SUBCLINICAL CARDIAC DAMAGE IN CARDIOPULMONARY POLYMORBIDITY (REVIEW) PART 1

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Abstract

Hypertension and chronic obstructive pulmonary disease are one of the frequent comorbid conditions in internal medicine and are subject to meaningful cooperation among physicians, cardiologists, and pulmonologists.

A combination of chronic obstructive pulmonary disease and hypertension presents certain diagnostic and therapeutic challenges. These conditions share common risk factors, similar clinical presentations and some common parts of pathogenesis. The problem of association between chronic obstructive pulmonary disease and hypertension may be currently discusses both as a simple combination of various clinical entities, and as chronic obstructive pulmonary disease resulting in development of factors contributing to hypertension. One way or another, either a simple combination, or a mutually aggravating syndrome, but we state there is a cardiorespiratory continuum where chronic obstructive pulmonary disease acts as a valid component of hypertension development, and vice versa. Thus, it seems to be relevant to study peculiarities of the structural and functional status of the cardiovascular system and microcirculation, systemic remodeling mechanisms, endothelial dysfunction and inflammation in presence of chronic obstructive pulmonary disease -associated hypertension. Problems of additional cardiovascular risk marker development, treatment efficiency assessment remain topical.

Use of electrocardiography and echocardiography with dopplerometry has been an important diagnostic principle of subclinical cardiovascular damage in presence of hypertension and chronic obstructive pulmonary disease comorbidity. Non-invasive imaging methods play a central part in diagnostics of subclinical target organ damage. Wide implementation thereof is based on high diagnostic accuracy, common availability, safety and relatively low price.

Keywords: *hypertension, chronic obstructive pulmonary disease, comorbidity, electrocardiography, echocardiography with dopplerometry.*

Hypertension (HT) is one of the most serious common chronic diseases in humans causing disability and significantly reducing life length by 15–20 years on average. According to the WHO, between 10% and 30% of adult population in developed countries have HT.

A deeper investigation into clinical complications of HT resulted in development of a cardiovascular risk concept. A sufficient body of statistical data based on numerous epidemiological studies was collected allowing saying that every studied factor contributes to development, course, progression and outcome of this cardiac pathology.

Experts from the European Society of Hypertension (ESH) and the European Society of Cardiologists (ESC) extensively study the issues of concern related to stratification of the cardiovascular risk, treatment approaches, develop promising areas for future research. The major conclusions are summarized in units. The first unit addresses the following issues of concern: evaluation of subclinical target organ

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damage for complete cardiovascular risk stratification; treatment approaches; treatment strategy; therapeutic approach in particular conditions; treatment of concomitant risk factors.

Of particular note is the concept of target organs damage - heart, vessels, kidneys – by HT with the rationale for analysis methodology of subclinical damage thereof for the purpose of quantifying the overall cardiovascular risk which is of particular importance for optimization when treatment initiation, intensity and goals are decided.

Chronic obstructive pulmonary disease (COPD) is defined as a condition characterized by partially irreversible airflow restriction which is constantly progressing and associated with inflammatory reaction of pulmonary tissue to irritation by various pathogenic agents and gases [1].

A prevailing verification component in COPD identification is bronchopulmonary manifestations; however, extrapulmonary signs of COPD have been increasingly discussed lately, because clinical studies prove that development of COPD extrapulmonary effects have an important clinical and prognostic significance and define COPD as a systemic condition.

Cardiovascular diseases are diagnosed in at least 50% of patients with chronic obstructive pulmonary disease (COPD), which significantly increases risk of cardiovascular disease development two- or threefold [2]. HT and COPD are one of the frequent comorbid conditions in the internal medicine and are subject to meaningful cooperation among physicians, cardiologists, and pulmonologists [3].

A combination of COPD and HT presents certain diagnostic and therapeutic challenges. These conditions share common risk factors, similar clinical presentations and some common parts of pathogenesis. The problem of association of COPD and HT may be currently discusses both as a simple combination of various clinical entities, and as COPD resulting in development of factors contributing to HT. One way or another, either a simple combination, or a mutually aggravating syndrome, but we state there is a cardiorespiratory continuum where COPD acts as a valid component of HT development, and vice versa.

Development of these conditions is underpinned by a complex of pathogenic mechanisms aiming target organs directly or indirectly - through damaging a vessel wall, developing endothelial dysfunction, and increasing arterial stiffness. Those factors include hypoxemia at rest or on exertion, smoking, oxidative stress, systemic inflammation. Mutual aggravation and progression in case of combination of bronchopulmonary conditions and cardiovascular pathology are based on similar parts of pathogenesis (pulmonary and cardiac microcirculation impairment, pulmonary hypertension) causing early development of cardiorespiratory complications [4, 5].

According to numerous researchers, COPD and HT are mainly associated through endothelial dysfunction and systemic inflammation.

Endothelial Dysfunction

Cardiovascular effects, including endothelial damage leading to endothelial dysfunction (ED), are considered to be among the potential systemic presentations of COPD. Endothelium of vascular intima fulfils barrier, secretory, hemostatic and vasotonic functions, plays an important part in vascular wall inflammation and remodeling processes. ED may be defined as an imbalance between relaxing and constricting factors, anti- and procoagulant mediators, growth factors and inhibitors thereof. COPD patients show early ED development in pulmonary and systemic circulations associated with changes in collagen-elastin exchange in vascular walls due to hypoxemia, exposure to cigarette smoke pollutants, hemodynamic and oxidative stress, systemic inflammation, and proteinase-proteinase inhibitor system imbalance.

The literature data suggest that ED development is currently one of the major factors of pulmonary hypertension (PH) pathogenesis associated with COPD. Pulmonary heart disease development with change of the right and, at certain stages, left compartments of heart may be considered COPD systemic presentation. The concept of endothelial regulatory role in PH pathogenesis is mainly based on findings from *in-vitro* animal tests or tests with human preparations, meanwhile there are only few *in-vivo* studies. ED role in PH pathogenesis was studied predominantly in patients with primary PH where vascular wall structural impairments are acknowledged as the basis for pathogenesis.

ED is one of the first presentations of COPD-associated vascular complications which are identified at early stages of the condition, aggravate increasing respiratory disturbance, hypoxemia and tissue hypoxia. The association between bronchial obstruction and bronchial inflammation accompanied by increase in neutrophil and macrophage counts in bronchoalveolar lavage fluid presenting as

decrease in FEV1 (forced expiratory volume), and systemic inflammatory response with endothelial damage was proven. ED has been an object of interest lately, since ED is associated with high cardiovascular risk. Therefore, it is feasible in COPD-associated HT treatment to prescribe antihypertensive drugs which should both lower blood pressure efficiently, and exert positive effect on endothelial function, reduce pulmonary hypertension, decrease severity of systemic inflammatory response having no negative impact on one's respiratory system [6].

Chronic Systemic Inflammation

Chronic systemic inflammation syndrome, which plays a predominant role in the pathogenic cascade both for HT, and for COPD, may be considered as another global association mechanism. Chronic systemic inflammation is a typical multi-syndrome pathological process developing in response to the systemic damage and characterized with total inflammatory responsiveness of endotheliocytes, plasma and cell blood factors, connective tissue, and, at terminal stages, forms pathological microcirculation disturbances in vital organs and tissues [7, 8].

In presence of COPD, even if clinically stable, subclinical systemic inflammation accompanied by significant effect of pro-inflammatory cytokines on skeletal muscle metabolism, specifically, on their regeneration, is often observed. Fabbri and Rabe suggest viewing COPD as a "chronic systemic inflammatory syndrome" [9-11].

Subclinical systemic inflammation is considered to potentially induce development of systemic presentations in the presence of COPD [12, 13].

Fabbri et al. proposed a new approach to diagnosis, severity assessment and management of COPD and its frequent concomitant conditions, which lies in identification of the *"chronic systemic inflammatory syndrome"* signs [14]. Patients with moderate and severe COPD both during its acute condition, and its steady course, were proven to show signs of systemic inflammation confirmed by increase in circulating cytokines (TNF α [tumor necrosis factor α], IL-6 [interleukin 6], and IL-8 [interleukin 8]), chemokines and proteins of acute phase [15].

COPD patients display impairment of vasoactive endothelial function, pro-inflammatory cytokine balance, and increase in circulating immune complex concentration even at an early stage of the condition. The developed systemic inflammation and endothelial dysfunction (ED) directly and indirectly contribute both to development of pulmonary hypertension and chronic pulmonary heart disease, and development of left ventricular failure; increase in plasma endothelin concentration associated with COPD may be viewed as one of the signs of ED presence. This biologically active substrate activates receptors on smooth muscle cells, induces steady vasoconstriction and proliferation of small vascular media, stimulates further activation of pro-inflammatory cytokine cascades, maintains persistence of the chronic inflammation, and enhances platelet adhesion and microthrombi formation [16].

Clinical studies suggest that COPD is accompanied by development of pulmonary hypertension in 30–50% of cases. Presence of pulmonary hypertension complicates prognosis and is one of the major factors which determine survival in COPD patients. It has been determined that life prognosis in COPD patients becomes unfavorable when pulmonary hypertension becomes stable and circulation deficiency develops. Two thirds of COPD patients die during the period between 15 months and 5 years after circulatory decompensation development which occupies the third place after hypertension and chronic coronary insufficiency among causes of death in the age group of over 50. Despite the fact that decompensated chronic cor pulmonale (CCP) causes death in 30–37% due to circulatory deficiency and in 12.6% of all cases – due to cardiovascular diseases, early diagnosis of CCP, its decompensation and development of effective treatment remain topical; finding solutions to these problems is inseparable from understanding CCP pathogenesis. An inflammatory response which is excessive in intensity and duration intensifies the endocrine system activity with enhanced release of hormones and neurotransmitters into blood, and cytokine regulation imbalance. It is no doubt that there is a correlation between the systemic inflammation and cardiovascular diseases [17]. Haplotypes associated with increase in C-reactive protein (CRP) concentration do not cause cardiovascular pathologies as such [18]. Thus, CRP is more likely to be a marker rather than a cause of such concomitant diseases. In presence of COPD, there is a direct association between a level of the systemic inflammatory response and artery rigidity [19].

The major mediators of the chronic systemic response include pro-inflammatory interleukins

(IL-1, 2, 6, 8, 9, 12, 18) [20], tumor necrosis factor (TNF?) [21], matrix metalloproteinases [22].

Biomarkers specific for COPD-associated inflammation may include desmosine isomers [23], leukotriene B4 [24], IL-8, neutrophil elastase and surfactant protein D [25].

Among HT pathogenic mechanisms in COPD patients, the major role is played by primary sympathoadrenal system (SAS) activation. Thus, COPD-associated HT pathogenesis involves a renal part which lays in hyperactivity of renin-angiotensin-aldosterone system (RAAS), enhancement of juxtaglomerular system activity, renin and angiotensin 2, with the renal mechanism of COPD-associated HT quickly becoming a predominant one. In presence of bronchial obstruction in combination with HT, high RAAS activity is observed as early as at the initial COPD stage and hyperactivity of its tissue components is reported. Enhanced RAAS activity may cause hypokalemia in COPD patients leading to progression of respiratory disturbance through diminution of breathing muscular strength [26].

Thus, it seems to be relevant to study the peculiarities of the structural and functional status of the cardiovascular system and microcirculation, systemic remodeling mechanisms, endothelial dysfunction and inflammation in presence of COPD-associated HT. Problems of additional cardiovascular risk marker development, treatment efficiency assessment remain topical.

Use of electrocardiography and echocardiography with dopplerometry has been an important diagnostic principle of subclinical cardiovascular damage in presence of HT and COPD comorbidity. Non-invasive imaging methods play a central part in diagnostics of subclinical target organ damage. Wide implementation thereof is based on high diagnostic accuracy, common availability, safety and relatively low price. EchoCG allows for fast evaluation of the heart size, valvular heart apparatus status, systolic and diastolic functions of ventricles.

Structural biomarkers of subclinical organ damage
Electrocardiography

Electrocardiography (ECG) still remains the most available and relevant method in various diagnostic algorithms. PAC-COPD Study – 2013 [27] results show presence of myocardial structural and functional pathology in 64% of chronic obstructive pulmonary disease (COPD) patients when they are referred to an in-patient department for the first time, with 27% of patients displaying left heart damage, and 48% displaying right heart damage.

ECG signs of Right Atrial Hypertrophy

Right atrial myocardial hypertrophy results in increase of its excitation vector, leading to increased amplitude and duration of the first portion of the P-wave, with virtually no changes in left atrial depolarization processes; in this regard, the right atrial excitation ends almost simultaneously with the left atrium. The sum of the right and the left atrial vectors results in a high sharpened P-wave, often referred to as P-pulmonale (*Fig. 1*).
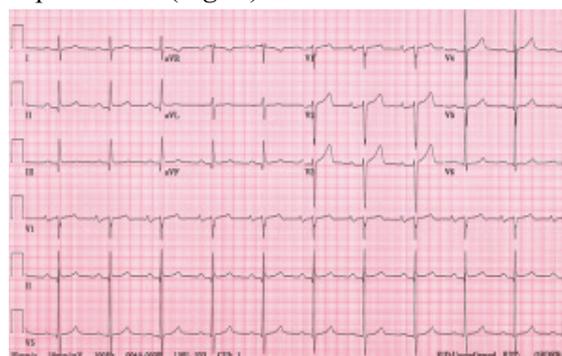

Fig. 1. Right Atrial Hypertrophy (P-pulmonale)

ECG findings show the following:

1. High (over 2.5-mm amplitude), sharpened, symmetrical P-wave with normal duration (0.1 second) in leads II, III, AVF.

2. P-wave electrical axis deviation to the right (PIII > PII > PI), with a somewhat smoothed P-wave in leads I and AVL.

3. In AVR: a deep, sharpened negative P-wave is recorded.

4. In chest leads – V1, V2 a high-amplitude (over 1.5-mm) sharpened or diphasic P-wave with predominant positive first phase (+/-). Depending on hypertrophy severity, similar changes may be recorded for the leads between V_1 and V_5; however, the P-wave amplitude in V_{5-6} leads lowers.

5. In leads III, AVF and V1: activation time elongation for 0.04 seconds is recorded [28].

Right atrial myocardial hypertrophy may be additionally confirmed with the Macruz index calculation:

$$\frac{\text{P-wave (seconds)}}{\text{PQ segment (seconds)}}$$

In presence of the right atrial hypertrophy, it will be less than 1.1.

The amplitude criteria (P II>2 mm, P V_1>1 mm) displayed high P-pulmonale specificity: for men – 100%, for women – 94%; however, the performed analysis comparing these ECG criteria with echocardiography findings, namely, with the right atrial volume index recommended as a determinant for the right atrial size, showed

somewhat low sensitivity of these markers; P V_1>1 mm (66.%) and P II>2 mm (48%) showed the highest sensitivity without any gender differences [29]. Similar data were also displayed for structural and volumetric findings with cardiovascular magnetic resonance: ECG was 96 – 100% specific, but its sensitivity made up 17% [30].

ECG signs of Right Ventricular Hypertrophy

In presence of the right ventricular hypertrophy (RVH), sum excitation vector of the QRS complex shifts to the right and anteriorly resulting in the increased R-wave amplitude in right precordial leads. The more severe the RVMH is, the more the balance of cardiac ventricular vectors changes and the more the dominant effect of the left ventricular excitation vector reduces.

Electrocardiographic findings may include several presentations of RVH: the first one: predominance of the R-wave (in the QRS complex) in the right precordial leads, so-called R-type: such changes are specific for severe RVH and pressure overload; the second variant: ECG is comparable to the picture of the incomplete right bundle branch block and may be recorded in case of pressure overload, and the third variant: presence of deep S-waves in all chest leads at moderate RVH – S-type. The first and the second variants are often recorded in patients with chronic obstructive pulmonary diseases, the third variant is recorded for chronic non-obstructive pulmonary diseases.

Severe RVH, hypertrophied right half of the interventricular septum changes orientation of the initial sum excitation vector right to left; with further depolarization, two oppositely directed vectors interface: left and right ventricles – a sum vector is formed due to a hypertrophied right ventricle and is oriented toward it, i.e. left to right. In the context of delayed depolarization in the hypertrophied right ventricle, its repolarization processes start near endocardium, while in the left ventricle they start as usual from epicardium leading to change in normal direction of the sum repolarization vector, and it deviates to the left (*Fig. 2*).

Fig. 2. Right Ventricular Hypertrophy

ECG displays so-called R-type right ventricular hypertrophy:

1. High R-wave (more than 7 mm) in V_{1-2} leads, with R $V_1 \geq$ S V_2

2. Deep S-wave (more than 7 mm) in V_{5-6} lead

3. Decrease in amplitude R V_5, V_6 <5 mm

4. R/S ratio in V_6 leads α 1

5. R V_1 + S V_5 or R V_1 + S V_6> 10.5 mm (Sokolow index)

6. The QRS complex in the right precordial leads is graphically displayed as qR or R, less often as Rs, and in the left leads – as rs or RS; furthermore, the more severe the right ventricular myocardial hypertrophy is, the higher the R-wave in V_{1-2} leads and the deeper the S-wave in V_{5-6} leads are.

7. ST segment: a downsloping or upward-oriented curve depression is recorded in V_{1-2} leads with V_{5-6} elevation

8. The T-wave is negative, asymmetric in V_{1-2} leads, and positive in V_{5-6} leads.

9. The electrical cardiac axis (ECA) deviation to the right has an α angle $\geq$110°.

Moderate Right Ventricular Hypertrophy or S-Type

In the presence of this type, there is no severe interventricular septal hypertrophy and the sum excitation vector has a typical left-to-right orientation, ongoing depolarization processes in the right and left ventricles result in formation of the excitation vector oriented right to left; however, its size will be somewhat smaller than normal due to the dominant effect of the excitation vector of the hypertrophied right ventricle. Repolarization processes often have a typical course (*Fig. 3*).

In presence of this type of hypertrophy, ECG changes may be absent or may be displayed as insignificant changes in R- and S-wave amplitudes in chest leads and ratio thereof, namely, as
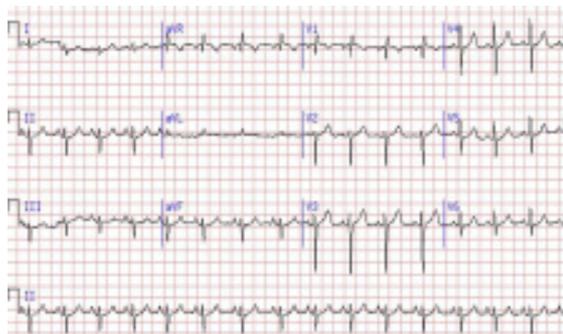

Fig. 3. Moderate Right Ventricular Hypertrophy or S-Type

somewhat increased R-wave amplitude in V_{1-2} leads (up to 6 mm) with decrease in V_{5-6} down to 3 mm [31], with decreased intensity of the S-wave depth in V_{1-2} and increase thereof in V_{5-6}. The heart apex turning posteriorly displayed at ECG as deep S-waves in standard (S_I–S_{II}–S_{III}, with maximum in the second lead) and precordial leads with the rS complex graphical pattern and transitional zone shifting to the left, and ECA deviation to the right with the α angle ≥110° are recognized as typical criteria. The ST interval changes are insignificantly displayed or absent.

Right Ventricular Hypertrophy with Incomplete Right Bundle Branch Block

In this RVH type, initial depolarization processes have a typical course with formation of a left-to-right-oriented sum excitation vector; however, the right interventricular septal hypertrophy may result in the dominant influence of a vector of the left half being levelled out, leading to decreased sum vector amplitude. Similar changes are also observed in ventricles aggravated by the delayed depolarization course in the right ventricle which continues after the end of the left ventricular myocardial excitation leading to formation of a left-to-right-oriented vector. A hypertrophied right ventricle also affects repolarization processes shifting its sum vector to the left (*Fig. 4*).
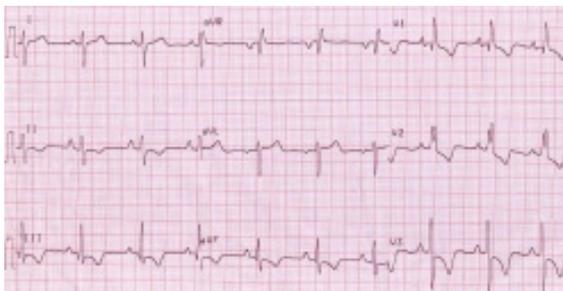

Fig. 4. Right Ventricular Hypertrophy with Delayed Excitation and Incomplete Right Bundle Branch Block

ECG findings display the following:

1. The pattern of the complex is rsR' or rSR' (R' v1 > r v1) in V1 and qRS in V1 with its duration not more than 0.12 seconds.

2. Decrease in the R-wave amplitude in V_6 and the S-wave depth in V_1.

3. Increase in the S-wave depth and duration in V_{5-6}.

4. The right ventricular (RV) activation time in V_1 is increased up to 0.05 seconds.

5. The ECA deviation to the right has an α angle ≥110°.

6. ST segment: a downsloping or upward-oriented curve depression is recorded in V_{1-2} leads with V_{5-6} elevation.

7. The T-wave is negative, asymmetric in V_{1-2} leads, and positive in V_{5-6} leads.

Other amplitude criteria of RVH include presence of a delayed R-wave with its amplitude at least 4 mm in the AVR lead, with development of the QR complex or rSR' pattern; the Lewis index (R I + S III)–(S I + R III) is less than 15 mm; the Butler-Leggett index (maximum R V1,2+ maximum S I, V_6 – S V_1) is more than 6 mm.

RVH identification criteria show high specificity and sensibility both during ECG findings assessment and its comparison with the cardiac magnetic resonance imaging findings; the most sensitive (89%) and specific (93%) LVH criteria included ECA deviation to the right with the α angle >90°, presence of a high-amplitude R-wave > 5 mm in V1, R/S> 1 and the QRS complex pattern in V1 as rsr' or rsR' [32]; however, other criteria, such as the Butler-Leggett index, turned out to be a highly specific (100%), but insensitive (74%) RVMH marker [33].

ECG signs of Left Atrial Hypertrophy

Depolarization processes in a hypertrophied left atrium (LAH) are more prolonged leading to increase in sum excitation vector shifting it to the left and somewhat downward; ECG findings display a two-humped wide P-wave (p-mitrale) – the first portion of the wave reflects an unchanged right atrial excitation vector, and the second one reflects a hypertrophied left atrium and is displayed by the apex increased in duration and amplitude (*Fig. 5*).
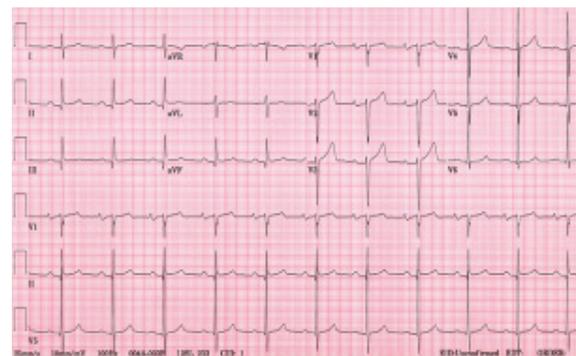

Fig. 5. Left Atrial Hypertrophy

ECG findings show the following:

1. A wide (more than 0.1–0.12 seconds in duration), two-humped P-wave with an interval between apices more than 0.02–0.04 seconds in left leads (I, II, AVL, V_{5-6})

2. A negative, wide, two-humped P-wave in AVR.

3. P-wave ECA deviation to the left (α = -30°–90°), with a high-amplitude P-wave in lead I and formation of the ratio: P I> P II> P III.

4. In V_1, the P-wave is displayed as a negative or diphasic (+/-) wave with significant (>1 mm deep), wide (0.04 seconds and more) negative portion.

The Macruz index may serve as an additional LAH confirmation criterion:

$$\frac{\text{P-wave (seconds)}}{\text{PQ segment (seconds)}}$$ In presence of the right atrial hypertrophy, it will be more than 1.6.

LAH criteria for the standard ECG and cardiac computed tomography findings were compared suggesting that, among all the diagnostic criteria, the increased P-wave duration (more than 0.11 seconds) showed the highest sensitivity (71%) and specificity (55%), other parameters did not have sufficient diagnostic accuracy [34]; however, in 2014, sensitivity was demonstrated to increase with simultaneous presence of two criteria (P-wave duration > 0.12 seconds and its diphasic nature in V_1), its specificity was up to 100% [35], studies continued in 2016 with experimental voxel-based biatrial models and demonstrated directly associated, statistically significant correlations between the left atrial wall thickness and increase in the second phase duration of the P-wave in V_1 (more than 0.4 seconds) [36].

ECG signs of Left Ventricular Hypertrophy

In presence of left ventricular hypertrophy (LVH), excitation vector of the interventricular septum and ventricles increases and shifts to the left, which is displayed in ECG as increase in QRS complex amplitude in left leads, and ECA shift to the left. In this situation, repolarization processes in the thickened left ventricular (LV) and interventricular septal walls progress slowly and start at the endocardium, leading to an ECG left-to-right change in the repolarization vector and shift of the ST segment below an isoline in left leads and above an isoline in right leads extending to a concordant, asymmetric T-wave (*Fig. 6*).

ECG findings show the following:

1. In limp leads:

R I ≥ 15 mm; R AVF >20 mm; R AVL>11 mm; Q or S AVR>19 mm;

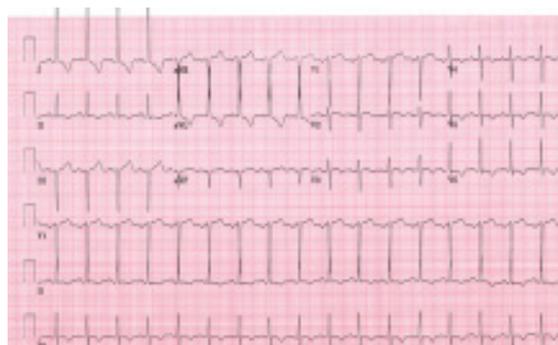R I+ S III >25 mm (Gubner index); (R I- S I)+(S III- R III) >16 mm (Lewis index).

Fig. 6. Left Ventricular Hypertrophy

2. In precordial leads:

S V_1 >23 mm; S V_2 >25 mm; R V_5 >33; R V_6 >25 mm;

S $V_1(V_2)$ + R $V_5(V_6)$ >35 mm for individuals of over 40, and S V1(V2) + R $V_5(V_6)$ >45 mm for individuals under 40 (modified Sokolow-Lyon index)

3. Combined criteria (precordial and limb leads):

RS AVF +V_2 +V_6 >59 mm for individuals over 30 and RS AVF +V_2 +V_6 >93 mm for individuals under 30;

S V_3 +R AVL >28 mm for men, and S V_3 +R AVL >20 mm for women (Cornell voltage index)

(S V3 +R AVL)* QRS (ms) for men, and (S V3 +R AVL+8)* QRS (ms) for women >2400 mm*ms (Cornell product) [31.37]

Additional criteria are believed to include:

The ratio for the R-wave: R I> R II > R III; R V_6 ≥ R V_5 ≥ R V_4; ECA deviation to the left; insufficient R-wave amplitude buildup in right precordial leads, in presence of a deep, occasionally wide S-wave; the S segment changes displayed as downsloping depression in V_5, V_6.

The Romhilt-Estes score system is also known; the following parameters are used for assessment: [38]

• R or S amplitude in any limb lead ≥ 20 mm • S V_1 or SV_2 amplitude ≥ 30 mm • R V_5 or V_6 amplitude ≥ 30 mm	3 scores
ST segment or T-wave discordant to the QRS complex in V_5 or V_6 • without digitalis administration • with background digitalis administration	 3 scores 1 score
P-wave: presence of a negative deep (≥ 10 mm) and prolonged (≥ 0.4 seconds) wave in V_1	2 scores
ECA deviation to the left (α angle ≤ -30°)	2 scores
QRS duration ≥ 0.09 ms	1 score
Time of internal deviation V_{5-6} ≥ 0.05 ms	1 score
According to the Romhilt-Estes score system, 5 or higher scores suggest presence of LVH, 4 scores suggest possible LVH, 3 and lower scores suggest low likelihood of LVH.	

Despite availability of numerous LVH identification criteria, they display quite low sensitivity (10.5%–68%) with high specificity (89%–99%) [39–42].

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