Sapporo Medical Journal
Volume 56, Issue 02, February, 2022

Features of changes in plasma ST2 and troponin I levels in patients with NSTEMI, depending on the nature of the anatomical lesion of the coronary arteries.

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Abstract— The aim of the study is to evaluate the dependence of associations of ST2 and Troponin I levels on the nature of the anatomical lesion of the coronary arteries.

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. In the association of relatively high levels of ST2 and relatively high levels of Troponin I, there is a positive correlation between the degree of coronary arteries damage, while in the association of relatively low levels of ST2 and Troponin I, severe stenotic coronary arteries lesions can be ruled out.

Conclusions. Determining the associations of ST2 and Troponin I before coronary angiography allows to predict the degree of stenotic lesions of the coronary arteries and to determine the expected intervention strategy in patients with NSTEMI.

Keywords: NSTEMI, Troponin I, ST2, coronary arteries.

Резюме.

Цель исследования – оценить зависимость ассоциаций уровней ST2 и тропонина I от характера анатомического поражения коронарных артерий.

Материалы и методы. Обследовано 200 пациентов с ИМбпST в возрасте от 38 до 80 лет, экстренно госпитализированных в Винницкий областной клинический центр сердечно-сосудистой патологии. У всех пациентов проведено лабораторное исследование уровней ST2 и тропонина I в плазме с помощью иммуноферментного анализа в первый день госпитализации перед коронарной ангиографией.

Полученные результаты. Выявлена положительная корреляция между относительно высокими уровнями ST2 и относительно высокими уровнями тропонина I со степенью повреждения коронарных артерий, в то время как в сочетании с относительно низкими уровнями ST2 и тропонина I возникновение серьезных стенозирующих поражений коронарных артерий могут быть исключены.

Выводы. Определение ассоциаций ST2 и тропонина I перед коронарной ангиографией позволяют предположить наличие высокой степени стенотического поражения коронарных артерий и определить стратегию вмешательства у пациентов с ИМбпST.

Ключевые слова: ИМбпST, тропонин I, ST2, коронарные артерии.

შ ემაჯამებელი.

კვლევის მიზანი იყო ST2 და ტროპონინ I დონის ასოციაციების დამოკიდებულების შეფასება კორონარული არტერიების ანატომიური დაზიანების ბუნებაზე.

მ ასალა და მეთოდები. კვლევაში მონაწილეობდა 38-დან 80 წლამდე ასაკის 200 პაციენტი NSTEMI, რომლებიც სასწრაფოდ ჰოსპიტალიზებული იყვნენ ვინიცის გულ-სისხლძარღვთა პათოლოგიის რეგიონალურ კლინიკურ ცენტრში. ყველა პაციენტს ჩაუტარდა პლაზმური ST2 და ტროპონინ I დონის ლაბორატორიული ტესტირება ELISA ჰოსპიტალიზაციის პირველ დღეს კორონარული ანგიოგრაფიამდე.

შედეგები. დაფიქსირდა დადებითი კორელაცია შედარებით მაღალ ST2 დონეებსა და შედარებით მაღალ ტროპონინ I-ის დონეებს შორის კორონარული არტერიის დაზიანების ხარისხთან, ხოლო შედარებით დაბალ ST2 და ტროპონინ I-ის

დონეებთან ერთად შეიძლება გამოირიცხოს კორონარული არტერიის მძიმე სტენოზირების დაზიანებები.

დასკვნები. ST2 და ტროპონინ I ასოციაციების განსაზღვრა კორონარული ანგიოგრაფიის წინ მიუთითებს კორონარული არტერიების სტენოზური დაზიანების მაღალი ხარისხის არსებობაზე და განსაზღვრავს ჩარევის სტრატეგიას NSTEMI მქონე პაციენტებში.

საკვანძო სიტყვები: NSTEMI, ტროპონინი I, ST2, კორონარული არტერიები.

Introduction.

A large number of adverse events and endpoints in NSTEMI remain the focus of study due to the leading role of myocardial infarction (MI) among the causes of death [4]. In addition to the immediate consequences after undergoing MI, it is of great interest to study the long-term prognosis in this category of patients. Despite the achievements of modern science in treatment, the percentage of patients with an unfavorable prognosis remains quite high, which encourages further search for clinical and prognostic markers of destabilization of NSTEMI.

The already known markers of myocardial damage have recently received increasing attention to the growth stimulating factor expressed by gene 2 (ST2) [1]. ST2 plays a key role in regulating the myocardial response to biomechanical overload in cardiac fibroblasts and cardiomyocytes and is, in fact, a system that controls cardiomyocyte hypertrophy and cardiac fibrosis [8].

The aim. The aim of the study is to evaluate the dependence of associations of ST2 and Troponin I levels on the nature of the anatomical lesion of the coronary arteries.

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. For all patients coronary ventriculography (CVG) was performed.

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 [3]. 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 Troponin I (Tp I) levels in blood plasma was performed by quantitative enzyme-linked immunosorbent assay in all patients on the first day of hospitalization before CVG.

Results.

Using the variation statistics method, the ST2 level gradations group were selected. Thus, the relatively low (RL) corresponded to less than 25, and the relatively high (RH) level of ST2 to more than 75 persons in the group, respectively. For patients in the main group, these levels were <26 and> 56 ng / ml, respectively. Instead, the relatively moderate (or intermediate) ST2 level (RM) for these patients was 26-56 ng / ml [2].

Similar calculations made for the level of Tp I in plasma showed that the average level of the factor was 7.07 ng / ml at the minimum and maximum values of 0.31 and 18.41 ng / ml, respectively, and the standard deviation of the mean value (σ) – 4.84. The median was 5.96 and the interquartile range was 3.49 and 10.11 ng / ml, respectively. Therefore, the obtained data showed that in 75% of the examined NSTEMI patients the level of Tp I in plasma ranged from 3.49 to 10.11 ng / ml. To assess the degree of CA damage, we used our own severity of atherosclerotic stenosis score in points [2].

The distribution of the value of the total score of the CA lesion at different associations of ST2 and Tp I levels in plasma (Fig. 1) showed the the following patterns. Thus, at different associations of ST2 and Tp I in plasma milder lesions of the CA (≤ 3 points) were registered from 65.8% to 40.5%, while more severe (> 3 points) – from 34.3 to 59 , 5% of cases. The largest number of cases with more severe and, accordingly, the smallest – with milder lesions of the CA, was observed in the association of RH ST2 / RH Tp I (59.5% vs. 34.2%, 35.0% and 24 , 4% and 40.5% against 65.8%, 65.0% and 75.6%, p according to the criterion $\chi 2$ was 0.03, 0.03 and 0.002, respectively).

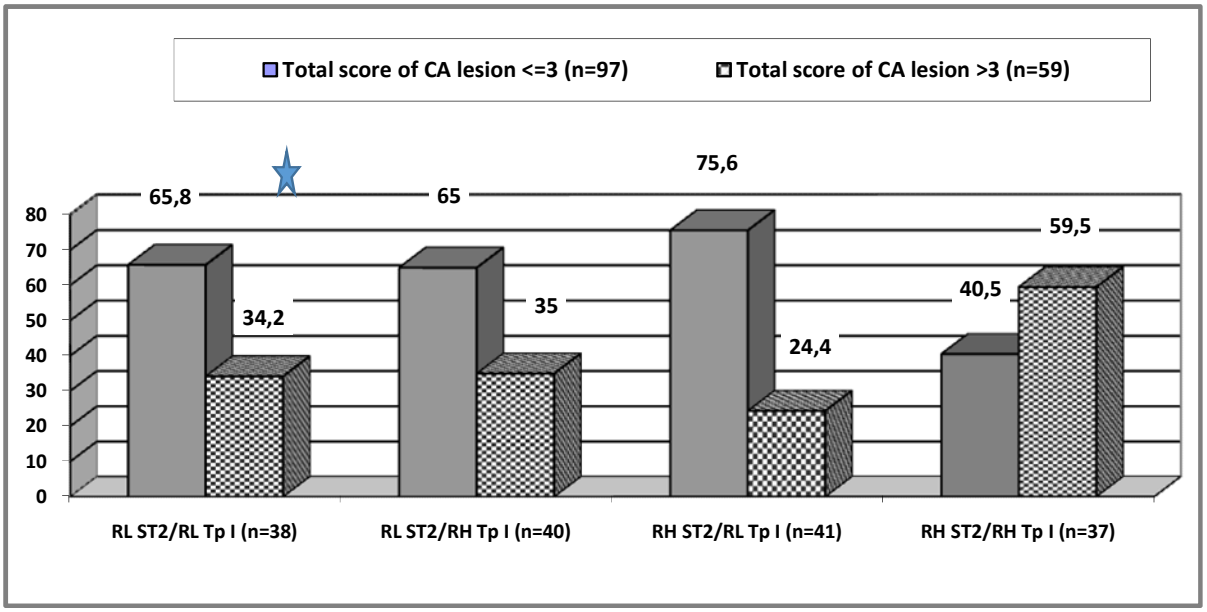

Fig.1 The total score of CA lesions depending on the association of ST2 and Tp I levels in plasma in patients with NSTEMI

Notes:

RL and RH – relatively low and relatively high levels in plasma, respectively;

It was observed that the largest number of different correlations with CVG indicators was determined for associations of ST2 and Tp I levels, which combined the same category of plasma factor level – RL ST2 / RL Tp I and RH ST2 / RH Tp I. A positive was determined correlation of RL ST2 / RL Tp I association with the absence of atherosclerotic plaques in the pool left anterior descending artery (LAD) (R = 0.15, p = 0.04), left circumflex artery (LCx) (R = 0.21, p = 0.003) and the absence of hemodynamically significant stenosis (HSS) CA (R = 0.19, p = 0.01). In addition, this association found a negative correlation with the presence

of HSS LAD (R = -0.17, p = 0.02) and the presence of 2 vascular lesions CA (R = -0.18, p = 0.01), as well as the nature of the LCx lesion in points (R = -0.16, p = 0.01) and the total CA lesion score (R = -0.16, p = 0.02) (Tab. 1).

The highest correlations of the RL ST2 / RL Tp I association were registered with the absence of atherosclerotic plaques in LCx and the absence of HSS CA. Based on the data obtained, it should be assumed that the presence of RL ST2 / RL Tp I association in NSTEMI patients precludes severe CA lesions.

In turn, the presence of the association RH ST2 / RH Tp I revealed positive correlations with the presence of HSS right coronary artery (RCA) (R = 0.17, p = 0.01), LAD (R = 0.15, p = 0.03) and LCx (R = 0.21, p = 0.003) and the presence of 3 vascular lesions CA (R = 0.23, p = 0.001), as well as the nature of the lesion LCx in points (R = 0, 23, p = 0.0009) and the total CA score (R = 0.21, p = 0.004). In addition, a negative correlation was found between the RH ST2 / RH Tp I association and the absence of atherosclerotic plaques in the LCx (R = −0.27, p = 0.0001).

Thus, the results of the analysis showed that the biochemical association RH ST2 / RH Tp I identified in NSTEMI patients is accompanied by more severe CA lesions compared to other analyzed associations.

Discussion.

As a result of our study, we found a positive correlation between ST2 and Tp I levels and the degree of coronary artery disease. The results of such studies were based on determining the degree of damage to the coronary arteries on the Hensini score and assessing the risk of major adverse cardiac events (MACE) in this category of patients [9, 10, 11, 12]. It was found that increasing levels of these biomarkers directly affect the increase in MACE and reduce the one-year survival of patients with myocardial infarction.

Previous studies have also shown that marked increases in Tp I in patients with NSTEMI have been associated with more severe clinical manifestations and culprit stenotic lesions with more complex morphological features on coronary angiography [7]. However, these studies did not assess ST2 levels and there are no data to predict the development of MACE. Instead, there is information that apelin-12 affects Tp I levels in the acute phase of

MI, while in the non-acute phase low levels of apelin are associated with a high frequency of MACE [5].

Also, some studies have found a significant moderate positive correlation between high specific Tp I levels and the complexity of coronary artery lesion, as assessed by the SYNTAX score. However, a weak correlation was found between this biomarker and the clinical prognostic scores of TIMI and GRACE [6].

Thus, there is an indisputable positive correlation between the degree of CA damage and the increase in the levels of biomarkers that characterize myocardial damage. Determination of these biological markers will allow not only to predict the nature of CA lesions, but also to predict the likelihood of MACE in this category of patients.

In addition, we first analyzed the associative relationship of ST2 and Tp I levels, markers that reflect the processes of myocardial damage and fibrosis, with the degree of coronary arteries lesions. This analysis convincingly demonstrated not only the relationship between these parameters, but also the fact that the association of relatively elevated levels of ST2 and Tp I should expect more significant damage of the coronary arteries, which in turn is associated with an increased risk of adverse events.

Conclusions.

1. It is established that at association of relatively high level of ST2 and relatively high level of Tp I there is a positive correlation of degree of lesions of CA.

2. No correlations have been established between relatively low ST2 and relatively high Tp I associations.

3. Associations of relatively low levels of ST2 and Tp I exclude severe stenotic lesions of the CA.

There is no conflict of interest.

References.

[1]. Çağrı Kokkoz, Adnan Bilge, Mehmet Irik et al. Prognostic value of plasma ST2 in patients with non-ST segment elevation acute coronary syndrome. Turkish Journal of

Emergency Medicine. Volume 18, Issue 2, June 2018, Pages 62-66. https://doi.org/10.1016/j.tjem.2018.01.003

[2]. Ivanov V.P., Mezhievska I.A., Maslovskyi V.Yu.. Characteristics of anatomic injury of coronary arteries in patients with acute myocardial infarction without ST elevation depending on plasma level of gene 2 growth stimulating factor and risk of adverse events. Acta Medica Leopoliensia Vol. 26 No. 1 (2020): P. 20-25. https://doi.org/10.25040/aml2020.01.020

[3]. Jean-Philippe Collet, Holger Thiele, Emanuele Barbato et al. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: The Task Force for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). European Heart Journal, Volume 42, Issue 14, 7 April 2021, Pages 1289–1367, https://doi.org/10.1093/eurheartj/ehaa575.

[4]. Kovalenko, V. M., Kornatskiy, V. M. (Eds.) (2014). Circulation system diseases as medical-social and social-politic problem. Kyiv, 279.

[5]. Krasniqi, X., Berisha, B., Gashi, M. et al. Influence of apelin-12 on troponin levels and the rate of MACE in STEMI patients. BMC Cardiovasc Disord 17, 195 (2017). https://doi.org/10.1186/s12872-017-0633-z

[6]. Monique Rodrigues Cardoso, Delcio Gonçalves da Silva Junior, Eduardo Alves Ribeiro, Alfredo Moreira da Rocha Neto. Correlation Between the Complexity of Coronary Lesions and High-Sensitivity Troponin Levels in Patients with Acute Coronary Syndrome. Int. J. Cardiovasc. Sci. 31 (3) • May-Jun 2018. https://doi.org/10.5935/2359-4802.20180014

[7]. Silvia López-Fernández, Ángel Cequier, Emili Iràculis et al. Elevated Troponin I Levels in Patients With Acute Coronary Syndrome Without ST Elevation Are Associated With Increased Complexity of the Culprit Lesion. Revista Espanola de Cardiologia. 2004; Vol.57. Issue 4:291-298. DOI: 10.1016/S1885-5857(06)60152-7

[8]. Shoji Sanada, Daihiko Hakuno, Luke J. Higgins, et al. IL-33 and ST2 comprise a critical biomechanically induced and cardioprotective signaling system. J Clin Invest. 2007; 117(6):1538-1549. https://doi.org/10.1172/JCI30634.

[9]. Weir RA, Miller AM, Murphy GE, et al Serum soluble ST2: a potential novel mediator in left ventricular and infarct remodeling after acute myocardial infarction. J Am Coll Cardiol. 2010; 55: 243–50. DOI: 10.1016/j.jacc.2009.08.047

[10]. Wei S, Mao L, Liu B, et al Serum biomarkers and the prognosis of AMI patients. Herz. 2014; 39: 384–9. DOI: 10.1007/s00059-013-3828-9

[11]. Yan-Peng Wang, Jian-Hua Wang, Xiao-Long Wang et al. Roles of ST2, IL-33 and BNP in predicting major adverse cardiovascular events in acute myocardial infarction after percutaneous coronary intervention. J Cell Mol Med. 2017 Nov; 21(11): 2677–2684. doi: 10.1111/jcmm.13183

[12]. Yeh RW, Kereiakes DJ, Steg PG, et al Benefits and Risks of Extended Duration Dual Antiplatelet Therapy After PCI in Patients With and Without Acute Myocardial Infarction. J Am Coll Cardiol. 2015; 65: 2211–21. DOI: 10.1016/j.jacc.2015.03.003

Table 1. Spearman's rank correlation between associations of levels of ST2 and Tp I in plasma with CVG indicators in patients NSTEMI

CVG indicators	Spearman R	P-value
RL ST2/RL Tp I in plasma (yes - 1, no - 0)		
Absence of plaques in LAD (yes - 1, no - 0)	0,15	0,04
Availability HSS in LAD (yes - 1, no - 0)	-0,17	0,02
Absence of plaques in LCx (yes - 1, no - 0)	0,21	0,003
The nature of the LCx lesion in points (0-3)	-0,16	0,01
The presence of 2-vascular lesions CA (yes - 1, no - 0)	-0,18	0,01
Absence HSS CA (yes - 1, no - 0)	0,19	0,01
Total CA score (0-9)	-0,16	0,02
RL ST2/RL Tp I in plasma (yes - 1, no - 0)		
No reliable relationships ($p < 0.05$) were found		
RH ST2/RH Tp I in plasma (yes - 1, no - 0)		
The presence of 3-vascular lesions CA (yes - 1, no - 0)	-0,19	0,007
RH ST2/RH Tp I in plasma (yes - 1, no - 0)		
The presence HSS RCA (yes - 1, no - 0)	0,17	0,01
The presence HSS LAD (yes - 1, no - 0)	0,15	0,03
Absence of plaques in LCx (yes - 1, no - 0)	-0,27	0,0001
The presence of LCx (yes - 1, no - 0)	0,21	0,003

The nature of the lesion LCx (0-3)	0,23	0,0009
The presence of 3-vascular lesions CA (yes - 1, no - 0)	0,23	0,001
Total CA score (0-9)	0,21	0,004

Note: CA – coronary artery, HSS – hemodynamically significant stenosis, RCA – right coronary artery, LAD – left anterior descending artery, LCx – left circumflex artery.