Original Article

Metabolic syndrome and chronic heart failure: a modern aspect of the problem

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Abstract

Objective: 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 chronic heart failure (CHF). The combination of several atherogenic mechanisms (abdominal obesity (AO), insulin resistance (IR), arterial hypertension (AH), hyperglycemia, dyslipidemia), combined as "metabolic syndrome" (MS), causes a more rapid development of CHF.

Materials and methods: The research finding of 74 patients with class II-III of CHF, including 37 patients (50%) with MS, are presented. The age structure of the pathology, severity of clinical course, data of laboratory and instrumental examination in various groups of patients were evaluated. A special program included an echocardiographic test with an assessment of various myocardial parameters.

Results and Discussion*:** Research materials find out a number of characteristics of CHF clinical course (its earlier development and severe course) in patients with MS. Echocardiographic tests reveal an increase of heart chambers sizes, thickness of left and right ventricle, pulmonary hypertension. Myocardium morpho-functional changes are more significant in patients with CHF and MS than in those without MS. An increase in leptin levels, a marker of obesity, fibrosis and inflammation, has been found. Leptin, C-reactive peptide (CRP) and high-sensitive troponin in patients with MS significantly exceeded those in patientswithout MS. Correlations of leptin levels, adiponectin, CRP and left ventricular mass, thickness of epicardial fat (TEF), ejection fraction were established. ***Conclusion: Materials of the research indicate the important role of inflammatory and dysmetabolic processes in development and progression of CHF in patients with MS.

Keywords: adiponectin; C-reactive peptide; chronic heart failure; high-sensitive troponin; leptin; metabolic syndrome.

Bangladesh Journal of Medical Science Vol. 21 No. 01 January'22 Page : 105-113
DOI: https://doi.org/10.3329/bjms.v21i1.56335

Introduction

Chronic heart failure (CHF) is one of the most important medical and social problems due to its increasing prevalence in economically developed countries. More than 23 million people suffer from CHF worldwide.[1] According to the "ЭПОХА-О-ХСН" study, in Russia about 7.9 million people have signs of CHF. The prevalence of functional class I-IV (FC) in the European part of the Russian Federation is 12.3% among women and 9.86% among men.[2] In the age group 70-79 years, the prevalence of CHF increases manifold, reaching 34.3%. The annual mortality rate in clinically expressed CHF is 612 thousand patients.[2]

The increase in the incidence of CHF is largely associated with an increase in the life expectancy

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of the population and the number of elderly patients (the average age of outpatients with CHF is 59.6 years). An important role in this is played by improving the quality of diagnosis and treatment, including myocardial infarction, effective surgical treatment of coronary heart disease (IHD), heart defects, and rhythm disturbances. At the same time, epidemiological studies indicate that in Russia, an increase in CHF is associated with a wide spread of risk factors (arterial hypertension (AH), diabetes mellitus (DM), etc.).[3]

A combination of several atherogenic factors (abdominal obesity (AO), insulin resistance (IR), AH, hyperglycemia, dyslipidemia) is combined into the concept of "metabolic syndrome" (MS) and causes more rapid development of CHF.[4] AO in 2005 at the International Congress on Pre-Diabetes and MS (IDF criteria, 2005) was recognized as a fundamental criterion for the diagnosis of MS.

According to research data, there is a high prevalence of MS, which in the general population ranges from 14 to 25%. In Russia, according to the World Health Organization (WHO), MS is diagnosed in men under the age of 40 in 18.6%, from 40 to 55 years - in 44.4%. In women, it is less common - in 7.3% and 20.8%, respectively. MS is more common in middle-aged and older people (30-40%). Accordingly, its prevalence is also growing: in people over 60 years of age, MS is detected in 45% of cases.[4] The research results indicate that patients with CHF and MS have a higher mortality rate compared with patients without MS.[5,6]

Visceral adipose tissue is an active endocrine organ that synthesizes and secretes biologically active substances into the bloodstream with many effects.[7,8] Along with various proinflammatory cytokines that support the processes of subacute inflammation in MS, factors such as leptin and adiponectin, responsible for metabolic disorders, play a significant role.

Leptin activates the essential tissue fibrogenesis factor (TGF-β), which increases the rate of fibrosis in the heart muscle. Leptin reduces the sensitivity of peripheral tissues to insulin, which is accompanied by an increase in the severity of IR, which is the main link in the violation of carbohydrate metabolism. A number of studies have established a link between hyperleptinemia and the presence of coronary atherosclerosis, while the level of another adipose tissue hormone, adiponectin, remained normal.[8]

In patients with CHF, a high level of protective adipokine, adiponectin, is determined, which increases the sensitivity of peripheral tissues to insulin, has antiatherogenic, antidiabetic and angioprotective effects. It is known that AO, type 2 diabetes, dyslipidemia, and hypertension are accompanied by a decrease in adiponectin levels. There is evidence that a low level of this adipokine is associated with the development of left ventricular (LV) hypertrophy and its diastolic dysfunction in patients with CHF.[7]

The dynamics of the level of highly sensitive troponin (hsTr) and its significant increase are observed in ischemic and non-ischemic acute and chronic heart failure, which makes TrI and TrT an unreliable marker in the diagnosis and monitoring of CHF. A meta-analysis of 16 studies has shown that increased hsTr levels in patients with CHF are associated with a high risk of mortality and adverse cardiovascular events.[9] It was found that hyperglycemia promotes the development of myocardial damage with an increase in the level of hsTr and makes a significant contribution to the development of CHF.

The aim of this work was to study biomarkers of metabolic disorders and myocardial damage and to assess their role in myocardial remodeling and CHF progression in patients with MS.

Materials and methods

We examined 74 patients with CHF II-III FC, including 37 patients (50%) with signs of MS, who were treated at the City Clinical Hospital named after S.P. Botkin in the period from 2014 to 2019 and followed up on an outpatient basis for six months.

The diagnosis of CHF was established according to the National Recommendations of the Russian Society of Cardiology (RSC) and Society of Heart Failure Specialists. The functional class of CHF was assessed according to NYHA criteria.

The diagnosis of MS was established according to the RSC criteria from 2009: based on the presence of AO in the patient (waist circumference> 80 cm in women and> 94 cm in men) and two of the following criteria: AH (blood pressure (BP)> 140/90 mm Hg), an increase in triglycerides (TG)> 1.7 mmol / L, a decrease in the concentration of high density lipoproteins (HDL) <1.0 mmol / L in men and <1.2 mmol / L in women, an increase in low density lipoprotein (LDL)> 3.0 mmol / L, fasting hyperglycemia (fasting plasma glucose> 6.1 mmol

/ L), impaired glucose tolerance (IGT) (plasma glucose 2 hours after glucose loading in range> 7.8 and <11.1 mmol / L).

Routine clinical, laboratory and instrumental examination of patients included collection of complaints, anamnesis, physical examination, measurement of body weight, height, waist and hip circumference, calculation of body mass index, complete blood count, biochemical blood test (including fasting glucose, glycosylated hemoglobin, total cholesterol, HDL, LDL, TG), urinalysis, electrocardiography.

A special research program included:

- Determination of the level of highly sensitive CRP (hsCRP) by immunoturbodimetric method on the KONELAB20 analyzer;
- Determination of leptin and adiponectin in blood serum by enzyme immunoassay;
- Determination of hsTr by the immunochemiluminescent method (CLEIA) using the PATHFAST test system;
- Determination of the level of brain natriuretic peptide (NTproBNP) using an automated system for heterogeneous immunochemical analysis with continuous loading of samples Elecsys 2010 rack / disk (Roche, Switzerland).

Echocardiographic examination (echocardiography) was carried out using Tehnos and MaLab 90 ultrasound devices (EsaoteSpA, Italy) with sector anular mechanical and sector phased transducers with a frequency of 2.5-5.0 MHz using standard echocardiographic approaches: left parasternal, apical and subcostal.

The morphological and functional parameters of the myocardium were assessed, including LV myocardial hypertrophy, the size of the heart chambers, LV systolic function (LV ejection fraction (LVEF)), the state of the valve apparatus, the degree of mitral regurgitation, mitral valve prolapse, and aortic regurgitation.

All patients underwent determination of TED (epicardial fat thickness) when performing a standard two-dimensional echocardiography study from the parasternal access. TED was measured behind the free wall of the right ventricle.

The studies were carried out upon admission to the hospital. The dynamics of the patients' condition was assessed clinically for 6 months.

All patients received standard CHF therapy, including angiotensin-converting enzyme (ACE) inhibitors, beta-blockers, spironolactone, loop diuretics, if necessary, digoxin (36.4%), hypolipidemic (9.5% of patients) and hypoglycemic drugs (27%), insulin therapy (5.4%).

Statistical processing of the results was carried out on a personal computer using the SPSS version 21 and Microsoft Excel 2010 software package. The mean value (M) and standard error of the mean (m) were determined. To compare the mean values of dependent samples, the Wilcoxon test was used, to compare independent samples - the median method, the Mann-Whitney, Kolmogorov-Smirnov test. Quantitative indicators are presented as M ± m (mean value ± standard error of the mean). All parameters were also estimated using correlation analysis with determination of the correlation coefficient (r). The level of 0.05 was taken as the critical level of reliability of differences.

The studies were carried out in two groups of patients. Group I consisted of patients with CHF and MS, group II (control) - patients with CHF without signs of MS.

Criteria for inclusion in group I: age over 18 years, proven CHF (clinical picture, physical examination, echocardiography), the presence of signs of MS.

Criteria for inclusion in group II: age over 18 years, proven CHF (clinical picture, physical examination, echocardiography), no signs of metabolic syndrome.

The study did not include patients with acute myocardial infarction, acute surgical pathology, infective endocarditis, acute myocarditis, chronic obstructive pulmonary disease and bronchial asthma in the acute stage.

Ethical clearance: The authors declare that the work is written with due consideration of ethical standards. The study was conducted in accordance with the ethical principles approved by the Experiments Ethics Committee of I.M. Sechenov First Moscow State Medical University (Sechenov University)(Protocol № 5 of 21.03.2018).

Results

Patients under 60 years old accounted for 17.6% (13 people), from 60 to 80 years old - 43.2% (32 people), over 80 years old - 39.2% (29 people). The peak incidence of CHF was in elderly and senile patients

(in men - from 60 to 80 years old, in women - over 80 years old). The average age of men and women was 67.7 ± 13.8 and 79.5 ± 7.9 years, respectively. Upon admission of FC II, CHF was established in 19 people (25.7%), FC III - in 55 people (74.3%).

The cause of CHF in all patients was ischemic heart disease. 18 patients (24.3%) had a history of myocardial infarction (MI), among whom two (2.7%) had recurrent MI. The average age of patients with the first MI was 64.6 ± 11.4 years. 15 patients (20.3%) had degenerative heart defects. Three patients (4%) had previously undergone coronary artery bypass grafting and / or mammary coronary bypass grafting due to multivessel coronary artery disease. Atrial fibrillation was detected in 41 patients (55.4%), of whom 8 patients (10.8%) had paroxysmal form, 34 patients (45.9%) had permanent form. The average length of hospital stay was 7.2 days. In the outcome of hospitalization, 22 patients (29.7%) showed improvement (a transition during treatment to a lower NYHA FC), without changes (the same NYHA FC remained) - 45 patients. A lethal outcome during hospitalization was observed in 7 patients (9.4%) with symptoms of increasing CHF and refractory to therapy. After 6 months of follow-up, 32 (47.8%) patients remained stable after hospitalization, 31 (46.3%) showed deterioration. Within six months of observation, 4 people died (5.9%). Among patients with CHF and MS, there were 21 men (56.8%) and 16 women (43.2%). Group II - 15 men (40.5%) and 22 women (59.5%). Group I consisted of 37 CHF patients with MS, group II - 37 CHF patients without signs of MS. In group I, 8 patients (21.6%) were under 60 years old, 15 patients (40.5%) aged 60 to 80 years, and 14 patients (37.8%) over 80 years old. In group II, the majority of patients were also between 60 and 80 years old - 17 people (45.9%), over 80 years old - 15 people (40.5%), under 60 years old there were 5 people (13.5%). The operation of coronary artery bypass grafting, according to anamnesis, was performed in two patients (5.4%) in group I and one (2.7%) in group II. In patients of group II, degenerative heart defects were more often determined (86.5%, in group I, 73%), atrial fibrillation occurred in both groups equally often (48.6%, in group I - 46.5%). In group I, CHF was clinically more severe: CHF FC was higher (FC III was 89.2% in group I and 75.7% in group II), dyspnea at rest was observed one and a half times more often (21.6% in group I and 16.2% in group II), congestion in the lungs (54.1% in group I and 40.5% in group II), pronounced edema of the lower extremities (78.4% in group I and 73% in group II), hydrothorax (30.6% in group I and 24.3% in group II), diffuse cyanosis (18.9% in group I and 10.8% in group II). In patients with MS, the onset of hypertension, type 2 diabetes mellitus (DM), ischemic heart disease, manifestation of CHF symptoms occurred earlier than in the control group. Patients of group I more often suffered from arterial hypertension, type 2 diabetes.

The most common MS options were:

- A combination of hypertension, low HDL cholesterol, increased fasting glucose (45.9%);
- AH, low HDL levels (13.5%);
- AH, low HDL, high fasting glucose, high LDL (8.1%).

In the outcome of hospitalization, patients in group I were discharged more often without significant improvement (62.2% of patients, in group II - 59.5%). Hospital mortality in group I was 10.8% (4 patients), in group II - 8.1% (3 patients). After 6 months of follow-up, 43.2% of patients from group I and 40.5% of patients from group II showed a clinical worsening of the course of CHF, an increase in FC according to NYHA. Mortality after 6 months of observation in group I was 16.2% (6 people), in group II - 13.5% (5 people).

The level of the most important marker of inflammation - CRP - was increased in 98% of patients with CHF and MS (group I) and 57% of patients with CHF (group II) (the norm is 0.0-5.0 mg / l). The average values in group I were 32.97 ± 6.36 mg / l. At the same time, in 15 of 37 patients, the protein level exceeded the reference values by 10 or more times, reaching 73.1-87.9 mg / l in some patients. In patients with FC II, the mean CRP level was 24.44 ± 6.3 mg / l, for FC III - 29.28 ± 4.11 mg / l ($p > 0.05$).

The level of leptin, which is a marker of obesity, fibrosis and inflammation, was increased in all patients with CHF and MS (the norm for men is 2.0-5.6 ng / ml, for women - 3.7-11.1 ng / ml). In 30% of patients with CHF, the indices exceeded the reference values by tens of times, in 11 cases they were above 70 ng / ml, in 7 - more than 100 ng / ml. In the CHF group without MS, in 15 out of 37 patients, the leptin level did not exceed the reference values, most of the indicators were in the range of 10-30 ng / ml. The average marker level in group I was 69.46 ± 13.84 ng / ml, in group II - 23.44 ± 13.84 ng / ml ($p < 0.01$). In general, in patients with FC III, leptin indicators are almost twice.

Table 1: Indicators of echocardiography in groups I and II

	All (n=74)	I group (n=37)	II 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 (length), mm	46.5±8.2	**50.1±10.3***	**47.3±5.9***
Left atrium (width), mm	50.2±8.8	**51.8±11.3***	**48.9±5.7***
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 dimension, mm	54.7±9.1	55.4±8.8	53.8±9.7
LV, mm	52±13.9	53.8±16.9	50.9±12.3
LV myocardial mass (LV MM), g	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***
Left ventricular posterior wall, mm	11.9±2.5	**12.9±2.9***	**10.8±2.2***
LV ejection fraction (LVEF, %)	46.8±12.5	47.9±13	45.8±12.2
Pulmonary hypertension, mm Hg Art.	52.2±17.7	53.4±18.4	50.7±17.2
Epicardial fat thickness (TED, mm)	5.19±1.3	**6.48±0.41****	**4.29±0.94****

** p<0.05, ** p<0.001*

In patients with MS and CHF, direct correlations were established between leptin and CRP levels (r = 0.37, p <0.001), hsTr (r = 0.279, p <0.05), NTproBNP (r = 0.315, p <0.05) , TED (r = 0.546, p <0.05), and LV MM (r = 0.68, p <0.05) and inverse with adiponectin (r = -0.444, p <0.001), LVEF (r = -0.239, p <0.05); direct relationships between CRP and the level of hsTr (r = 0.486, p <0.05), TG (r = 0.501, p <0.05), LDL (r = 0.452, p <0 , 05), interventricular septum (r = 0.423, p <0.05), left ventricular posterior wall (r = 0.543, p <0.005) and inverse with LVEF (r = -0.412, p <0.05); inverse correlation of adiponectin with NT proBNP (r = -0.379, p <0.05).

Discussion

CHF is the most important medical and social problem. The increase in the incidence of CHF is largely due to a number of risk factors included in the concept of MS.

The visceral-abdominal type of obesity is the main criterion for the diagnosis of MS, since visceral fat is a hormonally active adipose tissue, the amount of fat in which can reach 85%. Biologically active components produced by visceral adipocytes (leptin, adiponectin) can have a multifactorial effect. Their imbalances and inflammatory responses can contribute to cardiovascular remodeling.

In the course of this study, we compared two groups of patients with CHF, comparable in age and sex, with signs of MS (group I, n = 37) and without it (group II, n = 37). On admission, the clinical manifestations of the severity of CHF were assessed, the levels of biological markers of inflammation (hsCRP), metabolic disorders (leptin, adiponectin), myocardial damage (hsTr, NTproBNP) and morpho-functional parameters of the myocardium according to echocardiography (signs of myocardial hypertrophy, dimensions heart chambers, LV systolic function);epicardial fat thickness (TED). In the subsequent clinical course of CHF in the studied patients was monitored for 6 months.

The most common variants of MS were a combination of hypertension, low HDL cholesterol, increased fasting glucose (17 people, 45.9%), which is consistent with the data of a number of studies.[5,6]

In group I, CHF was clinically more severe: CHF FC was higher (FC III was 89.2% in group I and 75.7% in group II), dyspnea at rest was observed one and a half times more often (21.6% in group I and 16.2% in group II), pronounced edema of the lower extremities (78.4% in group I and 73% in group II), hydrothorax (30.6% in group I and 24.3% in group II), severe diffuse cyanosis (18.9% in group I and 10.8% in group II). After 6 months of observation, 43.2% of patients in group I and 40.5% in group II had a clinical worsening of the course of CHF, an increase in FC. Thus, there is a clinically more severe course of CHF in patients with MS, which is characterized by a higher functional class (FC) of CHF, a higher frequency of edema, and worse indicators of the six-minute walk test. The data obtained do not contradict

the results of other studies.[10]

Acute cerebrovascular accident (ACVI) was diagnosed in 4 patients of group I and 4 - II group, while the probable cause of ACVA among patients of group I was hypertension (1 out of 4 patients had atrial fibrillation), while in group II in 3 out of 4 patients revealed atrial fibrillation. This may be due to the predominant lesion of the vascular wall and the development of endothelial dysfunction in MS. However, in this case, the number of patients is very small to identify clear patterns. This requires further study, including the possible effect of metabolic changes on endothelial dysfunction in MS.

In the course of our study, the mortality in the CHF and MS group exceeded that in the CHF group without signs of MS. Thus, hospital mortality in the CHF and MS group was 10.8%, in the CHF group without MS - 8.1%. Mortality after 6 months of observation in group I was 16.2%, in group II - 13.5%. According to the world literature, when a large number of patients with CHF and MS are observed, mortality increases by at least 10% compared to patients without MS.[10]

It was interesting to study the role of inflammation in the development and progression of CHF in both groups, in connection with which we investigated CRP, leptin and adiponectin.

The CRP level was increased in 98% of patients with CHF and MS (group I) and 57% of patients with CHF (group II) (the norm is 0.0-5.0 mg / l). The average values in group I were 32.97 ± 6.36 mg / l. At the same time, in 15 of 37 patients, the protein level exceeded the reference values by 10 or more times and reached 73.1-87.9 mg / l in some patients. In patients with FC II, the mean CRP level was 24.44 ± 6.3 mg / l, for FC III - 29.28 ± 4.11 mg / l ($p > 0.05$). According to modern concepts, it is CRP, being a component of innate immunity, that, after its initiation, turns on the inflammatory process. CRP plays a key role in atherogenesis and atherothrombosis and is an informative predictor of cardiovascular events. Increased hsCRP is a key pathogenetic central component of the inflammatory process, which determines changes leading to endothelial dysfunction, thrombus formation, insulin resistance, impaired function of leptin, adiponectin, and cytokines.[11]Research results indicate that CRP is significantly associated with the severity and outcome of CHF.[7,12] In our study, there is a significant increase in CRP in CHF and MS, which indicates a more pronounced inflammation.

Leptin is one of the most important pro-inflammatory adipokines produced by adipose tissue. The leptin level was increased in all patients with CHF and MS and significantly exceeded that in patients without MS (the average level in group I - 69.46 ± 13.84 ng / ml, in group II - 23.44 ± 13.84 ng /ml, $p < 0.01$). The data of numerous studies confirm the presence of hyperleptinemia in obesity, type 2 diabetes, MS (in combination with left ventricular hypertrophy) and CHF.[7,13] In patients with FC III, leptin indices were almost two times higher than those in patients with FC II (52.84 ± 10.24 ng / ml and 27.96 ± 6.19 ng / ml, respectively), which allows us to consider a high level of leptin as a marker of severe course CHF.

Numerous experimental studies have proven the pro-inflammatory, pro-fibrotic effects of leptin; it is involved in the activation of β-oxidation of free fatty acids, reduces the synthesis and secretion of insulin, and activates the release of inflammatory cytokines. Against the background of chronic inflammation in patients with MS, apoptosis is noted, which in turn contributes to the development of fibrosis in the vascular wall and myocardium.[13]

The revealed correlations between the levels of CRP and leptin indicate the activation of inflammatory processes in MS, which can cause pronounced damage to the vessels and myocardium with the development of a more severe course of CHF. The relationship between inflammation and damage is obvious, and therefore the hsTr marker of damage was included in the study. Among biologically active molecules (adipokines) secreted by adipose tissue, adiponectin is one of the most important. Analysis of the results of determining adiponectin revealed significant differences in the groups of patients with CHF. In patients of group I, it was reduced and amounted to 12.96 ± 1.33 μg / ml, in patients of group II - 20.64 ± 1.44 μg / ml, the difference was statistically significant ($p<0.001$). It is known that AO,[12] type 2 diabetes, dyslipidemia,[14] and hypertension,[15]are accompanied by a decrease in adiponectin levels. At the same time, a number of authors did not find the use of adiponectin levels in MS patients.[16]It is known that the adiponectin polypeptide has antiatherogenic, anti-inflammatory and antidiabetic

effects.[17,18] A significant negative relationship was established between adiponectin and TG levels and a positive relationship between adiponectin and HDL levels in patients with abdominal obesity.[19] We found an inverse correlation between the levels of adiponectin and CRP (r = -0.389, p <0.05) and a positive correlation between adiponectin and HDL. Won et al. found that a decrease in adiponectin levels correlates with an increased level of CRP and is associated with a decrease in the anti-inflammatory effect of protective adipokine.[20] Obviously, with a combination of MS and CHF, these changes can contribute to the progressive remodeling of the myocardium. In obesity, especially in its abdominal form, the hormones of adipose tissue - adipokines - act as important regulators of energy metabolism and, in particular, energy substrates in heart cells. A special form of heart damage in obesity is described - "lipotoxic cardiomyopathy". In the cytoplasm of animal cardiomyocytes, the deposition of fat droplets and cell death were detected. Biopsy of the ventricular myocardium in obese patients with type 2 diabetes revealed an increase in cells that died by the mechanism of apoptosis.[21]

Based on our material, in the MS and CHF group, the hsTr level exceeded the reference values in all patients, in group II, increased hsTr indices were determined in 84% of patients. An increase in the level of hsTr, according to the literature, is observed in almost all patients with CHF.[21] The highest rates were found in patients of group I with FC III of CHF (0.0311 ± 0.007 ng / ml, with FC II - 0.0178 ± 0.004 ng / ml, p <0.001). A direct correlation between the level of hsTr and a number of clinical factors (age, early onset of coronary artery disease, type 2 diabetes, FC CHF) was established. A meta-analysis of 16 studies has shown that in patients with CHF, increased levels of hsTr are associated with a high risk of mortality and major adverse cardiovascular events.[9,22] The progression of CHF is accompanied by an intensification of the processes of cardiovascular remodeling, hypertrophy and apoptosis of cardiomyocytes, which may have an inducing effect on the active secretion and release of troponin I (trI) in violation of the structure of cardiomyocytes in non-coronary myocardial damage.[23] The level of hsTr in the group of CHF and MS patients correlates with the level of CRP, leptin and the N-terminal fragment of brain natriuretic peptide (NTproBNP), which has been confirmed in a number of clinical studies.[24,25]

In obesity, structural and functional restructuring of the heart occurs with the development of an eccentric type of left ventricular hypertrophy. In patients with MS, with a combination of obesity and AH, concentric type of left ventricular hypertrophy is formed twice as often.[26] In this case, a certain contribution is made by both increased volume load and an increase in blood viscosity.[27]The indicators characterizing LV myocardial hypertrophy in group I were significantly higher than those in group II of the examined. MS patients had a large myocardial mass, LV diameter, hypertrophy of the interventricular septum, and posterior LV wall.[28]Patients of group I showed more pronounced dilatation of the right ventricle, which can be associated with the development of pulmonary hypertension in obese patients with MS. Pathophysiological changes are associated with the possible development of sleep apnea syndrome, which leads to an increase in pressure in the pulmonary artery, hypertrophy and dilatation of the right ventricle and impairment of its function.

With progressive obesity, hyperplasia and hypertrophy of adipocytes occurs in all ectopic local fat depots, including the epicardial one. Epicardial adipose tissue, being in close proximity to the myocardium, influences it through the system of cytokines and peptides.[27]In patients with MS and CHF, direct correlations between leptin and TED (r = 0.546, p <0.05), LV MM (r = 0.68, p <0.05) and reverse correlations with LVEF (r = -0.239, p <0.05). Visceral obesity and, in particular, epicardial fat deposition is one of the main factors leading to cardiovascular remodeling.[29,30]

The revealed correlations between the levels of leptin, CRP, hsTR, NTproBNP, LV MM and TED indicate a natural relationship between inflammation, damage, development of myocardial hypertrophy and the formation of a more severe course of CHF in MS.

Conclusion

The multifactorial effects of the components produced by adipose tissue in patients with MS with the development of inflammatory and dysmetabolic processes have a significant effect on the clinical picture of CHF, which is characterized by earlier development and severe course; morpho-functional

parameters of the myocardium with significant hypertrophy of the ventricular myocardium, an increase in the size of the heart chambers, pulmonary hypertension. In this case, the degree of LV myocardial mass is associated with TED. In patients with MS, an increase in hsTr was found, significantly exceeding the levels in patients without MS. The established correlations indicate the important role of inflammation, dysmetabolic disorders in myocardial damage, its remodeling and the progression of CHF in this category of patients.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest. The authors declare no conflicts of interest.

Authors' contribution:

Data gathering and idea owner of this study: ST and AM;

Study design: TF, ST, and TS;

Data gathering: NS, AM, and TS;

Writing and submitting manuscript: TF andNS;

Editing and approval of final draft: TF,NS,ST,AM, and TS.

References

1. McMurray JJ, Adamopoulos S, Anker SD, Auricchio S, Böhm M, Dickstein K, et al. ESC Guidelines for the diagnosis and treatment of acute and chronic HF 2012: The task force for the diagnosis and treatment of acute and chronic HF in collaboration with the HF European Society of Cardiology. *Eur Heart J* 2012;**33**(14):1787-1847.
2. Belenkov YN, Mareev VY. The first results of a national epidemiological study - an epidemiological examination of patients with heart failure in real clinical practice. *Heart Failure* 2003;**4**(3):116-120.
3. Drapkina OM, Ivashkin VT, Korneeva ON. Clinical variants of metabolic syndrome. Moscow: Medical news agency, 2012.
4. Fukuta H, Ohte N, Wakami KGoto T, Tani T, Kimura G. Relation of Plasma Levels of Adiponectin to Left Ventricular Diastolic Dysfunction in Patients Undergoing Cardiac Catheterization for Coronary Artery Disease. *Am J Card* 2011;**108**:1081-1085. https://doi.org/10.1016/j.amjcard.2011.06.005
5. Tadaki S, Sakata Y, Miura Y, Miyata S, Asakura M, Shimada K, et al. Prognostic impacts of metabolic syndrome in patients with chronic heart failure. *Circ J* 2016;**80**:677-688. https://doi.org/10.1253/circj.CJ-15-0942
6. Tamariz L, Hassan B, Palacio A, Arcement L, Horswell

R, Hebert K. Metabolic Syndrome increases Mortality in Heart Failure. *Clin Cardiol* 2009;**32**:327-331. https://doi.org/10.1002/clc.20496

7. Kochegura TN, Makarevich PI, Ovchinnikov AG, Zhigunova LV. Circulating markers associated with metabolic disorders in patients with post-infarction heart failure. *Diabetes Mellitus* 2013;**14:**191-199.
8. Krikunova OV, Vasyuk YA, Viskov RV,Krikunov PV, Ivanova SV. Differential diagnostic and prognostic value of troponin tests in heart failure. *Heart Failure* 2015;**16(**4):254-260.
9. Tang ZH, Wang L, Zeng F, Zhang K. Association and predictive value analysis for metabolic syndrome on systolic and diastolic heart failure in high-risk patients.*BMC Cardiovasc Disord* 2014;**14:**30. https://doi.org/10.1186/1471-2261-14-124
10. Ketelslegers J, Zannad F, Vincent J, Mukherje R, Rousseau M. Effect of neurohormons, cytokins and collagen markers on the risk of all-cause mortality: results from the ephesus trial. *Eur Heart J* 2006;**26:**439.
11. Vel'kov VV. C-reactive protein: new opportunities for laboratory diagnosis.Pushchino: ZAO «Diakon», 2010.
12. Fedorova MM. The effect of weight loss on adiponectin concentration in patients with obesity and type 2 diabetes.Klin Lab Diagn 2009;8:10-11.
13. Drapkina OM, Deeva TA, Volkova NP. Fibrosis in patients with metabolic syndrome.*Russian Medical News* 2014;**4**:25-40.
14. 14.MatsubaraM,MaruokaS,KatayoseS.Dicreasedolasma adiponectin concentrations in women with dyslipidemia. *J Clin Endocrinol Metab* 2002;**87**:2764-2769. https://doi.org/10.1210/jcem.87.6.8550
15. Billah SMB, Jahan MS, Al Jundi S, Rajab AM. Gender differentials of metabolic syndrome in Bangladesh taking menopause into consideration. *IJHHS* 2021;**5**:101-107. https://doi.org/10.31344/ijhhs.v5i1.242
16. Virsaladze DK, Charkviani NA, Adamiya N. Blood levels of adiponectin and leptin in menopausal metabolic syndrome. *Med Novosti Gruzii*2006;**134**(5):64-67.
17. Han S, Quon M, Kim J, Koh KK. Adiponectin and cardiovascular disease. *J Am Coll Card* 2007;**49**(5):531-538. https://doi.org/10.1016/j.jacc.2006.08.061
18. Guerre-Millo M. Adiponectin: An update. *Diabetes Metab* 2008;**34:**12-18. https://doi.org/10.1016/j.diabet.2007.08.002
19. Belyaeva OD, Bazhenova EA, Berezina AV,Bolshakova OO, Chubenko EA, Garanina AE, et al. Adiponectin levels, lipid and carbohydrate metabolism in patients with abdominal obesity. *Arterial Hypertension* 2009;**15**(3):309-313. https://doi.org/10.18705/1607-419X-2009-15-3-309-313
20. Al-Mahmood AK, Ismail AA, Faridah AR, Bebakar WMW, Tai ES.The metabolic syndrome in normal weight Malay subjects. *Bangladesh J Med Sci* 2016;**15**:123-128. https://doi.org/10.3329/bjms.v15i1.27149
21. Barouch LA, Gao D, Chen L, Miller KL, Xu W, Phan AC, et al. Cardiac myocyte apoptosis is associated with increased DNA damage and decreases survival in murine models obesity.*Circ Res* 2006;**98**:119-124. https://doi.org/10.1161/01.RES.0000199348.10580.1d
22. Al-Mahmood AK, Afrin SF, Hoque N. Metabolic syndrome and insulin resistance: Global crisis. *Bangladesh J Med Biochem* 2011;**4**:27-31. https://doi.org/10.3329/bjmb.v4i1.13779
23. Horwich TB, Patel J, MacLellan WR,Fonarow GC. Cardiac troponin I is associated with impaired hemodynamics, progressive left ventricular dysfunction, and increased mortality rates in advanced heart failure.*Circulation* 2003;**108**:833-838. https://doi.org/10.1161/01.CIR.0000084543.79097.34
24. Korff S, Katus NA, Giannitsis E. Differential diagnosis of elevated troponins. *Heart* 2006;**92**:983-993. https://doi.org/10.1136/hrt.2005.071282
25. ParmacekMS,SolaroRJ.Biologyofthetroponincomplexin cardiac myocytes. *ProgCardivasc Dis* 2004;**47:**159-176. https://doi.org/10.1016/j.pcad.2004.07.003
26. Veber VR, Rubanova MP, Kopina MP, Zhmailova SV, Shmatko DP, Prozorova IV. The effect of abdominal obesity on heart structural and functional changes and possibility of their medical correction in patients with arterial hypertension. *Ration PharmacotherCardiol* 2008;**4**:28-31. https://doi.org/10.20996/1819-6446-2008-4-4-28-31
27. Logacheva IV, Ryazanova TA, Makarova VR, Avzalova FR, Maksimov NI. Heart remodeling in patients with overweight and obesity with comorbid cardiac pathology. *Russ J Cardiol* 2017**;4:**40-46. https://doi.org/10.15829/1560-4071-2017-4-40-46
28. Afrin S, Mahmood AK, Bari K, Rahman F, Hassan Z. Pattern of lipid levels of subjects seeking laboratory services in an established laboratory in the Dhaka city. *Bangladesh J Med Sci* 2017;**16:**375-379. https://doi.org/10.3329/bjms.v16i3.32849
29. Eroglu S, Sade LE, Yildirir A, Bal U, Ozbicer S, Ozgul AS, et al. Epicardial adipose tissue thichness by echocardiography is a marker for the presence and severity of coronary artery disease. *Nutr Metab Cardiovasc Dis* 2009;**19**:211-217. https://doi.org/10.1016/j.numecd.2008.05.002
30. Shenkova NN, Veselovskaya NG, Chumakova GA,Osipova ES, Gritsenko OV, Ott AV. Prediction of the risk of subclinical atherosclerosis of brachiocephalic arteries in obese women. *Russ J Cardiol* 2017**;4**:54-60. https://doi.org/10.15829/1560-4071-2017-4-54-60