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Painless Cardiac Ischemia in Women with Rheumatoid Arthritis

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Abstract: Rheumatoid arthritis (RA) is an autoimmune rheumatic disease of unknown etiology characterized by chronic erosive arthritis and systemic inflammatory damage to internal organs. In Uzbekistan, RA affects about 1.5% of the entire adult population. RA most often affects people aged 30-50 years. Women get sick 5 times more often than men. The main cause of mortality in RA are cardiovascular catastrophes (myocardial infarction (MI), cerebral stroke (CS) den cardiac death (SCD). Let's start the discussion with the already established facts and try to clarify the mechanisms of the changes in the heart. So,rheumatoid arthritis (RA) is an autoimmune joint disease that affects 0.5–1.0% of the world's population. In RA, almost all joints are involved in the pathological process, almost always the joints of the hand, foot and knee joints, with the development of stiffness, pain and, eventually,destruction of bone and cartilage. It is known that RA is a systemic process in which not only joints are affected, but also various internal organs. However, until recently, it was believed that heart damage in RA was clinically insignificant. In recent years, it has been found that patients with RA, life expectancy decreases by 7-10 years, and the risk of coronary disease or myocardial infarction is comparable to that of diabetes mellitus. In general, patients with RA, the risk of development is approximately 50% higher cardiovascular events and cardiovascular death. At the same time, it should be taken into account that the magnitude of these risks may vary in different studies, which is associated with the characteristics of the examined cohorts of patients, with the peculiarities of treatment in different countries, with the effectiveness of achieving or not achieving the goal of treatment, depends on the time of observation and the specifics of the therapy performed. Thus, there are indications that the combined relative risk is 1.68 and 1.87 for myocardial infarction and congestive heart failure, respectively, and another study found that

patients with RA had an increased risk of myocardial infarction (MI) with a odds ratio (OR) of 2.50 (95% CI; 0.77–8.14)

Keywords: rheumatoid arthritis, coronary heart disease

Introduction

The course of coronary artery disease in patients with RA has its own characteristics, such as an increased frequency and early relapses of acute coronary syndrome (ACS), high mortality after the first MI, the prevalence of pain-free myocardial ischemia and asymptomatic MI, a high frequency of subclinical atherosclerotic vascular lesions, a low percentage of critical coronary artery stenosis, but at the same time a high frequency of "vulnerable" atherosclerotic plaques and pronounced signs of inflammation of the vascular wallTo date,information has been accumulated about possible causal relationships between the activity of inflammation and the accelerated progression of atherosclerosis, which is undoubtedly relevant in RA. According to the results of epidemiological studies, RA is recognized as an independent predictor of coronary heart disease in the general population. Asymptomatic atypical course of acute coronary syndrome was observed in every 5th RA patient. Almost half of the patients with RA were found to have painless ischemia based on the results of daily ECG monitoring. According to some data, pain-free ischemia occurred in 45% of RA patients, while a significant frequency (82.5%) of rhythm disturbances was noted, mostly due to supraventricular extrasystole in association with inflammatory activity. Perfusion single-photon emission computed tomography under pharmacological stress revealed signs of stable coronary heart disease in 59% of RA patients and 27% of the examined control group. Multivessel atherosclerotic lesion of the coronary arteries was diagnosed in a large number of patients with RA by coronary angiography. The

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causal relationship of endothelial dysfunction, the progression of which occurred in parallel with an increase in the activity of immunopathological inflammation, and the accelerated development of coronary atherosclerosis in RA patients was demonstrated by V.I. Mazurov et al. At the same time, the traditional risk factors – arterial hypertension (AH) and hypercholesterolemia – were less important in the formation and progression of coronary heart disease in this category of patients.

The most common factors that increase the risk of developing CVD in patients with RA include old age, male gender, genetic predisposition, burdened history of CVD (< 65 years in women, < 55 years in men), sedentary lifestyle (less than 150 minutes per week of moderate aerobic exercise), smoking (current, past, intensity, passive smoking), obesity (body mass index $\geq$ 30 kg/m^2, waist circumference $\geq$ 94 cm for men, $\geq$ 80 cm for women), body weight deficit (< 18.5 kg/m^2), arterial hypertension (>140/90 mmHg., systolic pressure >140/85 mmHg), dyslipidemia [low/moderate cardiovascular risk (SSR) – LDL cholesterol > 3.0 mmol/L; high SSR – LDL cholesterol > 2.6 mmol/L; very high SSR – LDL cholesterol > 1.8 mmol/L]. HDL CHOLESTEROL < 1.0 mmol/l for men and < 1.2 mmol/l for women; triglycerides > 1.7 mmol/l; type II diabetes; menopause; chronic heart disease; obstructive sleep apnea syndrome; periodontitis; hypothyroidism; insulin resistance; hypercoagulation; hyperhomocysteinemia, hyperuricemia; low vitamin D levels; adverse psychosocial status (social isolation, low socio-economic status, psychosocial stress, belonging to small ethnic groups); depression, anxiety. There are also risk factors that are directly related to RA, such as long-term moderate or high activity of RA; the duration of RA is more than 10 years; extra-articular manifestations; pronounced functional insufficiency of joints; highly positive levels of rheumatoid factor/antibodies to cyclic citrulline peptide; medications (GCS, NSAIDs, cyclosporine A) The disease-modifying therapy of RA, aimed at suppressing the activity of inflammation and slowing the progression of joint destruction, was often associated with an increase in HDL levels, which means it could have potentially anti-atherogenic properties.

The purpose of our study is to study the frequency, structure and features of the course of coronary heart disease in RA.

Materials And Methods

An analytical one-stage cross-sectional study of cardiovascular pathology was conducted in 77 patients with RA in a representative sample of Samarkand patients. Women prevailed (19 or 81.3%) with a moderate degree of activity according to DAS 28 (4.4±1.9), seropositivity according to RF (51 or 81.3%) and the III radiological stage of the disease (8 or 44.0%). Functional insufficiency of the joints corresponded in the overwhelming majority of cases to the II–III functional class. The average age of patients was 55.4±11.6 years, the duration of RA was 14.7 (2; 20) years. The diagnosis of coronary heart disease was verified on the basis of clinical, laboratory and instrumental data. All patients underwent an ECG in 12 standard leads for device Schiller AT-10 Plus (Schiller, Switzerland) and daily monitoring of blood pressure and ECG according to the generally accepted method using bifunctional monitors Cardio Tens-01 and Meditech card(x)plore (Hungary). The level of serum lipids was determined by the enzymatic method on an automatic analyzer In / M HITACHI 902 (Roche B/M, France). Endothelial function was assessed noninvasively using vasodilation tests by D.S. Celermajer. Statistical processing of the results was carried out using Epi info ver.6, Biostatistica 4.0 McGraw – Hill, Statistica application software packages 6.0 (Statsoft, USA).

Results

Coronary heart disease in RA after detailed verification of the diagnosis, taking into account daily ECG monitoring, was detected in 35 (45.9%) patients: typical angina pectoris was in 19 (52.5%), pain–free ischemia and rhythm disturbance - in 9 (25.4%) and 7 (22.1%) patients, respectively. At the same time, a high proportion of vertebrogenic cardialgia was noted – in 30 (48.8%) patients from among those who complained of pain in the heart area. This may create prerequisites for the erroneous interpretation of chest pain in this category of patients. In the vast majority of cases, cardialgia was diagnosed in postmenopausal women (88% vs. 12% in men, p<0.01), long–term RA patients (15.6±7.6 years), who in a large number of cases (41%) were prescribed glucocorticoids - GC (41%), including in the form of intra-articular injections (on average 7.5± 1.5 injections per year). This does not exclude the possible development of osteopenic syndrome in their spine and related complications.

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Detailed verification of the diagnosis of coronary heart disease was carried out by daily monitoring of an ECG diagnostic test alternative to a physical exercise test due to functional insufficiency of the joints in this category of patients. A comparative characteristic of the pathology detected during daily monitoring of ECG and resting ECG is presented in Table 1.

The method of daily ECG monitoring in RA patients made it possible to reliably verify ischemic changes, atrial fibrillation and atrioventricular conduction disorders more often than resting ECG, which must be taken into account in a wide clinical practice.

Significant risk factors for coronary heart disease in RA patients, according to the results of logistic regression, are presented in Table 2 in rating order.

From the data in Table. 2 it can be seen that the risk of coronary heart disease in RA increased significantly when combined with traditional cardiovascular risk factors – hypertension, smoking and anemia, early menopause in women, decreased GFR, burdened with heredity for cardiovascular diseases (CVD), overweight, high average daily heart rate, atherogenic profile dyslipidemia and hyperglycemia. Along with traditional predictors of cardiovascular risk, the contribution of factors associated with RA has been demonstrated. Thus, long–term use of GC and high activity of inflammation according to DAS 28 increased the risk of coronary heart disease in this category of patients by 5 and 3.5 times, respectively (5.06-2.66<HR<9.54, p<0.01 and 3.67– 1.93<HR<7.01, p<0.01).

Among RA patients with an established diagnosis of coronary heart disease, the frequency of endothelial dysfunction was 86.4% (n=31). As is known, the clinical equivalent of endothelial dysfunction is a tendency to vasoconstriction. In 9 patients with pain-free ischemia, endothelial dysfunction was found in the vast majority of cases (93%), which suggests that they have a close pathophysiological relationship of ischemia with vasospastic reactions.

The analysis of the lipid spectrum did not reveal a dominant hypertriglyceridemia and/or a predominant decrease in HDL levels, as previously shown in some studies. Thus, the average level of total CHOLESTEROL was 5.0 ± 1.9 mmol / l, LDL cholesterol – 3.0 ± 0.9 mmol / l, HDL cholesterol – 0.9 ± 0.3 mmol / L, triglycerides – 1.6 ± 0.5 mmol / l, the frequency of isolated hypercholesterolemia – 29.6%, various variants of dyslipidemia – 34.2%.

Thus, CHD, according to our observations, was established in 45.9% of RA patients. The features of the course of this pathology include frequent detection of rhythm disturbances and pain-free ischemia. Routine diagnostic methods, both clinical and instrumental, do not always allow to confirm the diagnosis of coronary heart disease in this category of patients. This is due to the high frequency of cardialgia, which can contribute to erroneous diagnosis. The inability to use the test with physical activity significantly limits diagnostic capabilities, therefore, other diagnostic tests should be used more widely, in particular daily ECG monitoring. The high frequency of endothelial dysfunction with a tendency to vasoconstriction, especially in pain-free ischemia, should be taken into account in clinical practice. Such patients are necessarily prescribed antagonists of slow calcium channels and beta-blockers with a vasodilating effect. Significant risk factors for coronary heart disease (along with traditional ones) directly associated with the consequences of chronic inflammation are the activity and duration of RA, your pain >50 mm, taking HA > 12 months in a total dose of > 3 g in terms of prednisone, as well as concomitant anemia as a frequent complication of RA.

Literature

1. Alisherovna, K. M., Baxtiyorovich, Z. M., & Anvarovich, N. J. (2022). To Assess The Condition Of The Myocardium In Patients Chronic Heart Failure On The Background Of Rheumatoid Arthritis. *Spectrum Journal of Innovation, Reforms and Development*, *4*, 210-215.
2. Alisherovna, K. M., Toshtemirovna, E. M. M., & Oybekovna, E. E. (2022). QUALITY OF LIFE OF PATIENTS WITH CIRRHOSIS OF THE LIVER. *Spectrum Journal of Innovation, Reforms and Development*, *4*, 197-202.
3. Erkinovna, K. Z., Davranovna, M. K., Toshtemirovna, E. M. M., & Xudoyberdiyevich, G. X. (2022). CORRECTION OF COMPLICATIONS IN CHRONIC HEART FAILURE DEPENDING ON THE FUNCTIONAL STATE OF THE KIDNEYS. *Web of Scientist: International Scientific Research Journal*, *3*(5), 565-575.

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4. Khabibovna, Y. S., & Buribaevich, N. M. (2020). STUDY OF PARAMETERS OF CENTRAL HEMODYNAMICS IN PATIENTS WITH CHRONIC GLOMERULONEPHRITIS. *Достижения науки и образования*, (13 (67)), 57-59.

5. Makhmudova, K. D., & Gaffarov, H. H. (2021, February). STUDYING THE LIVER FUNCTION IN BURN RECONVALESCENTS. In *Archive of Conferences* (Vol. 15, No. 1, pp. 208-210).

6. Rustamovich, T. D., & Hasanovich, B. D. (2021, February). COMORBID FACTORY OF HEART BLOOD VEHICLES AND METABOLIC SYNDROME IN PATIENTS. In *Archive of Conferences* (Vol. 14, No. 1, pp. 18-24).

7. Toirov, D. R., & Berdiyev, D. X. (2021). PODAGRA KASALLIGIDA KARDIOGEMODINAMIK BUZILISHLAR O'ZIGA XOSLIGI. *Scientific progress*, *2*(3), 775-784.

8. Toshtemirovna, E. M. M., Nizamitdinovich, K. S., Tadjiyevich, X. A., & Xudoyberdiyevich, G. X. (2022). ASSESSMENT OF RENAL DYSFUNCTION IN PATIENTS WITH CHRONIC HEART FAILURE.

9. Xaydarov, S. N., & Normatov, M. B. (2021). DETERMINATION OF IRON DEFICIENCY ANEMIA AT THE PREGNANCY PERIOD. *Scientific progress*, *2*(4), 325-327.

10. Yarmatov, S. T., & Xusainova, M. A. (2021). BRONXIAL ASTMA MAVJUD BO'LGAN BEMORLARDA GASTROEZOFAGIAL REFLYUKS KASALLIGI DIAGNOSTIKASI VA OLIB BORISH ALGORITMI. *Scientific progress*, *2*(2), 208-213.

11. Yarmatov, S. T., & Yarmahammadov, U. K. (2022). Semizlik–Zamonaviy Tibbiyotda Dolzarb Muammo Sifatida Qolmoqda. *Scientific progress*, *3*(4), 1196-1203.

12. Yarmukhamedova, S. (2020). SURUNKALI GLOMERULONEFRIT BILAN OG 'RIGAN BEMORLARDA ARTERIAL QON BOSIMINING SUTKALIK MONITORING KO 'RSATKICHLARINI BAXOLASH. *Журнал кардиореспираторных исследований*, *1*(1), 103-108.

13. Yarmukhamedova, S., & Amirova, S. (2021). ARTERIAL GIPERTENSIYA BILAN ORIGAN BEMORLARDA YURAK GEOMETRIK KO'RSATKICHLARINING O'ZGARISHI. *Scientific progress*, *2*(3), 944-948.

14. Yarmukhamedova, S., Nazarov, F., Mahmudova, X., Vafoeva, N., Bekmuradova, M., Gaffarov, X., ... & Xusainova, M. (2020). Features of diastolic dysfunction of the right ventricle in patients with hypertonic disease. *Journal of Advanced Medical and Dental Sciences Research*, *8*(9), 74-77.

15. Yarmukhamedova, S., Nazarov, F., Mahmudova, X., Vafoeva, N., Bekmuradova, M., Gafarov, X., ... & Xusainova, M. (2020). Study of indicators of intracardial hemodynamics and structural state of the myocardium in monotherapy of patients with arterial hypertension with moxonidin. *Journal of Advanced Medical and Dental Sciences Research*, *8*(9), 78-81.

16. Zikiryayevna, S. G., Makhmudovich, A. S., Fakhriddinovich, T. S., & Muxtorovna, E. M. (2022). NON-ALCOHOLIC FATTY LIVER DISEASE. *Web of Scientist: International Scientific Research Journal*, *3*(10), 414-422.

17. Zikiryayevna, S. G., Muxtorovna, E. M., Jurakulovich, U. I., & To'raqulovna, Q. S. (2022). PAINLESS CARDIAC ISCHEMIA IN WOMEN WITH RHEUMATOID ARTHRITIS. *Web of Scientist: International Scientific Research Journal*, *3*(10), 397-405.

18. Zokhidovna, K. Z., & Xudoyberdiyevich, G. X. (2022). " ISOLATED" DIASTOLIC MYOCARDIAL DYSFUNCTION IN DIABETES MELLITUS. *Spectrum Journal of Innovation, Reforms and Development*, *7*, 101-107.

19. Тоиров, Д. Р., & Махмудова, Х. Д. (2021). ПОДАГРА КАСАЛЛИГИ БИЛАН ОҒРИГАН БЕМОРЛАРДА ЮРАК ҚОН-ТОМИР ЗАРАРЛАНИШЛАРИ. *Scientific progress*, *2*(2), 242-249.

20. Хайдарова, З. (2021). ЭНТРОПИЯ И НАРУШЕНИЯ СЕРДЕЧНОГО РИТМА У БОЛЬНЫХ, ПЕРЕНЕСШИХ ИНФАРКТ МИОКАРДА. *Журнал кардиореспираторных исследований*, *2*(4), 59-62.

21. Хусаинова, М. (2021). CHRONIC HEART FAILURE IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS. *Журнал кардиореспираторных исследований*, *2*(4), 67-69.

22. Ярмухаммедова, С. (2020). ОЦЕНКА ПРИЗНАКОВ ДИАСТОЛИЧЕСКОЙ ДИСФУНКЦИИ ПРАВОГО ЖЕЛУДОЧКА У БОЛЬНЫХ С АРТЕРИАЛЬНОЙ ГИПЕРТОНИЕЙ. *Журнал кардиореспираторных исследований*, *1*(2), 88-92.

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