ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH CHRONIC HEART FAILURE

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ABSTRACT

One of the main factors determining the prognosis in patients with chronic heart failure (CHF) is endothelial dysfunction. The aim of the work was to determine the antithrombogenic and vasodilating activity of the vascular wall in patients with CHF. We examined 60 people, of which 40 were the main group — patients with Q-myocardial infarction and 20 people — the comparison group. To determine

We used the "cuff" test proposed by V.P. Baluda for the antithrombogenic properties of the vessel wall. The vasomotor function of the endothelium was studied in samples with reactive hyperemia (RH) and nitroglycerin (NG). In patients with CHF, there is a decrease in the antithrombogenic and vasodilating activity of the vascular wall.

In patients with CHF IV FC, who have a long duration of CHF symptoms, FW<33%, the number of repeated adverse cardiovascular events during 6 months of follow-up is significantly higher compared to patients I, II and III CHF FC.

Key words: chronic heart failure, endothelial dysfunction.

INTRODUCTION

Despite the successes of recent years in the field of pathogenesis research and the search for effective treatment options, chronic heart failure (CHF) remains one of the most severe and prognostically unfavorable diseases of the cardiovascular system. The main factors determining the prognosis are: the etiology of CHF, the functional class (FC) of CHF, the ejection fraction (EF), endothelial dysfunction. When analyzing the prognosis of patients depending on the initial left ventricular LV, it was shown that the development of adverse cardiovascular events, including mortality increases in parallel with a decrease in PV below 45%, while if this indicator is exceeded, the prognosis does not change for any amount of myocardial contractility. A decrease in the contractility of the left ventricular myocardium leads to the development of peripheral hemodynamic disorders, including the development of endothelial dysfunction. The endothelium is not just a barrier between the blood flow and the smooth muscles of the vessels, but is also the place of formation of compounds involved in the regulation of blood clotting, vascular tone, function platelets and vascular wall development. Endothelial dysfunction contributes to the further progression of CHF, a decrease in left ventricular LV and the development of adverse

cardiovascular events, including deaths.

PURPOSE OF THE STUDY: The aim of our study was to determine the antithrombogenic and vasodilating activity of the vascular wall in patients with impaired systolic function of the left ventricle, which developed after a Q-myocardial infarction, and its role in the prognosis of CHF.

MATERIALS AND METHODS

60 people were examined, of which 40 were the main group — patients with Q-myocardial infarction and symptoms of chronic heart failure; 20 people were practically healthy individuals included in the comparison group. Inclusion criteria: 1) the presence of chronic heart failure of various functional classes (FC), developed after a Q-myocardial infarction, and the ejection fraction (LV) of the left ventricle is less than 45%; 2) the patient's consent to participate in the study, confirmed by his signature in the observation protocol. Exclusion criteria: 1) destabilization of coronary heart disease (unstable angina, repeated myocardial infarction); 2) the presence of exacerbation of chronic processes at the time of the study.

The examination was carried out a week after the stabilization of the patient's condition. The average age of the examined patients was 54.5 years (from 42 to 70 years); men predominated — 34 (85%) people; the average number of heart attacks was 1.2; the duration of manifestations of heart failure in the group was 5.3 years; the majority of patients had symptoms of stable angina pectoris of functional class III — 39 (97.5%) people, 34 (85%) patients had arterial hypertension, the duration of an increase in blood pressure for 5.8 years, 6 (15%) people had type II diabetes mellitus, 2 (0.5%) patients had a permanent form of atrial fibrillation, more than half of the examined — 24 (60%) people smoked; the distance of a 6-minute walk was 319.25 m. All patients, depending on the results of the 6-minute test, were divided into four functional classes, the reliability of the differences between the groups was $p<0.001$. there were no significant differences in the studied signs between patients with different FC, except for except for the duration of manifestations of heart failure. In patients with IV FC, the symptoms of CHF were significantly ($p<0.01$) fixed for a longer time than in patients with other functional classes.

To determine the antithrombogenic (anticoagulant and fibrinolytic) properties of the vascular wall, we used a "cuff" test based on the creation of short-term (within 5 minutes) ischemia by applying a sphygmomanometer cuff to the patient's shoulder and creating a pressure in it 30 mm Hg higher than systolic, proposed by V.P. Baluda et al.. At the same time, prostacyclin, antithrombin III and plasminogen activator are released into the blood from the vessels. By the difference in the content or activity of these factors in the blood taken before and after the cuff samples are judged on the state of antithrombogenic activity. Antithrombin III accounts for more than 80% of all anticoagulant activity. According to the results of determining the activity of

antithrombin III in plasma obtained before and after the "cuff" test, the anticoagulant activity of the vascular wall is judged. The total anticoagulant activity is expressed by an index that is equal to the quotient of the division of the activity of antithrombin III after the cuff is applied to the activity of antithrombin III before the cuff is applied.

The determination of fibrinolytic activity of the vascular wall is based on the fact of accelerated lysis of euglobulins obtained from kaolin-treated platelet-poor plasma. A globulin fraction containing plasminogen, fibrinogen and blood clotting factors and not containing fibrinolysis inhibitors is isolated from blood plasma. When calcium chloride is added, a fibrin clot is formed, which is lysed by plasmin in 5-12 minutes. Endothelial cells are capable of synthesizing tissue-type plasminogen activator. Fibrinolytic activity of the vascular wall they were characterized by an index equal to the quotient of the time of lysis of the euglobulin clot after the "cuff" test to the time of lysis of the euglobulin clot before it. The time of clot lysis after compression is normally shortened by 1.5—2 times. Attenuation of activation of euglobulin fibrinolysis is a marker of endothelial damage. To carry out this study, sets of reagents of the NGO "Renam" were used.

Statistical processing was carried out using the STATISTICA 5.5 statistical software package. Among the processing methods, simple statistics were used, t is the Student's criterion, the compliance indicator is $\chi 2$.The difference between the studied parameters was recognized as significant at $p<0.05$.

RESULTS and DISCUSSION

We have revealed a significant decrease in the ejection fraction (PV) ($p<0.001$) in all groups of patients compared with healthy individuals. FV in patients I, II, III FC CHF were comparable and amounted to 40%. There was a significant ($p<0.05$) decrease in PV (33%) in patients with IV FC compared with patients of other groups. Patients with CHF significantly ($p<0.001$) have more CSR left atrium (LP), CSR, CDR, CSR and CDR of the left ventricle (LV); thickness of the anterior wall of the right ventricle, CDR of the pancreas; systolic pressure of the pulmonary artery (SDLA) compared with similar indicators of the comparison group. At the same time , the DAC LP and CDR LV, SDLA in patients with FC IV is significantly higher ($p<0.05$) compared with patients with CHF FC I, II, III. The thickness of the interventricular septum and the posterior LV wall in patients with CHF were comparable and significantly ($p<0.05$) greater than in healthy individuals. Diastolic function in all patients with CHF is impaired by restrictive type. The LV myocardial mass index in all patients with CHF was significantly ($p<0.01$) higher than in the comparison group. In two patients with IV FC CHF, blood clots were detected in the LV cavity.

Thus, in all patients with LV systolic dysfunction, remodeling processes occur in both the left and right parts of the heart. In patients with I, II, III FC CHF having comparable LV, there are no significant differences in heart remodeling indicators. In

patients with IV FC CHF, having a longer duration of manifestations of heart failure, a lower PV, remodeling indices — CSR LP, CDR LV and SDLA — are significantly higher ($p<0.05$) compared with patients with I, II, III FC CHF.

We evaluated the antithrombogenic (anticoagulant and fibrinolytic) activity of the vascular wall in patients with CHF. The examined patients with CHF initially showed no changes in the activity of antithrombin III before the PA occlusion test. The activity of antithrombin III after the test in patients with CHF is reduced, but with this number of examined patients does not reach the degree of reliability ($p>0.05$). Significant ($p<0.001$) was detected reduction of anticoagulant activity of the vascular wall in patients with II, III and IV FC CHF compared with healthy individuals. When studying the fibrinolytic activity of blood, it was revealed that the time of fibrinolysis before and after the cuff test tends to increase with increasing functional class of CHF and becomes significantly higher ($p<0.05$) in patients with IV FC CHF compared to persons of the comparison group. A marked decrease in the fibrinolytic activity of the vascular wall was found in patients with II, III and IV FC CHF compared with the same parameter of healthy individuals ($p<0.01$). Anticoagulant and fibrinolytic activity of the vascular wall in patients with I FC CHF is comparable with healthy faces.

In patients with I FC CHF with systolic myocardial dysfunction, the antithrombogenic activity of the vascular wall is not changed, which is associated with the work of neurohumoral systems and causes compensation for heart failure in these patients. In patients with II, III, IV FC CHF, anticoagulant and fibrinolytic activity of the vascular wall is reduced.

Depression of the fibrinolytic system was revealed in patients with IV FC CHF, which is an important condition for the formation of blood clots in the vascular bed. Vasomotor function of the endothelium in patients with different functional classes of CHF It was studied in samples with reactive hyperemia (RG) and nitroglycerin (HTG). We revealed a significant increase in the initial diameter of the PA ($p<0.05$) and a decrease in the initial blood flow rate ($p<0.01$) in patients with I, II, III, IV FC CHF in comparison with similar indicators in the comparison group. Significant differences in the initial diameter PA and initial blood flow velocity in patients with CHF with different functional classes have not been established by us. During the test with reactive hyperemia, a significant increase in the initial diameter of the brachial artery ($p<0.05$) was noted in patients of all FC CHF in comparison with the indicators of the comparison group. According to the literature, the dilation caused by the flow is inversely proportional to the diameter of the vessel and in arteries with a diameter of 6 mm, less than the average expansion of the vessel is 10%. Its lesser value, or vasoconstriction, is considered pathological. Stream – dependent dilation at 60 seconds in patients with CHF is significantly lower ($p<0.05$) than in healthy individuals, and is at I FC 6.3%, at II FC — 8.1%, at III FC — 9.1%, at IV FC — 6.3%, which is

pathological. In one patient with CHF I FC, one patient with CHF II FC and two patients with CHF IV FC (10%), the diameter of the brachial artery did not change at the 60th second of the "cuff" test. Thus, patients with CHF and impaired systolic function of the left ventricle have initial disorders of brachial artery tone and the speed of blood flow in it. In all patients with CHF, violations of endothelium-dependent vasodilation were revealed. There was no endothelium-dependent vasodilation in 10% of patients with CHF to the effect of endogenous stimuli. Insufficient vasodilation in patients with CHF I and II FC leads to an increase in reactive hyperemia (% increase in speed), however, these changes are not reliable ($p>0.05$), and in patients with III and IV FC CHF, the flow rate decreases and becomes comparable with the data of the group of healthy individuals. In a sample with nitroglycerin, an increase in the diameter of the brachial artery was found in patients with II, III and IV FC CHF is more than 10%. However, endothelium-independent vasodilation in all patients with CHF was significantly ($p<0.01$) lower in comparison with healthy individuals. Significantly ($p<0.05$) lower indicators of endothelium-independent vasodilation in patients with FC I compared with FC IV CHF attract attention. Taking into account the proportional changes in nitroglycerin- and flow-dependent vasodilation, there were no significant differences in the "brachial artery reactivity" between patients with different functional classes of CHF and healthy individuals.

Thus, patients with I, II, III, IV FC CHF and impaired systolic function of the left ventricle have vascular tone disorders in the form of an increase in diameter and a decrease in blood flow velocity in the PA. In response to endogenous stimulation, there is not sufficient relaxation of the PA, and in 10% with CHF, vascular tone does not change, which indicates a violation of endothelium-dependent vasodilation. In patients with I, II, III, IV FC CHF and systolic myocardial dysfunction revealed disorders and endothelium-independent vasodilation, but to a lesser extent.

A decrease in cardiac output is accompanied by a violation of peripheral hemodynamics in the form of a decrease in blood flow velocity and, probably, compensatory vasodilation of the brachial artery. Systolic LV myocardial dysfunction in patients with I, II, III, IV FC CHF is accompanied by a violation of the vasomotor function of the endothelium, the causes are both insufficient synthesis of vasodilation factors (nitric oxide, endothelial hyperpolarizing factor, prostacyclin) and excessive formation of vasoconstrictors (angiotensin II, endothelin, free radicals of under-oxidized fatty acids, prostaglandin F2a and thromboxane A2). We conducted an analysis of the developed during 6 months of adverse cardiovascular events in the examined patients against the background of standard therapy with ACE inhibitors, beta-blockers, diuretics, aldosterone antagonists, nitrates, antiplatelet agents, statins in optimally selected doses for each patient. In patients with reduced LV systolic function, I and II FC CHF during 6 months of follow-up, there was no development of adverse

cardiovascular events. One patient with FC III CHF developed recurrent myocardial infarction. In half (50%) of patients with IV FC CHF and significantly reduced ejection fraction LV during 6 months of follow-up, the development of the following adverse cardiovascular events was recorded: one patient developed unstable angina, four patients had decompensation of CHF, one person died. To assess the significance of the differences of several compared values related by one attribute, the compliance indicator $\chi 2$ was used. Significant differences were revealed in the number of adverse cardiovascular events that developed in patients with IV FC, compared with patients I, II and III FC HSN ($\chi 1^2 > \chi 22$; $p<0.01$). There were no significant differences in the studied indicator in patients with CHF I, II and III FC ($\chi 1^2 > \chi 22$; $p<0.05$).

CONCLUSIONS

1. A violation of the systolic function of the left ventricle in patients with I, II, III and IV FC CHF who have suffered a Q-myocardial infarction is accompanied by a decrease in antithrombogenic and vasodilating activity of the vascular wall.

2. In patients with reduced systolic function of the left ventricle and I FC CHF, there were no violations of the antithrombogenic activity of the vascular wall.

3. In patients I, II, III and IV FC CHF, who underwent Q-myocardial infarction, PV below 45% there were no significant differences in the severity of endothelial dysfunction.

4. In patients with CHF IV FC, who have a longer duration of CHF symptoms, LV 33% or less, the number of repeated adverse cardiovascular events during 6 months of follow-up is significantly higher compared to patients I, II and III CHF FC.

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