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Clinical and Genetic Features of Unstable Angina Pectoris Depending on Various Psychosocial Risk Factors

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Abstract: In our study we investigated the association of several biopsychosocial risk factors on the progression of unstable angina pectoris, in particular blood uric acid level, cytokine imbalance, anxiety-depressive syndrome, polymorphism of proinflammatory genes, and basic lipid spectrum parameters. We analyzed the correlation between the studied MC parameters, anxiety parameters, production of immunoregulatory cytokines, polymorphism of proinflammatory genes IL-1β T/C 511 (rs16944) and IL-10 T/C 819 (rs1800871), as well as cholesterol metabolism parameters.

Keywords: Unstable angina pectoris, uric acid, anxiety-depressive syndrome, cytokine imbalance, polymorphisms of IL-1β T/C 511 and IL-10 C/T 819 genes.

Introduction. Currently, cardiovascular diseases play a crucial role in the evolution of total mortality worldwide. Coronary heart disease accounts for 26.6% in the structure of cardiovascular diseases. Among the various forms of coronary disease, angina pectoris occupies the leading place [1, 6]. An expert working group of the National Heart Foundation of Australia conducted a large study of systematic reviews of the evidence on major psychosocial risk factors to assess whether there are independent associations between psychosocial risk factors and the development, progression of coronary heart disease or the occurrence of acute cardiac events [4,5]. The expert panel concluded that there is strong and consistent evidence of an independent causal relationship between depression, social isolation and lack of quality social support and the development and progression of CHD, which has an impact on prognosis [7, 12, 16]. But there is no convincing evidence of a causal relationship between chronic life events, work-related stressors, hostility, anxiety disorders or panic disorders and CHD. The increased risk caused by these psychosocial factors is similar to more common CHD risk factors such as smoking, dyslipidemia, insulin resistance, and hypertension. The identified psychosocial risk factors should be considered in the assessment and risk management of individual CHD and have implications for public health policy and research [3, 5, 8]. The present studies showed that patients with unstable angina pectoris and TDS have frequent cases with elevated MC levels. And also the study noted frequent cases with high levels of OH, LDL. In this case, CVD and disturbed cholesterol metabolism in patients with NS are correlated. In addition, it was found an increase in the correlation relationship during the attack period between the indicators of MC and anxiety-depressive syndrome in patients with NS indicates the pathogenetic importance of HU in the mechanisms of formation of anxiety-depressive syndrome. High level of MC and clinically expressed anxiety especially in the period of NS attack testify to a single mechanism of their participation in cardiovascular disorders and formation of CHD.

Cardiovascular events and emotional disorders share a common epidemiology, suggesting fundamental pathways linking these various diseases. More and more facts in the literature emphasize the influence of psychological determinants in somatic diseases [13, 15]. Socio-economic aspects of the patient,

personality traits, health behavior, and even biological pathways can contribute to the development of cardiovascular diseases [17, 19]. Cardiac events often occur suddenly, and this episode can be traumatic for people who are not prepared for such an event. Many authors consider the issue of biopsychosocial mechanisms of stress within the framework of a pathophysiological approach to the fundamental pathways connecting the brain with the heart. Various psychological, biological, and genetic agents are cited to support the hypothesis that various etiological mechanisms may be involved. Finally, the authors consider biological and psychological strategies in the context of cardiovascular diseases [14]. Indeed, in this context, cardiac rehabilitation, with its global approach, seems to be an appropriate time to diagnose emotional disorders such as anxiety and depression and help people cope with stressful events. In this area, cardiac rehabilitation appears to be a critical step to improve patient outcomes by helping them understand the impact of biopsychosocial risk factors and develop strategies for managing daily stress [9, 10, 11]. However, the connection of psychosocial risk factors with a violation of purine metabolism is not taken into account by many scientists and remains a little-studied problem.

All of the above indicates that coronary heart disease associated with comorbid conditions remains an urgent problem of national and international health in most developed and developing countries of the world. Ways to solve this problem are being actively developed by national and international expert groups, including politicians, economists, financiers, health managers, practitioners and scientists, whose task is to develop and financially ensure optimal mechanisms for the functioning of a system for monitoring and managing global cardiovascular risk in the population.

Aim of the study: To study the peculiarities of clinical course and genetic polymorphism of patients with unstable angina pectoris with comorbid pathologies to calculate the prognosis of cardiovascular complications.

Materials and methods of the study: 202 patients with CHD, including 42 patients with stable angina pectoris (SS) and 160 patients with unstable angina pectoris (UA) were studied on the basis of Samarkand Branch of Republican Scientific Center of Emergency Medical Care in emergency department №1 and 2.

Among them, 102 females and 100 males were aged between 30 and 88 years. The mean age was 63.75 ±11.37 years. Among these patients, arterial hypertension was found in 150 patients (74.6%), DM - in 44 patients (21.8%), 52 patients (25.7%) had previous MI, rhythm disturbance 29 (14.35%), anemia 33 (16.3%), stroke 9 (4.5%), COPD 11 (5.4%), obesity 13 (6.4%), other diseases 27 (13.36%) (Fig.2). But in our study we studied the incidence of comorbid conditions such as anxiety-depressive syndrome (ADS) and asymptomatic hyperuricemia (AHI)

The diagnosis of unstable angina pectoris was established in patients on the basis of clinical findings, i.e. prolonged anginal attacks at rest, lasting more than 15 minutes, which are not controlled by taking nitroglycerin tablets; in addition, in patients with severe angina for the first time in the preceding 28-30 days, in those who had destabilization of pre-existing SS with the appearance of characteristics inherent in at least III FC according to the classification of the Canadian Heart Association, as well as attacks of pain at rest. All patients underwent laboratory investigations (general blood analysis, general urine analysis, biochemical studies: liver parameters, lipid spectrum (total cholesterol, LDL, HDL, TG), uric acid), pro- and anti-inflammatory cytokines (TNF-α, IL-1β, IL-4 and IL-10), as well as IL-1 T/C 511, IL-10 C/T 819 gene polymorphism. In the examination of patients with CHD we used: Hospital scale HADS. And also the Spielberger-Hanin scale, developed by Spielberger C.D. and adapted by Hanin Y.L. for the assessment of cognitive functions. The patients were monitored for 3 months.

Results of the study and discussion: To solve general clinical problems, patients with NS were conditionally divided into 4 groups: Group 1 patients with NS in comorbidity with TDS, Group 2 patients with NS with asymptomatic hyperuricemia (AHU), Group 3 patients with NS with AHU and TDS, Group 4 patients with NS alone**.** The distribution of patients into groups depending on the presence of comorbid pathology. The results showed that ECHOCG indices among patients with NS

and SS were practically no different than LVEF was reduced in the group of patients with NS and BSU. But in contrast to ECHO-CG data the indices of pro- and anti-inflammatory cytokines among patients with SS and NS varied. So pro-inflammatory cytokine IL-1β in patients with SS and NS without comorbid pathology had lower indices, but among patients with NS with TS and TDS IL-1β and TNFα in contrast to patients with SS and NS were strongly overestimated, by 19,58 pg/mL and 21,91 pg/mL respectively indices of IL-1 β and by 8,99 pg/mL, 11,64 pg/mL indices of TNFα. In the same way, it can be said that patients with NS with TDS and BSU are the main risk group, who are more prone to severe and longer course of the disease. Indicators of anti-inflammatory cytokines IL-4 and IL-10 did not show significant differences in these groups. Next, we evaluated lipid profile parameters and MC levels in blood. Where we saw no significant differences. However, it should be noted that among patients with NS with TDS and CVD, MC levels are excessively high than among patients with NS and CVD. Perhaps excessively elevated MC levels will lead to the development of TDS, which is supported by the results of many meta-analyses. A sufficient number of clinical trials of pharmacologic agents targeting the purinergic system have been conducted; most of these studies used xanthine oxidase allopurinol as adjunctive therapy in patients with bipolar disorder. The results of the meta-analysis demonstrated the positive efficacy of purinergic modulators (including allopurinol) as adjuvant therapy for bipolar mania compared with placebo

Finally, measures of TDS on the HADS and Spielberger-Hanin scales were examined. In Figure 4 we can see the average TDS scores and among patients with TDS these scores are increased almost 2 times, which leads to worsening of the course of the disease and more frequent development of cardiovascular complications. В связи с этим мы решили рассмотреть полиморфизм генов IL-1 T/C 511 (rs16944) и IL/10 C/T819 (rs1800871). Among patients with HC, a case with IL-1 T/C gene polymorphism 511 (rs16944) was found in 99 patients, of which 68 patients had a heterozygous C/T genotype and 31 patients had a homozygous T/T variant. It should also be noted that among patients with elevated MC levels, cases with polymorphism of this gene were much more common and amounted to 35%. Perhaps this was due to a violation of purine metabolism. Among patients with HC, there were 57 cases with the IL/10 C/T819 gene polymorphism (rs1800871) with the heterozygous variant of C/T and 71 cases with the homozygous variant of T/T. Cases with a heterozygous and homozygous variant of IL/10 C/T819 gene polymorphism (rs1800871) were noted in 65% of patients with TDS. Perhaps the replacement of the amino acid cytosine with thymine influenced the development of anxiety-depressive syndrome.

Conclusions: Thus, the hypothesis of the role of cytokines in depression by V. Sperlagh et al.(2012), who reviewed a large literature in order to explain the effects of the purine receptor, P2rx7 and its activation on mood associated with behavior due to the release of glutamate and changes in neuron plasticity in depressive disorders, was confirmed in this study. The results obtained by studying the polymorphism of the genes IL-1β 511 T/S (rs16944), IL-10 819 C/T (rs1800871) in HC with BSU and TDS, as well as without them, apparently, can allow us to talk about these genes no longer as candidates, but as the genes that make a great contribution to the formation of a hereditary predisposition to the development of the disease can be considered proven. All of the above indicates that coronary heart disease associated with comorbid conditions remains an urgent problem of national and international health in most developed and developing countries of the world. Ways to solve this problem are being actively developed by national and international expert groups, including politicians, economists, financiers, health managers, practitioners and scientists, whose task is to develop and financially ensure optimal mechanisms for the functioning of a system for monitoring and managing global cardiovascular risk in the population.

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