ETHIOPIAN INTERNATIONAL JOURNAL OF MULTIDISCIPLINARY RESEARCH

eISSN: 2349-5715 pISSN: 2349-5707

Volume: 11, Issue 03, March-2024 SJIF 2019: 4.702 2020: 4.737 2021: 5.071 2022: 4.919 2023: 6.980 2024: 7,662

SIGNIFICANCE OF THE SERUM MARKER OF CARDIAC FIBROSIS AND INFLAMMATION IN THE PROGNOSIS OF PERMANENT ATRIAL FIBRILLATION

Shokirova M. Sh., Usmanova D. N., Tulkinzhanova G. R.
Andijan State Medical Institute

Abstract: Indicators of cardiac fibrosis of mediators of systemic inflammation in patients withatrial fibrillation(AF) depending on the form of arrhythmia were studied. It was found that in AF, the levels of serum markers of fibrosis and inflammation increase: The C-terminal propeptide of procollagen type I (PICP), interleukin-6. There is a dependence of fibrosis indicators on the form of AF. The level of PICP increases in chronic permanent форме AF. In patients with recurrent AF, the IL-6 index has higher values compared to those in practically healthy people and increases even more in permanent AF. The level of tumor necrosis factor α is slightly increased in permanent AF.

Key words: Atrial fibrillation, terminal procollagen type I propeptide, tumor necrosis factory-α, interleukin-6.

Currently, atrial fibrillation (AF) is the most common persistent arrhythmia in adults worldwide, which is characterized by high morbidity and mortality, determining the extreme significance of socio-economic consequences for the health system of any state. Experts estimate that the prevalence of AF in adults ranges from 2% to 4%, and the number of patients with AF exceeds 5 million. in the United States and 30 million rubles. all over the world. In 2017, 0.75 million people were registered. new cases of AF in 54 member countries of the European Society of Cardiology (EOC), the average number of new cases, standardized by age, was 44.3 [39.7-47.5] per 100,000 inhabitants of each member country[1,2,]. Unfortunately, it should be noted that there is no accurate data on the prevalence of AF in the literature sources. more than that.

According to modern concepts, the occurrence of arrhythmia requires certain relationships between triggers, substrate, and modulating factors[5,6,6]. At the same time, it is structural remodeling of the left atrium that is identified as the key mechanism in which interstitial fibrosis can be the dominant factor [3]. A number of studies have attempted to study the histopathological substrate in various forms of AF. When studying biopsies from the area of the junction of the pulmonary veins to the left atrium and the tissues of the ear of the right atrium in patients with chronic AF, the presence of spotty fibrosis was revealed, and the average number of fibrosis sites in patients with AF is greater than in patients with sinus rhythm [4]. In more recent studies, it has been discussed that fibrosis and inflammation can disrupt the ordered propagation of electrical excitation, acting as direct obstacles [11].

As can be seen from the above, there is no data on the immediate and long-term prognosis of patients with atrial fibrillation of ischemic origin, and the data obtained are contradictory and need further in-depth study.

Objective: To study indicators of cardiac fibrosis and systemic inflammation in patients with various forms of AF.

Object and subject of the study: The study involved 15 relatively healthy people aged 35 to 49.6 years, a control groupя; the second group consisted of patients with AF of ischemic origin aged 50 to 71 years, the third group - patients with AF of idiopathic origin aged 45 to 69 years.

Methods and methods of research: The clinical parameters of the corresponding groups of AF patients of various origins, gender, and age were evaluated; an echocardiographic examination in modal and two-dimensional modes with an extended assessment of left atrial parameters and

eISSN: 2349-5715 pISSN: 2349-5707
Volume: 11, Issue 03, March-2024 SJIF 2019: 4.702 2020: 4.737 2021: 5.071 2022: 4.919 2023: 6.980 2024: 7,662

daily ECG monitoring with an assessment of heart rate variability were performed; a marker of cardiac fibrosis of the C-peptid terminal procollagen type I propeptide was determined (PICP) by enzyme-linked immunosorb assay using the Metra CIPC EIA Kit (Quidel Corporation, USA), determination of the levels of local myocardial inflammation indicators: tumor necrosis factor α (TNFa) and interleukin-6 (IL-6) by solid-phase enzyme-linked immunosorbent assay using standard test systems: DSL-10-42100 series07144-A LLC "Biohimmak"(Moscow).

Exclusion criteria from the study: age over 70 years; liver diseases; chronic kidney disease; pneumofibrosis and severe chronic obstructive pulmonary disease; malignant tumors; diffuse connective tissue diseases; installed pacemaker; cardioverter defibrillator; ischemic heart disease; cardiomyopathies; valvular heart defects; acute myocarditis; pericarditis; impaired heart function thyroid gland; circulatory failure of more II than NYHA functional class II NYHAand a left ventricular ejection fraction of less than 45%; diabetes mellitus; acute inflammatory diseases or exacerbations of chronic inflammatory diseases within 2 weeks. before being included in the study.

The obtained results were statistically processed cusing the computer program Statistica 6.1. Quantitative features with a normal distributionare represented as M ± σ (mean ± standard deviation), with an abnormal distribution — as the median and interqu artilerange. Correlation analysis was performed using Spearman's R criterion for quantitative values. At $p < 0.05$, the differences were considered statistically significant.

Results and discussion: The highest concentration of PICP was determined in patients with AF of ischemic origin (131 ng/ ml), slightly lower (125 ng/ ml). In patients with idiopathic AF, the PICP level PICP(84 ng/ ml) was significantly lower than y in patients with ФП ischemic AF ($p = 0.01$). Comparative assessment of fibrosis parameters in patients with ischemic origin revealed higher PICP values PICP, than y in patients with idiopathic AF (84 ng/ ml; $p = 0.001$) and practically healthy individuals (51 ng/ ml; $p = 0.0002$). Thus, an increase in the level of PICP in idiopathic AF in comparison with indicators y in healthy individuals allows us to assume a possible relationship of this marker именно with the presence of AF, but the presence более of higher values of PICP in ischemia indicates a significant impact её on the level of PICP. It should be noted that the association of PICP with cardiac fibrosis is more studied in hypertension and is represented as an abnormal increase in the level of PICP in the blood in isolated hypertension, which is confirmed by a number of studies [7-9]. In the literature , there are descriptions of fibrosis and inflammation in atrial tissues in isolated AF [10], but we have not seen any works specifically on the study of PICP.

When studying serum markers of inflammation, the TNF-α concentration in patients with AF significantly exceeded the parameters in practically healthy individuals (2.1 pg/ ml vs. 1.2 pg/ml; $p = 0.02$), and the IL-6 level significantly exceeded the parameters in healthy individuals (2.5 pg/ ml in AF vs. 1.6 pg/ml yin healthy individuals ($p = 0.01$).

When comparing TNF-α values in groups with pathology, the indicators were distributed as follows: the highest concentration was observed for AF of ischemic origin (2.1 pg/ml), which exceeded the values for idiopathic AF (0.2 pg/ml; $p = 0.03$).

The concentration of IL-6 was highest in patients with AF on the background of ischemia (2.5 pg/ml), which was higher than in patients with idiopathic AF (2.11 pg/ ml; $p = 0.7$).

Таблица Table 1. Indicators of fibrosis and inflammation y in patients with idiopathic AF, ФПischaemic AF , and practically healthy patients

eISSN: 2349-5715 pISSN: 2349-5707
Volume: 11, Issue 03, March-2024 SJIF 2019: 4.702 2020: 4.737 2021: 5.071 2022: 4.919 2023: 6.980 2024: 7,662

Indicator	Control group	Idiopathic	AF ischaemic AF
PICP, ng/ml	51 [37; 79]	84 [53; 102]	125 [66; 172]
TNFa, pg/ml	1,2,2 [0,8; 1,5]	0,2 [0; 2,3]	2,1 [1,2; 4,8]
IL-6, pg/ml	1,6 [0,9; 2,2]	2,1[0,6; 7,9]	2,5 [1,6; 4,8]

In permanent AF higher PICP concentrations (85.2 ng/ml vs. 182.4 ng/ml;p=0.01; Table 2) were . In comparison with practically healthy individuals, only an increase in the PICP level evident in recurrent and even more so in permanent AF (p = 0.003 and p = 0.002 respectively).

TTable 2. Indicators of fibrosis and inflammation in patients with various forms FA of AF compared to those in practically healthy patients

Indicator	Recurrent AF (n = 11)	Permanent AF (n = 11-4)	Control group (n = 10)
PICP, ng/ml	85,2 [54; 151]	182,4 [120; 282]	51 [37,2; 79,2]
TNFa, pg/ml	0,2 [0; 3]	2,4 [0; 5,2]	1,2 [0,8; 1,5]
IL-6, pg/ml	5,2 [1,6; 7,9]	7,7 [0,9; 141,2]	1,6 [0,9; 2,2]

The level of TNF-α was slightly higher in permanent AF (2.4 pg/ ml) по compared with recurrent AF (0.2 pg/ ml; p = 0.73), but did not differ при from its values in practically healthy individuals (1.2 pg/ ml; p = 0.6 and p = 0.3). The level of IL-6 also had a slight tendency to higher values in permanent AF (7.7 pg/ml) compared with recurrent AF (5.2 pg/ ml; p = 0.43); however , the level of IL-6 differed from the values in practically healthy individuals (1.6 pg/ml) only in recurrent AF(p = 0.007).

Conclusions

1. Atrial fibrillation is accompanied by an increase in the level of serum markers of cardiac fibrosis and inflammation, especially the C-terminal propeptide procollagen type I and interleukin-6, and to a greater extent AF of ischemic origin.
2. Serum показатели fibrosis values depend on the form of atrial fibrillation. The level of the C-terminal propeptide procollagen type I increases in chronic and recurrent forms, higher values are noted in chronic course.
3. The interleukin-6 parameter of serum inflammation has higher values in patients with recurrent atrial fibrillation and maximal values in patients with permanent atrial fibrillation compared to those in healthy individuals. The level tumor factor necrosis factor α is slightly increased in permanent atrial fibrillation.

Literature

1. Camm A., Kirchhof P., Lip G. et al. ESC Guidelines for the Management of Atrial fibrillation (2010 Version). Eur. Heart J. 2010; 6: 1—61.

eISSN: 2349-5715 pISSN: 2349-5707
Volume: 11, Issue 03, March-2024 SJIF 2019: 4.702 2020: 4.737 2021: 5.071 2022: 4.919 2023: 6.980 2024: 7,662

2. Savchenko A. P., Zhirov I. V., Rudenko B. A. et al. Endovascular application устройства of the WATCHMAN device for the prevention of thromboembolic complications in a patient with atrial fibrillation. Cardiology. 2012; 8: 93—6.
3. Aldhoon B., Melenovsky V., Peichl P., Kautzner J. New insights into mechanisms of atrial fibrillation. Physiol. Res. 2010; 59 (1): 1—12.
4. Nguyen B., Fishbein M., Chen L. et al. Histopathological substrate for chronic atrial fibrillation in humans. Heart Rhythm. 2009; 6 (4): 454—60.
5. Spach M., Boineau J. Microfibrosis produces electrical load variations due to loss of side-to-side cell connections: a major mechanism of structural heart disease arrhythmias. Pacing Clin. Electrophysiol. 1997; 20: 397—413.
6. Wolk R., Cobbe S., Hicks M., Kane K. Functional, structural, and dynamic basis of electrical heterogeneity in healthy and diseased cardiac muscle: implications for arrhythmogenesis and anti-arrhythmic drug therapy. Pharmacol. Ther. 1999; 84 (2): 207—31.
7. Gluba A., Bielecka A., Mikhailidis D., et al. An update on biomarkers of heart failure in hypertensive patients. J. Hypertens. 2012; 30 (9): 1681—9.
8. Lopez B., Gonzalez A., Querejeta R. et al. The use of collagen- derived serum peptides for the clinical assessment of hypertensive heart disease. J. Hypertens. 2005; 23 (8): 1445—51.
9. Macias B., Fatela-Cantillo D., Jiménez L. et al. Left ventricular mass, diastolic function and collagen metabolism biomarkers in essential hypertension. Med. Clin. (Barc). 2012; 138 (4): 139—44.
10. Frustaci A., Chimenti C., Bellocci F. et al. Histological substrate of atrial biopsies in patients with lone atrial fibrillation. Circulation. 1997; 96 (4): 1180—4.
11. Grigoryan S. V., Azarapetyan L. G., AdamyanK. G. Comparative assessment of markers of inflammation andfibrosisin patients withvarious clinical forms of atrial fibrillation. // Cardiovascular therapy andprevention. 2018;17(6):26–31. http://dx.doi.org/10.15829/1728-8800-2018-6-26-31