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MATHEMATICAL MODEL OF THE DEVELOPMENT OF ATRIAL FIBRILLATION IN PATIENTS WITH PREVIOUS MYOCARDIAL INFARCTION

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ABSTRACT — Background: Atrial fibrillation is one of the most common and heavy disorders of heart rhythm, which affects 0,4% of the general population and more than 5% among people aged 65 and older. The prevalence has increased six times in the last 25 years. AF occurs more often in men (10 times), less — in women (4 times). Therefore atrial fibrillation has lately become an issue of intensive clinical research. The challenges deal with a recurrent character of episodes, their unpredictiveness as well as a question of feasibility of attesting AF as a permanent disease. The answers to these questions may determine a choice of conservative or surgical treatment, which contributes to quality of life and life expectancy in patients.
Materials and methods: The study included 85 patients with atrial fibrillation and 30 somatically healthy individuals. All subjects underwent a comprehensive study of the protein, lipid oxidative stress and microcirculation indicators.
Findings: It was established that the formation of the clinical course of is-chemic heart disease is interconnected with the intensification of the processes of peroxidation of proteins, lipids and a change in superoxide dismutase activity. It has been proven that in patients with AF (both paroxysmal and permanent forms) in combination with a previous infarction, there is a change in peripheral microhemodynamics: a decrease in tissue perfusion and inhibition of active modulating mechanisms of tissue microcirculation.
Conclusion: According to the correlation and factor analysis, two factors have been identified that have a significant interrelation with the development of paroxysmal AF in patients with previous myocardial infarction: the level of advanced oxidation protein products and the microcirculation index. Our mathematical model for the risk of paroxysmal AF in patients with previous myocardial infarction has a level of statistical significance of 0,020, which indicates the reliability of the prediction results.

KEYWORDS — atrial fibrillation, previous myocardial infarction, oxidative stress, microcirculation index, advanced oxidation protein products.

INTRODUCTION

Atrial fibrillation (AF) is classified by the world medical community as one of the three cardiovascular «21st century epidemics» along with chronic heart failure (CHF) and diabetes mellitus [4].

It was established that AF is an independent predictor of death. Most frequently, AF occurs at various nosological units of ischemic heart disease (IHD).

Despite the large number of studies carried out in this area, the pathogenesis of the occurrence and progression of AF has not been fully explored [2].

It is now generally accepted, that there is a shortage of studies on prediction of the risk of the development of AF paroxysm in patients with IHD.

The available data are often inconsistent.

Early diagnosis of the factors of the development and progression of AF will improve not only the clinical status of patients, but also their prognosis [5].

The positions described above defined the purpose of our scientific research.

The purpose of the study

To create a mathematical model of atrial fibrillation paroxysm development in patients with previous myocardial infarction based on a comprehensive study of protein, lipid oxidative stress and microcirculation indicators.

MATERIALS AND METHODS

The Regional Ethics Committee (an extract of the record № 6 from 2 November 2015) approved this study.

In total 240 patients were examined, however, when criteria for exclusion were identified, patients dropped out of the study.

The main group consisted of 85 patients with AF. Of these, 39 patients had paroxysmal AF, 46 patients — a permanent form of AF. Of 39 patients with paroxysmal AF, 27 had angina pectoris, 13 had a previous myocardial infarction (MI), 12 had no angina pectoris, and 26 had no previous MI. Of 46 patients with permanent AF, 32 were diagnosed with angina pectoris, and 20 — with previous MI, 14 patients had no angina pectoris, 26 patients had no previous MI. The control group consisted of 30 somatically healthy individuals of the Astrakhan region. The average age

of the examined patients was 51.4 [40; 60] years. The average duration of the disease was 11.2 [3; 17] years. Groups of patients included in the study were comparable in age and gender parameters.

Determination of Cu/Zn — superoxide dismutase (SOD) concentrations in serum was carried out by the enzyme-linked immunosorbent assay (ELISA) using commercial test systems. Catalogue number — BMS 222. Company manufacturer — Bender Medsystems, Austria.

Determination of the advanced oxidation protein products (AOPP) in serum was carried out by the ELISA using commercial test systems. Catalogue number — K 7811w. Company manufacturer — Immundiagnostik, Germany.

Determination of the total enzymatic activity of all three types of SOD (Cu/Zn-SOD + Mn-SOD + Fe-SOD) in serum was carried out by the ELISA using commercial test systems. Catalogue number — 706002. Company manufacturer — BCM Diagnostics, USA.

To study the functional status of the vascular endothelium by means of laser Doppler flowmetry (LDF) there was used the laser analyzer of blood microcirculation «LAKK-02».

Statistical analyses were performed using STATISTICA 12.0 Stat Soft, Inc.

RESULTS

We attempted to conduct a comprehensive study of the processes of free radical oxidation as an example of AOPP and MDA, antioxidant protection, (SOD Cu/Zn with non-enzymatic activity and total SOD) and microvascular reactivity in order to identify meaningful indicators to predict such a terrible condition as a paroxysm of AF in patients with previous MI.

Correlation and factor analysis methods were used to identify factors that are related to paroxysmal AF in patients with previous MI: AOPP, microcirculation index (MI), flux, variation coefficient (Kv), alpha rhythm amplitude, vasomotion amplitude (LF), microcirculation efficiency index (index EfM), neurogenic tone (NT).

It was found that the formation of the clinical course of IHD is interrelated with the intensification of protein and lipid peroxidation and changes in the activity of SOD activity, activation of peroxidation in patients with paroxysmal and permanent AF with postinfarction cardiosclerosis.

However, in patients with a permanent form of AF, an increased activation of peroxidation processes led to the accumulation of peroxidation products in the blood serum of both protein and lipid molecules.

In patients with paroxysmal AF with the presence of previous MI an increased activation of peroxidation processes led to an increase in the total level of products of AOPP.

At the same time, the level of MDA in patients with paroxysmal AF in the group of patients with previous MI was comparable to the group of patients without previous MI, despite the fact that in comparison with the control group there was a significant difference.

Having studied the basal microcirculation (MI, flux and Kv) in patients with AF depending on the presence of previous MI, we found that in patients with both paroxysmal and permanent form of AF, in combination with a previous MI, there is a change in peripheral microhemodynamics: a decrease in tissue perfusion and inhibition of active modulating mechanisms of tissue microcirculation.

In the group of patients with paroxysmal AF and previous MI median MI was 3.54 perf.un., that was significantly lower both in comparison with the group of somatically healthy individuals ($p<0.0001$) and in comparison with the group of patients with paroxysmal AF without previous MI ($p=0.0369$).

In the group of patients with permanent AF with previous MI, the median flux was 0.11, that was significantly lower compared with the group of somatically healthy individuals ($p=0.0072$), compared with the group of patients with paroxysmal AF with previous MI ($p=0.0101$) and with the group of patients with permanent AF without previous MI ($p=0.0048$).

In the group of patients with paroxysmal AF with previous MI median Kv was 3.87%, that was significantly lower compared with the group of somatically healthy individuals ($p<0.001$) and with the group of patients with paroxysmal AF without previous MI ($p=0.0391$).

As a result of spectral decomposition of the dopplerogram into harmonic components of tissue blood flow oscillations (using mathematical Butterworth filters), we estimated the amplitudes of rhythmic components of the following frequency ranges: endothelial rhythms (Amax/M-α frequency 2–3 oscillations per minute), vasomotion (LF, frequency 4–12 oscillations per minute), respiratory rhythms of two ranges (HF1, frequency 13–30 oscillations per minute and HF2, frequency 31–49 oscillations per minute), cardiorhythms of two ranges (CF1, frequency 50–99 oscillations per minute and CF2, frequency 100–180 oscillations per minute).

As a result, we found that in patients with AF (both paroxysmal and permanent forms) there is an increase in the amplitude of cardiorhythms in patients with previous MI.

These micro hemodynamic disorders can exacerbate hypoperfusion of tissues and organs against the background of developing CHF, as well as be a risk factor for further vascular damage with the development of unstable conditions and complications.

Also, using the application program, we calculated a number of indices that allow to determine more objectify microcirculatory disorders in patients with AF: the index of microcirculation efficiency (index EfM), the neurogenic tonus of precapillary resistive microvessels (NT), the myogenic tonus of metarterioles and precapillary sphincters (MT), the shunting index (SI).

As a result, we came to the conclusion that both in the permanent form and in the paroxysmal form of AF, the presence of a previous MI was associated with a de-crease in peripheral capillary blood flow against the background of a decrease of NT, while in patients with a constant form of AF and with previous MI, microcirculatory disorders were deeper.

As a result of our scientific research on the data of correlation and factor analysis, we identified 2 factors that have a significant relationship with the development of paroxysmal AF in patients with previous MI: AOPP and MI.

Further, using binary logistic regression, we tried to create a mathematical model to predict the development of AF in patients with previous MI with the calcula-tion of the probability coefficient of AF.

p=1/1+e-z, where z=0,101*AOPP – 1,345*MI – 8,996

In this, AOPP means the total level of the advanced oxidation protein products; MI — microcirculation index in laser Doppler flowmetry.

Wald statistic was used for testing the significance of the coefficients.

The level of statistical significance of the model coefficients was 0.020, that was less than 0.05 and indicates the statistical significance of the prediction results of this model.

DISCUSSION

According to a number of researchers, AF is a common cardiac arrhythmia, leading to serious complications: heart failure, thrombosis, including stroke [1].

It is now generally accepted that over the time AF tends to progress from short and rare episodes of arrhythmia to the appearance of a stable permanent form of AF [3].

According to several researchers, the frequency of transition from a persistent form to a permanent form of AF is from 20% to 30% within 1–3 years [2].

Early diagnosis of AF progression factors, assignment of additional therapy for secondary prevention of arrhythmia and the choice of the correct treatment strategy can slow down the arrhythmia progression, which allows not only to improve the clinical status of the patient, but also his prognosis [6].

Thus, the purpose of our study is certainly relevant, and the results can open up new opportunities for specialists to predict paroxysm of AF.

In our scientific research, we decided to conduct a comprehensive study of antioxidant defence (AOD), protein and lipid peroxidation products and analysis of microcirculatory disorders in patients with AF.

We have established a significant decline of the AOD in patients with perma-nent form of AF, in this group of patients the decrease of AOD may be one of the factors modifying the clinical course of IHD with the development of painful forms.

A number of reseachers had long proved the direct relationship between AOD and peroxide oxidation.

Proteins are the most sensitive to oxidative stress, and therefore, along with MDA, we decided to investigate AOPP in the listed above groups of patients.

Intracellular accumulation of AOPP can induce apoptosis of podocytes, resulting oinproteinuria, and activation of the renin-angiotensin system in tubular cells [1].

Activation of protein and lipid peroxidation processes was revealed in patients with paroxysmal and permanent AF forms, with previous MI.

However, in patients with a permanent form of AF, increased activation of peroxidation processes led to the accumulation of peroxidation products in the blood serum of both protein and lipid molecules.

In patients with paroxysmal AF, the presence of previous MI led to the accumulation of mainly products of protein peroxidation.

We revealed a statistically significant decrease of MI and flux in groups of patients with previous MI in both paroxysmal and permanent AF, reflecting the development of peripheral hypoperfusion.

A statistically significant decrease of Kv in the groups of patients with previous MI was proved in both paroxysmal and permanent AF, reflecting a decrease in active propulsive movements of microvessels.

In patients with previous MI, correlation and factor analysis revealed a statistically significant relationship between the development of AF and MI.

Thus, the improvement of long-term prognosis of IHD depends of the level of diagnosis in the early stages of the disease, and the result of our study provides such an opportunity.

Conflicts of Interest

The authors declare no conflict of interest.

Contributors

OP and AA finally approved the manuscript for submission; EkP designed the study; ECh and EvP critically proved the work; RF and EK collected data, conducted statistical analysis; MF designed the study, interpreted the results, prepared the manuscript for submission.

REFERENCES

1. **Ciuntu A.O.** Advanced Oxidation protein products (AOPPS) in the development of glomerulonephritis in children // Международный научно-исследовательский журнал. 2017; Vol. 55(1–1), №1–1. P.178–181. (In Eng.). DOI: 10.2360/IRJ.2017.55.171
2. **Holmqvist F, Tristram D, Bahnson M.** Atrial fibrillation mapping strategies: The hunt is on // Heart Rhythm. 2018, Vol. 15, P. 1304–1305. DOI: 10.1016/j.hrthm.2018.05.007
3. **Kadyrova MV, Askerova NN, Stepanova YuA, Zhemerov NV, Malyshenko ES, Popov VA, Revishvili ASh.** Possibilities of echocardiography at the stages of surgical treatment of a patient with mitral valve posterior flap prolapse with the development of severe mitral insufficiency and atrial fibrillation (clinical observation). // Meditsinskaya vizualizatsiya. 2017; Vol. 21(2). P. 103–113. (In Russ.). DOI: 10.24835/1607-0763-2017-2-103-113
4. **Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, Cas-tella M, Diener H-C, Heidbuchel H, Hendriks J, Hindricks G, Manolis AS, Oldgren J, Popescu B., Schotten U, Putte B, Vardas P.** 2016 ESC guidelines for the management of atrial fibrillation developed in collaboration with EACTS. // European Heart Journal. 2016; Vol. 37: P. 2893-2962. DOI: 10.1093/eurheartj/ehw210
5. **Palagina I.A., Kudrya M.Ya., Melnikovskaya N.V., Kustova S.P., Ustenko N.V., Boyko M.A., Lalymenko O.S., Pavlenko T.A., Matveeva T.V.** Antioxidant properties of a cathiasine-based pharmaceutical composition studied on a model of the drug-induced liver impairment. // Проблемы эндокринной патологии. 2018; Vol. 3(65): P. 51–58. (In Eng.). DOI:10.21856/j-PEP.2018.3.06
6. **Podzolkov VI, Tarzimanova AI.** Changes in endothelial function in patients with paroxysmal atrial fibrillation in the treatment of propafenone. // Kardiovaskulyarnaya terapiya i profilaktika. 2018; Vol. 4: P. 40–45. (In Russ.). DOI: 10.15829/1728-8800-2018-4-40-45