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Evaluation of the GRACE scale in patients with acute myocardial infarction

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The aim was to study the clinical characteristics, echocardiographic data, N-terminal brain natriuretic peptide (NT-proBNP) levels at the hospital stage in patients with acute ST-segment elevation myocardial infarction (STEMI) in relation to the risk of in-hospital mortality (GRACE scale) and glomerular filtration rate (GFR).

Methods. Patients with STEMI who were followed in hospital were included on the first day of the cardiovascular event (n=150). The objective, laboratory data, including NTproBNP level, EchoCG in the dynamics of hospital treatment of patients depending on the risk level of the GRACE scale, GFR <60 ml/min/1.73 m2 and ⩾60 ml/min/1.73 m2 were evaluated. Statistical processing of the material was performed with "Statistica 10.0 for Windows".

Results. On the first day of STEMI, NT-proBNP concentration increased independently of the risk of in-hospital mortality (GRACE scale) and remained high at the in-hospital stage. Positive correlations: NTproBNP levels at hospital admission and discharge; NTproBNP levels at hospital admission with functional class of chronic heart failure and GRACE scale ($p<0.05$) indicated an unfavourable prognosis. High-risk STEMI patients on the GRACE scale were characterised by more severe diastolic and systolic myocardial function of the left ventricle. Patients with reduced GFR had a higher risk of in-hospital mortality with signs of left ventricular dilatation.

Conclusion. Patients at high risk according to the GRACE scale have older age, reduced left ventricular ejection fraction and the most severe changes in diastolic function. Evaluation of heart failure markers, GFR during the hospital stage of STEMI allows to choose the correct tactics of patient management.

Keywords: acute myocardial infarction, heart failure, glomerular filtration rate.

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Introduction

Modern cardiology expands the treatment options for acute myocardial infarction (AMI): correction of cardiovascular risk factors (RF), drug therapy and surgical tactics with an emphasis on the fact that the early initiation of treatment can improve prognosis. [1]. Risk stratification of AMI patients includes following criteria: Risk stratification of AMI patients includes demographic, clinical, laboratory and instrumental test results. In clinical practice it is possible to use risk scales in a calculator format. The GRACE scale — Global registry of acute coronary events assesses the risk of hospital mortality within six months. The parameters in the GRACE scale are: age, class of acute heart failure according to the T. Killip classification, the fact of cardiac arrest, systolic blood pressure (SBP), heart rate (HR), assessment of ST segment change according to electrocardiograms, blood creatinine level, markers of myocardial necrosis. The sum of all the indicators is used to calculate a score and the risk of in-hospital mortality is determined accordingly: low, intermediate or high risk in patients with acute coronary syndrome (ACS).

Laboratory markers contribute to the assessment of AMI prognosis. N-terminal brain natriuretic peptide (NTproBNP) levels are known to be elevated in patients with AMI, predicting the risk of heart failure [2, 3]. Currently, NTproBNP is widely used in modern practice. A number of studies have confirmed that NTproBNP is a prognostic marker for survival and the development of heart failure in patients with ACS [4]. The high levels of NTproBNP during a year in ACS patients predict an increase in mortality, risk of recurrent ACS, clinically significant heart failure. NTproBNP is one of the factors for sudden death, together with the following parameters: age, sex, arterial hypertension, diabetes mellitus, left ventricular (LV) ejection fraction (EF), troponin I [5].

Assessment of haemorrhagic complications RF in a patient with AMI allows timely selection of management tactics at the hospital treatment stage. According to clinical guidelines, in AMI with ST-segment elevation electrocardiogram 2020 it is necessary to assess the prognostic risks of patients with AMI for haemorrhagic complications (haemoglobin level, erythrocytes, platelets), the risk of thromboembolic complications, control carbohydrate metabolism, lipid metabolism data, calculate GFR [6]. Renal dysfunction in the general population occurs in 12-17 % of people, in patients with Non ST-elevation ACS- 42.9 %, in patients with ST-elevation ACS- 30.5 % [7].

The importance of studying and searching for new prognostic markers in patients with AMI in the hospital stage should be noted. Patients with AMI with ST-segment elevation (STEMI) have the most unfavourable prognosis on the first day and during the hospital stage. In our opinion, it is important to study the NT-proBNP prognostic marker in STEMI patients depending on the GRACE risk scale.

The aim was to study the clinical characteristics, echocardiographic data, N-terminal brain natriuretic peptide (NT-proBNP) levels at the hospital stage in patients with acute ST-segment elevation myocardial infarction (STEMI) in relation to the risk of in-hospital mortality (GRACE scale) and glomerular filtration rate (GFR).

Methods

The study included 150 patients with STEMI on day one. The trial was conducted in accordance with good clinical practice and the tenets of the Declaration of Helsinki. Written informed consent was obtained from all participants before enrolment. The diagnosis of STEMI was confirmed according to clinical guidelines (2020), taking into account data on symptoms, physical examination, markers of myocardial necrosis (CPK-MB and troponin I), and electrocardiogram dynamics [6].

Inclusion criteria: first-day STEMI, history of arterial hypertension. Exclusion criteria: known history of autoimmune diseases, connective tissue diseases, oncological diseases, diabetes mellitus type 1 and 2, acute kidney injury, liver failure, bronchial asthma, women of reproductive age, complicated percutaneous coronary intervention, infectious diseases at the time of enrolment.

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Clinical, laboratory and instrumental data of patients with STEMI on admission to the cardiology department and at discharge were evaluated. Those included:

- Clinical data: age, body mass index (BMI), SBP, diastolic blood pressure (DBP), HR.
- Laboratory data: clinical blood analysis, biochemical blood analysis, myocardial necrosis markers (CPK-MB, troponin I), lipidogram data (total cholesterol (TC), low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), triglycerides (TG)).

Plasma NTproBNT levels were determined by immunometric method using reagents from the VITROS immunodiagnostic products. Electrocardiograms and echocardiography were performed in all patients. We calculated the risk of in-hospital mortality of patients during hospitalization according to the GRACE scale: < 126 points — low risk (<2 %) of in-hospital mortality; 126-154 points — intermediate risk (2–5 %); >154 points — high risk (>5 %). Taking into account the GRACE risk score, the study population of STEMI patients was divided into low, intermediate and high risk groups [6].

Statistical processing of the obtained material was performed using the statistical software package "Statistica 10.0 for Windows". Statistical differences were evaluated using non-parametric Mann-Whitney, Wilcoxon criteria. The Spearman correlation coefficient method and its significance level were used to assess the dependencies between variables. The values studied are presented as mean values and mean errors (M±m). Differences in values were considered statistically significant at $p<0.05$.

Results

Characteristics of the general group of patients with STEMI on admission:

- Age: 61.70±2.96 years;
- Clinical data: BMI — 29.43±3.62 kg/m^2; SBP level — 135.00±27.60 mmHg, DBP level — 81.91±14.92 mmHg, HR — 81.62±18.50 beats/min.
- Laboratory data: Troponin I level — 13.22± 1.40 ng/ml, creatinine phosphokinase (CPK) — 320.21±35.64 U/L, CPK-MB — 61.60±14.93 U/L, alanine aminotransferase (ALT) — 45.01±2. 62 U/L, aspartate aminotransferase (AST) — 86.3±8.7 U/L, urea 6.6±2.3 mmol/L, creatinine 84.74±33.03 μmol/L, GFR — 81.17±1.98 ml/min/1.73 m^2; lipidogram data: TC level — 5.70±1.30 mmol/l, LDL — 2.87±0.06 mmol/l, HDL — 1.33±0.03 mmol/l, TG — 1.74±0.07 mmol/l.

According to the GRACE hospital mortality scale, the mean value in STEMI patients at the time of hospitalization was 162.21±2.53 points.

In our study in the general group of STEMI patients, the mean NTproBNP level at hospital admission — 2683.95±299.05 pg/ml, at discharge — 2489.46±275.06 pg/ml ($p>0.05$) did not differ statistically significantly in the dynamics of hospital treatment. The level of NTproBNP increased on the first day of STEMI and remained high throughout the hospital course. Positive correlations were found: between NTproBNP levels at admission and discharge $r=0.67$ ($p<0.01$); between NTproBNP levels at admission with functional class of chronic heart failure (CHF) $r=0.20$ ($p<0.04$) and GRACE scale $r=0.38$ ($p<0.01$), indicating an unfavourable prognosis. NT-proBNP levels have no significant dynamics in the hospital phase of treatment, which determines the further development of heart failure.

EchoCG parameters were calculated in the studied STEMI patients: Left atrium (LA) — 41.38±0.34 mm, left ventricular end-systolic dimension (LV ESD) — 40.84±3.59 mm, left ventricular end-diastolic dimension (LV EDD) — 53.43±3.48 mm, end-systolic volume (ESV) — 75.02±16.94 cm^3, end-diastolic volume (EDV) — 140.70±21.45 cm^3, stroke volume (SV) — 64.51±8.27 ml, peak transmittal blood flow velocity in the phase of early filling E — (50.19±0.99 cm/s), late filling (A) — 60.40±1.12 cm/s, right atrium (RA) — 32.84±0.21 mm, right ventricle (RV) — 29.95±0.19 mm, tricuspid valve (TV) V max –248.47±2.43 cm/s.

In AMI, there are changes in myocardial relaxation and impaired diastolic filling. There is a decrease in early ventricular diastolic filling (E), increase in peak late systolic filling (A), E/A ratio becomes less than 1. With the background of myocardial diastolic function progression, E/A ratio=1-1.5 with moderate increase in LA pressure reflects moderate degree of diastolic dysfunction. When the E/A ratio is >2, severe diastolic dysfunction (with restrictive filling) is observed with increased LA pressure and decreased LV compliance [8, 9].

Low-risk STEMI patients had a GRACE score of 117.00±1.66 points, intermediate-risk patients 144.36±2.23 points ($p<0.05$) and high-risk patients 182.53±2.72 points ($p<0.05$). A statistically significant

increase in GRACE score was found in STEMI patients as the risk rose. Table 1 shows the clinical and laboratory characteristics of STEMI patients according to GRACE scale risk (low, intermediate and high risk). High-risk GRACE patients were older, had higher creatinine levels and lower SBP, DBP, GFR (p<0.05). At the same time, low-risk patients had maximum troponin I levels. Other clinical and laboratory data did not show statistically significant differences (p>0.05).

According to EchoCG data, changes are observed depending on the risk level of in-hospital mortality. With increasing risk level according to the GRACE scale in patients with STEMI, there is a statistically significant decrease in E parameters, E/A ratio (p<0.05); increase in A (p<0.05), which confirms the presence of diastolic dysfunction. At the same time, there is a decrease in EF (p<0.05) with the lowest values in high-risk patients according to the GRACE scale (Table 1). Other EchoCG parameters were not statistically significantly different according to risk level (p>0.05).

Thus, diastolic dysfunction and reduced EF LV in the hospital setting in patients with STEMI have been shown to be associated with an increased risk of mortality according to the GRACE scale.

The study of the laboratory marker NTproBNP provided data to characterise the increased risk of developing heart failure in STEMI patients. Figure 1 shows the tendency for NTproBNP levels to increase (p<0.05) in STEMI patients with increasing risk according to the GRACE scale. Furthermore, NTproBNP concentration is three times higher in intermediate risk patients (p<0.05) and 8.3 times higher in high risk patients compared to low risk GRACE STEMI patients (p<0.05). The risk-related increase in NTproBNP levels may be related to the age of the patients. At the same time, NTproBNP levels did not change with treatment.

Thus, regardless of risk according to the GRACE scale, NTproBNP levels increase on the first day of STEMI. The highest NTproBNP levels are found in high-risk patients on admission to hospital and persist throughout the hospital course of STEMI patients, which is associated with the highest risk of heart failure.

Taking into account the statistically significant reduction in GFR in relation to the risk of death according to the GRACE scale, we analysed the data of patients with GFR <60 ml/min/1.73 m^2 and ⩾ 60 ml/min/1.73 m^2. According to the literature, an average of 30 % of patients with AMI experience a reduction in GFR. At the same time, GFR reduction is an exclusion criterion in most AMI randomized clinical trials.

Of the patients studied, 22 % (n=33) had reduced GFR and 78 % (n=117) had preserved GFR. STEMI patients with GFR <60 ml/min/1.73 m^2 were older than 69.48±2.01 years (p<0.05), haemodynamic data were not different: SBP — 132.18±5.54 mmHg, DBP — 80.21±3.50 mmHg, HR — 81.84±3.45 b/min compared

Table 1. **Parameters of STEMI patients according to the GRACE scale hospital mortality risk score (M±m)**

Parameter	Low risk	Intermediate risk	High risk	p low — intermediate risk	p low — high risk
Clinical data					
Age, years	44,15±2,13	54,47±1,17	67,65±0,96	<0,05	<0,05
SBP, mmHg	149,61±4,40	145,86±4,23	128,12±2,69	>0,05	<0,05
DBP, mmHg	88,46±2,73	86,63±1,89	78,51±1,62	>0,05	<0,05
HR, b/min	82,46±4,50	79,89±1,90	82,36±2,22	>0,05	>0,05
Laboratory data					
HGB, g/l	153,23±3,81	143,42±3,39	140,78±2,17	>0,05	0,03
HCT, %	48,69±4,65	41,90±1,33	41,07±0,96	>0,05	>0,05
CPK, U/l	182,58±60,87	354,73±64,14	323,63±44,77	>0,05	>0,05
CPK-MB, U/l	36,75±8,02	50,01±10,70	71,42±22,96	>0,05	>0,05
Troponin I, ng/ml	19,71±6,15	10,40±1,56	13,66±1,97	0,03	>0,05
Creatinine, mmol/l	65,69±6,46	83,80±3,52	87,49±3,87	0,02	0,04
GFR, ml/min/1,73 m^2	108,45±4,17	88,24±2,96	73,86±2,38	0,01	0,01
TC, mmol/l	5,82±0,28	5,81±0,20	5,68±0,14	>0,05	>0,05
EchoCG data					
EF, %	49,23±3,18	47,70±0,77	44,87±0,52	>0,05	<0,05
E, m/s	49,23±3,18	55,60±1,82	46,52±1,09	>0,05	<0,05
A, m/s	54,84±3,94	55,24±1,99	63,74±1,35	>0,05	<0,05
E/A	1,14±0,13	1,10±0,07	0,78±0,04	>0,05	<0,05

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to the group of patients with GFR ⩾60 ml/min/1.73 m^2: 60.26±1.11 years, SBP 135.77±2.43 mmHg, DBP 82.69±1.21 mmHg, HR 81.89±1.67 b/min (p>0.05). Notably, STEMI patients with reduced GFR had a higher risk of in-hospital mortality GRACE 181.15±5.84 than the group of patients with preserved GFR 159.83±2.79 points (p<0.05).

Biochemical data of STEMI patients were analysed according to GFR <60 ml/min/1.73 m^2 and GFR ⩾ 60 ml/min/1.73 m^2. The laboratory values of the group of patients with reduced GFR: AST 83.46±24.18 U/L, ALT 41.17±5.50 U/L, urea 10.38±2.94 mmol/L, CPK 319.78±90.19 U/L, CPK-MB 101.08±61.57 U/L and preserved GFR: AST 87.04±8.99 U/L, ALT 46.09±2.91 U/L, urea 9.5±1.64 mmol/L were comparable (p>0.05). In the group of STEMI patients with reduced GFR: creatinine values 118.67±7.57 mmol/l, calculated GFR 46.09±1.87 ml/min/1.73 m^2 and preserved GFR: creatinine 75.01±1.97 mmol/l, GFR 90.87±1.54 ml/min/1.73 m^2 were statistically significantly different (p<0.05). In patients with reduced GFR TC 5.89±0.23 mmol/l, LDL 3.11±0.14 mmol/l, HDL 1.40±0.05 mmol/l, TG 1.51±0.12 mmol/l and in patients with preserved GFR TC 5.70±0.12 mmol/l, LDL 2.80±0.07 mmol/l, HDL 1.31±0.03 mmol/l, TG mmol/l 3.67±1.32 mmol/l (p>0.05). In the analysis of myocardial necrosis markers, troponin I levels (13.81±3.51 and 13.05±1.51 ng/ml), CPK levels (319.78±90.19 and 320.36±37.89 U/L), CPK-MB (101.08±61.57 and 49.94±6.65 U/L) showed no statistically significant differences (p>0.05). However, potassium levels were higher in the group of patients with reduced GFR (5.60±1.15 mmol/L) compared to those with GFR⩾60 ml/min/1.73 m^2 (potassium 4.24±0.05 mmol/L (p<0.05)).

As a result, STEMI patients with reduced GFR were older and had a higher risk of hospital mortality according to the GRACE scale. There were no statistically significant differences in biochemical parameters and lipid metabolism depending on GFR.

Assessing the prognosis of patients in hospital is an urgent task. We performed a correlation analysis between GFR and the risk of acute heart failure, HCF, and the hospital mortality scale GRACE. We obtained negative correlations of GFR with the degree of acute heart failure in STEMI patients (r=–0.48, p=0.001), the degree of CHF progression (r=–0.23, p=0.038), hospital mortality according to the GRACE scale (r=–0.48, p=0.0001) and unfavourable prognosis at the hospital stage (r=–0.40, p=0.043).

Figure 2 shows the dynamics of NTproBNP levels during hospital treatment of STEMI patients with GFR < 60 ml/min/1.73 m^2 and GFR ⩾ 60 ml/min/1.73 m^2. There were no statistically significant differences in NT-proBNP levels according to GFR. At the same time, it should be noted that in the dynamics of hospital treatment of STEMI patients, there was a tendency for NTproBNP levels to decrease in the group with GFR ⩾60 ml/min/1.73 m^2 and for the studied marker to increase in patients with reduced GFR.

When examining the EchoCG data in STEMI patients depending on GFR, a statistically significant in-

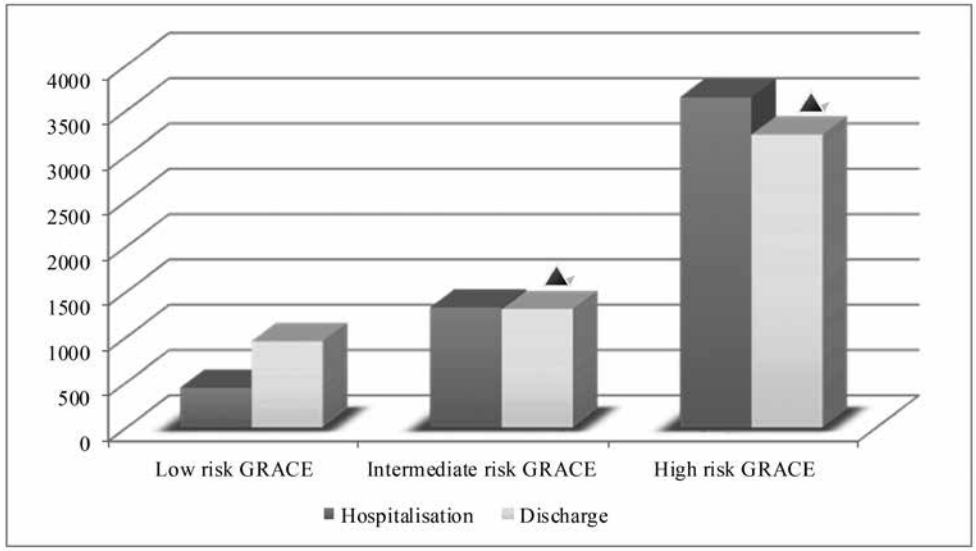

Fig. 1. Dynamics of NTproBNP level in STEMI patients depending on the risk of hospital mortality according to the GRACE scale
***Note**. p<0.05 in the studied groups with the increasing degree of the risk.

crease in LA 45.03±2.20 mm, LV ESD 44.41±2.12 mm, LV EDD 56.41±1.74 mm was observed in patients with reduced GFR compared to the group with preserved GFR: LA 41.48±0.65 mm, LV ESD 40.98±0.64 mm, LV EDD 53.48±0.52 mm ($p<0.05$). In the GFR < 60 ml/min/1.73 m^2 and GFR ⩾ 60 ml/min/1.73 m^2 groups, E (48.80±2.72 and 51.52±1.19 cm/s), A (62.09±2.91 and 60.68±1.28 cm/s), E/A (4.15±3.29 and 1.84±0.91) values were comparable ($p>0.05$).

Thus, changes in echocardiographic data with a tendency of increased left heart chambers size during the hospital follow-up period of STEMI patients are one of the important predictors of heart failure development in the future. Laboratory control of the increased NTproBNP level reflects the risk of heart failure progression.

Discussion

There are currently a large number of scales for assessing the prognosis of patients with AMI. In clinical trials and real-world clinical practice, the Killlip T. AMI patients' acute heart failure scale and the GRACE scale for assessing the risk of in-hospital mortality are widely used. The use of available criteria, objective and laboratory data in the GRACE scale allows timely assessment of the prognosis of ACS patients, and the use of the NT-proBNP increases the accuracy of heart failure prognosis. The obtained EchoCG data in high-risk patients according to the GRACE scale: decrease of E parameters, E/A ratio ($p<0.05$), increase of A ($p<0.05$) confirm the presence of diastolic dysfunction and progression of heart failure in STEMI patients at the hospital stage of treatment.

Clinical studies in ACS patients confirm the presence of varying degrees of renal failure in 35–40 % of patients [7]. Severe renal dysfunction is known to be associated with an unfavourable prognosis and is an independent predictor of cardiovascular complications in ACS patients [10]. GFR assessment is not only a prognostic marker of renal dysfunction, but also an important criterion for the selection of management tactics in patients with ACS. According to the literature, renal failure is common in patients after AMI, and the presence of chronic kidney disease is associated with high in-hospital and long-term mortality in patients with AMI [10, 11].

Among the STEMI patients we studied, 22 % had reduced GFR. Patients with STEMI GFR <60 ml/min/1.73 m^2 were older and had a high risk of in-hospital mortality according to the GRACE scale. Objective and laboratory data were comparable in patients with reduced and preserved GFR. According to the EchoCG data, patients with reduced GFR had increased LA and LV dimensions, a marker of heart failure progression. The calculated negative correlations of GFR with the degree of acute heart failure in patients with STEMI, the degree of CHF progression and hospital mortality according to the GRACE scale confirm the importance of GFR in assessing prognosis at the hospital treatment stage [11, 12].

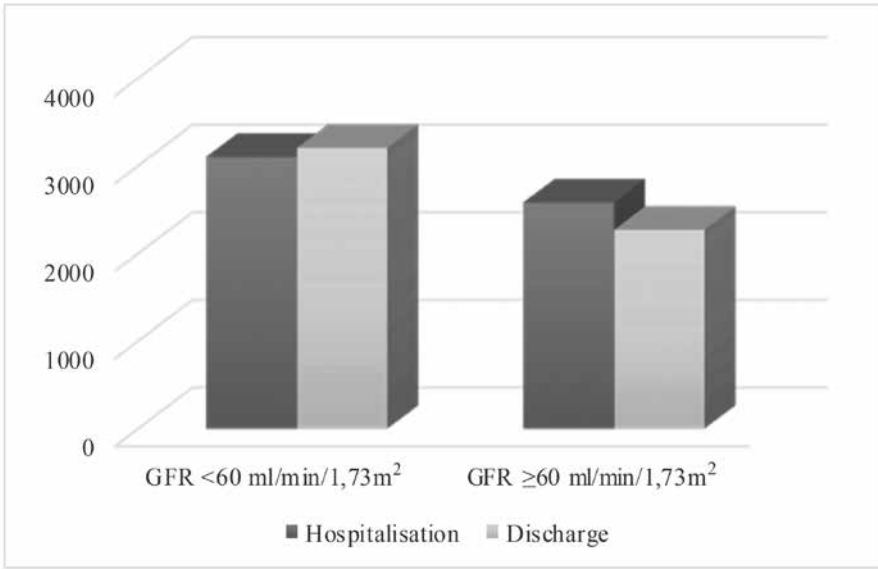

Fig. 2. NTproBNP levels during the hospitalization of STEMI patients depending on the GFR

Conclusion

The GRACE scale for in-hospital mortality is easy to use and can be applied in real-world clinical practice in patients with ACS. Patients at high GRACE risk tend to be older, with reduced LV EF and the severe diastolic dysfunction. NT-proBNP concentration increases with increasing GRACE risk and does not change at the end of the hospital phase of STEMI treatment. The detection of heart failure markers in the conditions of hospital treatment of STEMI allows the selection of the right tactics of patient management in the hospital and outpatient phases of treatment. Comprehensive assessment of patients with STEMI during the inpatient follow-up is an important guide to the future prognosis of patients.

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