*Огляди літератури, **оригінальні дослідження**, погляд на проблему, випадок з практики, короткі повідомлення*
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FEATURES OF CARDIAC ARRHYTHMIAS IN THE EARLY AND DELAYED PERIOD OF NSTEMI DEPENDING ON PLASMA LEVELS OF ST2 AND TROPONIN I.

©V. Yu. Maslovskyi

National Pirogov Memorial Medical University, Vinnytsya

SUMMARY. The search for highly sensitive markers for predicting the adverse course of myocardial infarction without ST-segment elevation is due to negative statistics of complications in the early and remote periods of the disease. Currently, one of these markers is considered to be a growth stimulating factor expressed by gene 2.

The aim – to determine the features of cardiac arrhythmias in the early and delayed period of NSTEMI depending on plasma levels of ST2 and troponin I.

Material and Methods. We conducted a comprehensive study of 200 patients with NSTEMI aged 38 to 80 years. All patients were examined according to the current treatment protocol for patients with acute coronary syndrome without ST segment elevation and daily Holter ECG monitoring was performed for 3–5 days after hospitalization.

Results. It was found that high levels of ST2 in the early period of NSTEMI are associated with a high risk of acute ventricular arrhythmias, a level in the early period. At the same time, elevated levels of ST2 and troponin I are not associated with the risk of developing acute arrhythmias in the long term NSTEMI.

Conclusions. Determining the level of ST2 in the early period of NSTEMI allows to predict the risk of fatal arrhythmias and to carry out appropriate preventive measures.

KEY WORDS: myocardial infarction without ST segment elevation; ventricular arrhythmias; ST2; troponin I.

Introduction. In the structure of overall mortality, coronary heart disease occupies a leading place [1]. Its form, such as myocardial infarction without ST-segment elevation (NSTEMI), remains one of its most dangerous manifestations due to the high risk of adverse events such as acute myocardial dysfunction, conduction disturbances and fatal cardiac arrhythmias [2]. The search for highly sensitive non-invasive predictors of destabilization of the NSTEMI course is aimed at timely stratification of the risk of adverse events, and appropriate prevention. One of the recent biomarkers that has been studied recently and is directly related to the development of acute myocardial dysfunction is the growth stimulating factor expressed by gene 2 (ST2). ST2 is a member of the family of interleukin-1 (IL-1) receptors with isoforms associated with membrane ST2 (ST2L) and soluble (sST2) forms. IL-33 / ST2L signaling protects the myocardium from hypertrophy and fibrosis of the heart after pressure overload. Soluble ST2 acts as a bait receptor for IL-33 and prevents IL-33 / ST2L interactions and subsequent cardioprotective cascade events. A number of scientific studies have already demonstrated its leading role in the progression of heart failure in the early and delayed period of NSTEMI [3].

The aim of the study. determine the features of cardiac arrhythmias in the early and delayed period of NSTEMI depending on plasma levels of ST2 and troponin I.

Material and Methods. We conducted a comprehensive study of 200 patients with acute myocardial infarction without ST-segment elevation (NSTEMI) aged 38 to 80 (mean 62.0 ± 0.71, median – 62 and interquartile range – 55 and 70) years, who were hospitalized in the Municipal Non-Profit Enterprise "Vinnytsia Regional Clinical Medical and Diagnostic Center for Cardiovascular Pathology" with urgent indications.

The criteria for including patients in the study were:

1. Verified NSTEMI, first diagnosed;
2. age up to 80 years;
3. the absence of contraindications to percutaneous coronary interventions and the use of the main groups of pharmacological agents included in the basic therapy of NSTEMI;
4. informed consent of the patient to participate in the study.

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;
7. malignancies, severe neuropsychiatric disorders, alcohol abuse;
8. the presence of contraindications to percutaneous coronary interventions and the use of the

main groups of pharmacological agents included in the basic therapy NSTEMI;

9. reluctance and refusal of the patient to participate in the study.

All patients were examined according to the NSTEMI protocol [4] and daily Holter ECG monitoring was performed for 3-5 days after hospitalization.

Results and Discussion. It was found that a convincing increase in ST2 plasma levels was recorded in patients with NSTEMI in the presence of paroxysms / episodes of persistent ventricular tachycardia / ventricular fibrillation (VT / VF), which was determined on the 1st day of MI and hospitalization of patients (Tab. 1). The latter fact demonstrates the important role of ST2 levels in plasma in predicting the course of NSTEMI. In this case, the median level of ST2 in the presence of paroxysms of the ventricle – 185 ng / ml, respectively, with a median value for the group as a whole of 36 ng / ml. Also, an increase in plasma ST2 levels was recorded in the presence of ventricular extrasystoles (VE), including high gradation (Lown IVb-V). At the same time, the level of (troponin I) Tp I did not show a significant connection with the development of acute arrhythmias.

Table 1. Plasma ST 2 and troponin I levels in patients in the early period of NSTEMI depending from various indicators on Holter ECG

Clinical characteristics of patients w/NSTEMI	ST2 level ng / ml)	Tp I level (ng / ml)
Frequent VE IVb-V gradations, 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 VT, 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/VF, 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

Analysis of ST2 and Tp I levels in plasma in NSTEMI patients depending on the nature of daily heart rate regulation, the structure of cardiac arrhythmias and ventricular repolarization (Tab. 2), which were determined by Holter ECG, showed no significant dependence of ST2 plasma levels on analyzed parameters. The data obtained were unexpected and needed some explanation, as we previously found that plasma ST2 levels to some extent depended on the severity of myocardial infarction, including the presence of severe and prognostic cardiac arrhythmias – paroxysms and frequent high-grade VE according to Lawn, which were observed during ECG recording or in-patient ECG monitoring on the first day of MI.

Table 2. Plasma ST 2 and troponin I levels in patients in the delayed period of NSTEMI depending from different parameters on the Holter ECG

Holter ECG indicators	ST2 level (ng / ml)	Tp I level (ng / ml)
1	2	3
CI > 1.5 (n=84)	36.9 (26.9; 55.6)	5.8 (3.4; 9.0)
CI ≤ 1.5 (n=116)	33.4 (23.4; 53.9)	5.9 (3.4; 10.3)
P by Mann-Whitney U test	0.21	0.34
The average number of SE per 1 hour > 10, yes (n=94)	36.9 (25.7; 56.1)	5.7 (2.9; 8.4)
no (n=106)	33.7 (22.3; 52.0)	7.3 (4.2; 11.4)
P by Mann-Whitney U test	0.10	**0.01**
The average number of SE per 1 hour > 100, yes (n=33)	36.9 (24.7; 63.7)	6.3 (2.4; 8.7)
no (n=167)	35.2 (24.2; 52.0)	5.9 (3.8; 10.3)
P by Mann-Whitney U test	0.42	0.33
Presence of episodes of SVT / AF during the day, yes (n=16)	37.9 (27.6; 83.8)	7.0 (2.5; 8.6)

Continuation of table 2

1	2	3
no, (n=163)	35.5 (24.0; 52.0)	5.9 (3.8; 10.3)
P by Mann-Whitney U test	0.33	0.45
The average number of VE per 1 hour > 10, yes (n=72)	36.2 (22.8; 56.1)	7.4 (4.3; 11.9)
no (n=128)	35.3 (24.3; 52.0)	5.8 (3.0; 8.7)
P by Mann-Whitney U test	0.91	**0.03**
The average number of VE per 1 hour > 100, yes (n=54)	36.2 (22.3; 56.1)	5.9 (3.9; 12.3)
no (n=146)	35.3 (24.4; 53.9)	5.9 (3.2; 9.3)
P by Mann-Whitney U test	0.80	0.39
Availability of paired / group VEs per day, yes (n=69)	36.2 (24.2; 56.1)	7.4 (4.2; 11.4)
no (n=131)	35.2 (24.2; 52.0)	5.8 (3.2; 9.0)
P by Mann-Whitney U test	0.89	**0.03**
The presence of polytopic VE per day, yes (n=41)	36.9 (22.3; 56.1)	7.5 (4.6; 11.5)
no (n=159)	35.2 (24.4; 53.9)	5.9 (3.4; 9.1)
P by Mann-Whitney U test	0.89	0.20
The presence of early (R on T) VE per day, yes (n=47)	33.7 (22.3; 56.1)	6.3 (4.5; 10.7)
no (n=153)	36.2 (24.2; 53.9)	5.9 (3.2; 9.0)
P by Mann-Whitney U test	0.77	0.25
The presence of episodes of VT per day, yes (n=25)	36.9 (22.3; 55.2)	7.4 (3.8; 11.4)
no (n=175)	35.4 (24.2; 53.9)	5.9 (3.4; 10.1)
P by Mann-Whitney U test	0.89	0.20
Availability of SMI episodes per day, yes (n=32)	35.0 (24.2; 47.2)	5.1 (3.3; 10.7)
no (n=168)	36.2 (24.2; 55.2)	5.9 (3.5; 9.9)
P by Mann-Whitney U test	0.92	0.61

Note. CI – circadian index, SE – supraventricular extrasystole, SVT / AF – supraventricular tachycardia / atrial fibrillation, VE – ventricular extrasystole, VT – ventricular tachycardia, SMI – silent myocardial ischemia.

Thus, it should be assumed that the level of ST2 in plasma, determined on the first day of MI, before percutaneous interventions, is primarily related to the nature of the most acute period of MI, namely the likelihood of severe and prognostic cardiac arrhythmias.

In turn, the registration of cardiac arrhythmias on day 3–5 of hospital stays, of course, reduces the likelihood of association of cardiac arrhythmias with acute myocardial dysfunction and therefore, in our opinion, has no definite relationship with plasma ST2 levels. On the other hand, the data obtained could indicate a positive effect of basic treatment, including percutaneous interventions, on the development of various cardiac arrhythmias in NSTEMI patients.

We found that an increase in plasma ST2 levels was observed in patients with NSTEMI in the presence of episodes of persistent VT/VF, which was determined on the 1st day of MI and hospitalization of patients. A number of studies have found a positive correlation between serum ST2 levels and 28-day mortality in patients with NSTEMI [5]. Also, it was found that the limit value for ST2 is 1000 pg / ml with a sensitivity of 72.2 % and a specificity of 80.0 %. In our study, it was found that an increase in plasma ST2 levels was recorded in the presence of VE, including high gradation (Lown IVb-V). At the same time, the level of Tp I did not show a significant association with the development of acute arrhythmias, which, in our opinion, is associated with the predominance of male patients among the examined patients [6].

In our opinion, the lack of association between ST2 and troponin I levels and the risk of developing acute arrhythmias in the long term NSTEMI is primarily due to the fact that these markers reflect the processes of acute remodeling and myocardial dam-

age in the first hours of infarction. In the long term, the remodeling processes are significantly affected by the consequences of reperfusion therapy, namely, early percutaneous intervention in high-risk patients with GRACE.

Conclusions. 1. High levels of ST2 in the early period of NSTEMI are associated with a high risk of acute ventricular arrhythmias, troponin I did not show a similar association.

2. Elevated levels of ST2 and troponin I are not associated with the risk of developing acute arrhythmias in the long term NSTEMI.

3. Determination of ST2 level in the early period of NSTEMI allows to predict the risk of fatal arrhythmias and to carry out appropriate preventive measures.

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Conflicts of interest. Author has no conflict of interest to declare.

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ОСОБЛИВОСТІ ПОРУШЕНЬ СЕРЦЕВОГО РИТМУ В РАННЬОМУ ТА ВІДТЕРМІНОВАНОМУ ПЕРІОДІ NSTEMI ЗАЛЕЖНО ВІД ПЛАЗМОВИХ РІВНІВ ST2 І ТРОПОНІНУ І

©В. Ю. Масловський

Вінницький національний медичний університет імені М. І. Пирогова

РЕЗЮМЕ. Пошук високочутливих маркерів прогнозування несприятливого перебігу інфаркту міокарда без елевації сегмента ST зумовлений негативною статистикою виникнення ускладнень у ранньому та віддаленому періодах захворювання. В даний час одним із таких маркерів вважається стимулювальний фактор росту, що експресується геном 2.

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Мета – визначити особливості порушень серцевого ритму в ранньому та відтермінованому періоді NSTEMI залежно від плазмових рівнів ST2 і тропоніну I.

Матеріал і методи. Нами було проведено комплексне обстеження 200 пацієнтів з NSTEMI у віці від 38 до 80 років. Усі пацієнти обстежені відповідно до діючого протоколу діагностики та лікування пацієнтів із гострим коронарним синдромом без елевації сегмента ST та проведене добове холтерівське моніторування ЕКГ протягом 3–5 днів після госпіталізації.

Результати. Встановлено, що високі рівні ST2 асоційовані з високим ризиком розвитку гострих шлуночкових аритмій у ранньому періоді NSTEMI. У той же час, підвищені рівні ST2 і тропоніну I не пов'язані з ризиком розвитку гострих аритмій у відтермінованому періоді NSTEMI.

Висновки. Визначення рівня ST2 в ранньому періоді NSTEMI дозволяє прогнозувати ризик фатальних аритмій та проводити відповідні профілактичні заходи.

КЛЮЧОВІ СЛОВА: інфаркт міокарда без елевації сегмента ST; шлуночкові аритмії; ST2; тропонін I.

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Електронна адреса для листування: vmaslovskyi@gmail.com