ORIGINAL ARTICLE

THE LEVEL OF GROWTH STIMULATING FACTOR EXPRESSED BY GENE 2 AND TROPONIN I IN THE BLOOD PLASMA OF NSTEMI PATIENTS DEPENDING ON DIFFERENT CLINICAL CHARACTERISTICS

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ABSTRACT

The aim of the study is to evaluate the relationship between ST2 and Troponin I with various clinical and instrumental parameters.

Materials and methods: We examined 200 patients with NSTEMI aged 38 to 80 years, who were urgently hospitalized in the Vinnytsya Regional Clinical Center of Cardiovascular Pathology. All patients underwent laboratory testing of ST2 and Troponin I levels in plasma by enzyme-linked immunosorbent assay on the first day of hospitalization before coronary angiography.

Results: Elevations in ST2 levels were significantly higher in patients with acute heart failure (Killip III) and the presence of acute arrhythmias, diabetes mellitus, and smoking. The increase in Troponin I was associated primarily with the nature of changes in the ECG, stratification on the GRACE score and the presence of concomitant arterial hypertension.

Conclusions: Determination of ST2 and Troponin I before coronary angiography makes it possible to predict the course of NSTEMI and make appropriate therapeutic corrections to prevent complications.

KEY WORDS: NSTEMI, Troponin I, ST2, GRACE score

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INTRODUCTION

Myocardial infarction (MI) is one of the leading causes of death and disability worldwide. In Ukraine, the frequency of registration of MI per capita is the highest in the European population, which puts this problem in the category of priority medical and social problems for our society [1].

Over the last 20 years, there has been an increasing trend in the frequency of NSTEMI, which, according to some data, accounts for about half of all registered MI [2]. The main problem with NSTEMI is that the long-term prognosis of these patients remains unsatisfactory, and mortality one year after the disaster equals or even exceeds that of STEMI.

Patients who have undergone NSTEMI remain one of the most difficult categories for invasive treatment, which requires systematization of experience and the development of a specific algorithm for the management of such patients. The data on the nature of coronary artery disease in patients with NSTEMI show that in 10-20% of patients there are intact coronary vessels, in 30-35% of cases there is a lesion of one, in 25-30% - 2 vessels and in 5-10% - lesions of the trunk of the left coronary artery of various nature [3, 4]. On the other hand, a number of studies show less significant anatomical changes in the coronary artery in women, compared with men, in various forms of acute coronary syndrome in all age groups [3, 4, 5]. Of some scientific interest are studies that develop the concept of predicting the nature of coronary artery disease using clinical and various non-invasive instrumental parameters, which allows using simple and affordable research methods to stratify patients for invasive treatment. In this sense, the study of the influence of various non-invasive biomarkers, such as Troponin I (Tp I), natriuretic peptide (BNP and NT-proBNP), galectin-3, stimulating growth factors expressed by gene 2 (ST2) and others, plays an important role. Among the latter, much attention is paid to ST2 [6, 7].

Circulating ST2 is a sensitive marker of cardiostress and ischemic injury, expressed by heart tissue during myocardial distension and mechanical stress. Circulating ST2 has prognostic significance in the case of acute coronary syndrome, in particular independently associated with 28-day mortality [7]. ST2 is a soluble protein expressed by heart cells in response to disease or injury. Unlike many other cardiomarkers, ST2 levels change rapidly depending on the patient's condition, allowing doctors to choose the most effective course of therapy.

THE AIM

The aim of the study is to evaluate the relationship between ST2 and Tp I with various clinical and instrumental parameters.

Table I. The analysis of the level of Tp I in plasma in patients with NSTEMI

Clinical characteristics of patients with NSTEMI	ST2 level (ng / ml)	Tp I level (ng / ml)
Anterior localization of MI (n=158)	36,5 (24,7; 56,1)	5,9 (3,2; 9,3)
Posterior localization of MI (n=42)	33,4 (22,3; 49,4)	6,8 (4,2; 10,3)
P by Mann-Whitney U test	0,35	0,10
Depression of the ST segment (n=129)	34,7 (24,2; 56,1)	6,4 (4,1; 10,3)
Inversion of the T-wave (n=71)	36,9 (24,2; 50,7)	5,3 (0,8; 8,3)
P by Mann-Whitney U test	0,45	**0,004**
Spearman's correlation with the value of ST depression	R=0,03; p=0,68	**R=0,21; p=0,006**
Killip III, yes (n=20)	110,2 (90,8; 189,8)	6,7 (4,1; 8,7)
no (n=180)	33,7 (23,4; 46,2)	5,8 (3,4; 10,3)
P by Mann-Whitney U test	**< 0,0001**	0,89
Frequent VE Lown II-V, yes (n=48)	36,8 (25,4; 86,6)	5,4 (2,5; 0,8)
no, (n=152)	33,7 (22,2; 51,4)	6,2 (3,5; 10,2)
P by Mann-Whitney U test	**0,04**	0,19
Unstable episodes of VE / VF, yes (n=22)	40,5 (25,3; 71,8)	5,3 (4,2; 8,7)
no (n=178)	34,3 (23,2; 52,9)	6,0 (3,4; 10,1)
P by Mann-Whitney U test	**0,04**	0,56
Persistent episodes of VT, yes (n=17)	184,5 (135,6; 195,7)	6,0 (2,5; 9,0)
no (n=183)	33,7 (24,0; 49,0)	5,9 (3,5; 10,1)
P by Mann-Whitney U test	**< 0,0001**	0,56
Paroxysmal AF, yes (n=18)	36,9 (22,7; 55,2)	6,0 (1,5; 9,0)
no (n=182)	35,2 (24,2; 53,9)	5,9 (3,5; 10,1)
P by Mann-Whitney U test	0,98	0,35
SA / AV-block of II-III degree, yes (n=19)	30,5 (18,8; 50,7)	5,8 (4,2; 10,3)
no (n=181)	36,2 (24,2; 55,2)	5,9 (3,4; 10,1)
P by Mann-Whitney U test	0,21	0,60
>140 points by GRACE (n=47)	36,9 (24,2; 49,4)	5,4 (4,2; 9,9)
<109 points by GRACE (n=30)	36,9 (25,9; 68,9)	3,6 (0,8; 5,9)
P by Mann-Whitney U test	0,92	**0,002**
AH, yes (n=171)	36,2 (24,4; 56,1)	6,2 (3,8; 10,1)
no (n=29)	34,7 (22,3; 43,7)	4,1 (3,2; 9,3)
P by Mann-Whitney U test	0,12	**0,02**
Spearman correlation with AH duration (years)	*R=0,14; p=0,06*	R=0,12; p=0,09
Angina pectoris I-III FC before MI, yes (n=86)	36,6 (25,9; 52,1)	6,2 (3,9; 10,1)
no (n=114)	35,2 (24,0; 55,2)	5,9 (3,2; 10,1)
P by Mann-Whitney U test	0,76	0,54
Spearman's correlation with the duration of angina (years)	R=0,007; p=0,91	R=0,06; p=0,41
Persistent AF, yes (n=23)	31,5 (24,2; 48,6)	7,5 (4,2; 11,5)
no (n=177)	36,2 (24,4; 56,1)	5,9 (3,2; 10,1)
P by Mann-Whitney U test	0,43	*0,06*
Spearman correlation with AF duration (years)	R=-0,05; p=0,46	R=0,11; p=0,11
Type II diabetes, yes (n=25)	46,2 (24,4; 100,4)	7,5 (4,2; 8,7)

no (n=175)	35,2 (24,2; 52,1)	5,9 (3,4; 10,3)
P by Mann-Whitney U test	**0,03**	0,78
Smoking, yes (n=84)	37,6 (27,0; 56,6)	4,8 (2,7; 6,0)
no (n=116)	33,2 (22,3; 52,3)	8,5 (4,4; 11,3)
P by Mann-Whitney U test	**0,04**	**< 0,0001**
Spearman correlation with smoking experience (years)	R=0,12; p=0,09	**R=-0,32; p< 0,0001**
Alimentary obesity, yes (n=73)	34,6 (24,4; 43,7)	5,4 (3,8; 8,4)
no (n=127)	36,2 (24,2; 56,6)	6,9 (3,3; 11,3)
P by Mann-Whitney U test	0,32	**0,02**
Spearman correlation with BMI (kg / m2)	R=0,03; p=0,67	**R=-0,14; p=0,04**

Note. MI - myocardial infarction, VE - ventricular extrasystoles, VT - ventricular tachycardia, VF - ventricular fibrillation, AF - atrial fibrillation, SA / AV - sinoatrial / atrioventricular block, AH - arterial hypertension, BMI – body mass index.

MATERIALS AND METHODS

All studies conform to the principles of the Declaration of Helsinki of the World Medical Association. The study protocol, the form of informed consent of patients and other documents related to the study were approved at the meeting of the Academic Council of the National Pirogov Memorial Medical University, Vinnytsya (excerpt from the protocol No. 2 from 27.02.2020). Informed consent to participate in the study was discussed and signed by all study participants.

We examined 200 patients with INSTEMI aged 38 to 80 (mean 62.0 ± 0.71, median – 62 and interquartile range – 55 and 70) years, who were urgently hospitalized in the Vinnytsya Regional Clinical Center of Cardiovascular Pathology.

The main criteria for inclusion of patients in the study were: NSTEMI, which emerged for the first time; age of patients up to 80 years and the patient's informed consent to participate in the study. The diagnosis of NSTEMI was established according to the recommendations of ESC, 2020. The criteria for exclusion from the study were: 1) STEMI, transferred in the past and recurrent acute myocardial infarction; 2) age of patients 80 years and older; 3) the presence of sinoatrial or atrioventricular block II-III degree, implanted or the need for implantation of an artificial pacemaker; 4) chronic heart failure NYHA-III, IV before the incident of acute myocardial infarction; 5) diseases of the respiratory system, kidneys and liver, which were accompanied by signs of pulmonary, renal and hepatic failure; anemic conditions with a hemoglobin level below 110 g / L; 6) the presence of rheumatic and congenital heart defects, idiopathic and inflammatory myocardial lesions and 7) malignancies, severe neuropsychiatric disorders, alcohol abuse. Laboratory testing of ST2 and Tp I levels in blood plasma was performed by quantitative enzyme-linked immunosorbent assay in all patients on the first day of hospitalization before coronary angiography.

RESULTS AND DISCUSSION

Analysis of ST2 and Tp I levels in plasma depending on the clinical characteristics of NSTEMI patients (Table I) showed that ST2 levels were significantly higher in patients with acute heart failure, which corresponded to Killip III (110.2 vs. 33.7 ng / ml, p <0.0001), in the presence of frequent ventricular extrasystoles Lown II-V (36.8 vs. 33.7 ng / ml, p = 0.04), episodes of unstable ventricular tachycardia (VT) (40.5 vs. 34.3 ng / ml, p = 0.04) and persistent / paroxysmal VT (184.5 vs. 33.7 ng / ml, p <0.0001), which were observed in the first days of MI.

In addition, plasma ST2 levels were significantly higher in patients with concomitant type II diabetes mellitus (46.2 vs. 35.2 ng / ml, p = 0.03), in the presence of a risk factor such as smoking (37.6 vs. 33.2 ng / ml, p = 0.04) in the absence of a significant correlation with his anamnesis (R = 0.12, p = 0.09). In turn, the tendency to reliability of connection of ST2 level in plasma with duration of arterial hypertension (AH) was defined (R = 0,14, p = 0,06).

It was found that the most convincing increase in plasma ST2 levels was recorded in patients with NSTEMI in the presence of acute heart failure (Killip III) and paroxysms / episodes of persistent VT, which was determined on the 1st day of MI and hospitalization. The latter fact demonstrates the important role of plasma ST2 levels in predicting the course of NSTEMI. The median level of ST2 in the presence of acute heart failure was 110, while in the presence of paroxysms of the VT - 185 ng / ml, respectively, with a median value for the group as a whole of 36 ng / ml.

Somewhat different patterns were recorded by us in the analysis of the level of Tp I in plasma in patients with NSTEMI (Table I). Thus, it was observed that the level was significantly higher in patients with ST-segment depression, compared with the inversion of the T-wave on the ECG (6.4 vs. 5.3 ng / ml, p = 0.004) in the presence of a positive correlation with the value of ST depression (R = 0.21, p = 0.006). In addition, the level of Tp I in plasma was significantly higher in patients in whom the GRACE score was determined > 140 points, compared with patients with < 109 points (5.4 vs. 3.6 ng / ml, p = 0.002), in the presence of a history of AH (6.2 vs. 4.1 ng / ml, p = 0.02) but no correlation with its duration (R = 0.12, p = 0.09).

Of particular interest to us was the fact that there was a significant reduction in the level of Tp I in the plasma of NSTEMI patients who smoked (4.8 vs. 8.5 ng / ml, p <0.0001) and patients with obesity (BMI > 30 kg / m2). (5.4 vs. 6.9 ng / ml, p = 0.02). Significant inverse correlations of Tp I level with experience of active smoking (R = -0.31, p <0.0001) and BMI (R = -0.14, p = 0.04) were determined.

Thus, the results of the analysis showed radically different dependences of the level of ST2 and Tp I in plasma with the initial clinical characteristics of NSTEMI patients. If the increase in ST2 levels was associated primarily with parameters that characterized the severity of MI (the presence of Killip III and severe ventricular arrhythmias) and such important risk factors as smoking and type II diabetes, the increase in Tp I in NSTEMI patients was associated, first of all, with the nature of ECG graphics, stratification on the GRACE score and the presence of AH in the anamnesis. The fact of association of a more significant increase in the level of Tp I with the absence of such risk factors as smoking and alimentary obesity needs some explanation.

The results of the analysis, which demonstrate the connection between ST2 level and the risk of acute arrhythmias in the early period of MI and the progression of acute heart failure, seem to be well-founded. These processes are primarily associated with acute myocardial remodeling on the background of mechanical myocardial distension. Changes in the levels of Tp I contribute to the risks on the GRACE score, which, in turn, is reflected in the choice of time for reperfusion.

In our opinion, the association of elevated levels of Tp I in patients without pre-existing risk factors, such as smoking and obesity, is due to the fact that patients in these groups are more likely to develop collaterals due to prolonged chronic myocardial hypoperfusion. As a result, myocardial remodeling is more compensated in the case of acute hypoperfusion.

CONCLUSIONS

1. The ST2 level determined before coronary angiography can predict such dangerous complications of NSTEMI as acute heart failure and dangerous ventricular arrhythmias.
2. Elevated levels of Tp I have a positive correlation with changes in the ECG and negative with such risk factors as obesity and smoking.
3. The combined determination of ST2 and Tp I makes it possible to predict the course of NSTEMI and to make appropriate therapeutic corrections for the prevention of complications.

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