STUDY OF THE COURSE OF CHRONIC HEART FAILURE IN PATIENTS WITH METABOLIC SYNDROME

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Chronic heart failure (CHF) is a major medical and social problem. The increase of morbidity results from both an increase of life expectancy of the population, and influence of various risk factors contributing to development and increase of heart failure. The combination of several atherogenic mechanisms (abdominal obesity, insulin resistance, arterial hypertension, hyperglycemia, dyslipidemia), combined as «metabolic syndrome» (MS), causes a more rapid development of CHF.

Key words: chronic heart failure, metabolic syndrome, echocardiographic parameters.

INTRODUCTION

In recent decades, there has been an increase in the prevalence of chronic heart failure (CHF) in economically developed countries [1,2,5]. The increase in the prevalence of CHF is largely associated with an increase in life expectancy. An important role is played by improving the quality of diagnosis and treatment, including myocardial infarction, effective surgical treatment of coronary heart disease (CHD), heart defects, and cardiac arrhythmias [3,4,7]. The combination of several atherogenic factors (abdominal obesity (AO), insulin resistance (IR), hypertension, hyperglycemia, dyslipidemia), united by the concept of “metabolic syndrome” (MS), causes a more rapid development of CHF [1,8,9].

Visceral adipose tissue is an active endocrine organ that synthesizes and secretes biologically active substances into the bloodstream with many effects [10,11]. The processes of subacute inflammation in MS are supported by various proinflammatory cytokines. Leptin and adiponectin, which are responsible for metabolic disorders, play an important role.

Thus, the main protein component of HDL is apolipoprotein A1 (apoA1) (65%). All lipoproteins that carry lipids to peripheral tissues have in their structure apolipoprotein B (apoB), receptors for which are found in almost all tissue cells, except for cells of the nervous system and red blood cells. In patients with CHF, there is a decrease in the level of apoA1, more pronounced in FC III–IV [13]. Low levels of apoA1 correlate with high levels of fibrinogen, a natriuretic peptide [6]. It has been established that low levels of apoA1 in patients with CHF increase the likelihood of death within five years [14].

The purpose of the study was to evaluate the relationship between metabolic syndrome and the severity of CHF, prediction of the severity of CHF based on ECHO-CG data, levels of leptin, apolipoproteins, HDL and LDL.

MATERIALS AND METHODS

74 patients with CHFfunctional class II–III were examined, including 37 (50%) patients with signs of metabolic syndrome(MS). The diagnosis of CHF was established according to the European guidelines for the diagnosis and treatment of CHF (ESC 2016). The FC of CHF was assessed according to the NYHA. When diagnosing MS, the International Diabetes Federation(IDF, 2009) diagnostic criteria for MS were used. The main components of MS were considered: abdominal obesity (AO) (>94 cm for men); triglyceride level (TG>1.7 mmol/l); high-density lipoprotein cholesterol (HDL-C <1.03 for men); blood pressure level (SBP >130 mmHg; DBP >85 mmHg), fasting glucose level (>5.6 mmol/l) or the presence of type 2 diabetes mellitus.

The examination of patients was carried out at the Republican Specialized Scientific and Practical Medical Center for Therapy and Medical Rehabilitation (RSSPMCTMR) of the Ministry of Health (Uzbekistan). Routine clinical, laboratory and instrumental examination of patients included collection of complaints, medical history, objective examination, measurement of body weight, height, waist and hip circumference, calculation of body mass index (BMI), general blood test, biochemical blood test, general urinalysis, electrocardiography (ECG).

The special research program included determining:

• CRP level by highly sensitive immunoturbidimetric method on the KONELAB20 analyzer;

• leptin level in blood serum using enzyme immunoassay;

• apolipoproteins (apoA1 and apoB-100) on a Turbox+ protein analyzer using the mephelometry method;

• HDL, LDL by enzymatic methods on the KONELAB20 biochemical analyzer.

Echocardiography (EchoCG) was performed on a Mindray device (China) in the supine position and on the left side in M and B modes in accordance with the requirements of the American Association of Echocardiography (ASE) using standard echocardiographic approaches - left parasternal, apical and subcostal. The study assessed the thickness of the interventricular septum, the posterior wall of the left ventricle, the end-diastolic size of the left and right ventricles, the diameter of the aorta, the size of the left atrium and the condition of the valve apparatus of the aorta, pulmonary artery, the number of papillary muscles and myocardial contractility of the left and right ventricles. The degree of mitral regurgitation, mitral valve prolapse and aortic regurgitation was determined. Left ventricular systolic function was assessed.

All patients had epicardial fat thickness measured using standard two-dimensional echocardiography. Visualization was carried out from a parasternal approach along the long axis of the left ventricle (the aortic annulus served as a

reference point). The thickness of the epicardial fat layer was measured at end systole behind the free wall of the right ventricle. The period of observation of patients was from the moment of admission to 6 months.All patients received standard therapy for CHF, including angiotensin-converting enzyme ingibitors(ACEis), beta-blockers, spironolactone, loop diuretics, and, if necessary, digoxin

Statistical processing of the results was carried out on a personal computer using the application package SPSS version 21 and Microsoft Excel 2010. The mean value (M) and standard error of the mean (m) were determined. To compare the average values of dependent samples, the Wilcoxon test was used; to compare independent samples, the method of medians and the Mann–Whitney test were used. Quantitative indicators are presented as M ± m (mean ± standard error of the mean). All parameters were also assessed using correlation analysis to determine the correlation coefficient (r). The critical level of significance of differences was considered to be 0.05.

RESULTS AND DISCUSSIONS

The study included 13 (17.6%) patients under 60 years of age, 32 (43.2%) from 60 to 80 years of age, and 29 (39.2%) patients over 80 years of age. The average age of men was 67.7 ± 13.8 years, women – 79.5 ± 7.9 years.

The peak incidence of CHF occurred in elderly and senile age (in men - from 60 to 80 years, in women - over 80 years).

Upon admission to the hospital, FC II CHF was established in 19 (25.7%) cases, FC III – in 55 (74.3%).

The cause of CHF in all patients was ischemic heart disease. 18 (24.3%) patients suffered myocardial infarction (MI), two (2.7%) - twice. The average age of patients with their first MI was 64.6 ± 11.4 years. 15 (20.3%) patients had

degenerative heart defects. Three (4%) underwent coronary artery bypass surgery and/or mammary coronary artery bypass grafting due to multivessel coronary artery disease. 41 (55.4%) patients had atrial fibrillation, eight (10.8%) of them had a paroxysmal form, and 34 (45.9%) had a permanent form. Eight (10.8%) patients suffered acute cerebrovascular accident (ACI), including two (2.7%) twice.

As a result of hospitalization, 22 (29.7%) patients showed an improvement (transition during treatment to a lower NYHA FC), while 46 (62.2%) patients showed no changes (the previous NYHA FC remained the same). Death occurred in six (8.1%) cases.

After six months of observation, 33 (45.6%) patients showed improvement, and 35 (48.6%) worsened. The overall six-month mortality rate was 14.9%.

Study participants were divided into two groups. The first included 37 patients with CHF and MS, the second (control) included 37 patients with CHF without signs of MS.

Criteria for inclusion in the first group:

• age over 18 years;

• proven CHF (clinical symptoms, objective examination, echocardiography);

• the presence of abdominal obesity (waist circumference in men > 94 cm, in women > 80 cm).

In addition, the first group included patients with two of the following symptoms:

• TG ≥ 1.7 mmol/l;

• HDL in men <1.0 mmol/l, in women <1.2 mmol/l;

• LDL > 3.0 mmol/l;

• BP ≥ 130/85 mmHg. Art.;

• fasting glucose ≥ 6.1 mmol/l;

• IGT ≥ 7.8 mmol/L and ≤ 11.1 mmol/L.

Criteria for inclusion in the second group:

• age over 18 years;

• proven CHF (clinical symptoms, objective examination, echocardiography);

• absence of signs of metabolic syndrome.

Criteria for non-inclusion and exclusion from the study:

• acute myocardial infarction within one month;

• acute surgical pathology;

• infectious endocarditis;

• acute myocarditis within one month;

• chronic obstructive pulmonary disease (COPD) in the acute stage;

• bronchial asthma in the acute stage.

The first group included 21 (56.8%) men and 16 (43.2%) women, the second group included 15 (40.5%) men and 22 (59.5%) women.

In the first group, eight (21.6%) patients were under 60 years of age, 15 (40.5%) patients were aged from 60 to 80 years, 14 (37.8%) patients were over 80 years of age. In the second group, patients aged from 60 to 80 years also predominated - 17 (45.9%), there were 15 (40.5%) patients over 80 years old, five (13.5%) were under 60 years old.

Coronary artery bypass surgery, according to medical history, was performed in two (5.4%) patients of the first group and one (2.7%) in the second group. In the first group, degenerative heart defects were recorded more often than in the second - 86.5 and 73%, respectively. The incidence of atrial fibrillation in both groups was the same (48.6% in the second, 46.5% in the first).

In the first group, CHF was clinically more severe: a higher FC of CHF (III FC - 89.2% in the first group and 75.7% in the second), shortness of breath at rest was observed one and a half times more often (21.6 and 16.2% respectively), congestion in the lungs (54.1 and 40.5%), severe edema of the lower extremities (78.4 and 73%), unilateral hydrothorax (30.6 and 24.3%), diffuse cyanosis (18.9 and 10.8% respectively).In the first group, the onset of hypertension, type 2 diabetes,

coronary artery disease and the manifestation of symptoms of CHF occurred earlier than in the control group (Table 2). Patients in the first group more often suffered from hypertension and type 2 diabetes. The incidence of acute stroke was determined equally often in both groups (10.8%). In the first group, repeated strokes were more often recorded.

An increased level of CRP was recorded in 98% of patients in the first group and 57% of patients in the second. The average values in the first group were 32.97 ± 26.36 mg/l. Moreover, in 15 of 37 patients, the protein level exceeded the reference values (0–5 mg/l) by 10 times or more and in some cases reached 73.1–87.9 mg/l (Fig. 3). In patients with FC II, the average level of CRP was 24.44 ± 6.3 mg/l, in patients with FC III – 29.28 ± 4.11 mg/l ($p > 0.05$).

The level of leptin, a marker of obesity, fibrosis and inflammation, was increased in all patients with CHF and MS. In 30% of patients, the values exceeded the reference values (2.0–5.6 ng/ml for men, 3.7–11.1 ng/ml for women) tenfold. In 11 cases, these values exceeded 70 ng/ml, in seven – 100 ng/ml. In 15 patients of the first group, leptin levels did not exceed reference values; most indicators were in the range of 10–30 ng/ml. The average apoA1 level in the first group was 1.23 ± 0.05 g/l, in the second group – 1.51 ± 0.28 g/l ($p > 0.05$). The difference in marker values in patients with FC II and III turned out to be unreliable.

ApoB levels in the majority of patients in both groups were within the reference values (0.6–1.38 g/l for men, 0.52–1.29 g/l for women). In eight patients of the first group and five patients of the second group, the level of apoB was increased. The average values in patients with CHF and MS were 1.21 ± 0.07 g/l, in the second group – 0.94 ± 0.05 g/l ($p > 0.05$). No significant differences in apoB in patients with FC II and III CHF have been established.

According to echocardiography, patients in both groups had dilatation of the left chambers of the heart. In patients of the first group, more pronounced dilatation of the right ventricle was revealed, which could be due to the development of

pulmonary hypertension against the background of obesity in MS, in addition to damage to the distal coronary arteries.

Characteristics of the examined patients

Indicator	First group(n=37)	Second group(n=37)
Arterial hypertension	100%	89.2%
Diabetes mellitus type	54,1%	10,8%
History of myocardial infarction	24.3%	24.3%
Abdominal obesity	100%	35.1%
Heart rhythm disturbances	51.4%	62.2%
Acute cerebrovascular accident	10.8%	10.8%
Onset of arterial hypertension	46. 5	57.5 years
Onset of chronic heart failure	62.4 years	69.4 years
Onset of type 2 diabetes mellitus	53.4 years	62.3 years

Onset of coronary heart disease	52.8 years	57.5 years
Chronic heart failure functional class III	89.2%	75.7%
Chronic heart failure functional class II	10.8%	24.3

Table No. 2.

Indicator	**All patients (n=74)**	**First group (n=37)**	**Second group (n=37)**
Right ventricle, mm	29,9 ± 8,3	32,6 ± 9,3*	27,8 ± 6,7*
Aorta, mm	34,9 ± 3,2	35,7 ± 3,6	34,5 ± 2,8
Left atrium, mm	46,5 ± 8,2	50,1 ± 10,3*	47,3 ± 5,9*
End-diastolic volume, ml	146,4 ± 70,1	151,9 ± 75,7	142,5 ± 67,3
End systolic volume, ml	90,4 ± 69,8	94,2 ± 63,8	84,4 ± 81,9
End diastolic size, mm	54,7 ± 9,1	55,4 ± 8,8	53,8 ± 9,7
Left ventricle, mm	52,0 ± 13,9	53,8 ± 16,9	50,9 ± 12,3
Left ventricular myocardial mass	279,2 ± 113,3	356,3 ± 115,1*	240,2 ± 52,9*
Interventricular septum, mm	13,4 ± 2,8	14,6 ± 3,3*	12,2 ± 2,3*
Posterior wall of the left ventricle, mm	11,9 ± 2,5	12,9 ± 2,9*	10,8 ± 2,2*

Left ventricular ejection fraction, %	46,8 ± 12,5	47,9 ± 13,0	45,8 ± 12,2
Pulmonary hypertension	52,2 ± 17,7	53,4 ± 18,4	50,7 ± 17,2
Epicardial fat thickness, mm	5,19 ± 1,3	6,48 ± 0,41**	4,29 ± 0,94**

Note •p<0.05, ••p<0.001

There was a direct correlation between epicardial fat thickness (EFT) and left ventricular myocardial mass and right ventricular size ($p < 0.05$).In patients with CHF and MS, a correlation analysis revealed direct correlations between leptin indicators and the level of CRP ($r = 0.371$; $p < 0.01$), left ventricular myocardial mass ($r = 0.68$; $p < 0.05$), EFT ($r = 0.546$; $p < 0.05$), inverse – with left ventricular ejection fraction ($r = 0.264$; $p < 0.05$), significant inverse correlation between apoA1 and CRP ($r = 0.239$; $p < 0.05$).

As a result of hospitalization, patients in the first group (62.2%) were discharged without significant improvement more often than patients in the second group (59.9%). Hospital mortality in the first group was 10.8% (four cases), in the second - 8.1% (three cases). After six months of observation, 43.2% of patients in the first group and 40.5% of patients in the second showed a clinical deterioration in the course of CHF and an increase in the FC of CHF. Mortality after six months of observation in the first group was 16.2% (six cases), in the second - 13.5% (five cases).

CONCLUSION

As the results of the study showed, in patients with metabolic syndrome, chronic heart failure has an earlier development and a more severe course. When conducting echocardiography, a significant increase in the size of the heart chambers, the thickness of the myocardium of the left and right ventricles, and pulmonary hypertension are noted. The degree of morphofunctional changes in a

number of parameters exceeds those in patients with CHF without MS. EVT is associated with increased left ventricular myocardial mass. The relationship between inflammatory and dysmetabolic processes that cause systemic and local changes, with a high level of CRP, a natural significant increase in the synthesis of leptin by adipose tissue, which has a pro-inflammatory effect and supports the processes of hypertrophy and fibrosis in the myocardium, disorders of lipid metabolism, in particular the ratio of apolyproteins, acquires pathogenetic significance and plays an important role in the development and progression of CHF in patients with MS.

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