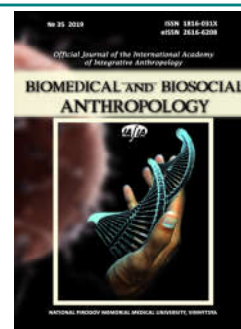




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The ratio of structural and functional status of myocardium to plasma level of stimulating growth factor expressed by gene 2 in patients with myocardial infarction without ST segment elevation

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Coronary heart disease remains one of the leading causes of temporary and persistent disability, invalidization and mortality in economically developed countries and is one of the most pressing problems in cardiology. Myocardial infarction is the most common manifestation of coronary heart disease and one of the main causes of the disability and mortality of the working population. The aim is to evaluate the structural and functional status of the myocardium in patients with acute myocardial infarction without ST segment elevation, depending on the plasma level of growth factor-stimulating factor expressed by gene 2 (ST2). 90 patients with acute myocardial infarction without ST segment elevation from 38 to 79 years old were examined. Among them, 60 (66.7 %) male patients. Echocardiography assessed the structural and functional status of the myocardium. By enzyme-linked immunosorbent assay determined ST2 levels in blood plasma. It has been determined that myocardial infarction without ST segment elevation is associated with more severe structural left ventricular remodeling, left atrial overload, and decreased left ventricular contractility. In patients, myocardial infarction without ST segment elevation is associated with an increase in cases of left ventricular concentric hypertrophy. Analysis of the nature of diastolic transmitral blood flow showed a significant increase in cases of blood flow by type of pseudonormalization (43.5 % versus 8.7 %). Therefore, the data obtained showed that in patients with myocardial infarction without ST segment elevation, ST2 elevation was associated with a more frequent manifestation of diastolic transmitral blood flow by type of pseudonormalization. Patients with myocardial infarction without ST segment elevation showed a predominance of systolic dysfunction in the group with relatively high levels of ST2 in the blood plasma, and no significant differences in remodeling types were found in all study groups.

Keywords: myocardial infarction without ST segment elevation, ST2, structural and functional state of the myocardium.

Introduction

For a long time, coronary heart disease (CHD), and especially its acute forms, remains the leading cause of mortality in Ukraine [7]. The most frequent and problematic, both in terms of prognosis and in terms of curation of patients, the consequence of coronary heart disease is myocardial dysfunction, which is asymptomatic in the initial stage and subsequently transformed into manifest heart failure. At the beginning of its origin, myocardial dysfunction in patients with coronary heart disease reveals impaired segmental myocardial contractility with preserved global ejection fraction and impaired diastolic function in the form of changes in myocardial relaxation. The described changes occur in the context of disorders of the neurohumoral

cascade with the activation of proliferative and profibrotic factors that initiate the formation of structural-geometric remodeling of the left ventricle and are a trigger for the development of severe myocardial dysfunction [4, 21].

The most accurate method for diagnosing disorders of myocardial structural and functional status is echocardiography, which allows you to diagnose these disorders in the early stages, while the most informative marker that accurately reflects the nature and severity of myocardial damage, especially in acute forms of coronary heart disease, to date not clarified. In this regard, various non-invasive biomarkers, such as: troponin I, natriuretic peptide, galectin-3, growth stimulation expressed gene 2

(ST2), have been studied very recently. Among the latter, enough attention is paid to ST2 today [2, 18, 20].

The physiological role of ST2 lies in two important mechanisms: it acts as a cardioprotector (the reverse process of remodeling (fibrosis) and hypertrophy), and also carries an immune response to inflammation [14, 17, 19]. With increasing concentration of ST2, there is a change in the extracellular matrix, which leads to an increase in the degree of fibrosis, the progression of hypertrophy and/or dilatation of the heart cavities, thereby reducing the contractility of the myocardium [3, 15, 24]. The response of healthy cardiac tissue to damage or mechanical stress involves the production and binding of IL-33 to ST2L, triggering a cardioprotective signaling cascade of fibrosis prevention, cardiac remodeling, and heart failure [1, 11, 23].

Based on the above, *the aim* of our study was to evaluate the relationship of structural and functional status of myocardium with plasma ST2 level in patients with myocardial infarction without ST segment elevation (NSTEMI). The latter, in the long run, provides an opportunity for the development of disease stratification and prognosis in this category of patients.

Materials and methods

The study is based on the results of a comprehensive survey of 90 patients with NSTEMI aged 38 to 79 (average 61.30 ± 1.10) years. Among them, 60 (66.7 %) patients were male and 30 (33.3%) were female, respectively, in the ratio of men to women - 2.0 to 1.0 ($p < 0.001$). All patients at the time of their inclusion in the study were hospitalized in the cardiology department for infarct patients of the Municipal non-profit enterprise "Vinnytsia Regional Clinical Medical Diagnostic Center for Cardiovascular Pathology" for 2016-2018 years.

As criteria for inclusion of patients in the study were considered: NSTEMI, which originated for the first time and the age of patients from 30 to 80 years. NSTEMI was diagnosed according to the order of the Ministry of Health of Ukraine No. 164 dated 03.03.2016 [10]. The criteria for not including in the study were: 1) past and repeated acute myocardial infarction; 2) the age of patients under 30 and over 80; 3) chronic heart failure (CHF) of IIB-III stages (at the time of inclusion in the study) according to the recommendations of the Working Group of the Ukrainian Association of Cardiologists (2016); 4) diseases of the respiratory system, kidneys and liver, which were accompanied by signs of pulmonary, renal and hepatic failure; anemic conditions with hemoglobin level < 110.0 g/l; 5) presence of rheumatic and congenital heart defects, idiopathic and inflammatory myocardial lesions; 6) malignancies, severe neuropsychiatric disorders, alcohol abuse.

Coronary-ventriculography (Siemens Anxiom) was performed in all subjects within 1 to 24 hours (an average of 6.8 ± 1.7 hours) from the moment of hospitalization. In 51

(56.7 %) patients, the procedure was performed in an emergency procedure (within 2 hours) and in 39 (43.3 %) - within 24 hours from the moment of hospitalization in the hospital.

Laboratory study of the level of ST2 in the blood plasma was performed by enzyme immunoassay on the first day of hospitalization before hospital coronary ventriculography.

Variation statistics were used to identify ST2 levels in the sample of patients. Thus, the relatively low relative level indicated a value of < 25 and a relatively high level of ST2 - > 75 percentile of the indicator. For NSTEMI patients, these levels were < 26 and > 56 ng/ml, respectively. Instead, the relatively moderate (or intermediate) ST2 level for these patients was 26-56 ng/ml. Further analysis of the data was performed in the selected three groups with relatively low, moderate and high levels of neurohormone. Comparison of percentages between groups was performed according to the criterion χ^2 , absolute values - by Kruskal-Wallis ANOVA & Mediantest.

Results

Time from the moment of destabilization of the patient's condition to hospitalization in the hospital ranged from 1 to 24 and averaged 10.60 ± 1.00 hours.

84.4 % of the surveyed patients had concomitant hypertension, 32.2 % - abdominal obesity of I-II degree and 50.0 % - aggravated hereditary cardiovascular morbidity, 45.6 % of patients were smokers.

Among clinical manifestations of NSTEMI, virtually all (95.6 %) patients identified typical anginal manifestations (pain or discomfort in the sternum). Only 4 (4.4 %) cases of myocardial infarction were atypical - the debut of the disease was dominated by symptoms of acute heart failure that corresponded to Killip III class. In 87.8 % of patients, ECG reported anterior localization of NSTEMI. All surveyed recorded an increase in plasma troponin levels compared to the reference rate of 2.5 to 18.4 (average 7.500 ± 0.500 ng/ml).

Complicated course of myocardial infarction was recorded in 22 (24.4 %) patients. In 15 (16.7 %), it was characterized by the occurrence of acute cardiac arrhythmias, in 3 (3.3 %) by conduction disturbances and in 4 (4.4 %) by acute heart failure (Killip-III). In 53.3 % of patients with acute cardiac arrhythmias, there were frequent high-grade ventricular extrasystoles (III - VI b Lown-Wolff gradations) with episodes of unstable ventricular tachycardia, 26.7 % had paroxysmal atrial fibrillation, and in 20.0 % cases there was a persistent ventricular tachycardia, which in all cases bore the character of monomorphic tachycardia. Out of 3 (3.3 %) patients with acute conduction disturbances, intermittent atrio-ventricular blockade of II-III were registered in 2 cases and in 1 case - sinoatrial blockade of II degree.

Percentile span of the parameters of the structural and functional status of the myocardium in patients with myocardial infarction without ST segment elevation

depending on the level of ST2 in the blood plasma are presented in table 1.

Analysis of the structural and functional status of the myocardium in patients from different groups revealed a correlation between echocardiographic indices and blood plasma ST2 levels. Thus, it was determined that significantly higher values of the left atrium ($p < 0.05$), left atrial index ($p < 0.05$), end-systolic size of the left ventricle ($p < 0.05$), end diastolic size of the left ventricle ($p < 0.05$), Ve/Va ratio ($p < 0.05$), local contractility index ($p < 0.05$), relative thickness of the myocardium ($p < 0.05$), left ventricular myocardial mass index ($p < 0.05$) were observed in patients with relatively high levels compared to relatively low ST2 levels; and smaller values of the ratio of the size of the right ventricle to the end-diastolic size of the left ventricle ($p < 0.05$), the magnitude of the ejection fraction ($p < 0.05$) and the ratio of the left atrium to the right atrium ($p < 0.05$).

Table 1. Percentile span of the parameters of the structural and functional state of the myocardium in patients with myocardial infarction without ST segment elevation depending on the level of ST2 in blood plasma.

Indicators	RL level of ST2 (n=23)	RM level of ST2 (n=44)	RH level of ST2 (n=23)
DA, mm	32 - 34	32 - 38	31 - 34
iDA, mm/m ²	15.9 - 18.6	15.9 - 19.1	15.6 - 18.4
BP, mm Hg/ml	0.41 - 0.75	0.41 - 0.67	0.42 - 0.77
LA, mm	35 - 39	37 - 41	37 - 42
iLA, mm/m ²	18.5 - 20.4	18.5 - 21.2	19.3 - 21.2
RA, mm	34 - 36	33 - 37	33 - 36
LA/RA	1.02 - 1.11	1.05 - 1.13	1.08 - 1.17
ESS, mm	31 - 36	33 - 36	34 - 38
EDS, mm	46 - 52	48 - 53	48 - 54
RV, mm	25 - 27	25 - 27	26 - 27
RV/EDS	0.50 - 0.58	0.48 - 0.54	0.47 - 0.53
EF, %	59 - 64	53 - 62	58 - 60
Ve/Va	0.56 - 0.78	0.58 - 0.74	0.60 - 1.20
ILC	1.12 - 2.70	1.62 - 3.03	1.80 - 3.25
TISd, mm	10 - 12	11 - 12	11 - 12
TBWd, mm	10 - 12	11 - 12	11 - 12
LV wall thickness	0.39 - 0.48	0.41 - 0.48	0.44 - 0.52
iLVM, g/m ²	91 - 117	100 - 127	106 - 130

Notes: here and in the future, RL - relatively low ST2 graduation rate; RM - relatively moderate ST2 graduation rate; RH - relatively high ST2 graduation rate; DA - aortic diameter; iDA - aortic diameter index; BP - blood pressure; LA - left atrium; iLA - left atrial index; RA - right atrium; LA/RA - the ratio of the left atrium to the right atrium; ESS - terminal systolic size of left ventricle; EDS - terminal diastolic size of left ventricle; RV - right ventricle; RV/EDS - the ratio of the size of the right ventricle to the end-diastolic size of the left ventricle; EF - ejection fraction; Ve/Va - velocity ratio peak E to peak A; ILC - local contractility index; TISd - the thickness of the interventricular septum in diastole; TBWd - thickness of back wall of left ventricle in diastole; LV wall thickness - the relative thickness of the left ventricular wall; iLVM - left ventricular myocardial mass index.

Table 2. Indicators of the character of structural-geometric remodeling of the left ventricle and the nature of diastolic transmitral blood flow in patients with myocardial infarction without ST segment elevation depending on the level of ST2 in blood plasma.

Indicators	RL level of ST2 (n=23)	RM level of ST2 (n=44)	RH level of ST2 (n=23)
The nature of structural-geometric remodeling of the left ventricle			
Normal geometry	5 (21.7 %)*	2 (4.5 %)	1 (4.3 %)
Concentric remodeling	5 (21.7 %)	14 (31.8 %)	4 (17.4 %)
Concentric hypertrophy	10 (43.5 %)	24 (54.5 %)	18 (78.3 %)*
Eccentric hypertrophy	3 (13.0 %)	4 (9.1 %)	0 (0 %)
The nature of diastolic transmitral blood flow			
Normal	4 (17.4 %)#	5 (11.4 %)	0 (0 %)
Violation of relaxation	17 (73.9 %)	28 (63.6 %)	13 (56.5 %)
Pseudonormalization	2 (8.7 %)	11 (25.0 %)	10 (43.5 %)*

Notes: * - significant differences between groups RL level of ST2 and RM level of ST2 (greater values are noted); # - significant differences between groups RL level of ST2 and RH level of ST2 (greater values are noted).

In addition, significantly higher values of left ventricular end-systolic size ($p < 0.05$), Ve/Va ratio ($p < 0.01$), and local contractility index are observed in patients with relatively high levels compared with patients with relatively moderate ST2 graduation levels ($p < 0.05$).

Analysis of structural-geometric remodeling of the left ventricle (Table 2), in turn, showed that in patients with relatively high levels of ST2 in the blood plasma compared with patients with relatively low levels of ST2, there was a significant increase in cases of concentric hypertrophy ($p < 0.05$). In turn, in patients with relatively moderate levels relative to the relatively low ST2 level, there was a significant reduction in cases of remodeling with normal geometry ($p < 0.05$). In patients, NSTEMI is associated with an increase in cases of left ventricular concentric hypertrophy (see Table 2). An analysis of the nature of diastolic transmitral blood flow showed a significant increase in cases of pseudonormalization of blood flow ($p < 0.01$), a decrease in normal diastolic transmitral blood flow ($p < 0.05$) in patients with relatively high levels compared to relatively low levels of ST2 in blood plasma (see Table 2).

Discussion

The nature of diastolic transmitral blood flow showed changes in the group of relatively high levels by type of pseudonormalization of blood flow. Our findings demonstrate an association of ST2 with structural myocardial abnormalities in this particular form of CHD. Increased ST2 levels greater than 56 ng/ml in patients with NSTEMI have been found to be associated with more severe left ventricular structural remodeling, left atrial overload, and decreased left ventricular contractility. The latter is manifested by a decrease in the magnitude of the ejection fraction and an increase in the value of Ve/Va, which changes towards the formation of a restrictive type of diastolic transmitral blood

flow. The ratio of the size of the right ventricle to the end-diastolic size of the left ventricle indicates the advantage of dilatation of the left ventricle over the right ventricle. Our findings indicate that in patients with NSTEMI, an increase in ST2 was associated with a more frequent manifestation of diastolic transmitral blood flow by type of pseudonormalization. The latter occurs in parallel with a decrease in the contractile capacity of the left ventricle.

According to the world literature, this relationship has been investigated in chronic heart failure [5, 16, 22], which has arisen against any background, and in acute myocardial infarction with ST segment elevation (STEMI) [6, 12], in while at NSTEMI, there is virtually no data available and the available studies relate to the closest (within 28 days) forecast [8, 9, 13], while structural remodeling is considered by us in the context of a more distant forecast.

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СПІВВІДНОШЕННЯ СТРУКТУРНО-ФУНКЦІОНАЛЬНОГО СТАНУ МІОКАРДА З ПЛАЗМОВИМ РІВНЕМ СТИМУЛЮЮЧОГО ФАКТОРУ РОСТУ, ЩО ЕКСПРЕСУЄТЬСЯ ГЕНОМ 2 У ПАЦІЄНТІВ З ІНФАРКТОМ МІОКАРДА БЕЗ ЕЛЕВАЦІЇ СЕГМЕНТУ ST
Межієвська І.А.

Ишемична хвороба серця залишається однією з провідних причин тимчасової та стійкої втрати працездатності, інвалідизації та смертності населення в економічно розвинутих країнах і є однією з найактуальніших проблем кардіології. Інфаркт міокарда є найчастішим проявом ІХС та однією з основних причин інвалідності й смертності працездатного населення. Мета роботи - оцінити структурно-функціональний стан міокарда у пацієнтів з гострим інфарктом міокарда без елевації сегменту ST залежно від плазмового рівня стимулюючого фактору росту, що експресується геном 2 (ST2). Обстежено 90 пацієнтів з гострим інфарктом міокарда без елевації сегменту ST віком від 38 до 79 років. Серед них 60 (66,7 %) пацієнтів чоловічої статі. За допомогою ехокардіографії оцінено структурно-функціональний стан міокарда. Імуноферментним аналізом визначено рівень ST2 у плазмі крові. Визначено, що інфаркт міокарда без елевації сегменту ST асоціюється з більш тяжким структурним ремоделюванням лівого шлуночка, перевантаженням лівого передсердя та зниженням скоротливої здатності лівого шлуночка. У пацієнтів інфаркт міокарда без елевації сегменту ST асоціюється зі зростанням випадків концентричної гіпертрофії лівого шлуночка. Аналіз характеру діастолічного трансмітрального кровотоку показав суттєве збільшення випадків кровотоку за типом псевдонормалізації (43,5 % проти 8,7 %). Отже, отримані дані показали, що у пацієнтів з інфарктом міокарда без елевації сегменту ST підвищення рівня ST2 було асоційовано з більш частим виявленням діастолічного трансмітрального кровотоку за типом псевдонормалізації. У пацієнтів з інфарктом міокарда без елевації сегменту ST встановлено переважання ознак систолічної дисфункції в групі відносно високого рівня ST2 в плазмі крові, а суттєвих відмінностей стосовно типів ремоделювання у всіх групах обстежених виявлено не було.

Ключові слова: інфаркт міокарда без елевації сегмента ST, ST2, структурно-функціональний стан міокарда.

СООТНОШЕНИЕ СТРУКТУРНО-ФУНКЦИОНАЛЬНОГО СОСТОЯНИЯ МИОКАРДА С ПЛАЗМЕННЫМ УРОВНЕМ СТИМУЛИРУЮЩЕГО ФАКТОРА РОСТА, КОТОРЫЙ ЭКСПРЕССИРУЕТСЯ ГЕНОМ 2 У ПАЦИЕНТОВ С ИНФАРКТОМ МИОКАРДА БЕЗ ЭЛЕВАЦИИ СЕГМЕНТА ST
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Ишемическая болезнь сердца является одной из самых актуальных проблем кардиологии и остается одной из ведущих причин временной и стойкой утраты трудоспособности, инвалидизации и смертности населения в экономически развитых странах. Инфаркт миокарда является наиболее частым проявлением ИБС, а также одной из основных причин инвалидности и смертности трудоспособного населения. Цель работы - оценить структурно-функциональное состояние миокарда у пациентов с острым инфарктом миокарда без подъемов сегмента ST в зависимости от плазменного уровня стимулирующего фактора роста, который экспрессируется геном 2 (ST2). Обследовано 90 пациентов с острым инфарктом миокарда без элевации сегмента ST в возрасте от 38 до 79 лет. Среди них было 60 (66,7 %) пациентов мужского пола. При помощи эхокардиографии оценили структурно-функциональное состояние миокарда. Иммуноферментным анализом определили уровень ST2 в плазме крови. Инфаркт миокарда без элевации сегмента ST ассоциируется с более тяжелым структурным ремоделированием левого желудочка, перегрузкой левого предсердия и снижением сократительной способности левого желудочка. У пациентов инфаркт миокарда без элевации сегмента ST ассоциируется с ростом случаев концентрической гипертрофии левого желудочка. Анализ характера диастолического трансмитрального кровотока показал существенное увеличение случаев кровотока по типу псевдонормализации (43,5 % против 8,7 %). Таким образом, полученные данные показали, что у пациентов с инфарктом миокарда без элевации сегмента ST повышение уровня ST2 было ассоциировано с более частым выявлением диастолического трансмитрального кровотока по типу псевдонормализации. У пациентов с инфарктом миокарда без элевации сегмента ST установлено преобладание признаков систолической дисфункции в группе относительно высокого уровня ST2 в плазме крови, а существенных различий в отношении типов ремоделирования во всех группах обследованных выявлено не было.

Ключевые слова: инфаркт миокарда без элевации сегмента ST, ST2, структурно-функциональное состояние миокарда.