ASSOCIATION OF INFLAMMATORY CYTOKINES AND ECHOCARDIOGRAPHIC REMODELING IN PATIENTS WITH ATRIAL FIBRILLATION

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Introduction. Atrial fibrillation (AF) is the most common type of abnormal heart rhythm or arrhythmia. In AF, the rhythmic beating of the atrial chambers of the heart is replaced by an irregular and rapid beat [1]. The link between inflammatory processes and AF is becoming increasingly clear as more evidence comes to light. The pathogenesis of AF involves initiation of the arrhythmia by certain triggers and the maintenance of it by abnormal atrial tissue substrate. The initiating triggers are often in the form of rapidly firing ectopic foci located inside one or more pulmonary veins [2]. The role of inflammatory mediators is implicated in both the initiation of AF as they can alter the atrial electrophysiology and the maintenance of AF by causing abnormalities in structural substrates [2].

The inflammatory mediators thought to be involved in atrial structural and electrical remodelling, atrial fibrosis and oxidative stress include interleukin-6 (IL-6), TNF-б, interleukin-1-beta (IL-1в), C-reactive protein (CRP), ROS, NLRP3 inflammasome, TGF-в [3]. An established understanding of the correlation between inflammatory cytokines and atrial fibrillation can lead to innovative treatment tactics as well as better prediction of the prognosis.

Aim of the study is to establish association of inflammatory cytokines (CRP and IL-1B) and echocardiographic parameters in patients with AF.

Materials and methods. The study included 80 patients with coronary artery disease and/or hypertension who were admitted to the Grodno Regional Clinical Cardiological Centre for treatment. 42 patients (52%) had paroxysmal or persistent form of AF, while 38 patients (48%) had sinus rhythm.

Exclusion criteria from the study were: recent acute myocardial infarction, chronic rheumatic heart disease, valvular pathology of the heart requiring surgical correction, prosthetic heart valves, coronary artery bypass grafting, or coronary angioplasty (less than 3 months before enrollment in the study); oncological diseases and severe concomitant extracardiac pathology.

Echocardiography was performed on Phillips iE33 device with a multi-frequency sensor (frequency 2.5-5.0 MHz). Determination of the concentration of CRP and IL-1b in the blood serum of patients was carried out using the FineTest ELISA kits (China) on the SUNRISE TECAN automatic ELISA analyzer (Austria). The procedures for preparing samples, reagents and the experimental scheme were carried out according to the instructions of the manufacturer of the test systems.

Statistical analysis was performed using the STATISTICA 12.0 software package with a preliminary check for normal distribution using a distribution histogram. Quantitative data, the distribution of which was not normal, were given as a median, 25% and 75% quartiles. Since most of the quantitative characteristics did not obey the normal distribution law, non-parametric methods were used for

comparison. The Mann-Whitney test was used to assess differences in quantitative traits between two independent groups. At a significance level of p less than 0.05, it was believed that the studied indicator in the compared groups had statistically significant differences.

The study was performed in accordance with Good Clinical Practice standards and the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants prior to inclusion in the study.

Results. Patients with AF and sinus rhythm were comparable in age and gender, p>0.05). Patients with sinus rhythm more often suffered from hypertension (92.1% vs 50%, p=0.026), especially stage 2 (p<0,001). It is interesting to say, that patients with sinus rhythm more often had stable angina (81.6% vs 40.5%, p<0.001) and more often suffered from myocardial infarction (9.5% vs 26.3%, p=0.049) than patients with AF.

Patients with sinus rhythm were characterized by higher prevalence of HF NYHA class 2 (p=0.012), however in patients with AF Class 3 was more common.

In biochemical blood test patients with AF were characterized by higher levels of urea (p=0.017), however their creatinine levels and eGFR were comparable (p>0.05). However, patients with AF had significantly higher levels of potassium (4.7 [4.3; 5.1] vs 4.4 [4.2; 4.6], p=0.040) and NT-proBNP (1041.4 [634; 1042.5] pg/mL vs 283.3 [71.5; 336.5] pg/mL, p<0.001).

According to the results of transthoracic echocardiography, patients with AF had significantly higher left atrial (LA) and right atrial (RA) diameters in both 2-chamber and 4-chamber positions (p<0.001) than patients with sinus rhythm. It is interesting to say that patients with AF had significantly larger left ventricle (LV) linear and volumetric parameters as well as LV ejection fraction (p>0.05), with the only exclusion being end-diastolic diameter and volume, which were comparable. Patients with AF also were characterized by higher grade of both mitral and tricuspid regurgitation (p<0.05).

When conducting an enzyme immunoassay in patients of the AF group, the CRP level was 7.83 [6.89; 8.87] mg/L, and in patients with sinus rhythm – 6.15 [4.34; 7.69] mg/L, these differences were statistically significant (p=0.023). However, there were no intergroup differences in IL-1B level (0.31 [0.25; 0.36] vs 0.32 [0.24; 0.39] pg/mL, p>0.05) (fig. 1).

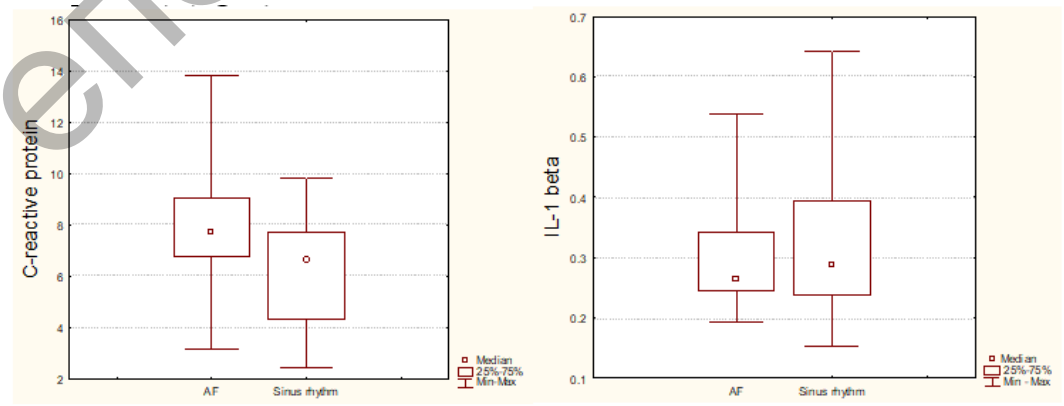

Figure 1 – Levels of CRP and IL-1B in studied groups of patients

When conducting a correlation analysis, a statistically significant correlation was revealed between the level of CRP and a number of echocardiographic parameters. Positive correlations were established between CRP level and LA diameter (R=0.41, p<0.001) and RA diameter (R=0.33, p<0.001). Negative correlation was found between CRP level and LVEF (R=-0.28, p<0.05).

Conclusion. Correlations between CRP level and linear and volumetric echocardiographic parameters were established. Further research on the causative role of inflammatory cytokines in AF can lead to new therapeutic strategies such as anti-inflammatory medication for AF.

References

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ВЗАИМОСВЯЗЬ ВОСПАЛИТЕЛЬНЫХ ЦИТОКИНОВ И ЭХОКАРДИОГРАФИЧЕСКОГО РЕМОДЕЛИРОВАНИЯ У ПАЦИЕНТОВ С ФИБРИЛЛЯЦИЕЙ ПРЕДСЕРДИЙ

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Целью исследования было установить взаимосвязь между уровнями провоспалительных цитокинов (С-реактивный белок (СРБ) и интерлейкин-1-бета) и эхокардиографическими параметрами у пациентов с фибрилляцией предсердий. Положительные корреляции были установлены между уровнем СРБ, диаметром левого предсердия (R=0,41, p<0,001) и диаметром правого предсердия (R=0,33, p<0,001). Отрицательная корреляционная связь выявлена была между уровнем СРБ и фракцией выброса левого желудочка (R=-0,28, p<0,05).