ABDOMINAL OBESITY AND POSTINFARCTION CARDIOSCLEROSIS: CARDIOMETABOLIC CONTINUUM IN THE DEVELOPMENT OF CHRONIC HEART FAILURE

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The aim of the study was to evaluate the influence of abdominal obesity (AO) on left ventricular myocardium (LV) postinfarction remodeling, readaptation to physical exertion and the course of chronic heart failure in patients of working age with newly diagnosed large-focal myocardial infarction (MI).

Methods. At the first stage of the study we examined 318 patients of working age who were admitted to hospital with the diagnosis of acute coronary syndrome during the calendar year. According to the selected criterion (newly diagnosed large-focal MI) 91 patients of working age were included and examined in the study: 82.4% (n = 75) – males, 17.6% (n = 16) – females. The main group included 60 patients with AO, the comparison group consisted of 31 patients without AO. These groups were matched by sex, age, localization of ischemic damage, types of reperfusion therapy and drug therapy tactics in the postinfarction period. Design: a prospective, comparative study with a follow-up period of 36 months. Examination of patients which included questioning, taking a case history, clinical examination, laboratory and instrumental investigations (echocardiography of the heart) and a six-minute walking test was conducted in the acute MI period (10±2 days), 1st (30±2 days), 6th (180±2 days) and 12th (364±2 days) months of postinfarction follow-up period. The levels of adiponectin, leptin and the N-terminal fragment of proBNP (NT-proBNP) were determined for all patients. In addition, the information on the state of health was obtained to reveal repeated coronary events in patients with postinfarction cardiosclerosis 36 months after the onset of the disease.

Results. After 12 months of follow-up the proportion of patients with postinfarction cardiosclerosis and AO who developed maladaptive prognostically unfavorable types of postinfarction LV remodeling made up 75.0% vs. 9.7% of patients without AO ($F = 0.399$; $p < 0.001$). The development of maladaptive type of postinfarction LV remodeling after 12 months was accompanied by a diastolic dysfunction (84.6% vs. 58.1% of patients without AO ($\chi^2 = 7.24$; $p < 0.01$), decrease in myocardial LV contractility < 50% (78.8 % vs. 19.4 % of patients without AO ($\chi^2 = 28.0$; $p < 0.001$), low exercise tolerance as a result of a six-minute walking test, as well as increase in the functional class of CHF and in the number of the deceased among the patients with obesity.

Despite the achievements of domestic and foreign healthcare, chronic heart failure (CHF) has been and remains the focus of priority areas of modern medicine. The socio-economic significance of the problem is due to the prevalence of pathology, a steadily progressive increase in the number of people with CHF, the growth and duration of hospitalizations (including repeated ones), expensive cardiac surgery, early disability and high mortality in this category of people [1–5].

Numerous studies both in our country and abroad have been devoted to the issues of epidemiology, etiopathogenesis and tactics of managing patients with CHF. In developed countries heart failure occurs in about 1–2% of the adult population. About 17% of hospitalized patients and more than 7% of outpatients suffering from chronic heart failure die during the year and patients with a progressive CHF course prevail in the structure of mortality. About 5 million Americans suffer from CHF, about 550,000 new cases are diagnosed annually and result in approximately 287,000 deaths per year. In Russia more than 8 million people have obvious clinical signs of CHF, of which more than three million have a severe, III–IV functional class of the disease [3, 4]. According to the Belarusian Association of Heart Failure, the moment prevalence CHF rate in the city of Minsk as of 01.12.2012 was 13.2% [2]. Demographic aging of the population contributes to the CHF epidemiology [1, 2, 5]: in people over 55 the risk of developing

heart failure during the remaining life is over 33% in men and 28% in women. More than 10% of the total population of developed countries over 75 years are CHF victims. Early disability, especially at working age, additional costs of the healthcare system for ensuring demographic security by means of resources for preventing premature mortality due to CHF progression make heart failure one of unresolved global socio-economic problems [1–5].

CHF associated cardiovascular diseases frequently occurring against the background of metabolic disorders largely contribute to the structure of total mortality in Europe and the Republic of Belarus: in 80% of all cases CHF is associated with arterial hypertension (AH) and in 60% – with coronary heart disease (CHD) [2, 3]. One of the factors that affect the duration and preservation of quality of life after major myocardial infarction (MI) is the structural and functional state of the left ventricular myocardium (LV) [6, 7]. The morphological substrate of postinfarction LV changes are processes occurring at all the levels of the structural organization of the heart, associated with its dilatation, changes in the shape and thickness of the walls. The triggering mechanism of the pathophysiological processes of postinfarction remodeling is the loss of part of viable cardiomyocytes, which stimulates the compensatory processes of myocardial changes in the areas bordering on the infarction site and those distant from the lesion. The most important determinants of the intensity of postinfarction remodeling are considered to be expansion of the infarction zone, dilatation of the left ventricle and hypertrophy of the viable segments. In some cases postinfarction LV remodeling acquires decompensated character, which is a key point in the pathogenesis of ischemic cardiomyopathy, the development and rapid progression of heart failure [6–9]. The significance of the contribution of numerous predictors of postinfarctional transformation of the left ventricle (LV) into the pathogenesis remains one of the most pressing and debatable problems of modern cardiology. The leading position in the high cardiovascular risk group is occupied by patients with abdominal obesity (AO) and metabolic syndrome [9–11].

Aim of the study. To analyze the effect of abdominal obesity (AO) on postinfarction remodeling of the left ventricular myocardium, readaptation to physical exertion and the course of CHF in people of working age with a newly identified large-focal myocardial infarction.

Materials and methods. At the first stage of the study we examined 318 patients of working age who were admitted to the 9th City Clinical Hospital of Minsk with the diagnosis of acute coronary syndrome (ACS) during the calendar year. We analyzed outpatient cards and inpatient case-histories, collected anamnestic data, carried out clinical examination, made up an anthropometric patient passport, assessed cardiovascular risk factors, recorded ECG at rest, performed cardiac echocardiography (ECHO-CG) and laboratory tests.

According to the selected inclusion criterion (newly diagnosed large-focal MI), 91 patients aged 40 to 60 years became participants of this prospective comparative study [9]. Exclusion criteria were: MI in history; pathologically changed dimensions of the left ventricle according to ECHO-CG at the time of inclusion in the study; non-coronary myocardial diseases; congenital and acquired valvular heart disease; past cardiac or interventional surgery performed in the process of follow-up; the use of implantable antiarrhythmic devices that provide constant cardiac pace; the presence of tachyarrhythmias that cannot be corrected with drug therapy; alcohol abuse; progressive hepatic and renal disease; cancer pathology; hypoventilation of the upper and lower respiratory tract. The gender distribution was as follows: 82.4% (n = 75) were males, 17.6% (n = 16) were females. Patients were monitored for three years.

Taking into account the characteristics of the anthropometric passport of the subjects included in the study (weight, height, body mass index (BMI), waist circumference (WC), hip circumference (HC), WC/ HC), the diagnosis of abdominal obesity was conducted [10, 11]: men – BM I> 30.0 kg/m^2, WC > 94 cm., WC/HC > 0.9; for women – WC > 80 cm., WC/HC > 0.85 and BMI > 30.0 kg/m^2. Two study groups were formed. The main group consisted of 60 patients (48 men and 12 women) with postinfarction cardiosclerosis and abdominal obesity; the comparison group included 31 patients (27 men and 4 women) without overweight and abdominal obesity. Statistically significant differences between the examined groups by sex, age composition, presence of bad habits, comorbidities (AH and DM) (Table 1), reperfusion tactics, localization of the affected area, linear, volumetric and indexed echocardiographic characteristics of the left ventricle as well as drug therapy conducted in the post-infarction period were not established.

The main checkpoints were: acute period of MI (10±2 days), 1st (30±2 days), 6th (180±2 days) and 12th (364±2 days) months of postinfarction follow-up. To identify repeated coronary events in patients with postinfarction cardiosclerosis additional information on the state of health was collected 36 months after the onset of the disease.

An echocardiographic study of the heart was performed on the Vivid-7 apparatus of General Electric Medical Systems (USA) in three modes (M-, B-modal and color Doppler) with 3.5 MHz ultrasound transducer and according to the standard procedure with a permissible measurement error of 2, 5, 4–10% respectively. A decrease in systolic function, LV remodeling according to linear, volumetric, and indexed echocardiographic characteristics [8, 9, 12, 13] at the time of randomization served as an exclusion criterion for individuals of both groups.

To determine the functional class of CHF according to the classification of the New York Heart Association (NYHA) and exercise tolerance assessment we used a 6-minute walking test. Readaptation to physical activity was evaluated over time by the criterion of the minimum significant improvement in the result – an increase in the distance covered in 6 minutes by 70 m compared to the baseline, obtained on 10±2 days with MI data.

The concentration of the brain natriuretic peptide precursor (NT-proBNP), adiponectin and leptin was determined on 30±2 day of postinfarction period in vitro using ELISA method and commercial kits of DRG International, Inc. (United States) [11–14]. The threshold of serum NT-proBNP concentration for adults younger than 75 years, according to the manufacturer, was 125.0 pg/ml. As the normal levels of adipocytokines the following manufacturer's standard indicators were adopted: adiponectin – 10–35 ng/ml; leptin – 3.84±1.79 ng/ml in men and 7.36±3.73 ng/ml in women.

Statistical packages Excel and Statistica (version 10.0, StatSoft, Inc., USA) were used to process the obtained data. The obtained data were interpreted as reliable and the differences between the indicators were considered significant when the magnitude of the error-free forecast was 95% or more ($p < 0.05$).

Results and discussion. Over 12 months death from cardiovascular causes was observed in 3.3% (n = 2) of patients with AO and it was not registered in the comparison group. 36 months after MI the proportion of patients who died of cardiovascular causes in the group with AO was 15% (n = 9); in the group without abdominal obesity no episodes of patient death were revealed ($F = 0.057$; $p < 0.05$). In the structure of cardiovascular mortality over 36 months of postinfarction observation, the proportion of people with CHF decompensation prevailed – in 77.8% (n = 7) of cases, with acute coronary insufficiency – 22.2% (n = 2) ($p < 0.05$) (figure 1) [9].

Variable	MI with AO (n = 60)	MI without AO (n = 31)
Age, years, Me (25–75%)	53.15 (47.0–59.0)	53.29 (48.0–59.0)
Male sex,% (n)	80.0 (48)	87.0 (27)
Smoking,% (n)	30.0 (18)	32.3 (10)
Arterial hypertension, % (n)	78.3 (47)	77.4 (24)
Family history of early coronary artery disease,% (n)	58.3 (35)*	35.5 (11)
Abdominal obesity,% (n)	100.0 (60)*	–
Diabetes,% (n)	16.7 (10)	16.1 (5)

Note – * – reliability of differences in comparison with the myocardial infarction (MI) group without abdominal obesity (AO), $p < 0.05$.

Table 1.
Cardiovascular risk characteristics of patients

In the group of patients with AO the obtained values of adiponectinemia were 7.3 (5.5–11.8) ng/ml versus 10.8 (7.1–19.1) ng/ml ($U = 483.5$; $p < 0.01$), and the detection rate of hypoadiponectinemia was 72.0% (n = 36) versus 43.3% (n = 13) in the group without AO ($\chi^2 = 6.49$, $p < 0.05$). The average leptin rate and the proportion of patients with hyperleptinemia in the group with AO statistically significantly exceeded the corresponding values in patients without abdominal obesity and amounted to 12.0 (8.2–25.8) ng/ml versus 3.2 (2.0–5.2) ng/ml ($U = 40.0$; $p < 0.001$) and 100% (n = 50) versus 20% (n = 6) ($F = 0.7$; $p < 0.001$) respectively. In the group with abdominal obesity the level of NT-proBNP was 151.5 (128.0–201.0) ng/l versus 121.5 (115.0–131.0) ng/l ($U = 188.0$; $p < 0.001$)), the proportion of individuals with a peptide concentration of more than 125 ng/l was 76.7% (n = 23) versus 26.7% (n = 8) ($\chi^2 = 15.0$; $p < 0.001$).

There were no significant echocardiographic differences between the groups in the acute MI period. Despite the changes in the geometric LV parameters in both groups of patients

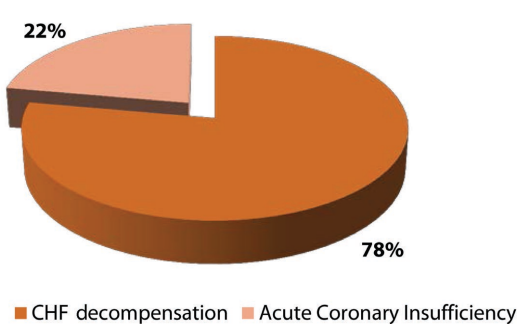
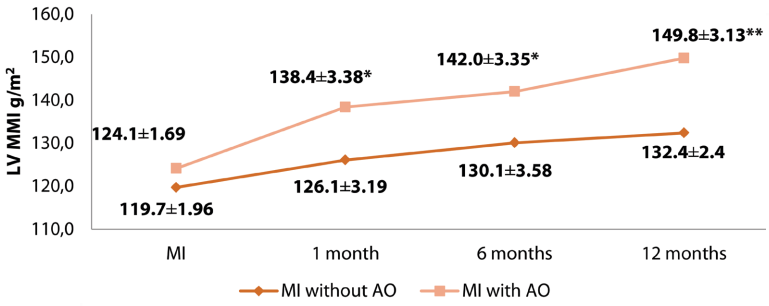
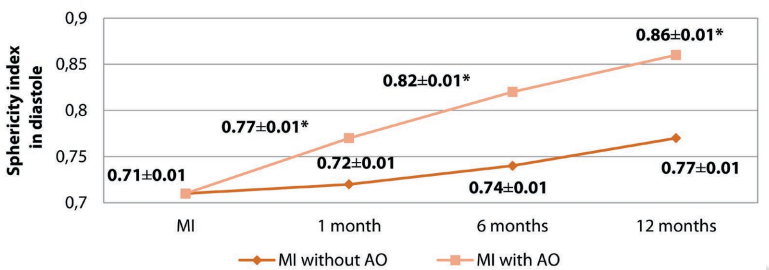


Figure 1.
The structure of mortality causes of patients after large-focal myocardial infarction over 36 months of follow-up, $p < 0.05$



N o t e – * – reliability of differences in comparison with the myocardial infarction (MI) group without abdominal obesity (AO), $p < 0.05$; ** – $p < 0.001$

Figure 2. Dynamics of left ventricle myocardial mass index (LV MMI) in patients with postinfarction cardiosclerosis over 12 months.

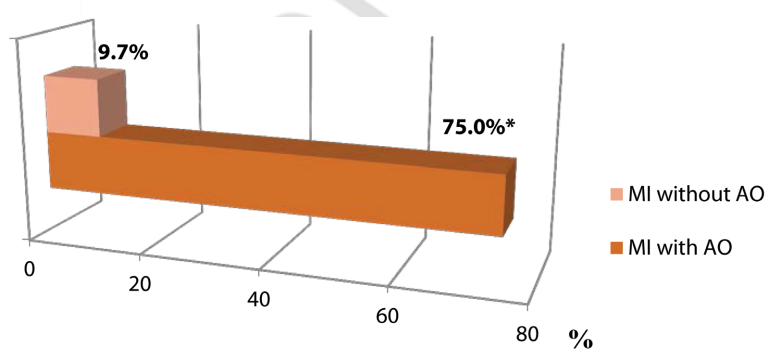


N o t e: * – reliability of differences in comparison with the myocardial infarction (MI) group without abdominal obesity (AO), $p < 0.001$.

Figure 3. Sphericity index in diastole in patients with postinfarction cardiosclerosis

observed during the postinfarction follow-up year, the absolute increase in the number of echocardiographic characteristics of LV dilatation was higher in the AO group and remodeling acquired a pathological form. 12 months after MI greater expression of LV dilatation was observed in AO patients according to the values of end systolic (ESI) and diastolic (EDI) indices (41.2 ± 1.47 ml/m² versus 29.2 ± 2.56 ml/m² and 74.7 ± 1.94 ml/m² versus 66.0 ± 2.48 ml/m²; $p < 0.001$p and $p < 0.01$), LV myocardial mass index (LV MMI) (149.8 ± 3, 13 g/m² versus 132.4 ± 2.4 g/m²; $p < 0.01$) and the sphericity index in diastole (SId) (0.86 ± 0.01 versus 0.77 ± 0.01; $p < 0.001$). Absolute increase in LV MMI in the group of AO patients over 12 months of the follow-up period amounted to 22.5 (10.0–42.2) g/m² versus 11.4 (6.0–18.0) g/m² in the group without AO ($U = 493.5$; $p < 0.01$) (Figure 2).

Figure 4. Proportion of patients with a maladaptive type of left ventricle remodeling 12 months after myocardial infarction



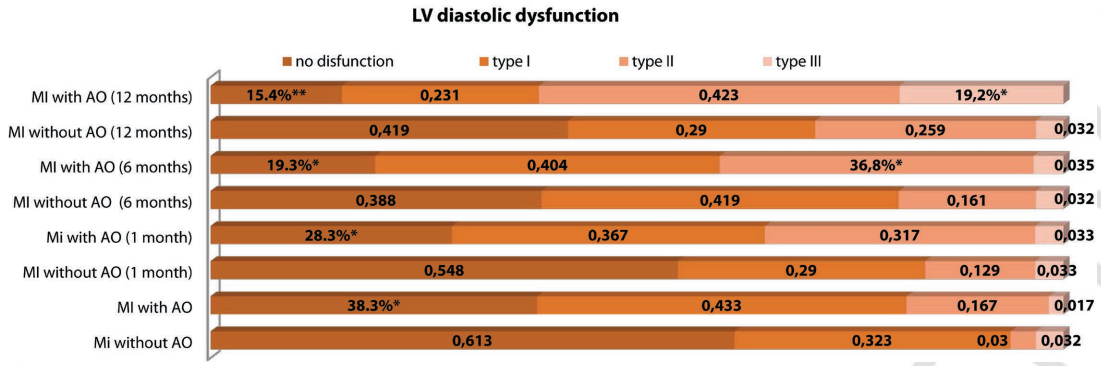
N o t e: * 75.0% – reliability of differences in comparison with the myocardial infarction (MI) group without abdominal obesity (AO), $p < 0.001$.

Analysis of the annual dynamics of one of the main LV geometry characteristics [12] – the sphericity index in diastole showed a statistically significant increase in patients of both groups: from 0.71 ± 0.01 to 0.77 ± 0.01; 0.82 ± 0.01 and 0.86 ± 0.01 ($\chi^2 = 72.1$; $p < 0.001$) in the AO group and from 0.71 ± 0.01 to 0.72 ± 0.01; 0.74 ± 0.01 and 0.77 ± 0.01 ($\chi^2 = 19.0$; $p < 0.001$) in the comparison group. At the same time, the absolute increase in SId over 12 months of follow-up in patients with AO was significantly higher and amounted to 0.15 ± 0.01 versus 0.05 ± 0.01 in the group without AO ($p < 0.001$) (Figure 3).

Depending on the severity of changes in the LV geometry according to the presence of 2 or 3 criteria of pathological remodeling – myocardial hypertrophy according to the LV MMI, the relative wall thickness index of the left ventricle in diastole (RWTI) less than 0.33 or over 0.45 and SId over 0.8 – prognostically unfavourable maladaptive type of postinfarction LV remodeling was diagnosed [13], associated according to the literature with a decrease in the contractile ability of the myocardium, decreased exercise tolerance, development and progression of CHF and reduced life expectancy of patients. According to the data of the present study, the proportion of patients with the formation of a maladaptive type of postinfarction LV remodeling in the AO group was 75.0% (n = 39) versus 9.7% (n = 3) in the group without AO ($F = 0.399$; $p < 0,001$) (Figure 4).

Intra-group analysis of LV systolic function over 12 months of postinfarction follow-up demonstrated a decrease in the contractile ability of the myocardium in AO patients (from 59.6 ± 1.54% to 57.6 ± 1.14%, 51.6 ± 1.51% and 45.1 ± 1.30%) ($\chi^2 = 51.7$; $p < 0.001$). Statistically significant annual dynamics of the LV ejection fraction (EF) in the group without AO was not obtained. 12 months after myocardial infarction LV ejection fraction in patients with abdominal obesity compared with patients without AO was 45.1 ± 1.30% versus 58.9 ± 1.66% ($p < 0.001$), the proportion of subjects with LV systolic function < 50% was 78.8% (n = 41) versus 19.4% (n = 6) ($\chi^2 = 28.0$; $p < 0.001$).

In the group with AO compared with patients without AO after 12 months of follow-up the cardiac index (CI) values were: 2155.5



Note – * – reliability of differences in comparison with the myocardial infarction (MI) group without abdominal obesity (AO), $p < 0.05$ and ** – $p < 0.01$

Figure 5. Results of the structural analysis of left ventricle (LV) diastolic dysfunction in groups of patients with postinfarction cardiosclerosis after 12 months of follow-up

(1667.5–2363.5) versus 2461.5 (2033.0–2833.0) ($U = 436.5$; $p < 0.001$), integral systolic remodeling index (ISRI) – 66.5 ± 2.98 versus 76.7 ± 2.95 ($p < 0.05$). Intra-group analysis of ISRI after 12 months of the postinfarction period revealed a significant tendency to the reduction of this indicator in patients with AO (from 84.1 ± 2.37 to 76.0 ± 1.81; 64.1 ± 2.98 and 66.5 ± 2.98 ($\chi^2 = 43.5$; $p < 0.001$), the negative growth rate was –28.7 (–43.3 – 17.0). In the group without AO a slight decrease of this indicator after 12 months was not relevant.

The proportion of AO patients diagnosed with LV diastolic dysfunction according to echocardiographic criteria [12] in the main checkpoints was 61.7% (n = 37) versus 38.7% (n = 12) ($\chi^2 = 4.3$; $p < 0.05$), 71.7% (n = 43) versus 45.2% (n = 14) ($\chi^2 = 6.14$; $p < 0.05$), 80.7% (n = 46) versus 61.3% (n = 19) ($\chi^2 = 3.92$; $p < 0.05$) and 84.6% (n = 44) versus 58.1% (n = 18) ($\chi^2 = 7.24$; $p < 0.01$) in the acute period of myocardial infarction and after 1st, 6th and 12th months after myocardial infarction, respectively. In the AO group an increase in the proportion of patients with verified (excluding the type) LV diastolic dysfunction from 61.7% (n = 37) to 84.6% (n = 44) ($\chi^{2MN} = 17.42$; $p < 0.001$) was detected during the follow-up period. In the group without AO no significant change of this indicator was observed. The results of the LV diastolic dysfunction structural analysis are presented in Figure 5. 12 months after MI a significant increase in the proportion of patients with the most prognostically unfavorable, restrictive type of LV diastolic dysfunction (from 1.7% (n = 1) to 19.2% (n = 10)) ($F = 0.087$; $p < 0.01$) in combination with low LV EF associated with decompensated CHF [17, 18] was noted in the AO group.

12 months after MI functional class III (FC) according to the classification of the New York Heart Association (NYHA) prevailed in AO patients: 59.6% (n = 31) versus 6.4% (n = 2) in patients without AO ($F = 0.180$; $p < 0.001$). In the group of patients without AO FC I and FC II of heart failure according to NYHA prevailed: 9.7% (n = 3) and 83.9% (n = 26) versus the absence of patients with FC 1 ($F = 0.063$; $p < 0$, 05) and 40.4% (n = 21) with FC 2 ($\chi^2 = 14.95$; $p < 0.001$) among patients with AO (Table 2).

In the group without AO the proportion of patients who demonstrated increased tolerance to physical activity during a 6-minute walking test after 1st, 6th and 12th months after MI: 64.5% (n = 20) versus 23.3% (n = 14) ($\chi^2 = 14.8$; $p < 0.001$), 83.9% (n = 26) versus 35.1% (n = 20) ($\chi^2 = 19.2$; $p < 0.001$) and 87.1% (n = 27) versus 50.0% (n = 26) ($\chi^2 = 11.6$; $p < 0.001$) of patients with AO, respectively.

A direct moderately strong relationship between BMI and LV remodeling according to the maladaptive type ($r = 0.45$, $p < 0.001$) and inverse moderately strong relationship between BMI and LV EF ($r = –0.36$, $p < 0.001$)

FC, NYHA	Distance, m	MI+AO				MI without AO			
		10±2 day (n = 60)	1 month (n = 60)	6 months (n = 57)	12 months (n = 52)	10±2 day (n = 31)	1 month (n = 31)	6 months (n = 31)	12 months (n = 31)
0	>551	0	0	0	0	0	0	0	0
I	426–550	0*	0*	0*	0*	9.7(3)	9.7(3)	9.7(3)	9.7(3)
II	301–425	60.0 (36)*	58.3 (35)**	45.6 (26)***	40.4 (21)***	3.9 (26)	87.1 (27)	87.1 (27)	83.9 (26)
III	151–300	36.7 (22)**	40.0 (24)***	54.4 (31)***	59.6 (31)***	9.7(3)	3.2(1)	3.2(1)	6.4(2)
IV	<150	3.3(2)	1.7 (1)	0	0	0	0	0	0

Note – * – reliability of differences in comparison with the myocardial infarction (MI) group without abdominal obesity (AO), $p < 0.05$, ** – $p < 0.01$ and *** – $p < 0.001$.

Table 2.
6-minute walking test: heart failure functional class assessment according to NYHA in patients after myocardial infarction with and without abdominal obesity, % (abs.)

12 months after MI were revealed. An inverse moderately strong relationship between the data obtained during a 6-minute walking test 12 months after MI, the formation of LV maladaptive remodeling (r = –0.48, p <0.001) and LV EF (r = –0.50, p < 0.001) was found. A direct moderately strong relationship between leptin amount and NT-proBNP levels (r = 0.53, p < 0.001) was observed. A direct moderately strong relationship between NT-proBNP, development of LV remodeling according to the maladaptive type (r = 0.42, p < 0.01) 12 months after MI, as well as death from cardiac causes within the next 3 years (r = 0, 43, p < 0.001) was established.

Conclusion. In patients with abdominal obesity compared with patients without overweight and abdominal obesity the maladaptive type of left ventricular remodeling, associated with impaired systolic and diastolic function, low exercise tolerance, development of a high functional class of chronic heart failure prevailed 12 months after a large-focal myocardial infarction; after 36 months the maladaptive type of left ventricular remodeling was associated with increased proportion of deaths from decompensated chronic heart failure.

Conflict of interests: none.

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