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EFFECT OF PREHOSPITAL SYSTEMIC THROMBOLYSIS ON LEFT VENTRICULAR DIASTOLIC FUNCTION IN ST-SEGMENT ELEVATION ACUTE MYOCARDIAL INFARCTION

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ABSTRACT:

Objective:

To study the effect of prehospital thrombolysis on left ventricular diastolic function in patients with acute ST-segment elevation coronary syndrome.

Material And Methods:

We examined cases of LV diastolic function in 108 STEMI patients aged 35 to 67 years.The average age was 44.2 ± 1.3 years. All 108 patients underwent echocardiography (1 day after myocardial revascularization and 3 months later. Patients were randomized into two groups: group 1 - 50 patients receiving standard therapy, and prehospital hospital TLT. Group 2 included 58 patients who underwent standard therapy and hospital TLT.Transmitral blood flow (TMBF) parameters were assessed using Doppler echocardiography to assess diastolic dysfunction of the left ventricular myocardium.

Results:

According to the initial state of TMBF, the groups of patients did not differ significantly among themselves. The maximum speed of early LV filling (E) in patients of groups 1 and 2 was 58.0 ± 2.4 and 56.0 ± 2.6 cm /s, respectively. The integrated indicator of LV diastolic function - the E / A ratio - was 0.83 ± 0.02 and 0.79 ± 0.02, respectively. The integral of the rate of early LV filling (VTIE) was 9.8 ± 0.6 and 9.6 ± 0.5 cm, while no significant intergroup differences were found. The time of is volumetric relaxation of the LV myocardium in the group of patients receiving prehospital thrombolysis and hospitalized patients was 100 ± 5.0 and 103 ± 5.6 ms, respectively (p> 0.05).

Conclusion:

Thus, changes in LV diastolic function indicators during stress Doppler echocardiography with dobutamine are associated with the presence of reversible myocardial dysfunction. The use of prehospital thrombolytic therapy leads to the development of reversible diastolic dysfunction in the area of ischemic myocardial damage.

Keywords: STEMI, left ventricular diastolic function, prehospital thrombolytic therapy.

INTRODUCTION:

Currently, the incidence of ST-segment elevated myocardial infarction remains high worldwide, as well as in Uzbekistan, and the development of death from acute complications and disability from late complications is still a pressing problem in cardiology. Underlying in the ST segment elevation myocardial infarction lies acute complete closure of the coronary arteries due to atherothrombosis. As a result, ischemic and lethal damage to myocytes leads to impaired diastolic and then systolic activity of the left ventricle. The results of studies (1,2) have shown the role of impaired diastolic function in the pathogenesis of coronary heart disease (CHD). In some types of acute forms of CHD, only the left ventricular diastolic function is disturbed without damage to systolic function (i.e., contractile function is normal).

Underlying diastolic dysfunction in STEMI is coronary occlusion, myocardial ischemic injury, structural and functional reconstruction of functional cardiomyocytes and interstitium, resulting in increased myocardial stiffness. If during the systole the Ca2+ ion is actively released from the sarcoplasmic reticulum to the cytosol, during the diastole the Ca2+ ion must be re-entered by active transport from the cytosol to the SRP against the concentration gradient, and this process is energy-intensive. Due to impaired Adenosine triphosphate synthase (ATS) synthesis in ischemic cardiomyocytes, an energy deficit state is observed. Due to energy deficit, excess calcium ions remain in the cytosol, leading to disruption of the relaxation process in cardiomyocytes. Disruption of diastolic relaxation of left ventricular myocytes, in turn, leads to an increase in the position of the left ventricle in its diastolic filling. Insufficient thickness of the left ventricular wall, lack of compensatory capacity, leads to an increase in its size and subsequent enlargement of the left atrium, an increase in pressure in the pulmonary veins. This, in turn, can lead to the development of heart failure. The presence of diastolic dysfunction subsequently leads to systolic dysfunction, or its concomitant presence to exacerbation of left ventricular dysfunction.

Restoration of early antegrade blood flow in the coronary arteries serves to stop the process of necrosis, preserve vital myocardial areas, and thus limit the final volume of myocardial infarction. According to experimental studies, experiments in dogs have shown that myocardial necrosis begins 20 minutes after the onset of coronary artery occlusion and has a wavy spread from the endocardium to the epicardium. However, ischemic time has been found to be a major factor limiting the development of myocardial necrosis. At 20-40 minutes of coronary artery occlusion responsible for infarction, dogs develop necrosis of the subendocardial layer of the heart muscle. However, with 40-minute occlusion, 72% of the ischemic myocardium can be preserved by restoring coronary blood flow. If reperfusion was performed 3 hours after the start of the procedure, this figure could be maintained at 33% and 16% if it lasted 6 hours. If coronary arteryrecanalization and myocardial reperfusion are completed before the onset of irreversible injury, then necrosis does not develop, but depression of myocardial function continues at the level of energy exchange in the cells. To describe post-ischemic myocardial dysfunction without necrosis, the term “stunned myocardium” has been proposed after the transient and cardiomyocyte energy potential has stabilized. As a rule, the condition of the human body is more complex, the life of the myocardium largely depends on the anatomy of the coronary arteries: injury of one or more vessels, the development of collateral circulation, the degree of occlusion, the state of the blood coagulation system. After the initial

functional impairment, necrosis spreads rapidly (depending on the size of the active collaterals) from the inside to the outside and, as a rule, peaks within a few hours. If the collateral circulation is well developed or the coronary artery occlusion responsible for infarction is intermittent or incomplete (according to K. Rentrop, in 33% of patients), then the time during which the myocardium can be preserved can be significantly prolonged.

Experimental data were confirmed in subsequent clinical trials. In parabolic dependence, it is known that the effectiveness of thrombolytic therapy decreases over time: the sooner this therapy is used, the greater the chances of saving the patient's life. Restoration of coronary blood flow during the first 2 hours of disease can even prevent the development of large focal myocardial necrosis, which is called a "stopped infarction". It can be seen that the use of prehospital thrombolysis in STEMI can accelerate reperfusion time and improve disease treatment outcomes.

Based on the above data, the restoration of early antegrade blood flow in the coronary arteries responsible for infarction in STEMI can also have a positive effect on the diastolic activity of the myocardium by stopping the process of necrosis. However, given the lack of data in the literature on the effect of early pre-hospital thrombolysis on diastolic activity of the left ventricle in STEMI, we aimed to conduct this study in view of the lack of work in this area.

The Purpose of this Study:

To study the effect of left ventricular diastolic activity on patients with pre-hospital thrombolysis in ST elevated acute myocardial infarction.

Materials and Methods:

In this study, indicators of left ventricular diastolic function were studied in 108 patients aged 35 to 67 years with STEMI. The mean age of the patients was 44.2 ± 1.3 years. Patients underwent pharmacological reperfusion within the first 6 hours after the onset of the disease. Patients were randomly divided into two groups:

Group 1 included 50 patients receiving prehospital thrombolytic therapy and standard therapy, and group 2 included 58 patients receiving TLT and standard therapy at the hospital. All 108 patients received echocardiography (1 day after myocardial revascularization and 3 months after). Doppler-echocardiography evaluated transmitral circulatory parameters to assess diastolic dysfunction of the left ventricular myocardium.

Left ventricular diastolic function was assessed using pulsed Doppler during the study of transmitral blood flow in all patients: left ventricular early diastolic filling - E, atrium systole rate A (cm/s) and their ratio (E/A), left ventricular isovolumic relaxation time - IVRT, ms, deceleration time DT, ms. Also, 4 main criteria currently recommended for the detection of diastolic dysfunction were assessed: early diastolic velocity of the interventricular septal (ICS) movement e'sep < 7 cm/s, early diastolic velocity of the left ventricular side wall e'lat < 10 cm/s, the ratio of the mean rate of early diastolic mitral blood flow of the coccyx to the mean early diastolic rate of mitral ring movement E/e'> 14, indexed left ventricular volume> 34 ml/m^2, maximum rate of tricuspid regurgitation (TR)> 2.8 m/s.

Statistical data processing was performed using the program STATISTICA-5.0. In analyzing the material, average values, their mean standard errors, and a 95% confidence interval were calculated. The mean equality hypothesis was evaluated by the Student t-test.

Statistical differences between the samples were set at $p < 0.05$.

RESULTS AND DISCUSSION:

All 108 patients were found to have decreased left ventricular systolic activity when echocardiography was administered on the first day of illness, but no significant statistical difference was found (on day 1, left ventricular ejection fraction was 50.3% and 49.5%, respectively, in both groups). The left ventricular regional wall motion abnormality index (WMAI) was 1.40 ± 0.04 and 1.55 ± 0.04, respectively, in groups 1 and 2.

To assess diastolic dysfunction of the left ventricular myocardium, Doppler-echocardiography studied transmitral flow parameters. As can be seen from Table 1, the maximum frequency (E) (87.0 ± 2.2 and 89.3 ± 2.4 cm/s, respectively) of premature ejaculation in patients with transmitral blood flow in group 1 patients compared with group 2, left; the maximum rate of lateral ventricular filling of the ventricle was (A) (106.2 ± 2.5 and 115.1 ± 2.3 cm/s, respectively). The integrated measure of left ventricular diastolic function - i.e., the E/A ratio - was 0.82 ± 0.02 and 0.77 ± 0.02 ($p > 0.05$), respectively. The left ventricular premature filling rate integral was 9.9 ± 0.6 and 9.8 ± 0.5 cm, respectively, and no reliable differences were found between the groups. The isovolumetric relaxation time of the left ventricular myocardium was 98 ± 5.0ms and 101 ± 5.2ms ($p > 0.05$), respectively, in patients who underwent prehospital thrombolysis in the group and were admitted to the hospital.

Table 1. Indications of left ventricular diastolic function in patients with STEMI

Indicator	Group 1 (pre-hospital TLT),n=50		Group 2 (TLT in the hospital), n=58	
	baseline	After 3 months	baseline	After 3 months
E, cm/s	87,0±2,2	98,0±2,2	89,3±2,4	90,3±2,4
A, cm/s	106,2±2,5	101±2,5	115,1±2,3*	110,2±2,3*
E/A	0,82±0,02	0,97±0,02	0,77±0,02	0,82±0,02
AT, cm	107,0±2,0	110,0±2,1	109,0±2,0	112,0±2,0
DT, cm	190±8,0	186±6,7	195±8,8	198±8,3
VTIE, cm	9,9±0,6	9,7±0,5	9,8±0,5	10±0,3
VTIA, cm	7,8±0,5	7,9±0,4	7,6±0,5	7,3±0,5
VTIE/VTIA	1,27±0,1	1,23±0,1	1,3±0,1	1,36±0,1
IVRT, cm	98±5,0	100±5,0	101±5,2	110±4,8
Left atrium volume index, ml/m²	35±1,0	35,2±1,0	38±0,9*	39±0,9*^
$e'_{average}$, cm/sec	6,6±0,1	7,6±0,1*	6,2±0,1	6,4±0,1^
$E/e'_{average}$	13,2±0,13	12,7±0,1	14,35±0,11	14,1±0,11^
Tricuspid regurgitation rate, m/s	2,82±0,02	2,5±0,02	3,0 ±0,03	2,9 ±0,03^

*p<0.05 difference within the group; ^p<0,05-intergroup difference.

It was noted that the volume index of the left atrium was statistically significantly higher in the group of patients undergoing thrombolysis in the hospital (39 ± 0.9 ml/m²) than in the main group (35 ± 1.0 ml/m²) ($p<0.05$). An increase in the volume of the left atrium indicates an increase in left ventricular filling pressure.

In tissue myocardial dopplerography (TDI mode), the detection of mitral valve fibrosis ring early diastolic rate (e') is one of the indicators explaining myocardial relaxation. The mean value of early diastolic velocity of the left ventricular myocardium was 6.6 ± 0.1 cm/s in the first group and 6.2 ± 0.1 cm/s in the second group ($p<0.05$). We analyzed the fact that this indicator was not significantly reduced in group 1 patients, early group TLT in group 1 patients, and faster reperfusion, which in turn prevented serious damage to the process of myocardial diastolic relaxation of the left ventricle.

In many studies in recent years, the E/e ratio has been shown to be correlated with left abdominal filling pressure. The E/e' ratio was 13.2 ± 0.13 and 14.35 ± 0.11 in groups 1 and 2, respectively, and no significant statistical difference was found between the groups ($p>0.05$).

The rate of regurgitation in the tricuspid valve was 2.82 ± 0.02 m/s in group 1 patients and 3.0 ± 0.03 m/s in group 2 patients. This indicator is significantly increased ($p<0.05$) in group 2, indicating an increase in left ventricular filling pressure.

According to Doppler-echocardiography, left ventricular diastolic dysfunction was diagnosed as grade 1 in all patients in the first group (100%), while diastolic dysfunction of the left ventricle in 2 patients in the second group was grade 2 (3.4%), the remaining 56 patients had grade 1 (96.6%). It can be seen that although left ventricular diastolic function was impaired in both groups, it was more pronounced in the group of patients treated with thrombolysis in the hospital.

On re-examination of patients after 3 months, it was found that the improvement of left ventricular systolic activity on echocardiography was more pronounced in group 1 (left ventricular ejection fraction was 52.0% and 49.8%, respectively, in both groups). The WMAI of the left ventricle was 1.18 ± 0.02 and 1.3 ± 0.04 in groups 1 and 2 ($p<0.05$).

The first table shows that in both groups, the high E value after 3 months was reliably higher than the baseline data, while the high E value was relatively greater in the group of patients who underwent pre-hospital TLT. In both groups, a reliable decrease in the high value of A was observed. The E/A ratio was 0.97 ± 0.02 and 0.82 ± 0.02, respectively, and it was significantly increased in the group using pre-hospital TLT. The change in the duration of the transmitral blood flow time-related indicators was not reliable.

No significant dynamics in AT and IVRT readings was observed in all patients after 3 months. The time to decrease left ventricular early diastolic filling (DT) tended to decrease in group 1 and increase in group 2.

A significant increase in left atrium volume and maximum rate of tricuspid regurgitation was observed after 3 months in group 2 patients, and an improvement in these parameters was noted in group 1. $E/e_{average}$ was reduced in both groups, but a single statistical decrease was observed in those who underwent prehospital thrombolysis. $e'_{average}$ (cm/sec) was reliably increased after 3 months in patients treated with TLT before hospitalization, indicating an improvement in diastolic parameters in the areas of myocardial infarction based on early thrombolysis.

Correlation analysis revealed a reverse mean correlation between the E / A ratio and the WMAI ($r = -0.7$; $p<0.05$). The study also found a direct mean correlation between IVRT values and the number of stunned segments ($r = -0.56$; $p<0.05$).

CONCLUSION:

Thus, a positive change left ventricular diastolic function indicators in pre-hospital thrombolytic therapy is associated with the presence of myocardial reversible dysfunction. Reperfusion with early prehospital TLT prevents the development of diastolic dysfunction in the ischemic damaged area of the myocardium.

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