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Sid' E.[1], Iatsenko O.[2]
[1] Zaporizhzhia Medical Academy of Postgraduate Education, Zaporizhzhia, Ukraine
[2] Zaporizhzhia State Medical University, Zaporizhzhia, Ukraine

Сидь Е.В.[1], Яценко О.В.[2]
[1] Запорожская медицинская академия последипломного образования, Запорожье, Украина
[2] Запорожский государственный медицинский университет, Запорожье, Украина

The Levels of Markers of Systemic Inflammatory Response among Patients with Acute Myocardial Infarction and Permanent Premature Ventricular Contractions

Уровни маркеров системного воспалительного ответа у пациентов с острым инфарктом миокарда со стойкими желудочковыми экстрасистолами

Abstract

Introduction. Despite significant advances in modern cardiology in improving the treatment of patients with coronary heart disease, its clinical form called acute myocardial infarction is a potentially fatal event and cause of death in the adult population. The immune system reacts to acute myocardial infarction and the development of its complications. It is believed that immuno-inflammatory reactions may be the root cause of arrhythmias. However, the mechanisms of these reactions in the development of ventricular arrhythmias remain poorly understood. It seems appropriate to study the state of the systemic inflammatory response in patients with acute myocardial infarction with ventricular arrhythmias. It will allow to assess the role of inflammation in the development of ventricular arrhythmias, as well as to determine the predictor value of the markers of systemic inflammatory response in this group of patients.

Purpose. To analyze the levels of markers of systemic inflammatory response among patients with acute myocardial infarction and permanent premature ventricular contractions.

Materials and methods. The study involved 351 patients with coronary artery disease (CHD): 185 patients with acute myocardial infarction with stable ST segment elevation and 91 ones with acute myocardial infarction without ST segment elevation; the control group consisted of 75 patients with angina pectoris. The sample of patients was carried out in the period from 2015 to February 2018. In the study, the ST segment elevation myocardial infarction (STEMI) group included 96 (51.9%) residents of the city and 89 (48.1%) ones of the village; the non-ST segment elevation myocardial infarction (NSTEMI) group consisted of 42 (46.2%) residents of the city and 49 (53.8%) ones of the village. The groups were comparable in the proportion of patients from the city and village. All the surveyed persons were comparable in age, social status and sex (the ratio of men and women was 4 to 1).

The levels of the acute myocardial infarction biomarkers were determined at the first contact. The blood was taken 24 hours after the onset of clinical manifestations of AMI to determine the biomarkers of inflammation.

The premature ventricular contractions (PVCs) were identified with the help of Holter ECG monitoring that lasted for 24 hours. Identification of the PVCs was conducted in 5 days after STEMI. The PVCs of the 1–2 gradations by B. Lown and heart rate turbulence were the criteria for inclusion in the study.
Results. The highest level of high-sensitivity C-reactive protein (hs-CRP) was in the group of STEMI patients – 10.63 [9.20–13.44] mg/l and noticeably exceeded the level of this indicator in the group of NSTEMI patients – 8.47 [7.05–10.61] mg/l ($p<0.05$). In comparison with the group of patients with stable CHD, where the level of hs-CRP was 4.78 [3.60–6.45] mg/l, in the group of patients with STEMI, its level was 2.3 times higher ($p<0.05$). The hs-CRP level in patients with STEMI with premature ventricular contractions was 11.82 [9.86; 14.00] mg/l, and it was significantly higher than 9,67 [7.43; 12.00] mg/l in the group STEMI without PVCs ($p<0.05$). The hs-CRP had the largest area under the ROC curve (AUC=0.695, 95% CI 0.624–0.761) among the analyzed markers of immuno-inflammatory response. At the cut-off point >10.05 mg/l, the sensitivity was 70.25% and specificity was 64.06%. The relative risk of occurrence of PVCs in patients with STEMI for hs-CRP >10.05 mg/l was 1.646, 95% CI 1.273–2.129.
Conclusions. The systemic inflammatory response behind the values of hs-CRP, tumor necrosis factor-α, and interleukin-6 levels are more pronounced in patients with STEMI than in those with NSTEMI. The relative risk of premature ventricular contractions increases by 1.646 times in patients with acute myocardial infarction with the increase of the level of hs-CRP higher than 10.05 mg/l.
Keywords: acute myocardial infarction, acute myocardial infarction with stable ST segment elevation, inflammation, coronary heart disease, premature ventricular contractions.

Резюме

Введение. Несмотря на значительные достижения современной кардиологии в совершенствовании лечения пациентов с ишемической болезнью сердца, ее клиническая форма – острый инфаркт миокарда – является потенциально фатальным событием и причиной смерти среди взрослого населения. Иммунная система реагирует на острый инфаркт миокарда и развитие его осложнений. Считается, что первопричиной аритмий могут быть иммуновоспалительные реакции. Однако механизмы развития этих реакций при образовании желудочковых аритмий остаются малоизученными. Представляется целесообразным изучить состояние системного воспалительного ответа у пациентов с острым инфарктом миокарда с желудочковыми экстрасистолами. Это позволит оценить роль воспаления в развитии желудочковых аритмий, а также определить прогностическое значение маркеров системного воспалительного ответа у данной группы пациентов.
Цель. Проанализировать уровни маркеров системного воспалительного ответа у пациентов с острым инфарктом миокарда со стойкими желудочковыми экстрасистолами.
Материалы и методы. В исследовании принял участие 351 пациент с ИБС: 185 человек было с острым инфарктом миокарда со стабильным подъемом сегмента ST и 91 пациент с острым инфарктом миокарда без подъема сегмента ST, контрольную группу составили 75 пациентов со стабильной стенокардией. Выборка пациентов проводилась в период с 2015 г. по февраль 2018 г. В исследовании группа STEMI включала 96 (51,9%) жителей города и 89 (48,1%) жителей из сельской местности, группа NSTEMI состояла из 42 (46,2%) жителей города и 49 (53,8%) жителей из сельской местности. Группы были сопоставимы по доле пациентов из города и из сельской местности. Все обследованные лица были сопоставимы по возрасту, социальному положению и полу (соотношение мужчин и женщин составило 4 к 1).
Уровни биомаркеров острого инфаркта миокарда определяли при первом контакте. Для определения биомаркеров воспаления кровь брали через 24 часа после начала клинических проявлений острого инфаркта миокарда.
Желудочковые экстрасистолы были выявлены при помощи холтеровского мониторирования ЭКГ в течение 24 часов. Выявление желудочковых экстрасистол проводили через 5 дней после

STEMI. Критерием включения в исследование было наличие желудочковых экстрасистол 1–2 градаций по B. Lown и турбулентность сердечного ритма.

Результаты. Самый высокий уровень высокочувствительного С-реактивного белка был в группе пациентов STEMI и составил 10,63 [9,20–13,44] мг/л и достоверно превышал уровень этого показателя в группе пациентов NSTEMI – 8,47 [7,05–10,61] мг/л ($p<0,05$). По сравнению с группой пациентов со стабильной ИБС, где уровень высокочувствительного С-реактивного белка составлял 4,78 [3,60–6,45] мг/л, в группе пациентов STEMI его уровень был в 2,3 раза выше ($p<0,05$). Уровень высокочувствительного С-реактивного белка у пациентов STEMI с желудочковой экстрасистолией составил 11,82 [9,86; 14,00] мг/л и был достоверно выше – 9,67 [7,43; 12,00] мг/л – в подгруппе STEMI без желудочковой экстрасистолией ($p<0,05$). Наибольшую площадь под кривой ROC (AUC=0,695, 95% ДИ 0,624–0,761) среди анализируемых маркеров иммуновоспалительного ответа имел высокочувствительный С-реактивный белок. В точке отсечения >10,05 мг/л чувствительность составила 70,25%, а специфичность – 64,06%. Относительный риск возникновения желудочковой экстрасистолии у пациентов со STEMI при уровне высокочувствительного С-реактивного белка >10,05 мг/л составил 1,646, 95% ДИ 1,273–2,129.

Выводы. Системная воспалительная реакция, лежащая в основе значений уровней высокочувствительного С-реактивного белка, фактора некроза опухоли-α и интерлейкина-6, более выражена у пациентов со STEMI, чем у пациентов с NSTEMI. Относительный риск возникновения желудочковой экстрасистолии увеличивается в 1,646 раза среди пациентов с острым инфарктом миокарда при повышении уровня высокочувствительного С-реактивного белка выше 10,05 мг/л.

Ключевые слова: острый инфаркт миокарда, острый инфаркт миокарда со стабильным подъемом сегмента ST, воспаление, ишемическая болезнь сердца, желудочковая экстрасистолия.

■ INTRODUCTION

Despite all the preventive, diagnostic and therapeutic possibilities, today diseases of the circulatory system are the leading causes of death in the adult population in the world. Even with significant advances in modern cardiology in improving the treatment of patients with CHD, its clinical form called acute myocardial infarction (AMI) is a potentially fatal event and cause of death in the adult population [1, 2].

The term «acute myocardial infarction» is used when the fact of myocardial damage is proven and there are clinical manifestations of myocardial necrosis, which makes it possible to assume the presence of ischemia of the heart. Modern guidelines of the cardiology European society have recommendations with many years of evidence-based experience in diagnosing both STEMI (ST-segment elevation myocardial infarction) and NSTEMI (non ST-segment elevation myocardial infarction) variants of acute myocardial infarction. They note that biomarkers of myocardial necrosis must meet modern requirements for accuracy, reproducibility, and especially sensitivity and specificity. However, the search for new biological markers for diagnosing acute myocardial infarction and predicting the occurrence of undesirable cardiovascular events is still underway [3, 4].

The immune system reacts to acute myocardial infarction and the development of its complications. Systemic and local inflammatory response occurs with the development of acute myocardial infarction. It

is believed that immuno-inflammatory reactions may be the root cause of arrhythmias. However, the mechanisms of these reactions development in the development of ventricular arrhythmias remain poorly understood. Ventricular arrhythmias occupy a special place among predictors of an unfavorable prognosis in patients with both acute myocardial infarction and postinfarction cardiosclerosis [5].

Currently, acute or chronic inflammatory processes are considered as pathogenetic mechanisms. All of them can lead to structural remodeling of the heart, through which premature ventricular contractions develop and progress [6, 7].

The spectrum of ventricular arrhythmias can range from asymptomatic single premature ventricular contractions (PVCs) to fatal arrhythmias. In addition, multiple forms of ventricular arrhythmias can be detected in patients with coronary heart disease [8, 9].

It seems appropriate to study the state of the systemic inflammatory response among patients with acute myocardial infarction with ventricular arrhythmias. It will allow to assess the role of inflammation in the development of ventricular arrhythmias, as well as to determine the predictor value of markers of systemic inflammatory response in this group of patients [10].

■ PURPOSE OF THE STUDY

To analyze the levels of markers of systemic inflammatory response among patients with acute myocardial infarction and permanent premature ventricular contractions.

■ MATERIALS AND METHODS

The results of the study are based on the data obtained from a comprehensive examination of 351 patients with CHD: with STEMI was 185 ones, with NSTEMI 91 patients, the control group consisted of 75 patients with angina pectoris (with II functional class (FC) was 38 ones and III FC had 37 patients). Screening of patients was carried out at the base of Municipal institution «Regional medical center of cardiovascular diseases» Zaporizhzhia Regional Council in the period from 2015 to January 2018. In the study, the STEMI group included 96 (51.9%) residents of the city and 89 (48.1%) ones of the village, the NSTEMI group consists 42 (46.2%) residents of the city and 49 (53.8%) ones of the village. The groups were comparable in the proportion of patients from the city and village. Almost 25 healthy volunteers were examined for determine the normal level of inflammatory markers on an outpatient basis (average age is 59.0 [55.0; 60.0] years) All 351 examined persons were comparable by age, social status and sex (the ratio of men to women was 4 to 1).

The criteria for inclusion in the study are male and female patients' age is from 46 to 75 years; the presence of AMI in the first 12 hours from the onset; detected the PVCs of 1–2 gradations by B. Lown and heart rate turbulence on 5 day after STEMI; informed consent of the patient to participate in the study.

The criteria for exclusion from the study are atrioventricular block of the II–III degree; the PVCs of 3–5 gradations by B. Lown gradation;

permanent atrial fibrillation; the PVCs in the anamnesis before STEMI; revealed congenital or acquired hemodynamically significant heart disease;

chronic heart failure of the III stage; revealed aneurysm of the left ventricle; decompensated comorbidities; acute inflammatory diseases or exacerbation of chronic ones; coronary artery bypass grafting in the anamnesis; cancer.

All patients underwent complex clinical, instrumental and laboratory examinations. Verification of the AMI diagnosis was performed based on the ESC/ACCF/AHA/WHF Third universal definition of myocardial infarction (2012), taking into account the recommendations of the ESC Fourth universal definition of myocardial infarction (2018) [11, 12]. The patients were divided into groups after the establishment of the compliance of patients regarding the criteria for inclusion / exclusion from the study depending on the presence/or absence of ST-Segment elevation and stable CHD:

- the first group includes 185 patients with STEMI (average age is 60.0 [52.0; 64.0] years);
- the second group consists of 91 patients with NSTEMI (average age is 61.0 [56.0; 66.0] years);
- the third group includes 75 patients with stable CHD (average age is 62.0 [57.0 ; 65.0] year).

Characteristics of patients involved in the study

The risk of death of patients was calculated on the GRACE 2.0 scale (Global Registry of Acute Coronary Events). The median values of scores on this scale had a noticeable difference between the groups of examined patients, and amounted to 104.5 [91.0–115.0] points in the group of STEMI patients versus 85.0 [75.0–95.0] points in the group of NSTEMI patients ($p<0.05$).

The levels of the AMI biomarkers were determined at first contact. The median seeking medical serves time of patients with STEMI was 205.0 [130.0; 350.0] minutes and had no significant difference with the value of 215.0 [115.0; 345.0] minutes in the NSTEMI group ($p>0.05$). According to the seeking medical serves time from the beginning of clinical manifestations of the disease, the groups of patients were comparable. The level of MB-CPK in STEMI patients was 47.63 [24.10–96.75] U/l and was considerably higher than the level of 32.70 [19.72–45.45] U/l in the NSTEMI group ($p<0.05$). The median level of troponin I was 4.90 [0.92–6.81] ng/ml in the group of STEMI patients and was significantly higher compared to the value of 1.28 [0.63–3.29] ng/ml in the group of NSTEMI patients ($p<0.05$).

ECG monitoring was carried out with calculation of heart rate turbulence indicators. The PVCs was identified by Holter ECG monitoring lasted 24 hours. Registration was carried out with the three-channel Cardiosens-K (KhAI-Medica, Ukraine), followed by an analysis of the record for the standard protocol. Identified the PVCs 5 days after STEMI. If less 6 PVCs were found suitable for heart rate turbulence analysis, than the data were not included in the study. Holter ECG was performed against the background of beta-blockers therapy among all patients [13].

Immunoenzyme analysis

The blood was taken 24 hours after the onset of clinical manifestations of AMI to determine biomarkers of inflammation. The blood sampling was carried out from the ulnar vein into 50 mg EDTA tubes, it was centrifuged at 3000 RPM for 15 minutes. The obtained plasma was separated, and then were immediately freezed and stored at a temperature not less than –24 °C

degrees until the time of the study. The level of highly sensitive C-reactive protein (hs-CRP), tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6) and interleukin-10 (IL-10) in blood plasma were determined by enzyme-linked immunosorbent assay method using standard «ELISA-Best» kits (Vektor-Best, Russia) according to the method described in the test systems instructions. The analysis was carried out using the «SUNRISE TS» enzyme immunoassay (Austria). The content of interleukin-6 (interleukin-10, TNF-α) in blood plasma was expressed in PG/ml.

Treatment of patients

Patients were treated in conformity with the recommendations of ESC (2012, 2017), according to the order No. 455 of the Ukraine's Ministry of health dated 02.07.2014 and No. 164 of the Ministry of health of Ukraine dated 03.03.2016. In the group of patients with STEMI was the following therapy: systemic thrombolytic therapy was performed among 42 (22.7%) patients, stenting was among 84 (45.4%) patients, combination of thrombolytic therapy and stenting were among 43 (23.2%) patients and conservative treatment was among 16 (8.7%) patients. The follow-up treatment was carried out with the anticoagulants, antiaggregants, selective β-blocker, inhibitors of angiotensin converting enzyme, lipid-lowering drugs and nitrates.

Statistical processing of the obtained results

The obtained data had a different distribution from the normal, and are presented in the form of median and inter quartile Me range [Q25; Q75]. The results of the study were processed by parametric or nonparametric statistics depending on the sample allocation using specialized computer applications ApacheOpenOffice (version 4.1) and PSPP (version 0.10.2, GNU Project, 1998–2016).

While comparing more than two independent variables, they used a variance analysis (One-way ANOVA), followed by a posteriori test. Equality of variances was checked using Leven's test. They used the criterion Scheff while equality of variances in the studied groups, and they used to test T2-Tamhane while the absence of equality of variances was. In the case of distribution of data distinct from normal, they used the analogue of dispersion analysis by the Kruskal – Wallis method followed by post-hoc analysis using the Dunn criterion.

ROC analysis (ROC-Receiver Operating Characteristic curve) was also performed, area under ROC curve (AUC – Area under the ROC curve) and its 95% confidence interval (CI), sensitivity (Se) and specificity (Sp) were calculated. The model was considered to be adequate at statistically significant at AUC value more than 0.5. Cut off was determined using Youden index J, using the Cut off values, relative risk was calculated.

■ RESULTS

Conducted the determination of the levels of biomarkers among patients with STEMI, NSTEMI and group stable CHD are given in the table 1.

The highest level of hs-CRP was in the group of STEMI patients and amounted to 10.63 [9.20–13.44] mg/l and noticeably exceeded the level of this indicator in the group of NSTEMI patients was 8.47 [7.05–10.61] mg/l

Table 1
The levels of biomarkers in patients with STEMI, NSTEMI and the group with stable CHD (Me [Q_{25}–Q_{75}], n=351)

Variable	STEMI (n=185)	NSTEMI (n=91)	Stable CHD (n=75)
	1	2	3
hs-CRP, mg/l	10.63 [9.20–13.44]	8.47 [7.05–10.61]	4.78 [3.60–6.45]
P-value	p_{1-2}<0.001	p_{2-3}<0.001	p_{1-3}<0.001
TNF-α, PG/ml	1.92 [1.43–2.78]	1.62 [1.03–2.15]	0.87 [0.56–1.68]
P-value	p_{1-2}<0.001	p_{2-3}=0.009	p_{1-3}<0.001
IL-6, PG/ml	10.87 [7.98–14.87]	7.20 [5.65–8.40]	2.00 [1.18–3.39]
P-value	p_{1-2}<0.001	p_{2-3}<0.001	p_{1-3}<0.001
IL-10, PG/ml	3.57 [2.40–5.77]	4.15 [2.89–4.83]	4.67 [3.41–6.65]
P-value	p_{1-2}=1.0	p_{2-3}=0.02	p_{1-3}=0.002
IL-6 / IL-10	2.82 [1.81–4.55]	1.78 [1.44–2.32]	0.47 [0.24–0.70]
P-value	p_{1-2}<0.001	p_{2-3}<0.001	p_{1-3}<0.001

(p<0.05). In comparison with the group of patients with stable CHD, where the level of hs-CRP was 4.78 [3.60–6.45] mg/l, in the group of patients with STEMI, its level was 2.3 times higher (p<0.05).

The level of TNF-α was significantly higher in the STEMI group of 1.92 [1.43–2.78] PG/ml versus 1.62 [1.03–2.15] PG/ml in the NSTEMI group of patients, (p<0.05) and was 2.4 times higher than the level of 0.87 [0.56–1.68] PG/ml in the group of patients with stable CHD (p<0.05). The TNF-α level of 1.62 [1.03–2.15] PG/ml in the group of NSTEMI patients was seriously 1.9 times higher than in the group of patients with stable CHD (p<0.05).

In AMI patients in both STEMI and NSTEMI groups, there was a great increase in IL-6 levels compared to the group of patients with stable CHD, where this indicator was 2.00 [1.18–3.39] PG/ml, 5 times and 3.2 times, respectively (p<0.05). At the same time, the level in the group of STEMI patients was considerably higher than the level of 7.20 [5.65–8.40] PG/ml in the group of NSTEMI patients (p<0.05). There was no significant difference between the level of IL-10 in all three study groups (p>0.05).

The ratio of IL-6 / IL-10 was noticeably higher in the group of patients with STEMI compared to NSTEMI – 2.82 [1.81–4.55] versus 1.78 [1.44–2.32], respectively (p<0.05). There was a highly reliable difference between the value of this indicator 0.47 [0.24–0.70] in the group of patients with stable CHD and the groups of patients with STEMI and NSTEMI (p<0.05).

We analyzed biomarkers of immuno-inflammatory response among patients with STEMI with and without PVCs. The results are shown in table 2.

The hs-CRP level among patients with STEMI with PVCs was 11.82 [9.86; 14.00] mg/l and was significantly higher than 9.67 [7.43; 12.00] mg/l in the group the STEMI without PVCs group (p<0.05). The TNF-α level in the group of patients with STEMI with PVCs was no significantly higher and amounted to 2.22 [1.46; 2.97] PG/ml versus 1.79 [1.35; 2.36] PG/ml in the group of patients with STEMI without PVCs (p>0.05).

There was no significant difference in level IL-6 in the groups of patients with STEMI with PVCs 11.53 [8.75; 15.02] PG/ml vs 9.39 [7.07; 14.10] PG/ml in the STEMI without PVCs group, (p>0.05). There was no significant difference

Table 2
The levels of biomarkers of immuno-inflammatory response in patients with STEMI (n=185)

Variable	STEMI with PVCs (n=121)	STEMI without PVCs (n=64)	Healthy volunteers (n=25)
	1	2	3
hs-CRP, mg/l	11.82 [9.86; 14.00]	9.67 [7.43; 12.00]	1.44 [1.12; 2.08]
P-value	p_{1-2}<0.001	p_{2-3}<0.001	p_{1-3}<0.001
TNF-α, PG/ml	2.22 [1.46; 2.97]	1.79 [1.35; 2.36]	0.44 [0.15; 0.56]
P-value	p_{1-2}=0.06	p_{2-3}<0.001	p_{1-3}<0.001
IL-6, PG/ml	11.53 [8.75; 15.02]	9.39 [7.07; 14.10]	1.10 [0.90; 1.25]
P-value	p_{1-2}=0.20	p_{2-3}<0.001	p_{1-3}<0.001
IL-10, PG/ml	3.45 [2.36; 5.63]	3.83 [2.50; 5.79]	4.98 [4.44; 6.43]
P-value	p_{1-2}=0.99	p_{2-3}=0.03	$p_{1-3=}$0.18
IL-6 / IL-10	3.02 [1.97; 4.98]	2.26 [1.54;3.67]	0.20 [0.18; 0.22]
P-value	p_{1-2}=0.02	p_{2-3}<0.001	p_{1-3}<0.001

in such indicator of immuno-inflammatory response as IL-10 among the examined persons. The IL-6/IL-10 ratio was higher in the group of patients with STEMI with PVCs.

Further, using two data sets: the first group of patients with STEMI with PVCs (n=121) and the second one with STEMI without PVCs (n=64) are performed ROC-analysis. The results are presented in table 3.

The largest area under the ROC curve (AUC=0.695, 95% CI 0.624–0.761) among the analyzed markers of immuno-inflammatory response had the hs-CRP level. At the cut-off point >10.05 mg/l sensitivity was 70.25% and specificity was 64.06%. The average quality of the model (AUC=0.615, 95% CI AUC 0.541–0.685) had the TNF-α level and the IL-6 / IL-10 ratio (AUC=0.636, 95% CI 0.562–0.705). Immuno-inflammatory response indicators such as the levels IL-6 and IL-10, although they had significant prognostic value according to ROC-analysis (AUC>0.5) for PVCs detection, however, their models were unsatisfactory (AUC 0.5–0.6).

Using the Cut off values, relative risk was calculated for analyzed indicators the indicators of immuno-inflammatory response. Obtained result are shown in the table 4.

For Variable IL-10 the value of RR was unreliable because 95% CI crossed a RR of 1. In the group with STEMI and PVCs were 36 patients with hs-CRP below 10.05 mg/l and 85 ones had a level higher than 10.05 mg/l in the group with STEMI without PVCs, respectively 40 patients below 10.05 mg/l and 24 above 10.05 mg/l. Relative risk of occurrence for PVCs among

Table 3
The cut off of indicators of immuno-inflammatory response for PVCs

Variable	Cut off	AUC	95% CI AUC	Se, %	Sp, %
hs-CRP, mg/l	>10.05	0.695	0.624–0.761	70.25%	64.06%
TNF-α, PG/ml	>2.47	0.615	0.541–0.685	45.45%	81.25%
IL-6, PG/ml	>8.16	0.594	0.519–0.665	78.51%	42.19%
IL-10, PG/ml	≤3.87	0.539	0.464–0.612	58.68%	50.00%
IL-6 / IL-10	>2.62	0.636	0.562–0.705	62.81%	62.50%

Table 4
The relative risk of occurrence of PVCs in patients with STEMI

Variable	Cut off	RR	95% CI RR
hs-CRP, mg/l	>10.05	1.646	1.273–2.129
TNF-α, PG/ml	>2.47	1.434	1.178–1.746
IL-6, PG/ml	>8.16	1.429	1.067–1.914
IL-10, PG/ml	≤3.87	1.104	0.891–1.367
IL-6 / IL-10	>2.62	1.449	1.155–1.818

patients with STEMI for hs-CRP >10.05 mg/l was 1.646, 95% CI 1.273–2.129. In the group with STEMI and PVCs were 66 patients with level TNF-α below >2.47 PG/ml and 55 ones above >2.47 PG/ml, in the group STEMI without PVCs, 51 patients had level TNF-α below >2.47 PG/ml and 13 ones had level TNF-α above >2.47 PG/ml respectively. Relative risk for TNF-α was 1.487, 95% CI 1.10–1.76. Relative risk for IL-6 was 1.429, 95% CI 1.067–1.914, cut-off point >8.16 PG/ml. The relative risk was related to the IL-6 / IL-10 ratio 1.449, 95% CI 1.155–1.818, cut-off point >2.62.

■ DISCUSSION

The processes of destruction and repair caused by myocardial necrosis are inextricably linked with the concept of «inflammation». They play an important role in post-infarction remodeling of the heart. The immuno-inflammatory response of various degrees is determined in almost all major forms of cardiac pathology, and AMI is a classic example of an aseptic inflammatory reaction that develops after the development of necrosis. Although there are certain limitations of the study, which is that until now, there is no standard cut-off point for the inflammatory process behind the IL-6, IL-10 markers [14], [15].

Prognostic value of PVCs at the present time remains understudied. The role of frequent PVCs as a predictor of unfavorable prognosis was demonstrated in the population of patients with myocardial infarction. Of particular importance is the stratifying the risk of PVCs among patients who have undergone STEMI [16].

Further studies will aim to determine whether an increase in plasma levels of hs-CRP, IL-6, or the IL-6/IL-10 ratio is associated with a high risk of adverse CHD. Thus, according to the results of the study by K. Suryana et al. (2017) reported that a high IL-6/ IL-10 ratio is a predictor of cardiovascular events in patients with acute coronary syndrome [17].

Thus, our data indicate significantly higher levels of markers of systemic inflammatory response in AMI in particular in the STEMI group, both in comparison with NSTEMI and the stress angina group. Identification of relevant differences between AMI subtypes, as shown here for proinflammatory cytokines, allows for a deeper understanding of the unique pathobiology of CHD. However, there is currently some disagreement about the activity of cytokines on the daily terms after STEMI, which demonstrates the lack of consensus on this issue. Also, the most optimal diagnostic timing of cytokine assessment in patients with acute myocardial infarction remains uncertain.

■ CONCLUSIONS

1. The systemic inflammatory response behind the values of hs-CRP, TNF-α, and IL-6 levels is more pronounced in patients with STEMI than in those with NSTEMI.
2. The relative risk of premature ventricular contractions increases in 1.646 times among patients with acute myocardial infarction with an increase in the level hs-CRP higher than 10,05 mg/l.

The authors certificate that the procedures and experiments we have done respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008 (5), as well as the national law.

The authors declare no conflict of interests.

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Contacts/Контакты: sidev@mail.ru