LEFT VENTRICLE REMODELING IN PATIENTS WITH POSTINFARCTION CARDIOSCLEROSIS AND OBESITY, TAKING INTO ACCOUNT FABP 4 AND CTRP 3 LEVELS

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The objective – to study the structural-functional condition of the left ventricle myocardium (LV) in patients with postinfarction cardiosclerosis and surplus body weight taking into account the levels of adipokines FABP4 and CTR3.

Material and methods. The study involved 189 patients. The first group consisted of 60 patients with postinfarction cardiosclerosis, the second group included 68 patients with postinfarction cardiosclerosis and excess body weight (EBW), the third group comprised 61 patients with postinfarction cardiosclerosis and obesity. The content of FABP 4 and CTRP 3 was determined by enzyme-linked immunosorbent assay. Statistical processing of the survey results was performed using the licensed software package "IBM SPPS Statistics 27.0". According to the sample size and distribution of indicators, the parametric Student's test was used. Evaluation of the significance of the difference between the means of multiple comparisons for quantitative traits with normal distribution using Bonferroni correction was performed by one-way analysis of variance (ANOVA). The mean and the error of the mean were determined. The correlations of the indicators were determined using the Pearson correlation coefficient (r). At a value of p<0.05, the difference was considered significant.

Results. Patients with post-infarction cardiosclerosis and obesity in comparison with patients without excess body weight were found to have an increase in end-systolic volume (ESV), end-diastolic volume, end-diastolic size (EDS), end-systolic size (ESS), stroke volume, thickness of interventricular septum, thickness of the posterior wall of the left ventricle, size of the left atrium, mass of the left ventricular myocardium, LVMMI. A direct relationship between FABP 4 and ESS, ESV, LVMMI in patients with postinfarction cardiosclerosis and obesity was determined. There was a significant inverse correlation between CTRP 3 and EDS, ESS, ESV, LVMMI in patients with postinfarction cardiosclerosis and obesity.

Conclusions. The study showed that in patients with postinfarction cardiosclerosis and obesity there was an increase in echocardiographic parameters. The influence of FABP 4 and CTRP 3 content on the structural and functional state of the left ventricular myocardium was determined.

Key words: adipokines, echocardiography, myocardial infarction, obesity, remodeling.
різниці між множинними порівняннями кількісних ознак із нормальним розподілом проводили за допомогою одностороннього дисперсійного аналізу (ANOVA) з урахуванням корекції Бонферроні. При значенні р<0,05 різниця вважалася достовірною.

Результати. У пацієнтів із постінфарктним кардіосклерозом та ожирінням порівняно з пацієнтами без надмірної маси тіла та після інфаркту міокарда збільшилися кінцево-систолічний об’єм (КСО), кінцево-діастолічний об’єм, кінцево-діастолічний розмір (КДР), кінцево-систолічний розмір (КСР), ударний об’єм, товщина міжшлуночкової перетинки, товщина задньої стінки ЛШ, розмір лівого предсердя, маса міокарда ЛШ, ИММЛШ. Визначено пряме взаємозв’язок між FABP 4 та КСР, КСО, ИММЛШ у пацієнтів із постінфарктним кардіосклерозом та ожирінням. Виявлено достовірний зворотний кореляційний зв’язок між CTRP 3 та КДР, КСР, КСО, ИММЛШ у пацієнтів із постінфарктним кардіосклерозом та ожирінням.

Висновки. 1. Встановлена наявність взаємозв’язку між показниками структурно-функціонального стану міокарда ЛШ, FABP4 і CTRP3 у пацієнтів із постінфарктним кардіосклерозом і ожирінням спостерігається зростання ИММЛШ і ВТЗСЛШ, що відповідає концентричному ремоделюванню серця.

РЕМОДЕЛИРОВАНИЕ ЛЕВОГО ЖЕЛЕДУЧКА У ПАЦИЕНТОВ С ПОСТИНФАРКТНЫМ КАРДИОСКЛЕРОЗОМ И ОЖИРЕНИЕМ С УЧЕТОМ УРОВНЯ FABP 4 И CTRP 3

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Цель исследования – изучить структурно-функциональное состояние миокарда левого желудочка (ЛЖ) у пациентов с постинфарктным кардиосклерозом и избыточной массой тела с учетом уровней адипокинов FABP4 и CTRP3.

Материалы и методы. Обследовано 189 пациентов. Первую группу составили 60 пациентов с постинфарктным кардиосклерозом, вторую группу – 68 пациентов с постинфарктным кардиосклерозом и избыточной массой тела (ИМТ), третью группу – 61 пациент с постинфарктным кардиосклерозом и ожирением. Содержание FABP 4 и CTRP 3 определено с помощью иммуноферментного метода. Статистическую обработку результатов исследования осуществлено путем использования лицензионного пакета программ "IBM SPSS Statistics 27.0". Согласно размера выборки и распределения показателей применим параметрический метод Стьюдента. Корреляционные связи показателей определены с помощью коэффициента корреляции Пирсона (r). Показатели приведены как среднее значение и ошибка среднего арифметического. Оценку значимости различий между множественными сравнениями применены критерий Стьюдента и поправка Бонферроні. При значении р<0,05 разница считалась достоверной.

Результаты. У пациентов с постинфарктным кардиосклерозом и ожирением по сравнению с пациентами без избыточной массы тела и после инфаркта міокарда увеличилась конечно-систолический объем (КСО), конечно-диастолический объем (КДР), конечно-диастолический размер (КСР), ударный объем, толщина межжелудочковой перегородки, толщина задней стенки ЛЖ, размер левого предсердия, масса міокарда ЛЖ, ИММЛШ. Определены прямые взаимосвязи между FABP 4 и КСР, КСО, ИММЛШ у пациентов с постинфарктным кардиосклерозом и ожирением. Выведена достоверная обратная корреляционная связь между CTRP 3 и КДР, КСР, КСО, ИММЛШ у пациентов с постинфарктным кардиосклерозом и ожирением.

Выводы. Показано наличие взаимосвязи между показателями структурно-функционального состояния миокарда ЛЖ, FABP4 и CTRP 2. У пациентов с постинфарктным кардиосклерозом и ожирением наблюдается увеличение ИММЛШ и ВТЗСЛШ, что соответствует концентрическому ремоделированию сердца.

Ключевые слова: адипокины, эхокардиография, инфаркт миокарда, ожирение, ремоделирование.

Introduction

Obesity is one of the risk factors for acute myocardial infarction (AMI). The production of adipokines by adipose tissue is known to be associated with the development and progression of heart failure after myocardial infarction [2]. C1q tumor necrosis factor related protein 3 (CTRP3)
and fatty acid binding protein 4 (FABP4) are adipokines involved not only in the regulation of carbohydrate and lipid metabolism, but also affect the structural and functional parameters of the left ventricle (LV) of myocardium. FABP4 content increased in patients with CHF [2; 11]. The researchers investigated that systolic and diastolic function decreased in experimental subjects with increasing FABP4 content. FABP4 concentration is associated with left ventricular myocardial remodeling and further contributes to the progression of heart failure [7; 15]. It is noted that FABP4 affects cardiac function via a direct effect on cardiomyocytes [14]. Therefore, FABP4 affects the structural and functional state of the myocardium through paracrine or endocrine pathways.

CARTP3 has a cardioprotective effect and reduces the development of pathological remodeling of the left ventricular myocardium after myocardial infarction through the process of restoring the state of ischemic cardiomyocytes [13]. However, the study of the effect of FABP4 and CARTP3 on the structural and functional parameters of the left ventricular myocardium in patients with postinfarction cardiosclerosis and excess body weight remains insufficiently studied today.

The objective of the study

To study the structural-functional condition of the left ventricle (LV) myocardium in patients with postinfarction cardiosclerosis and excess body weight taking into account the levels of adipokines FABP4 and CARTP3.

Material and methods of the study

The study was performed between 01 September 2018 and 31 December 2020. The cross-sectional study involved 189 patients with postinfarction cardiosclerosis in the presence and absence of excess body weight (EBW) and obesity, who were treated in the State Institution “L. T. Malaya National Institute of Therapy of the National Academy of Medical Sciences of Ukraine” and in the Kharkiv Clinical Hospital of Rail TransportNo.1 of the branch of the “Health Center” of the Public Joint Stock Company “Ukrainian Railways”. The first group consisted of 60 patients with postinfarction cardiosclerosis, the second group included 68 patients with postinfarction cardiosclerosis and EBW, the third group consisted of 61 patients with postinfarction cardiosclerosis and obesity.

The criterion includes patients with postinfarction cardiosclerosis depending on body mass index.

Exclusion criteria were type 1 and 2 diabetes, diffuse connective tissue diseases, pituitary and hypothalamic diseases, autoimmune diseases, thyroid disease, CHF IV FC before myocardial infarction, the presence of chronic obstructive pulmonary disease, disorders of the heart valve, symptomatic hypertension, kidney or liver malfunction, cancer, severe anemia.

The diagnosis of postinfarction cardiosclerosis was formulated in accordance with the Order of the Ministry of Health No. 152 of 03.02.2016 and as amended 09.23.2016 No. 994 “Unified clinical protocol of primary, secondary (specialized) and third (highly specialized) medical care stable ischemic heart disease” [3]. Signs of obesity were detected by body mass index (BMI) by the formula: weight (kg)/height (m)^2. The value of normal body weight was from 18.5 to 24.9 kg/m^2. Signs of EBW were measured by BMI from 25 to 29.9 kg/m^2. Signs of obesity were BMI exceeding 30 kg/m^2 [12].

Doppler echocardiography was performed on a Radmir ULTIMA Pro 30 ultrasound scanner to determine end-diastolic size (EDS), end-systolic size (ESS) of the left ventricle (LV), thickness of the interventricular septum (TIVS), size of the aorta, size of left atrium (LA) and posterior wall of LV (TPWLV) in diastole. LV myocardial mass (LVMM), LVMMI2 index (LVMMI2=LVMM/body surface area (m^2)), LVMMI1 (LVMMI1=LVMMI/height (m^2)^2) was calculated, which is important to measure in obesity. The upper limit of LVMMI1 was 44 g/m^2 for women and 48 g/m^2 for men. LV hypertrophy was diagnosed in more than 110 g/m^2 for women and more than 125 g/m^2 for men. The relative wall thickness (RWT) of the LV was determined by the formula (TPWLV+TIVS/EDSLV) and the type of LV remodeling was identified with the help of LVMMI1 and LVMMI2 indicators. Concentric LV remodeling was diagnosed in RPPWLV≥0.45 and normal LVMMI [10].

The content of FABP 4 and CARTP 3 was measured using ELISA (enzyme-linked immunosorbent assay) using kits from Elascience Biotechnology, USA and Human CARTP 3 (Aviscera Bioscience Inc, Santa Clara, USA) in the biochemical department of the Central Research Laboratory of Kharkiv National Medical University. The studies were performed in accordance with the standards of Good Clinical Practice and the principles of the Declaration of Helsinki. The study protocol was approved by the Ethics Committee of Kharkiv National Medical University (Minutes No.2 of 2 April 2018). Prior to inclusion in the study, all participants signed written informed consent.

Statistical processing of the study results was performed using the licensed software package “IBM SPSS Statistics 27.0” (IBM Inc., USA). Parametric Student's t-test was used according to the sample size and distribution of indicators. The correlations of the indicators were determined using the Pearson correlation coefficient (r). Evaluation of the significance of the difference between the means of multiple comparisons for quantitative traits with normal distribution using Bonferroni correction was performed by one-way analysis of variance (ANOVA). Indicators are given as mean (M) and the error of the mean (m). At a value of p<0.05, the difference was considered significant.

Results and their discussion

Patients with postinfarction cardiosclerosis and EBW in comparison with patients with postinfarction cardiosclerosis were found to have an increase in EDS by 3.57% (p = 0.047); the size of LA by 11.5% (p = 0.000), LVMM by 10.29% (p = 0.019) (Table 1).

Patients with postinfarction cardiosclerosis and obesity compared to patients without obesity and EBW had an increase in EDS by 24.67% (p = 0.001); EDV by 18.42% (p = 0.000), EDS by 7.54% (p = 0.000); ESS by 10.14% (p = 0.000), SV by 11.19% (p = 0.025), TIVS by 6.3% (p = 0.031), TPWLV by 6.25%, 01), the size of LA by 13.86% (p = 0.000), LVMM by 23.21% (p = 0.000), LVMMI by 11.22% (p = 0.000).
A direct correlation (Fig. 1) between FABP 4 and ESS, ESS, ESV, LVMMI1 in patients with postinfarction cardiosclerosis and obesity was determined. There was a significant inverse relationship between CTRP 3 and EDS, ESS, ESV, LVMMI1 in patients with postinfarction cardiosclerosis and obesity (Fig. 1).

It has been proved that the presence of postinfarction cardiosclerosis in obese patients is associated with thinning of the left ventricular wall, which leads to a decrease in myocardial contractility. These changes occur due to high blood pressure, the presence of atherosclerotic cardiosclerosis, resulting in the deepening of the decrease in LV myocardial systolic function and leading to the development of ischemic myocardial remodeling. It is known that LV myocardial hypertrophy, detected in hypertension, coronary heart disease, CHF and myocardial infarction, has different mechanisms of development [1; 4]. FABP4 and CTRP3 are known modern adipokines involved in the restructuring of myocardial geometry after myocardial infarction [5; 7].

The study revealed an increase in the concentration of FABP4 and a decrease in the content of CTRP3 in patients with AMI depending on the presence and absence of excess weight [8; 9]. The study showed an increase in structural and functional parameters in patients with postinfarction cardiosclerosis, EBW and obesity. This indicates the effect of excess weight on the course of postinfarction cardiosclerosis. The authors note that there is a significant correlation between FABP4 concentration and LV mass in excess weight [6]. We found that the concentration of FABP 4 was significantly higher in patients with AMI in the presence of obesity compared with patients in the absence of signs of excess body weight. At the same time, the concentration of CTRP3 is likely to be significantly reduced in patients with AMI in the presence of obesity. This indicates the effect of excess weight on the course of postinfarction cardiosclerosis. The authors note that there is a significant correlation between FABP4 concentration and LV mass in excess weight [6].

Table 1

| Indicator, units of measurement | Patients with postinfarction cardiosclerosis | Patients with postinfarction cardiosclerosis and EBW | Patients with postinfarction cardiosclerosis and obesity | Probability (p) |
|---------------------------------|--------------------------------------------|-----------------------------------------------------|--------------------------------------------------------|-----------------|
|                                 | 1                                          | 2                                                   | 3                                                     |                 |
| EDS, cm                         | 5.04±0.06                                 | 5.22±0.00                                          | 5.42±0.07                                             | p<0.047, p<0.000 |
| ESS, cm                         | 3.65±0.07                                 | 3.76±0.06                                          | 4.02±0.07                                             | p<0.025, p<0.000 |
| EDV, ml                         | 122.35±3.3                                | 132.21±3.92                                        | 144.89±4.59                                          | p<0.060, p<0.000 |
| ESV, ml                         | 59.18±2.43                                | 62.72±2.71                                         | 73.78±3.29                                           | p<0.338, p<0.001 |
| SV, ml                          | 63.65±1.86                                | 68.19±1.88                                         | 70.77±2.52                                           | p<0.091, p<0.025 |
| EF, %                           | 52.48±1.01                                | 53.31±0.95                                         | 50.1±1.05                                            | p<0.568, p<0.119 |
| TIVS, cm                        | 1.11±0.02                                 | 1.15±0.02                                          | 1.18±0.017                                           | p<0.183, p<0.031 |
| TPWLV, cm                       | 1.12±0.021                                | 1.14±0.02                                          | 1.19±0.016                                           | p<0.421, p<0.01  |
| LA, cm                          | 3.39±0.077                                | 3.78±0.07                                          | 3.86±0.08                                            | p<0.000, p<0.000 |
| Aorta, cm                       | 3.15±0.06                                 | 3.13±0.07                                          | 3.27±0.05                                            | p<0.837, p<0.145 |
| LVMM, g                         | 261.99±7.81                               | 288.95±8.15                                        | 322.8±9.28                                           | p<0.019, p<0.000 |
| LVMMI, g/m²                     | 50.31±1.44                                | 52.65±1.35                                         | 64.34±1.61                                           | p<0.240, p<0.000 |
| LVMMI, g/m²                     | 142.15±4.17                               | 144.69±3.86                                        | 158.1±4.31                                           | p<0.656, p<0.009 |
| RTPWLV                          | 0.45±0.01                                 | 0.45±0.01                                          | 0.45±0.01                                            | p<0.822, p<0.918 |
Conclusions

There is a relationship between the indicators of the structural and functional state of the left ventricular myocardium and FABP4 and CTRP3 in patients with postinfarction cardiosclerosis with concomitant obesity.

In patients with postinfarction cardiosclerosis and obesity, there is an increase in LVMMI and RTPWLV, which corresponds to the concentric remodeling of the heart.

Prospects for further research

We consider promising studies of the effect of FABP4 and CTRP3 on the condition of the coronary arteries in patients with AMI depending on the presence and absence of excess body weight.

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