superior division of the right branch: RECD (block of the anterosuperior zone of the right ventricle)
3) Advanced or complete left bundle branch block: (ALBBB or CLBBB)
4) Wolff-Parkinson-White syndrome: WPW
5) Inferior or diaphragmatic infarction
6) Association of inferior infarction, LAFB or CLBBB
7) Certain types of emphysema: pseudo deviation of ÂQRS to the left
8) Hyperpotassemia;
9) Acute pulmonary embolism (APE) (Chan, Logue, & Kligfield, 2006).
10) Right ventricular ectopic rhythm;
11) Congenital heart diseases: endocardial cushion defects, tricuspid atresia, 15% of VSD, single ventricle, anomalous onset of coronary artery of pulmonary artery, giant AV fistulae;
12) Left ventricular hypertrophy.

Romhilt-Estes LVH Point Score System (Romhilt & Estes, 1968)

ECG finding	Scoring
Voltage criteria Voltage Criteria (any of): R or S wave in limb leads ≥20 mm S wave in V1 or V2 ≥30 mm R wave in V5 or V6 ≥30 mm	Excessive amplitude 3 points
ST-T segment pattern of LV strain ST-T vector opposite to QRS without digitalis ST-T vector opposite to QRS without digitalis	 3 points 1 point
Left atrial abnormality; terminal negativity of the P wave in V1 >1 mm in depth with a duration of ≥0.042	3 points
Left axis deviation ≥30º	2 points
QRS duration >90 ms	1 point
Delayed ventricular activation time, R peak time or intrinsicoid deflection in V5 or V6 (>0.05 sec) or ≥50 ms	1 point

The authors attribute values from 1 to 3 points to the different existing criteria, 5 or more points: certain LVH; 4 points: probable LVH. **If the score equals 4, LVH is present with 30% to 54% sensitivity. If the score is greater than 5, LVH is present with 83% to 97% specificity.**

Cornell limb lead criterion, Cornell index (CI) (Casale et al., 1985) or Casale criterion for LVH

***Cornell criteria*:** Add the R wave in aVL and the S wave in V3. If the sum is >28 mm in males or >20 mm in females, then LVH is present.

CI = R aVL + SV3: >28 mm (>2.8 mV) in men or >20 mm (>2.0 mV) in women suggests LVH.

Gender-specific Cornell voltage (SV3 + RaVL >2.8 mV in men and >2.0 mV in women. The criterion has high sensitivity and specificity for LVH and is the best ECG criterion to evaluate LVH.

***Modified Cornell Criteria*:** Examine the R wave in aVL. If the R wave is >12 mm in amplitude, then LVH is present.

Cornell product index (Molloy, Okin, Devereux, & Kligfield, 1992) (CP)*Cornell voltage-duration product: 12-lead QRS voltage–duration product. It is the product of QRS voltage and QRS duration (QRS voltage-duration product); Cornell voltage-duration product (RaVL + SV3 with 6 mm added in women x QRS duration). Values ≥2440 mm/ms are diagnostic of LVH (Positive criteria of LVH CP≥2440 mm x ms).

The Lifestyle Interventions and Independence for Elders (LIFE) Study shows that evaluation of both baseline and in-study ECG LVH defined by Cornell product criteria, Sokolow-Lyon voltage criteria or ECG strain improves prediction of CV events and that regression of ECG LVH during antihypertensive treatment is associated with better outcome, independent of blood pressure reduction (Bang, Devereux, & Okin, 2014). This trial was based upon promising results from a pilot study among 424 sedentary older adults who were randomized to a physical activity intervention or a successful aging health education intervention. The primary aim is to assess the long-term effects of the proposed interventions on the primary outcome of major mobility disability, defined as inability to walk 400 m. Secondary aims focus on assessing the relative effects of the interventions on the following outcomes: cognitive function; serious fall injuries; persistent mobility disability; the combined outcome of major mobility disability or death; disability in activities of daily living; cardiovascular and pulmonary events; and cost-effectiveness. Tertiary aims relate to assessing the relative effects of the interventions on (a) the combined outcome of mild cognitive impairment or dementia and (b) physical performance within pre-specified subgroups defined on the basis of race, gender and baseline physical performance. The proposed trial will provide definitive evidence regarding whether lifestyle modification interventions are effective and practical for preventing major mobility disability. Eight sites around the country participate in the LIFE study.

The CP is a useful ECG marker, reflecting not only LV mass but also LV geometry and diastolic function in Japanese hypertensive patients (Shirai, Kasao, Nozaki, & Nitta, 2007).

Reduction in CP ECG LVH during antihypertensive therapy is associated with fewer hospitalizations for HF, independent of blood pressure lowering, treatment method, and other risk factors for HF (Okin et al., 2007).

To determine if persistence of ECG-LVH during aggressive systolic blood pressure (SBP) lowering would identify patients at increased risk. Adjudicated outcomes were examined in relation to the presence of LVH by mean in-treatment CP in 463 hypertensive patients with mean in-treatment SBP ≤ 130 mmHg randomly assigned to losartan- or atenolol-based treatment. During mean follow-up of 4.4 ± 1.3 years, persistence of mean CP > 2440 mm ms in 211 patients (45.6%) was associated with significantly higher 4-year rates of cardiovascular death, myocardial infarction, stroke, the composite endpoint of these events (20.0% vs 7.0%, $p < 0.001$) and all-cause mortality. In multivariate Cox analyses, adjusting for a propensity score for CP LVH, randomized treatment and Framingham risk score entered as standard covariates and in-treatment diastolic BP and Sokolow-Lyon voltage LVH entered as time-varying covariates, persistence of CP LVH remained associated with statistically significant increased risks of cardiovascular death, stroke and the composite endpoint. These findings suggest that persistence of LVH in a subset of these patients may in part explain the lack of benefit found in hypertensive patients despite treatment to lower SBP (Okin, Hille, Kjeldsen, Dahlof, & Devereux, 2014).

Perugia Score System for LVH (Verdecchia et al., 1998)

The Perugia score carried the highest population-attributable risk for cardiovascular morbidity and mortality compared with classic methods for detection of LVH. Traditional interpretation of standard electrocardiography maintains an important role for cardiovascular risk stratification in essential hypertension. ECG-LVH.

Perugia Score requires positivity of one or more of the following criteria:

- SV3+ RaVL >2.4 mV (men) or >2.0 mV (women)
- Left ventricular strain pattern
- Romhilt-Estes score of ≥5 points

The Perugia score has low sensitivity. They showed that the prevalence of LVH in the hypertensive population is highest using the Perugia score, followed by the Sokolow-Lyon voltage criteria.

When compared with traditional criteria for ECG diagnosis of LVH, the Perugia score showed the highest sensitivity (34%) at the expense of a slight decrease in specificity (93%), whereas, for example, the Cornell voltage yielded a sensitivity of 16% and a specificity of 97%.

Cornell/strain index (Verdecchia et al., 2003)

The Cornell/strain [C/S] index, a simple electrocardiographic (ECG) index for left ventricular hypertrophy (LVH) defined by the presence of either a classic strain pattern or a Cornell voltage (sum of R in aVL + S in V(3) >2.0 mV in women or 2.4 mV in men, or both).

After adjustment for age, sex, smoking, and other confounders, the C/S index identified subjects with hypertension at increased risk of events (relative risk 1.76; 95% confidence interval 1.32-2.33). The C/S index achieved the highest population-attributable risk (16.1%) for cardiovascular events in hypertensive patients. Sex affects both the prevalence rates and prognostic values of ECG LVH criteria in the general population, while showing higher prognostic value of ECG LVH in women than in men. The composite of the Sokolow-Lyon voltage and the Cornell voltage seems to be a good option (Porthan et al., 2015).

Framingham score for LVH

Framingham Score, as coexistence of definite strain pattern and at least one of the following 4 criteria:

I) Sum of the amplitude of the R-wave (I) and the S-wave (III) > 2.5 mV;

II) Sum of the amplitudes of S-wave (V_1) or S-wave (V_2) and R-wave (V_5) or R-wave (V_6) ≥ 3.5 mV; c) S-wave (V_1) or S-wave (V_2) ≥ 2.5 mV; d) R-wave (V_{4-5}) ≥ 2.5 mV (Levy et al., 1990).

Adult ECG criteria for left ventricular hypertrophy in young competitive athletes

The ECG diagnosis of LVH in young athletes is challenging due to low sensitivity of the commonly used criteria. Speranza et al. sought to establish whether adult ECG criteria can be appropriate to make diagnosis of both common and uncommon patterns of LVH in young trained athletes. A total of 122 athletes, ages 16.2±3.8 years, training at least 5 h per week, were studied with Sokolow-Lyon voltage, Romhilt-Estes, Cornell voltage, Cornell Product, Perugia and Framingham scores. Garson Criteria were also investigated in athletes under 16. Participants were divided into 2 groups based on the presence (group-A, n=56) or absence (group-B, n=66) of at least one positive ECG score. Test performance was calculated with respect to accurate echocardiographic diagnosis of LVH. There were no inter-group differences regarding physical characteristics and training burden. 9 athletes from group-A (16%) and 2 from group-B (3%) were found to

have LVH, likely to be pathological in 2 cases from group-A. Criteria gathering both QRS voltages and ST-T anomalies, like Perugia-score, best identified this subgroup and should be preferred to those based on QRS voltage analysis alone (Speranza, Magaudda, & de Gregorio, 2014).

Coexistence of a definite strain pattern and at least one of the following voltage criteria:

1. Sum of the amplitudes of the R wave on lead I and the S wave on lead III ≥2.5 mV
2. Sum of the amplitudes of the S wave on lead V1 or V2 and the R wave on lead V5 or V6 ≥3.5 mV
3. The S wave on the right precordial lead ≥2.5 mV and the R wave on the left precordial lead ≥2.5 mV

Combination criteria of LVH (Erice et al., 2009)

The combination of Cornell (RaVL+SV3>2.8 mV in men and>2.0 mV in women) with Lewis (RI+SIII-RIII-SI>1.7 mV) and Gubner-Ungerleider (RI+SIII>2.5 mV) indices displayed the highest net sensitivity (80.0% and 76.7%, respectively) while retaining excellent specificity (88.9% and 91.6%, respectively).

The combination of the Cornell and the Lewis or Gubner voltage criteria showed the greatest net sensitivity and specificity for the LVH diagnosis of HCM in a cardiovascular examination conducted in young people. Erice et al. examined the strongest predictor within ECG voltage criteria for LVH in HCM to be applied in cardiovascular examination of young people. The ECGs of 36 healthy individuals with high voltages, mimicking HCM (i.e., false-positive), were statistically compared with those of 30 subjects with an ECG diagnosis of HCM. The most striking ECG voltages observed in HCM patients were those included in leads I, aVL (R wave) and V_3 (S wave), typically present in the Cornell, Gubner and Lewis voltage criteria. In a stepwise logistic regression analysis model, these indices were the most significant predictors of HCM. The combination of Cornell with Lewis or Gubner-Ungerleider indices displayed the highest net sensitivity (80.0% and 76.7%, respectively) while retaining excellent specificity (88.9% and 91.6%, respectively) (está repetido) showed the greatest net sensitivity and specificity for the LVH diagnosis of HCM in a cardiovascular examination conducted in young people (Erice et al., 2009).

Twelve-lead ECG is a powerful instrument for risk-stratification in HCM.

Table Electrocardiographic scoring system to assess risk for this population

Any deviation in QRS-axis		1point
Pathological T-wave inversion limb leads		1 point
Pathological T-wave inversion precordial leads		2 points
ST-segment depression ≥2 mm		2 points
Dominant S in V4		2 points
Limb-lead QRS-amplitude sum	≥7.7 mV ≥10.0 mV ≥12.0 mV	1 point 2 points 3 points
12-lead amplitude–duration product		1 point 2 points 3 points
QTc		1 point

Max score = 14.; QTc = corrected QT-interval.

The two points for precordial T-wave inversion does not get added on top of the 1 point for limb-lead T-wave inversion, thus total score available for T-wave abnormalities is 2 points (Ostman-Smith et al., 2010).

VI. Indirect criteria for Left Ventricular Hypertrophy/Overload

1) Left atrial enlargement (LAE) in absence of right ventricular hypertrophy/enlargement;
2) Left anterior fascicular block (LAFB);
3) Incomplete left bundle branch block (ILBBB);
4) Advanced LBBB or Complete LBBB;
5) Morphology of left ventricle in multiple leads;
6) Deep and narrow (<40 ms) q waves in inferior leads, mainly leads III and aVF and less often in lead II;
7) Absence of q waves in left leads;
8) Notching and prolongation of QRS complexes or complexes in “M” in I and aVL or V_3 and $V_{4;}$

9) Poor R wave progression in precordial leads. Absence of growth of r wave in the right precordial leads from V_1 to V_3, with sudden increase in V_4;
10) Pseudo septal or anteroseptal infarction pattern;
11) R wave of increased voltage in V2 by dislocation of transition zone to the right;
12) ST elevation in the right precordial leads V1-3 ("discordant" to the deep S waves).
13) Secondary alteration of T wave;
14) Negative U wave in left precordial leads;
15) Prominent U waves (proportional to increased QRS amplitude).
16) Acute atrial fibrillation in myocardiosclerosis;

Common electrocardiographic criteria for the diagnosis of left ventricular hypertrophy (LVH) (Okin et al., 2004)
Cornell voltage criteria SV3 + RaVL ≥ 2.0 mV (28 mm) in men SV3 + RaVL ≥ 2.8 mV (20 mm) in women (some variations use a lower cutoff value in men)
Cornell product criteria SV3 + RaVL (+8 in women **A**) × QRS duration ≥ 2.440 mm × ms
Sokolow-Lyon voltage criteria SV1 + RV5 or RV6 ≥3.5 mV (35 mm) B or RaVL ≥1.1 mV (11 mm)
Romhilt-Estes point score system (a score ≥5 is diagnostic of LVH, a score of 4 is "probable" LVH). Voltage criteria (3 points): Any S or R in limb leads ≥20 mm SV1, SV2, RV5, or RV6 ≥30 mm ST-T wave changes of LVH (3 points, 1 point on digitalis) Left atrial abnormality (3 points): Terminal component of the P wave in V1 ≥1 mm and ≥40 ms Left axis deviation (2 points): QRS axis of ≥−30° Prolonged QRS duration (1 point): ≥90 ms Prolongation of ventricular activation time or delayed intrinsicoid deflection time (1 point): ≥50 ms in V5 or V6

A modification of +6 instead of +8 in women may be more accurate and was used in the Losartan Intervention for Endpoint Reduction in Hypertension (LIFE) study (1)

B A cutoff value of 38 mm has also been used; e.g., in the LIFE study

A systematic review of 21 studies (Pewsner et al., 2007), found that all the criteria were less sensitive than specific:

Of note, the ranges of the published values were extremely broad. For example, the ranges in sensitivity were:

Cornell voltage—median sensitivity 15%, median specificity 96%

Cornell product—median sensitivity 19.5%, median specificity 91%

Sokolow-Lyon voltage—median sensitivity 21%, median specificity 89%

Romhilt-Estes point score—median sensitivity 17%, median specificity 95%.

The ranges in sensitivity were:

Cornell voltage—2% to 41%

Cornell product—8% to 32%

Sokolow-Lyon voltage—4% to 51%

Romhilt-Estes point score—0% to 41%.

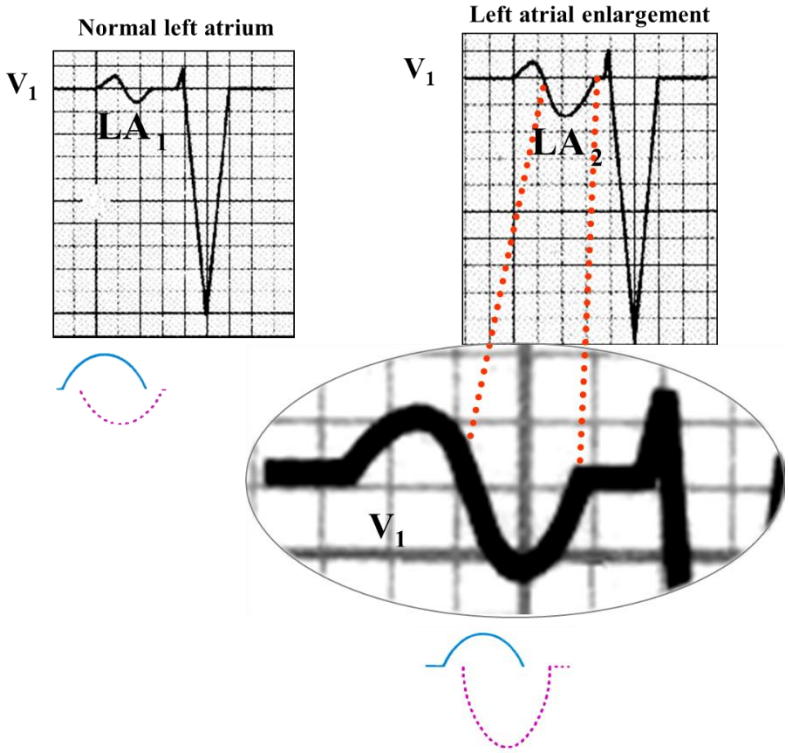
The LIFE study shows that evaluation of both baseline and in-study ECG LVH defined by Cornell product criteria, Sokolow-Lyon voltage criteria or ECG strain improves prediction of CV events and that regression of ECG LVH during antihypertensive treatment is associated with better outcome, independent of blood pressure reduction (Bang et al., 2014).

Reduced myocardial conduction velocity which is either diffuse or regional, or reduced intracellular coupling, may account at least in part for the changes in the QRS patterns observed in patients with LVH (**Bacharova 2014**).

VI. Indirect criteria of LVH

Increase in depth and duration of final negative component of the wave in V_1 (left atrial enlargement Morris' index) (Morris, Estes, Whalen, Thompson, & McIntosh, 1964); slow and deep of P in V_1 or V_1-V_2. PTFV1. P terminal force in lead V_1 equal or more negative than 0.04 mm/s

Greater than 0.03 mm/s: product of the duration of the final negative component (duration expressed in seconds; while depth is expressed in mm). Values above 0.03 mm/s constitute a highly sensitive criterion for the diagnosis of LAE.



Electrocardiographic diagnosis of LVH in the presence of LBBB

The presence of LBBB on 12-lead ECG may obscure the diagnosis of LVH.

The criterion of SV2 + RV6 greater than 4.5 mV demonstrated a sensitivity of 86% and a specificity of 100% for LVH diagnosis in the presence of LBBB.

QRS duration greater than 160 ms plus left atrial enlargement strongly supports the diagnosis of LVH in the presence of LBBB (Klein, Vera, DeMaria, & Mason, 1984).

There are no differences in limb lead voltage, intrinsicoid deflection, or mean frontal plane QRS axis.

The following criteria can be helpful in left bundle branch block: QRS voltage increase, left atrial enlargement, QRS duration >155 ms (Oreto, Saporito, Messina, Lanteri, & Luzza, 2007).

LVH can be diagnosed in the presence of LBBB with an accuracy at least similar to that observed in patients without this conduction defect. Computer-assisted interpretation of the ECG may be useful in the diagnosis of LVH as it enables the implementation of more accurate algorithms. Diagnostic algorithms, voltage-duration products, and certain compound criteria had the best sensitivities (Rodriguez-Padial et al., 2012).

LA abnormality is significantly diagnostic of LVH in the presence of LBBB. Age, body mass index, body surface area, frontal axis, and QRS duration are also significant predictors of LV mass (Mehta, Jain, Mehta, & Billie, 2000).

Kafka parameters for the diagnosis of LVH in presence of LBBB

Kafka et al (Kafka, Burggraf, & Milliken, 1985) selected and used 5 ECG parameters in cumulative fashion for the diagnosis of LVH in the presence of LBBB:

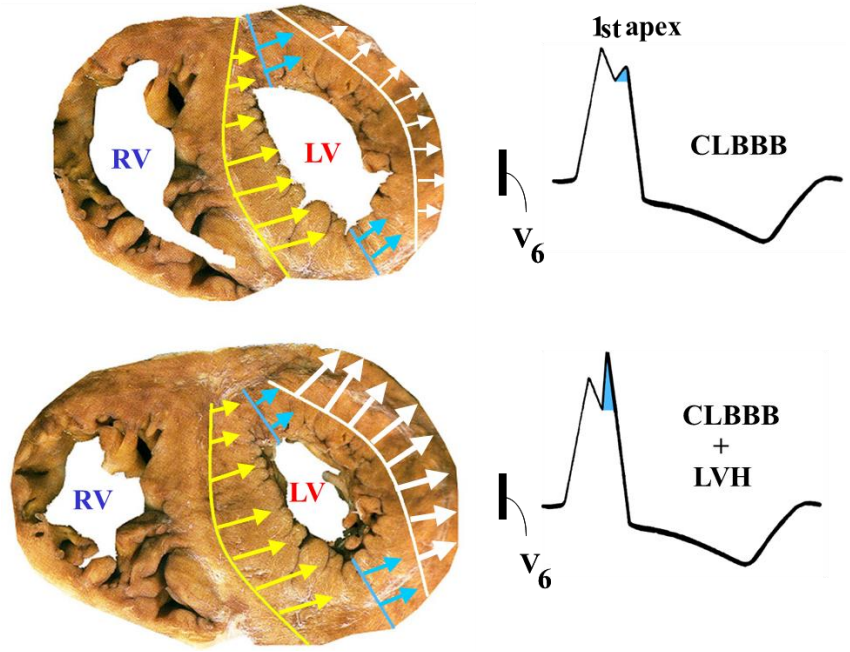
1. RaVL ≥11 mm;
2. QRS axis ≤40º or SII greater than RII;
3. SV1 + RV5 to RV6 ≥40 mm;
4. SV2 ≥30 mm
5. SV3 ≥25 mm.

This cumulative approach was superior to using single conventional criterion such as SV1 + RV5 or RV6. When LVH was defined as an M-mode index of at least 115 g/m2, the sensitivity was 75% and specificity 90%. Using M-mode, a mass of at least 215 g was the standard, the sensitivity was 73% and the specificity 66%.

LVH can be diagnosed by ECG criteria in the presence of LBBB at least as reliably as in normal conduction.

LVH criteria in the presence of Complete Left Bundle Branch Block

According to the apex of R wave in V_6, of greater amplitude than the first apex. As the LV free wall has more mass to be depolarized, the last apex is of greater voltage than the first.



ECG Diagnosis of LVH in the Presence of RBBB

With RBBB, ECG criteria for LVH using right precordial S waves and combination criteria of right precordial S waves and left precordial R waves have a marked reduction in sensitivity, whereas left precordial R wave criteria have modestly reduced sensitivity. Limb lead criteria for LVH have increased sensitivity in the presence of RBBB. Acceptable sensitivity for the diagnosis of LVH in patients with bundle branch block requires a combination of limb and precordial lead voltage criteria and/or other nonvoltage ECG criteria, since the prevalence of LVH in the presence of RBBB appears higher than the sensitivity of individual criteria.

1. Presence of Morris criteria for left atrial enlargement in absence of mitral valve stenosis. Specificity: 90%, sensitivity: 32%;
2. SÂQRS deviation to the left beyond -30°: specificity: 68%, sensitivity: 61%;
3. Voltage of R wave of I > than 10 mm. Specificity: 90%, sensitivity: 39%;
4. Voltage of R wave of aVL > than 7 mm. Specificity: 74%, sensitivity: 50%;
5. In I and aVL, qRs pattern, with q and R wave of greater voltage and s wave of reduced voltage;
6. rSr' pattern in the leads of the inferior wall: II, III and aVF;
7. Unipolar morphology of right precordial leads observed in intermediary precordial leads V3 and V4;
8. Increase in S wave depth in V1: rSr'. The S corresponds to vector III of the hypertrophic LV free wall that gets away from V1;
9. Voltage of R wave of V5 ≥ than 20 mm. Specificity: 90%, sensitivity: 20%;

10. S wave of V1 + R of V5 or V6 > 35 mm. Specificity: 100%, sensitivity: 4%;
11. R-wave peak time of V5 and V6 ≥ than 50 ms.

In right bundle branch block, LVH is suggested by a left atrial enlargement pattern, secondary repolarization changes, and a sum of S wave in lead III plus the maximal R+S in a precordial lead ≥ 35 mm (Oreto 2007)

Chan et al. (Chan et al., 2006) examined the instantaneous effect of RBBB on QRS amplitudes and LVH voltages in 40 patients who had intermittent complete RBBB during a single 10 s standard 12-lead ECG recording. RBBB was associated with an increase in initial QRS forces (RV1, RV2, and QV6) but significant decreases in mean mid-QRS amplitudes that reflect LV depolarization (RaVL, SV1, SV3, RV5, and RV6).

All late QRS forces were increased with RBBB (R` V1, SV5, SI). As a result, combined voltages used for LVH criteria were significantly reduced by RBBB: Sokolow-Lyon voltage decreased from 1520 to 1014 microvolts ($p < 0.001$), and Cornell voltage decreased from 1438 to 746 microvolts ($p < 0.001$). (See the next 4 slides). The authors conclude that RBBB is associated with significant reduction in "left ventricular" QRS amplitudes of the standard ECG, consistent with cancellation, rather than unmasking, of left ventricular mid-QRS forces by altered septal and delayed RV depolarization. Because QRS voltages that are routinely combined for the detection of LVH are reduced in RBBB, standard LVH criteria will perform with lower sensitivity in patients with RBBB.

Other criteria for RBBB: Max R/S precordial lead (with LAD) > 29 mm; S V1 >2 mm; R V5,V6 >15 mm; S III+max R/S precordial (with LAD) >40 mm; RI >11 mm (Vandenberg & Romhilt, 1991).

Amplitudes are given in millimeters, where 1 mm=0.1 mV. LAD indicates left axis deviation.

ECG Diagnosis of LVH in the Presence of left anterior fascicular block

The following criteria have been used: S V1+R V5+S V5 >25 or S V1,2+R V6+S V6 >25 (Bozzi & Figini, 1976); S III+max R/S any lead (men) >30 and S III+max R/S any lead (women) >28 (Gertsch, Theler, & Foglia, 1988).

Complex criteria using computerized recording and interpretation system

These include:

a) Indices based on products of voltage and QRS duration (Okin, Roman, Devereux, & Kligfield, 1995);

b) Computation of QRS area (Okin et al., 1996);
c) Composite use of several criteria (Schillaci et al., 1994),
d) Indices based on scores derived from regression equations that incorporate multiple electrocardiographic and nonelectrocardiographic factors (Norman & Levy, 1995; P. M. Rautaharju et al., 1996).

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