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Головний редактор:

Соколенко Л.С. кандидат педагогічних наук, доцент, професор кафедри медико-біологічних основ фізичної культури Уманського державного педагогічного університету імені Павла Тичини

Редакційна колегія:

Бойко Ю.С. кандидат педагогічних наук, доцент кафедри медико-біологічних основ фізичної культури
Танасійчук Ю.М. доктор філософії, старший викладач кафедри медико-біологічних основ фізичної культури

Відповідальний за випуск:

Танасійчук Ю.М. доктор філософії, старший викладач кафедри медико-біологічних основ фізичної культури

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*Kseniia Voroniuk, Larysa Sydorchuk, Oleksandr Hinhuliak,
Alina Sokolenko, Yuliia Repchuk, Marianna Semianiv*

**THE RELATIONSHIP BETWEEN ALTERATIONS IN HYPERTROPHIC
GEOMETRIC MODELS OF THE LEFT VENTRICLE AND CLINICAL,
ANTHROPOMETRIC, METABOLIC-HORMONAL FACTORS, AND
MINERAL METABOLISM MARKERS**

Left ventricular hypertrophy (LVH) is an adverse prognostic marker for the development of fatal cardiovascular events, including in patients with arterial hypertension (AH).

In some clinical and experimental studies, a relationship between LVH, interstitial myocardial fibrosis, and parathyroid hormone (PTH) has been demonstrated. It has been found that PTH is associated with interstitial myocardial fibrosis in patients with primary hyperparathyroidism, end-stage renal disease with secondary hyperparathyroidism, and AH. The relationship between PTH and LVH has been shown not only in the disease state, but also for the general population and elderly people [1,2,3,4].

Vitamin D may play an important role in reducing LVH through modulation of the renin-angiotensin system (RAS). RAS plays a key role in regulating the volume and homeostasis of arterial pressure, and excessive RAS activation is a major pathogenic factor in hypertension, cardiac hypertrophy, and atherosclerosis [5].

Concentric LVH (CLVH) is most commonly seen in patients with AH and is associated with a 30% increased risk of cardiovascular events (CVD) [6]. However, some researchers have found myocardial hypertrophy of the interventricular septum in individuals with borderline hypertension, in the absence of chronic volume and pressure overload. Eccentric or dilated LVH (dLVH), the second most common form after AH, is associated with a decrease in myocardial contractile function and a 15% increase in CVD [7,8]. On the other hand, the risk of cardiovascular complications (CVC) for isolated increase in relative wall thickness of the LV (concentric remodeling – CR LV) is unclear.

Material and methods. The case-control study involved 100 patients with EAH stage II, 1-3 degrees of blood pressure (BP), high and very high cardiovascular risk. Among the patients there were 21% (21) men, 79% (79) women. The mean age of patients was 59.86 ± 6.22 y.o. The control group consisted of 60 almost healthy individuals, relevant in age (49.13 ± 6.28 y.o.) and gender distribution (63% - women, 37% - men). The lipid panel parameters, such as: TC (Total cholesterol), TG (Triglycerides), LDL-C (Low-density lipoprotein cholesterol), HDL-C (High-density lipoprotein cholesterol) were investigated in blood plasma. All recruited subjects were tested for serum levels of fasting glucose, ionized calcium, parathyroid (PTH) hormone, 25-hydroxyvitamin D (Vit D). Left ventricular hypertrophy (LVH) and LVH models were assessed by echocardiography. Conducted clinical and anthropometric examination methods.

Laboratory and clinical data collection

All recruited patients were observed by general physicians, cardiologists and underwent a complex of basic clinical examinations: clinical anamnesis recording, anthropometric parameters, body mass index (BMI, kg/m²), complete blood count,

total cholesterol level, low / high density level cholesterol (LDL-, HDL-C), serum uric acid, office SBP, DBP and heart rate (HR) measurement, ECG in 12 leads, EchoCG, kidneys' ultrasound examination and Daily Holter BP monitoring in undetermined conditions according to Ukrainian standards (2019) and European recommendations ESC/ESH (2018, 2021).

All patients and healthy subjects were tested for serum level of ionized calcium (Ca²⁺) (potentiometry, "SINNOWA", China), parathyroid hormone (PTH) and 25-hydroxyvitamin D (Vit D) (immune luminescent test "MAGLUMI", "SNIB", China).

Left Ventricular Hypertrophy Patterns

The LVH was estimated using the established ECG criteria: Sokolow-Lyon index and Cornell scoring system.

The transthoracic echocardiography (Echo-CG) in M- and B-modes was utilized to confirm the LVH and the structural and functional myocardium state analysis, including the LV geometry. The standard linear Echo-CG indicators were measured by Ultrasonography complex "ACCUVIX A30" (Samsung Medison, South Korea). The LV mass (LVM) was calculated according to the Penn Convention. LVM index (LVMI) was assessed by LVM / body surface area ratio (g/m²). LVMI cut off values of echocardiographic LVH diagnostic criteria were >115 g/m² for men and >95 g/m² for women (ESC/ESH, 2018). According to LVMI and LV relative wall thickness (RWT) the following geometric models of LV were identified (ESC/ESH, 2009): normal geometry of LV (NGLV), concentric remodeling of LV (CRLV), eccentric LVH (ELVH), concentric LVH (CLVH).

Study design and patients

The study was conducted in full compliance with the main ethical principles of the European Convention on Human Rights and Biomedicine, according to the standards of the Helsinki Declaration, GLP and GCP, EUC directive #609 and other EU and international legislations on bioethics. Each participant signed a consent form to participate in the study. The Research is defined as prospective, cohort, case-control study.

Diagnosis. Inclusion / Exclusion criteria.

Hypertension was defined according to European Societies of Hypertension and Cardiology (ESH/ESC) recommendations: office systolic BP (SBP) values ≥ 140 mmHg and/or diastolic BP (DBP) values ≥ 90 mmHg at least for three measurements during a month [10, 11].

The study enrolled EAH patients with hypertensive-mediated organ damage (HMOD) estimated according to European Societies of Hypertension and Cardiology recommendations (ESH/ESC 2018, 2021) [10, 11]: target-organs damage – 2nd stage (asymptomatic EAH), moderate-high-very high cardio-vascular risk (CVR), from the 1st through to the 3rd grade of BP elevation.

Exclusion criteria were presented in our former publications: EAH patients with complicated /symptomatic HMOD (coronary heart disease, heart attack, stroke, heart failure, aneurysm, chronic kidney diseases, thickened, narrowed or torn blood vessels in the eyes, carotid arteries intima-media thickness enlargement, peripheral artery disease, etc); secondary arterial hypertension; malignant or uncontrolled arterial hypertension; diabetes mellitus type I (DM 1), sub- and decompensated diabetes mellitus (DM) type 2 (with diabetic target-organ damage); sub- and decompensated liver diseases; bronchial asthma, chronic obstructive pulmonary disease of III-IV stage with C or D risk value (GOLD 2019); exacerbated infectious diseases or during unstable remission of any location, including systemic immune system diseases; severe dementia; psychological/psychiatric disorders/diseases; malignancies of any location; multiple organ failure; use of oral corticosteroids or contraceptives; pregnancy or lactation.

Results.

The frequency of complaints of general weakness, fatigue, as well as shortness of breath and pain in the heart area did not differ significantly between groups. However, relatively frequent ECG signs of myocardial conduction disturbance and cardiac arrhythmias (predominantly monophasic, solitary, rare, monomorphic extrasystoles - supraventricular, ventricular, occasionally parasystoles,

supraventricular tachycardia, etc.) were found in individuals with ELVH compared to those with CLVH by 25.76% ($\chi^2=3.92$; $p=0.048$). Among cerebrovascular symptoms in patients with EAH with ELVH, headache was more often registered by 23.02% ($p=0.05$) and sleep disturbances by 30.79% ($\chi^2=5.46$; $p=0.019$).

The frequency of anxiety symptoms for complaints of stress, inner trembling, feeling of fear, danger, or appearance of restless/anxious thoughts and/or panic attacks did not differ between groups depending on LVH models. However, signs of depression dominated in patients with EAH with ELVH due to a decrease in positive thoughts or a decrease in a sense of optimism, something "joyful" or "positive" by 34.60% ($\chi^2=6.69$; $p=0.01$).

In addition, individuals with ELVH predominated among those with a high and very high risk of fatal cardiovascular events in the next 10 years according to the SCORE scale (>5.0 uo) compared to those with EAH and CLVH by 27.29% ($\chi^2=4.01$; $p=0.045$). No significant differences were found in the frequency of peripheral edema, complaints from the gastrointestinal tract, changes in organ vision, and neurological symptoms between observation groups.

It was established that the SBP and DBP levels in patients with ELVH were higher than those of patients with CLVH by 3.95% ($p=0.04$) and 3.29% ($p=0.05$). Similarly, anthropometric indicators such as BMI by 7.80% ($p=0.051$) and WC, but only in women – by 7.40% ($p=0.048$). Biochemical parameters did not differ statistically significantly between groups.

When analyzing the parameters of the lipid profile and blood glucose level in patients, depending on the geometric model of the LV, no significant differences were established. The glucose level and CA index in patients probably exceeded those in the control group. HDL cholesterol regardless of gender, on the contrary, was lower than in the control group, especially according to CLVH.

Regarding the hormonal and metabolic indicators of the regulation of mineral metabolism depending on the hypertrophic geometric models of the left ventricle, in patients with EAH with ELVH, a lower level of ionized Ca^{2+} blood was found than

with CLVH by 2.54% ($p=0.021$) with a compensatory higher level of parathyroid hormone by 23.86% ($p=0.047$)

Conclusions. Lipid profile, blood glucose and Vit D concentration do not determine the development of any type of the LVH. ELVH is associated with lower level of Ca^{2+} and consequently elevated level of PTH. The formation of ELVH in patients with EAH is accompanied by a higher level of blood pressure than according to CLVH, and is also associated with higher BMI and WC.

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Oleksandr Hinhuliak

THE CLINICAL USEFULNESS OF MEASURING CERTAIN BIOMARKERS IN PATIENTS WITH SUBCLINICAL SYMPTOMS OF ATHEROSCLEROSIS

The proposed definition of clinical conditions in cardiology, which can serve as a manifestation of subclinical atherosclerosis, including asymptomatic patients at risk for coronary heart disease (CHD), atypical course, changing the development of acute coronary syndrome, long preclinical period against the background of confirmed coronary atherosclerosis cause a changes in diagnostic and treatment strategy according to the latest European guidelines.

The study of biomarkers in the development of atherosclerosis, the spread of components of ischemia, destabilization of coronary heart disease is extremely relevant in view of the search for the latest ways of influencing the treatment of such a complex diagnostic and treatment plan of the contingent patients as patients with coronary heart disease.

In recent years, the role of nonspecific markers of inflammation, including PSA, neopterin, selectins (E- and P-), tumor necrosis factor- α , interleukins, molecules of intercellular adhesion-(sICAM-1), vascular endothelium adhesion molecules 1 type (sVCAM-1) [7,8,11,12].

In recent years, research on Pregnancy-Associated Protein-A has attracted interest plasma (Pregnancy-associated plasma protein-A -PAPP-A), especially in correlation with C-reactive protein (CRP) [4,5].