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Prognostic Value of Cytokines in Acute Coronary Syndrome

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Abstract: The article is devoted to the study and development of prognostic criteria for the severity of acute coronary syndrome, which is of great importance for health authorities in the organization of specialized cardiology and rehabilitation services. The proposed method allows early diagnosis and prevention of myocardial infarction, which is of great practical importance.

Keywords: cardiovascular diseases, acute coronary syndrome, cytokines, prognosis.

Introduction.

Coronary heart disease is the leading cause of death worldwide. Despite the fact that the prevalence of coronary heart disease continues to increase, there has been a decrease in the mortality rate associated with coronary heart disease in Europe over the past decades [3].

Some domestic and foreign scientists have studied the features of clinical manifestations and treatment of cardiovascular diseases in men and women. It was determined that women are more likely to have a more severe course of coronary heart disease (CHD) than men and a greater number of risk factors [2].

Of particular interest are the issues of gender differences in patients with coronary artery disease, an atypical form of angina pectoris. CHD is not a linearly progressive, stable process. CHD is characterized by a change of phases of stable course and exacerbation of the disease. In the population, only about 40-50% of all patients are aware of the presence of the disease and receive appropriate treatment, while in 50-60% the disease remains unrecognized [1.5].

Patients diagnosed with stable angina pectoris die from coronary heart disease 2 times more often than those without this disease [4].

The aim of the study was to study the cytokine status in acute coronary syndrome of gender dependence in order to develop criteria for the severity of its course.

Materials and methods of research:

The study included 120 patients with acute coronary syndrome (ACS) aged 25 to 85 years (the average age of men was 62.6 ± 1.47 years, and women 63.4 ± 1.14 years). The comparison group consisted of patients with progressive angina pectoris (PS), a total of 65 patients, including 31 women and 34 men (average age 64.2 ± 1.37 years).

ACS verification was carried out according to the requirements of the World Health Organization (WHO), classified according to the International Classification of Diseases (ICD-10).

Statistical processing of the results was carried out using Excel programs from the Microsoft Office XP application package (Microsoft, USA).

Results and their discussion.

The ratio of men-66 (55.0%) and women-54 (45.0%) was 1.2:1.0. A comparative analysis of the frequency of ACS, taking into account gender, showed an increase in cases of ACS in men aged 50 years and older - 57 (86.4%), in women aged 50 to 74 years - 44 (81.5%). An important element of the study is the study of gender characteristics of the mechanism of ACS development, which requires a comprehensive study of immunological and biochemical parameters of blood.

For a comparative evaluation of the results of the study, the patients were distributed taking into account gender:

Group 1 includes 54 women with ACS

Group 2 includes 66 men with ACS

Comparison group 3 includes 65 patients with PS

When calculating the indicators of the general blood test, depending on gender, anemia was found in patients of group 1 -107.1±2.01 g/l and an increase in ESR to 17.9±1.22 mm/h against the indicators of group 2: 115.3±1.33 g/l and 13.8±0.78 mm/h, respectively (Table 1).

Table 1. General laboratory blood tests, (M ±m)

Indicators	1-group n=54	2-group n=66	3-group n=65
Hemoglobin (Hb), g/l	107,1±2,01*	115,3±1,33	110,9±1,98
RBC,x10 9 /l	3,6±0,07	3,8±0,04	3,6±0,06
WBC,x10 10/l	7,4±0,29	7,6±0,28	7,2±0,22
ESR, mm/h	17,9±1,22*	13,8±0,78	16,1±1,14
Lymphocytes (%)	24,7±0,79	24,6±0,79	25,0±1,04
Monocytes (%)	4,4±0,34	4,8±0,28	4,5±0,30

*Note: * The values are reliable in relation to the indicators of group 2 (P<0.05)*

In the comparison group, the indicators of the general blood test were at the level of the indicators of group 1.

Thus, a comparative blood test showed the course of ACS in women against the background of anemia of the 1st degree and an increase in ESR to 17.9 mm/h.

To study the biochemical status of patients with ACS, taking into account gender, the levels of glucose, total protein, creatinine, urea, total bilirubin, ALT, AST, fibrinogen were determined.

The obtained results of a biochemical study of the patients' blood showed distinctive sides in the comparison group (Table 2).

Table 2. Biochemical spectrum of blood (M ±m)

Indicators	1-group n=54	2-group n=66	3-group n=65
Glucose, g/l	7,6±0,62	6,9±0,44	6,7±0,36
Total protein, g/l	64,4±1,0	63,7±1,02	62,3±1,37
Total bilirubin	17,8±0,56	18,5±1,5	17,4±0,57
Indirect bilirubin	4,3±0,29	4,3±0,81	4,2±0,28
ALT	31,2±3,61	32,1±1,61^	39,2±1,45*
AST	31,4±1,79	31,3±1,87^	39,5±2,02*
Urea, mmol/l	7,8±1,11	7,9±0,43^	6,4±0,23
Creatinine, mmol/l	49,2±1,05	48,7±1,11^^	63,6±0,84**
Fibrinogen, g/l	3,1±0,12	3,2±0,1	3,2±0,12

*Note: * The values are reliable in relation to the indicators of group 2 (P<0.05)*

In the comparison group, the indicators of the general blood test were at the level of the indicators of group 1.

Thus, the concentrations of hepatic transaminases in women with ACS on average are: ALT - 31.2±3.61 mmol/l, in men -32.1 ±1.61 mmol/l and AST -31.4±1.79 mmol/l, in men -31.3±1.87 mmol/L.

At the same time, ALT and AST in patients of the comparative group were increased to 39.2±1.45 mmol/l and 39.5±2.02 mmol/l, respectively, against the indicators of both group 1 and group 2 patients. Consequently, hepatic transaminases (ALT and AST) are an indicator of the transition of ACS to PS.

Such an increase in creatinine levels was detected in PS, against the indicators of the 1st and 2nd groups ($p<0.001$), (Table 3).

The study of the nature of inflammation in ACS allows predicting the transition of ACS to myocardial infarction (MI) or progressive angina pectoris (PS) and the choice of tactics for further management of patients in this category.

The results obtained do not have statistical significance, although they show the development of ACS in women against the background of anemia.

Thus, the analysis of biochemical blood parameters in ACS allowed us to establish the absence of a gender connection between the mechanism of its formation and the transition to MI and/or PS.

The study of cytokines in ACS showed an increase in the level of IL-1 to 77.6±1.29pg/ml in relation to the indicators of patients of the comparative and 2nd groups: 60.6±1.14pg/ml and 65.0±2.12 pg/ml, respectively, $P<0.05$ (Table 3).

Table 3. Cytokines in ACS

Indicators	1-group n=54	2-group n=66	3-group n=65
IL-1, пpg/ml	77,6±1,29	65,0±2,12*	60,6±1,14*
IL-10, pg/ml	29,7±2,71	43,8±2,19*	34,5±0,28^
VEGF, pg/ml	92,7±3,51	104,5±2,15*	98,4±0,06

*Note: * The values are reliable in relation to the indicators of group 2 (P<0.05)*

In the comparison group, the indicators of the general blood test were at the level of the indicators of group 1.

At the same time, the threshold level indicating the development of inflammation in ACS in women is the concentration of IL-1>67.0 pg/ml.

ACS in women is also accompanied by a decrease in the level of IL-10 by 1.5 times, against the values of the 2nd group-43.8 ± 2.19 pg/ml. Consequently, in women, ACS is accompanied by a decrease in IL-10, while the threshold level is IL-10<6.25 pg/ml.

It should be noted that IL-10 of the comparative group was reduced to -34.5±0.28 pg/ml, against the indicators of the 2nd group ($p<0.05$). This means that during the transition of ACS to PS, there is a decrease in IL-10, which indicates the depletion of the protective mechanisms of immunity.

It is known that IL-10 under certain conditions can stimulate the synthesis of immunoglobulins, activate T cells with cytotoxic action [8].

Consequently, the results obtained confirm the process of microcirculation disorders in the myocardium and a decrease in the activation of protection in ACS in women. At the same time, ACS in men is characterized by activation of the body's defense system by 1.5 times, which shows an increase in the level of IL-10 compared to ACS in women.

The study of the state of vascular endothelin factor in ACS revealed an increase in the concentration of VEGF in men to-104.5±2.15 pg/ml in relation to the indicators of group 1 -

92.7±3.51pg/ml (p<0.05). Consequently, in men with ACS, in response to damage to the vascular wall as a result of impaired microcirculation in the myocardium and spasm of coronary vessels, there is an increase in vascular endothelin factor in the blood by 1.12 times compared to the values of group 1 (in women).

Thus, the mechanism of ACS development in women is closely interrelated with the violation of intercellular interaction at the level of cellular structures, which is determined by the state of synthesis of pro and anti-inflammatory cytokines. The activity of inflammatory markers has an important prognostic value for assessing the progression of CVD. Postmenopausal women have a high risk of developing and progressing CVD and developing ACS. Regular examination and cytokine status study are important for early detection of ACS risk and prevention.

Thus, in women, ACS without ST segment elevation occurs against the background of anemia and lymphocytopenia.

A comparative analysis of the studied blood parameters in men, depending on the state of the ST segment, with ACS with a rise in the ST segment showed an increase in the level of Hb to 120.7 ± 1.33 g / l against these men without its rise -113.9± 2.35 g /l. The remaining indicators did not depend on the ST shift and were at the same level in men.

Thus, men are characterized by the lack of connection of laboratory blood parameters with the shift of the ST segment.

The pathomechanism of the ACS course at the molecular level was interesting. For a comparative evaluation of the data obtained, studies were conducted to study the cytokine profile.

A significant increase in IL-1 concentration was revealed in women with ST segment elevation - 103.4±3.0 pg/ml versus the values of the 1a group -61.3±1.69 pg/ml (p<0.001). The obtained result proves the development of systemic inflammation in women with ACS with ST segment elevation (Table 4).

Table 4. Cytokines in ACS depending on the state of the ST segment

Indicators	1a-group n=45	1b-group n=35
IL-1, ıpg/ml	61,3±1,69	103,4±3,0**
IL-10, pg/ml	44,9±2,42	35,5±2,96*
VEGF, pg/ml	88,5±3,32	45,4±2,53**

*Note: * The values are reliable in relation to the indicators of group 2 (P<0.05)*

In the comparison group, the indicators of the general blood test were at the level of the indicators of group 1.

In a study of the concentration of IL-10 in ACS in women, a statistically significant decrease was found to 35.5±2.96 pg/ml in ACS with ST segment elevation, compared to group 1a data-44.9±2.42 pg/ml (P<0.05).

Consequently, the result of studying IL-10 in ACS in women it indicates the depletion of compensatory defense mechanisms aimed at preserving coronary microcirculation.

It has a strong effect on vascular permeability, is a powerful angiogenic protein in various experimental systems, takes part in the processes of neovascularization in pathological situations.

The vascular endothelin factor index determines the risk of transformation of ACS into MI and/or angina pectoris.

The study found a statistically significant increase in the level of VEGF by 1.9 times (88.5±3.32pg/ml) in women of group 1a in relation to the indicators of group 1b-45.4±2.53pg/ml (p<0.05).

Consequently, an increase in the level of vascular endothelin factor indicates an increase in vascularization in women with ACS without lifting the segment.

A comparative assessment of the cytokine status in men with ACS showed an increase in the level of IL-1 by 1.7 times (up to 93.3±2.94 pg/ml) against the indicators of group 2a - 54.0±1.15 pg/ml ($p<0.05$), (Table 5).

Table 5. Cytokines in ACS depending on the state of the ST segment

Indicators	1a-group n=45	1b-group n=35
IL-1, ıpg/ml	54,0±1,15	93,3±2,94*
IL-10, pg/ml	60,7±1,72	28,9±2,11**
VEGF, pg/ml	151,7±5,97	89,0±3,66*

*Note: * The values are reliable in relation to the indicators of group 2 (P<0.05)*

In the comparison group, the indicators of the general blood test were at the level of the indicators of group 1.

At the same time, a decrease in IL-10 by 2.1 times and VEGF by 1.7 times was also found in men with ACS with a rise in the segment, ($P<0.001$).

Thus, the cytokine status in men with ACS without lifting the segment is aimed at preserving the compensatory mechanisms of the body's defense to improve coronary and cerebral circulation. In ACS with an increase in the ST segment in men, the cytokine status showed depletion of the body's reserve defense mechanisms, which indicates a high risk of its transformation into MI.

Taking into account the above, the established research data allowed predicting the outcome of ACS and determining informative indicators of the development of complications, taking into account gender.

At the same time, for both women and men, the threshold level indicating the development of inflammation in ACS is the concentration of IL-1 >67.0 pg/ml. Indicators of the severity of ACS in women are anemia, leukocytosis and lymphocytopenia.

Conclusions:

1. It has been established that ACS, regardless of age, is more common at the age of 50 years and older.
2. It has been established that hepatic transaminases (ALT and AST) are an indicator of the transition of ACS to PS.
3. ACS without ST segment elevation in women occurs against the background of anemia and lymphocytopenia. Men are characterized by the lack of connection of laboratory blood parameters with the shift of the ST segment.
4. The absence of a gender link between the mechanism of ACS development and its transition to MI and/or PS has been established
5. With ACS in men, there is an increase in vascular endothelin factor in the blood by 1.12 times, IL-1 by 1.7 times.
6. The threshold level indicating the development of inflammation in ACS for both women and men is the concentration of IL-1 >67.0 pg/ml
7. Indicators of the severity of ACS in women are anemia, leukocytosis and lymphocytopenia.

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