PREDICTORS OF MYOCARDIAL ISCHEMIA AND CENTRAL HEMODYNAMIC DISORDERS IN PATIENTS WITH CORONARY HEART DISEASE

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Introduction. Coronary heart disease (CHD) ranks first among mortality causes in the world over the years [1]. Present scientific studies prove the leading role of chronic systemic inflammation (CSI) in the onset and progression of atherosclerosis (ASVD), which has been the morphological basis of CHD [2, 3]. Taking into account the above-mentioned, it is relevant to study the interaction of components of the pathogenetic process in the ASVD and CHD, the factors of formation and progression of the specified pathology in order to determine the diagnostic markers for the development and destabilization of these diseases and developing rational therapeutic approaches.

The purpose of our research was to study the relationship between the indicators of systemic inflammation, the lipid spectrum of blood and the structural and functional condition of the heart in patients with stable CHD, and the search for predictors of its progression.

Materials and methods. One-time, open-label, single group clinical trial involved 115 patients with CHD: stable angina pectoris, FC II, HF 0-I (62 men and 53 women aged 54±6.2).

Patients were given laboratory and instrumental studies. The levels of total cholesterol, low density lipoprotein cholesterol (LDL), high density lipoprotein cholesterol (HDL), triglycerides (TG) by sedimentation, fibrinogen (Fg) concentration in blood by gravimetric analysis, the level of cytokines (CK) in the blood (interleukin 1β (IL-1β), tumor necrosis factor (TNFα), interleukin 10 (IL-10)) by the immune enzyme method, the content of circulating endothelial microparticles (EMP) of $CD32^+CD40^+$ in blood by cytofluorometry, mRNA gene expression of kappa B-alpha inhibitor (IkBα) of the nuclear kappa B transcription factor (NF-kB) in mononuclear cells of the peripheral blood by real-time polymerase chain reaction (Real-time PCR) were being determined [4, 5, 6]. Echocardiography and the 24 hour Holter ECG monitoring were performed by the standard method. A correlation and regression analysis was conducted.

Results. Moderate direct correlation between IL-1β level and blood lipid spectrum indicators, TNFα levels and LDL cholesterol levels has been detected. Fibrinogen (Fg) concentration was positively correlated with all investigated blood lipid spectrum indicators, as well as TNFα, IL-1β and IL-10 levels. Also, a direct moderate correlation between the amount of IL-1β and EMP $CD32^+$ $CD40^+$, which characterizes inflammatory activation and endothelial dysfunction, was determined. The level of mRNA IkB expression positively correlated with the the level of cytokines, total cholesterol and LDL cholesterol in a moderate way.

Investigation of the ratio of central hemodynamics indices and CSI markers revealed inverse correlation between left ventricular (LV) ejection fraction (EF) and TNFα ($r=-0.340$, $p<0.05$), LVEF and Fg ($r=-0.336$, $p<0.01$), direct correlation

between LV isovolumetric relaxation time (IVRT) and EMP $CD32^+CD40^+$ (r=0.311, p<0.05), DT and EMP $CD32^+CD40^+$ (r=0.383, p<0.01), as well as inverse ones — between the ratio of the phases of the transmitral flow (E/A) and IL-1β (r=0.333, p<0.05).

Analysis of the correlation between Holter ECG indicators and inflammatory markers revealed a direct moderate correlation between total ischemic burden (ΣtST depr), and TNFα and Fg, the same association was found in relation to the number of episodes of depression in the ST segment.

To determine the independent predictors of cardiovascular risk regression analysis has been conducted. The values of TNFα and Fg were found to be prognostic markers affecting LVEF, proving the role of CSI in the development of LV systolic dysfunction: LVEF=60.74–0.33* TNFα–1.32*Fg.

For the E/A parameter of the transmitral flow, the linear regression equation has had the form: E/A=0.96–0.02*IL-1β, for deceleration time (DT) — DT=199.17+3.72*EMP $CD32^+CD40^+$. The linear regression equation has also been obtained: IVRT=87.44+1.04*EMP $CD32^+CD40^+$. The indicated regression models prove the association of CSI markers and inflammatory endothelial activation with the development and progression of LV diastolic dysfunction

Myocardial ischemia prognosis has been presumable by CSI markers — TNFα and Fg: ΣtST depr =23.01+1.13* TNFα–4.58* Fg.

Conclusion. Thus, we have identified the central role of CSI in the pathogenesis of CHD, the relationship between CSI and dyslipidemia, endothelial dysfunction and coagulation potential of blood. According to the results of the correlation and regression analysis, it has been found out that CSI negatively affects the systolic function of LV and the components characterizing the diastolic function of LV (IVRT, DT, E/A), it has influence on the development of ischemic changes and electrical myocardial instability.

Prospects for further research. The data obtained are the basis for an active study of the efficiency of anti-inflammatory agents in patients with CHD in order to develop new pathogenetically based therapeutic approaches.

Recommendations. It is relevant to introduce actively into the clinical practice the use of certain predictors of myocardial ischemia and central hemodynamic disorders in order to stratify cardiovascular risk in patients with CHD.

Key words: coronary heart disease, chronic systemic inflammation, endothelial dysfunction, central hemodynamics, myocardial ischemia, correlation and regression analysis, predictors of cardiovascular risk.

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