ИММУНОВОСПАЛИТЕЛЬНЫЕ МАРКЕРЫ СИНТРОПНЫХ СЕРДЕЧНО-СОСУДИСТЫХ ЗАБОЛЕВАНИЙ

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Резюме. Целью исследования явилось изучить иммуновоспалительные маркеры ишемической болезни сердца, артериальной гипертензии и их сочетанного течения.

В исследовании приняли участие 116 пациентов с сердечно-сосудистыми заболеваниями среднего и пожилого возраста. Средний возраст пациентов составляет 62,4±1,27 года. Все пациенты были обследованы в Бухарском филиале Республиканского научно-практического центра неотложной медицинской помощи. В ходе анализа было установлено, что уровень систолического артериального давления напрямую зависит от концентрации фибриногена – r = 0,3 и противоположно зависит от концентрации прокальцитонина (ПКТ) – r = -0,3 и IL-6 – r = -0,26. В то же время также была выявлена заметная положительная связь частоты сердечных сокращений с уровнем креатинина в крови – r = 0,35. Установленные связи показывают вклад синдрома воспаления (иммунного) в прогрессирование артериальной гипертензии, точнее, показателями прогрессирования артериальной гипертензии при ишемической болезни сердца являются креатинин, фибриноген, ПКТ и IL-6. Благодаря высокой и заметной корреляции с изучаемыми иммунобиохимическими показателями крови и функциональными показателями сердца, IL-6 является более информативным показателем прогрессирования ишемической болезни сердца с риском осложнений и полиорганной недостаточности. Таким образом, установленные связи в наших исследованиях позволяют включить вывод о том, что, наряду с вышеизложенным, факторами риска развития разрыва и/или аневризмы аорты при ИБС являются повышение уровня комплемента C3, IL-17 и ПКТ в крови. Следовательно, с повышением уровня VEGF в крови при ИБС AS возрастает риск увеличения толщины ЛЖ в диастолу, а повышение IL-6, IL-17A и мочевины в крови свидетельствует об уменьшении толщины ЛЖ в диастолу. диастола, которая позволяет дифференцировать рестриктивный вариант от гипертрофической формы при атипичной стенокардии. Благодаря высокой и заметной корреляции с изучаемыми иммунобиохимическими показателями крови и функциональными показателями сердца, IL-6 является более информативным показателем прогрессирования ишемической болезни сердца с риском осложнений и полиорганной недостаточности.

Ключевые слова: сердечно-сосудистые заболевания, ишемическая болезнь сердца, артериальная гипертензия, иммунитет

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Образец цитирования:

Ш.Ш. Ганиева, М.У. Эргашева, Х.Ш. Паноев «Иммуновоспалительные маркеры синтропных сердечно-сосудистых заболеваний» // Медицинская иммунология, 2023. Т. 25, № 4. С. 933-938.
doi: 10.15789/1563-0625-IIM-2763

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For citation:

Sh.Sh. Ganieva, M.U. Ergasheva, Kh.Sh. Panoev "Immunoinflammatory markers of syntropic cardiovascular diseases", Medical Immunology (Russia)/Meditsinskaya Immunologiya, 2023, Vol. 25, no. 4, pp. 933-938.
doi: 10.15789/1563-0625-IIM-2763

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DOI: 10.15789/1563-0625-IIM-2763

IMMUNO-INFLAMMATORY MARKERS OF SYNTROPIC CARDIOVASCULAR DISEASES

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Abstract. Objective: To study the immuno-inflammatory markers of coronary heart disease, arterial hypertension and their combined course.

The research work included 116 patients with cardiovascular disease of middle and old age. The average age of patients is 62.4±1.27. All patients were examined at the Bukhara branch of the Republican scientific and practical Center for emergency medical care. During the analysis, it was found that the level of systolic arterial blood pressure directly depends on the concentration of fibrinogen – r = 0.30 and oppositely depends on the concentration of procalcitonin (PCT) – r = -0.3 and IL-6 – r = -0.26. At the same time, a noticeable positive association of heart rate with creatinine in the blood – r = 0.35 was also revealed. The established connections show the contribution of inflammation syndrome (immune) in the progression of hypertension, or rather, indicators of the progression of hypertension in coronary heart disease are creatinine, fibrinogen, PCT and IL-6. Due to the high and noticeable correlation with the studied immuno-biochemical parameters of blood and functional parameters of the heart, IL-6 is a more informative indicator of the progression of coronary heart disease with the risk of complications and multiple organ failure. Thus, the established connections in our studies allow us to include the conclusion that, along with the above, risk factors for the development of rupture and/ or aneurysm of the aorta in CHD are an increase in the blood level of complement C3, IL-17 and PCT. Consequently, with an increase in the level of VEGF in the blood in CHD AS, the risk of an increase in the thickness of the LV in the diastole increases, and an increase in IL-6, IL-17A and urea in the blood shows a decrease in the thickness of the LV in the diastole, which makes it possible to differentiate the restrictive variant from the hypertrophic form in atypical angina. Due to the high and noticeable correlation with the studied immuno-biochemical parameters of blood and functional parameters of the heart, IL-6 is a more informative indicator of the progression of coronary artery disease with the risk of complications and multiple organ failure.

Keywords: cardiovascular diseases, ischemic heart disease, arterial hypertension, immunity

Introduction

In modern literature, the term “remodeling of the heart” has appeared, which includes the whole complex of changes in the mass, volume and shape of the left ventricle due to cardiomyocyte hypertrophy, as well as hypertrophy and hyperplasia of interstitial cells and endothelium, leading to a violation of the biochemical and functional properties of the myocardium under the influence of various factors, including hypertension [1].

Age is a recognized risk factor for cardiovascular diseases and mortality, including in patients with hypertension. In many ways, this influence is realized through age-related changes in the structure and function of blood vessels [6]. The results of research in recent decades confirm the crucial role of vascular endothelium in the regulation of vascular homeostasis, while a significant contribution of endothelial dysfunction (ED) to the development of cardiovascular diseases (CVD) has been established, in particular, participation in the pathogenesis of hypertension. It is generally recognized that the endothelium maintains a balance between the processes of vasoconstriction and vasodilation, produces inflammatory factors and vascular proliferation, participates in vascular remodeling and in thrombosis [2, 3, 4].

Transforming growth Factor-β (TGF-β) is a cytokine, a protein growth factor that plays an important role in the regulation of cell growth, differentiation and regeneration of various tissues. In the heart, TGF-β1 is induced by MI, pressure overload, with the introduction of angiotensin II, norepinephrine and is inhibited by nitric oxide [5]. In the myocardium, TGF-β1 is synthesized by fibroblasts and cardiomyocytes and plays a key role in the development of tissue fibrosis. Thus, along with the already “gold standard” biomarker of heart failure pro-BNP, new biomarkers are being intensively studied, such as markers of apoptosis, remodeling of connective tissue extracellular matrix and inflammation, which allow not only to more accurately diagnose, but also to determine the risk of developing or progressing heart failure and death [7, 8].

Objective: to study the immuno-inflammatory markers of coronary heart disease, arterial hypertension and their combined course.

Materials and methods

The study included 116 middle-aged and elderly patients with an average age of 62.4±1.27 years.

All patients were examined for cytokine status: IL-17A, TNFα, C3 complement component, VEGF

and a marker of the acute phase of inflammation – procalcitonin (PCT), the lipid spectrum of blood was studied, an echocardiogram (ECHOCG) and a biochemical blood test were performed.

The inclusion criteria were patients aged 45 to 74 years with a diagnosis of arterial hypertension (AH), coronary heart disease (CHD), confirmed by clinical and laboratory-instrumental methods, hospitalized in a hospital.

The patients of the study groups were comparable in age, gender, and the presence of CVD risk factors. AH verification was carried out according to the requirements of the World Health Organization (WHO), classified according to the International Classification of Diseases (ICD-10).

At the same time, the ACC/AHA Hypertension Guidelines (2017) classification was adhered to.

The exclusion criteria from the study were patients with acute myocardial infarction, acute coronary syndrome, acute infectious diseases, myocarditis and cardiomyopathies, chronic renal and hepatic insufficiency, pulmonary hypertension, congenital and acquired heart defects, systemic diseases, oncological and hematological diseases.

The research was carried out in accordance with the Helsinki Declaration.

Statistical processing of the results was carried out using Excel programs from the Microsoft Office XP application package (Microsoft, USA), correlation analysis was carried out using the Pearson method and evaluated on the Cheddock scale.

Results and discussion

To develop specific indicators of the progression of AH in CHD, a correlation analysis of the relationship of the studied blood parameters with the parameters of ECHOCG in patients with CHD selected for examination was carried out.

The dependence of the aortic diameter on the studied immunological parameters of the blood was established: a weak positive relationship with C3 – $r = 0.20$, with IL-17A – $r = 0.21$, with PCT – $r = 0.25$, a negative relationship between the aortic diameter and TNFα – $r = -0.21$, VEGF – $r = -0.2$.

The established relationships show a directly proportional positive dependence of the aortic diameter on the level of inflammatory markers: complement C3, IL-17A and PCT ($r = 0.2$-0.25).

In patients of this group, the average concentration of PCT was 0.2±0.01 ng/mL, which indicates the absence or low risk of infectious complications. The established weak positive association of PCT with the diameter of the aorta shows the risk of developing infectious complications in coronary heart disease and the importance of dynamic determination of PCT in this case.

Thus, the change in the diameter of the aorta depends on the degree of the infectious process in the body. Therefore, in case of CHD, it is important to take into account the state of syntropy, that is, the presence of concomitant diseases, for the prognosis of complications. At the same time, the longer the duration of chronization of the infectious process and the dynamic increase in the level of complement C3, IL-17 and PCT, the greater the risk of an increase in the diameter of the aorta in CHD.

It is known that the aorta regulates blood pressure and heart rate. Age-related enlargement of the aortic root leads to thinning of the aortic wall, increases the risk of aortic rupture and/or aortic aneurysm. Hypertension, hyperglycemia and hypercholesterolemia are risk factors for changes in the state of the vascular wall.

At the same time, negative weak connections of the aortic diameter with TNFα ($r = -0.2$) and VEGF ($r = -0.2$) were also revealed (Figure 1).

Consequently, the established negative associations of the aortic diameter with TNFα in CHD confirm the data of literature sources and allow the inclusion of TNFα in the list of indicators of the progression of hypertension in CHD as a marker of inflammation in CHD.

Taking into account the data of the above-mentioned modern literature sources, the negative connections between the diameter of the aorta and TNFα, VEGF in CHD indicate a compensatory phase of the body's defense system.

Thus, the established connections in our studies allow us to include the conclusion that, along with the above, risk factors for the development of rupture and/or aneurysm of the aorta in CHD are an increase in the blood level of complement C3, IL-17 and PCT. At the same time, the greater the degree of increase in the dynamics of the level of C3, IL-17 and PCT, the greater the risk of rupture and/or aneurysm of the aorta in CHD. Consequently, the more the level of TNFα, VEGF increases in coronary heart disease, the more the diameter of the aorta decreases. At the same time, it is necessary to take into account the state of syntropy.

In CHD revealed a noticeable positive association of final diastolic volume of the left atrium (FDV LA) with IGF-1 ($r = 0.30$), PCT ($r = 0.30$) and total blood protein ($r = 0.39$) against the background of a weak correlation with TGF-β1 – $r = 0.21$ (Figure 2).

The established features of the relationship show the effect of syntropy and chronic inflammation in CHD. At the same time, with coronary heart disease, an increase in the level of TGF-β1 and PCT in the blood against the background of an increase in total blood protein leads to an increase in FDV LA.

In CHD, the total blood protein has a noticeable negative relationship with final diastolic volume of the left ventricle (FDV LV) – $r = -0.31$, which makes it possible to determine it as an indicator of the shift of FDV LA and FDV LV. Consequently, in CHD, an increase in the level of total protein is accompanied

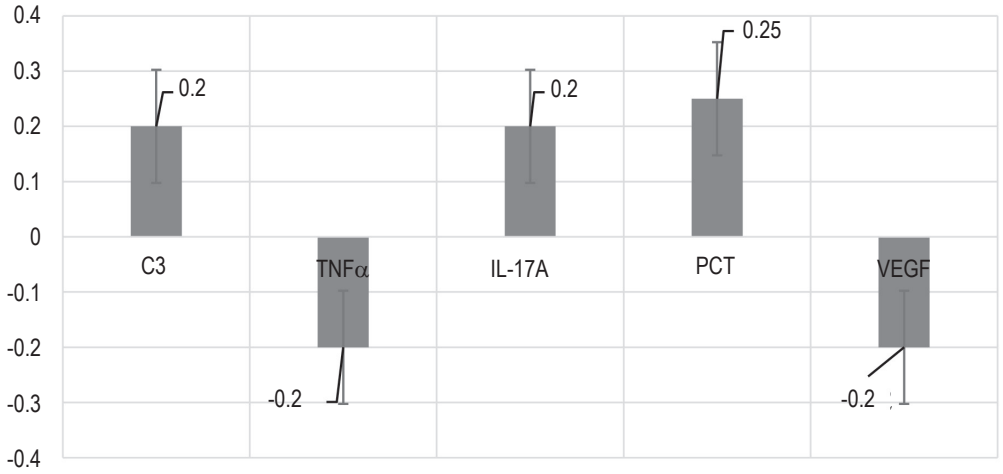

Figure 1. Relationship of aortic diameter with immuno-inflammatory markers in CHD

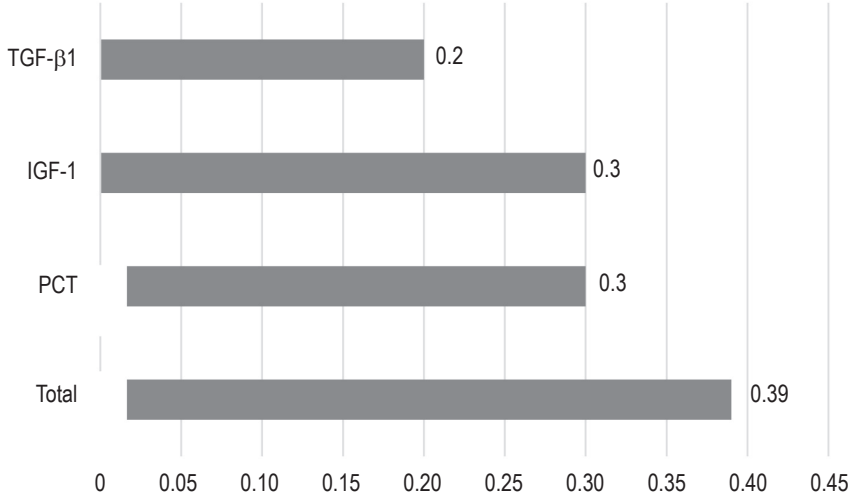

Figure 2. Relationship of the size of the left atrium with immuno-inflammatory markers in CHD

by an increase in FDV LA and a decrease in FDV LV. Thus, by determining the total protein in the blood, it is possible to predict the risk of developing LV dysfunction of the heart in CHD.

ECHOCG LV indices showed noticeable negative associations between muscle mass of the left ventricle (MMLV) and IL-6 – r = -0.31, a high negative association between LVEF and IL-6 – r = -0.41. At the same time, final systolic volume of the left ventricle (FSV LV) has a high positive relationship with IL-1 – r = 0.40, and specific volume of the left ventricle (SVLV) has a high positive dependence on the concentration of C3 in blood serum – r = 0.41 (Figure 3).

Consequently, SVLV decreases with an increase in IL-6, and MMLV increases with an increase in IL-1 in the blood, both cytokines are proinflammatory and show the role of immune inflammation at the level of the heart and blood vessels in coronary artery disease.

During the analysis, it was found that the level of SAP directly depends on the concentration of fibrinogen – r = 0.30 and oppositely depends on the concentration of PCT – r = -0.3 and IL-6 – r = -0.26.

At the same time, a noticeable positive association of heart rate with creatinine in the blood – r = 0.35 was also revealed.

The established connections show the contribution of inflammation syndrome (immune) in the progression of hypertension, or rather, indicators of the progression of hypertension in coronary heart disease are creatinine, fibrinogen, PCT and IL-6 (Figure 3).

Thus, revealed on the basis of correlation analysis of the relationship between the studied blood parameters and functional studies of the heart, the role of inflammation syndrome in the progression of hypertension in coronary heart disease has been established. At the same time, the development of cardiac restructuring dictates the need to develop

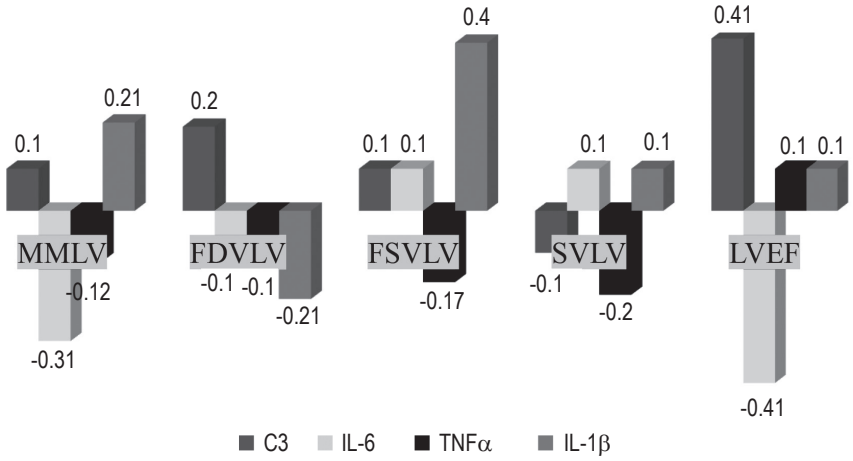

Figure 3. Relationship of ECHOCG indicators and cytokines in CHD

immunological and biochemical indicators for predicting the progression of hypertension in coronary heart disease in middle-aged and elderly people.

The dynamic study of immunological and biochemical blood parameters and the use of these recommendations allows the control and monitoring of hypertension, improving the effectiveness of diagnosis and the correct choice of treatment for patients with CHD, contributes to reducing mortality and disability at the same time.

In order to compare the relationship of immunological and biochemical parameters of blood with functional parameters of ECHOCG, a correlation analysis of the results obtained in patients with atypical angina was performed.

As a result, aortic diameter connections were established: weak positive with TNFα (r = 0.20), weak negative connections with IL-17A(r = -0.20), total blood protein (r = -0.20), PCT (r = -0.20) and VEGF (r = -0.26).

The obtained results of correlation analysis of the relationship allow a comparative assessment with the results of patients with CHD. Distinctive features of the relationship of the studied blood parameters with the diameter of the aorta in coronary artery disease were revealed: there is a weak positive relationship with TNFα (r = 0.20) against the background of a weak negative relationship between the diameter of the aorta and IL-17 (r = -0.20), total blood protein(r = -0.20), PCT(r = -0.20) and VEGF(r = -0.26). Consequently, in the atypical form of coronary angina, there is no risk of rupture and/or aneurysm of the aorta.

The study of the relationship between the FDV LA showed a noticeable positive relationship with the blood creatinine level in coronary artery disease (r = 0.32).

At the same time, weak negative associations of FDV LA with IL-17A (r = -0.21), fibrinogen (r = -0.20) and VEGF (r = -0.20). Consequently, in CHD, an increase in fibrinogen, IL-17A and VEGF in the blood is accompanied by a decrease in FDV LA. The degree of increase in creatinine shows the maximum size of the FDV LA. Therefore, with coronary artery disease, creatinine is an indicator of the prognosis of an increase in FDV LA.

In contrast to the correlation between FDV LA in CHD, in atypical angina, a noticeable positive relationship was established between FDV LV and PCT (r = 0.30), complement C3 (r = 0.40), weak noticeable connections with urea (r = 0.20), fibrinogen (r = 0.22), total blood protein (r = 0.22) against the background of a weak negative association with creatinine (r = -0.21).

The results obtained made it possible to determine the C3 complement of indicators of LV dysfunction in coronary artery disease in middle-aged and elderly people.

FDV LA in CHD has a high negative association with creatinine (r = -0.47) and TGF-β1 (r = -0.40), a noticeable negative association with IL-6 (r = -0.35), IL-1β (r = -0.30) and total blood protein (r = -0.30), a noticeable positive association with IGF-1 (r = 0.30). At the same time, the more creatinine and TGF-β1 increase in the dynamics in the blood, the more the FDV LA decreases. Consequently, creatinine and TGF-β1 are indicators of pancreatic hypertrophy in coronary artery disease atypical angina.

Consequently, in atypical angina, a decrease in TNFα in the blood in dynamics against the background of an increase in fibrinogen, VEGF and IL-1β in the blood indicates a threat of hypertrophy of the LV.

The state of the thickness of the posterior LV wall in the diastole (PWLV) is important. There was a noticeable positive association of PWLV with VEGF (r = 0.35) against the background of a noticeable negative association with IL-6 (r = -0.37), IL-17A (r = -0.30).

At the same time, weak associations of CSL were also revealed: negative with blood urea (r = -0.26) and positive with IGF-1 (r = 0.21), which shows a low risk of developing fibrosis in CHD.

The data obtained show that with coronary artery disease, an increase in IL-6, C3, and IGF-1 in the blood is accompanied by an increase in the size of the LV and vice versa, a decrease in these indicators in dynamics indicates an increase in LV with atypical angina in middle-aged and elderly people.

In general, a correlation analysis of blood parameters in CHD revealed a strong relationship between IL-6 and left ventricle ejection fraction (LVEF) (r = 0.44). At the same time, C3 complement and IL-6 were effective informative indicators of the severity of atypical angina.

Thus, the obtained high correlations made it possible to determine informative indicators of the risk of cardiac remodeling in CHD: an increase in IL-6 in the blood in dynamics predicts the risk of developing uremia (an increase in creatinine in the blood), tachycardia, a decrease in the thickness of the LV in the diastole, a decrease in LVEF, an increase in MMLV.

Conclusion

Thus, the established connections in our studies allow us to include the conclusion that, along with the above, risk factors for the development of rupture and/or aneurysm of the aorta in CHD are an increase in the blood level of complement C3, IL-17 and PCT.

Consequently, with an increase in the level of VEGF in the blood in CHD AS, the risk of an increase in the thickness of the LV in the diastole increases, and an increase in IL-6, IL-17A and urea in the blood shows a decrease in the thickness of the LV in the diastole, which makes it possible to differentiate the restrictive variant from the hypertrophic form in atypical angina.

Due to the high and noticeable correlation with the studied immuno-biochemical parameters of blood and functional parameters of the heart, IL-6 is a more informative indicator of the progression of coronary artery disease with the risk of complications and multiple organ failure.

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Поступила 13.04.2023
Отправлена на доработку 24.04.2023
Принята к печати 28.04.2023

Received 13.04.2023
Revision received 24.04.2023
Accepted 28.04.2023