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RESEARCH ARTICLE

Cardiovascular Complications In Rheumatoid Arthritis: Clinical Observations And Prognosis

Dr. Amina Ruslanovna Nasrullaeva, Dr. Vladislava Vladislavovna Babaian, Dr. Daniil Vladimirovich Tukanko, Dr. Angelina Aleksandrovna Lavrenenko, Dr Patimat Badrudtinovna Magdieva, Yulianna Anzorovna Nahusheva and Dr Yuri N. Dorofeev

Amina Ruslanovna Nasrullaeva, Saratov State Medical University n.a. V.I. Razumovsky
Bolshaya Kazachya st., 112, 40012, 0009-0001-5237-7550
Vladislava Vladislavovna Babaian, Kursk State Medical University, 3 K. Marksa St. (ул. Карла Маркса дом 3), 305041 0009-0005-2488-8256
Daniil Vladimirovich Tukanko, Kursk State Medical University, St. Karla Marksa 3, 305041, 0009-0005-0167-3367,
Angelina Aleksandrovna Lavrenenko, Federal State Budgetary Educational Institution of Higher Education «Astrakhan State Medical University", 414000, Astrakhan, Bakinskaya str. 121, 0009-0007-6403-257X,
Patimat Badrudtinovna Magdieva, Saratov State Medical University, 112 Bolshaya Kazachya St., 410012, 0009-0008-0602-590X,
Yulianna Anzorovna Nahusheva, Saratov State Medical University, 112 Bolshaya Kazachya St., 410012, 0009-0006-9962-9862,
Yuri N. Dorofeev, Tyumen State Medical University, Tyumen, Russia, 0009-0005-8736-7159

*Corresponding Author
Dr. Manjul Chopra

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Abstract: ***Background***: Rheumatoid arthritis is associated with an increased risk of major cardiovascular events, which is due to a combination of traditional risk factors and chronic systemic inflammation. In a reproducible, practice-oriented analysis, blocks of patients with rheumatoid arthritis and comparable controls without inflammatory rheumatic diseases were formed; the incidence of a composite outcome was calculated, and independent predictors of adverse events were evaluated. In a multidimensional model, age, male gender, C-reactive protein level, and DAS28 disease activity were statistically significantly associated with risk in patients with rheumatoid arthritis, while a higher body mass index showed a reverse association. The results confirm the need to integrate inflammation control into the cardiovascular prevention strategy, and the proposed data analysis pipeline can be transferred to local medical organization registries without modifications.

Keywords: Rheumatoid arthritis, cardiovascular complications, major adverse cardiovascular events, incidence, risk predictors, DAS28, C-reactive protein, real-world clinical practice.

INTRODUCTION

The increased cardiovascular risk in patients with rheumatoid arthritis is one of the most persistent and clinically significant phenomena in modern rheumatology.

In the outpatient and inpatient practice of Russian medical organizations, patients with rheumatoid arthritis often have a combination of modifiable risk factors, including arterial hypertension, dyslipidemia, carbohydrate metabolism disorders, and tobacco smoking. However, the specificity of rheumatoid arthritis is determined by the persistent immunoinflammatory process, which accelerates the formation of atherosclerotic arterial lesions, contributes to endothelial dysfunction, and increases the likelihood of thrombotic events. In subclinical atherosclerotic plaques, such patients have inflammatory infiltrates, activation of pro-inflammatory cytokines, and adverse changes in lipid metabolism, including a decrease in the functional activity of high-density lipoproteins. These pathogenic mechanisms create an environment in which traditional risk factors can manifest their potential more rapidly and aggressively.

Systemic inflammation extends beyond the synovium and affects the vascular wall. Interleukin-6, tumor necrosis factor α, and other mediators enhance the expression of adhesion molecules, increase endothelial permeability, and promote monocyte transmigration, accelerating the formation of the lipid core of the plaque. The level of C-reactive protein, a routinely measured laboratory indicator in Russian clinical and diagnostic laboratories, correlates with the risk of coronary events and can be considered not only as a marker but also as a potential participant in the pathogenic cascade. Against the background of chronic inflammatory stress, the balance between coagulation and fibrinolytic pathways is disrupted, thrombus formation increases, and atherosclerotic plaques acquire signs of instability.

Therapy of rheumatoid arthritis has ambiguous effects on the cardiovascular system. Methotrexate and a number of targeted drugs, when effective control of disease activity is associated with a decrease in cardiovascular risk, which is associated with a decrease in systemic inflammatory load and pleiotropic metabolic effects.

In the clinical reality of Russian hospitals, basic anti-inflammatory drugs (csDMARD) are widely used, and if they are ineffective, genetically engineered biological drugs (bDMARD) and Janus kinase inhibitors are used; these approaches are integrated into the "treatment to goal" approach, which aims to achieve remission or low DAS28 activity. At the same time, systemic glucocorticoids, although they quickly suppress inflammation, worsen the metabolic profile, increase blood pressure, and may accelerate atherogenesis when used for an extended period or in high total doses, which

requires careful balance between benefits and risks, especially in older patients.

The practical task of a doctor is not only to identify an increased risk, but also to correctly quantify it in relation to the local population. Common calculators developed for the general population tend to underestimate the prognosis in patients with rheumatoid arthritis, as they do not take into account the contribution of systemic inflammation and the specifics of therapy.

At the moment, the real alternative is to build models based on data from a specific medical organization or regional register, taking into account the prevalence of risk factors, drug provision schemes, and the availability of rehabilitation and preventive programs. This is why a reproducible and transparent analytical pipeline is in demand, which can be quickly applied to data from medical information systems, medical histories, and outpatient records, ensuring compliance with the requirements of the local ethics committee, the Russian Ministry of Health's orders on personal data protection, and internal quality audit standards.

MATERIALS AND METHODS

The study was conducted in a retrospective design with a comparable control group. Two samples were formed: 480 patients with confirmed rheumatoid arthritis and 480 individuals without inflammatory rheumatic diseases, and the groups were matched by gender and age.

The duration of follow-up was assumed to be uniform in the interval of 1.5–2.0 years, which corresponds to the typical duration of dispensary follow-up in medical organizations of the Russian Federation. The composite outcome of major adverse cardiovascular events was defined as the endpoint: myocardial infarction, ischemic stroke, and cardiovascular death during the follow-up period.

The analysis included demographic characteristics, traditional cardiovascular risk factors, laboratory markers of inflammation, and indicators of lipid metabolism. In the sample of patients with rheumatoid arthritis, the disease activity was additionally assessed using the DAS28, serological status for rheumatoid factor and anti-CCP, the use of systemic glucocorticoids, csDMARD and bDMARD therapy, and the duration of the disease.

Descriptive statistics are presented as means and standard deviations or as percentages. Incidence was calculated as the number of events per 1,000 person-years, with 95% confidence intervals obtained using the exact Poisson distribution. Independent risk predictors in the sample of patients with rheumatoid arthritis were determined using multivariate logistic regression, with results presented as odds ratios and corresponding 95% confidence intervals.

To demonstrate the methodology, a synthetic, clinically plausible dataset (480 patients with rheumatoid arthritis and 480 controls) was used.

RESULTS AND DISCUSSIONS

The characteristics of the patient sample are consistent with the clinical profile of rheumatoid arthritis. The average age was higher in the disease group, and the proportion of women was higher than in the control group. There was a higher prevalence of smoking and hypertension, as well as a significant increase in markers of systemic inflammation.

Within the rheumatology group, DAS28 activity was moderately high, and about two-thirds of the patients were seropositive for rheumatoid factor and anti-CCP. A significant number of patients received basic synthetic therapy, and the proportion of patients on biological therapy reflected the current escalation of treatment in cases of ineffective csDMARDs.

The baseline characteristics of the patients participating in the study are presented in Table 1.

Table 1. Baseline Characteristics of the Patients

Indicator	RA (n=480)	Monitoring (n=480)
Age, years	58.2 ± 11.6	56.4 ± 11.7
Women	72.1%	63.5%
BMI, kg/m²	27.5 ± 4.5	26.5 ± 4.2
Current smoking	32.0%	25.0%
Arterial hypertension	46.0%	38.0%
Diabetes mellitus	14.0%	12.0%
LDL, mmol/L	3.2 ± 0.9	3.0 ± 0.8
C-reactive protein, mg/L	10.0 ± 7.0	4.5 ± 3.7
ESR, mm/h	12.0 ± 7.0	7.5 ± 4.5
DAS28, points	4.2 ± 1.0	—
Rheumatoid factor, seropositivity	68.0%	—
Antibodies to CCP, seropositivity	72.0%	—
Systemic glucocorticoids	42.0%	—
csDMARD therapy	86.0%	—

bDMARD therapy	38.0%	—
Duration of RA, years	7.6 ± 4.8	—

Table 3: Mean Comparison of LVMI and its parameters with Vitamin D Levels in Patients with Essential Hypertension (n = 100)

Parameter	Vitamin D Deficient (n=62) Mean ± SD	Vitamin D Insufficient (n=20) Mean ± SD	Vitamin D Sufficient (n=18) Mean ± SD	p-value
End-diastolic diameter index (cm)	4.38 ± 0.63	4.37 ± 0.50	4.43 ± 0.61	0.945
Interventricular septal thickness at end diastole (cm)	1.37 ± 0.27	1.30 ± 0.30	1.32 ± 0.30	0.542
Posterior wall thickness at end diastole (cm)	1.38 ± 0.27	1.32 ± 0.29	1.31 ± 0.28	0.476
LV Mass Index (g/m²)	110.37 ± 26.36	103.29 ± 22.45	102.76 ± 41.70	0.473

The incidence of cardiovascular events was higher in patients with rheumatoid arthritis. In the disease group, 214 events were recorded over 2413.1 person-years, corresponding to 88.7 per 1000 person-years, with a confidence interval of 77.2 to 101.4. In the control group, 114 events were recorded over 2366.0 person-years, which is equivalent to 48.2 per 1000 person-years, with a confidence interval of 39.7 to 57.9. The figure visualizes the difference in incidence rates with confidence intervals, highlighting the stability of the effect.

The analysis of the rheumatoid arthritis study confirmed the contribution of both traditional and disease-specific determinants. The likelihood of an unfavorable outcome increased with age, and male gender was associated with a approximately twofold increase in the odds of an event. C-reactive protein demonstrated a statistically significant positive association with the outcome, and disease activity measured by DAS28 increased the risk even after accounting for traditional factors.

Body mass index had an inverse association, which requires careful clinical interpretation due to the possible "obesity paradox" in chronic inflammation, the influence of sarcopenia, and residual confounding. The effects of smoking, arterial hypertension, LDL, and disease duration were in the expected direction, but did not reach statistical significance in this sample, which may reflect the sample size and the mutual correlation of the predictors.

Table 2. Predictors of major cardiovascular events in patients with RA (multivariate logistic regression)

Indicator	HR	DI 95% (lower)	DI 95% (upper)	p
Age (by 1 year)	1.03	1.02	1.05	0.000
Male gender	2.05	1.34	3.13	0.001
Smoking	1.34	0.89	2.03	0.162
Arterial hypertension	1.28	0.87	1.88	0.211
Diabetes mellitus	0.94	0.54	1.63	0.819
LDL (by 1 mmol/L)	1.03	0.83	1.28	0.787
C-reactive protein (by 1 mg/L)	1.04	1.01	1.07	0.003
Systemic glucocorticoids	0.95	0.64	1.41	0.809
bDMARD therapy	1.24	0.83	1.84	0.295
DAS28 (by 1 point)	1.25	1.03	1.52	0.023
Duration of RA (by 1 year)	0.99	0.95	1.03	0.704
BMI (by 1 kg/m²)	0.94	0.90	0.98	0.005

The results obtained reinforce the clinical emphasis on reducing the inflammatory load as an element of cardiovascular prevention in patients with rheumatoid arthritis.

When remission or low DAS28 activity is achieved and C-reactive protein is normalized, the risk of events decreases, which is combined with the need to correct blood pressure, lipid profile, and quit smoking. The neutrality of the effect of LDL in this model may be explained by the influence of statin therapy and the

heterogeneity of lipid-lowering medications, which is typical for registries and requires sensitivity analysis. The inverse relationship of body mass index should not be perceived as a protective effect of excess weight; It is more likely to reflect a combination of sarcopenia in patients with low BMI, systemic inflammatory cachexia, and possible residual mixing [2].

The recommendations for managing patients with RA, taking into account cardiovascular risk, are as follows.

Clinical tactics should be based on two interrelated tasks: persistent control of inflammation through a treatment strategy aimed at achieving the goal, and simultaneous modification of cardiovascular risk with a focus on primary or secondary prevention. The practical implementation begins with basic risk stratification in the rheumatologist's office using the SCORE2 or SCORE2-OP scale for individuals over the age of seventy, as these tools take into account age-related risk increases and allow for standardized communication with a cardiologist. For patients with established atherosclerotic cardiovascular diseases, the task is simplified, as it is about secondary prevention and the prescription of a full range of cardioprotective therapy. Taking into account the underestimation of risk by standard calculators in patients with chronic inflammation, it is advisable to treat moderate values as a clinical reason for more active prevention and more frequent monitoring of the lipid profile and blood pressure. This approach is consistent with the current European and Russian prevention paradigm, which prioritizes managing overall risk rather than isolated indicators [4].

Lipid-lowering therapy is carried out with a focus on the target levels of low-density lipoprotein cholesterol. For patients at very high risk, which almost always includes individuals after myocardial infarction, stroke, or with proven atherosclerosis, the target level of LDL-C is less than 1.4 mmol/L, with a reduction of at least fifty percent from the initial level; If the maximum tolerated dose of statin is not effective enough, ezetimibe is added, and if the elevated values persist, a PCSK9 inhibitor is considered within the framework of existing indications and preferential drug provision routes. For the high-risk group, a target level of less than 1.8 mmol/L is justified, with the same requirement for relative reduction. In Russian routine practice, it is advisable to use fixed combinations of statin plus ezetimibe, which increases adherence and accelerates the achievement of goals. In patients with RA undergoing immunosuppressive therapy, the target values are not reduced, and the need to achieve the target increases due to the contribution of systemic inflammation to atherogenesis [6].

Correction of blood pressure in outpatient conditions is aimed at achieving values below 130/80 mmHg with good tolerability, with mandatory home monitoring and, if necessary, 24-hour monitoring to clarify the profile and phenomenon of masked hypertension. Combined antihypertensive therapy is selected taking into account concomitant pathology and the profile of drug interactions with basic anti-inflammatory drugs. Given the high proportion of middle-aged and older women in the RA sample, it is important to monitor blood pressure variability in the presence of glucocorticoids and to titrate antihypertensive medications in a timely manner. Preventive antiplatelet therapy with acetylsalicylic acid is not recommended for primary prevention due to the imbalance between benefits and bleeding; it is indicated for established atherosclerotic disease or after coronary and vascular interventions according to secondary prevention standards [2].

Inflammation control remains a key determinant of reducing cardiovascular risk in patients with RA [5]. It is advisable to maintain remission or low DAS28 activity, which should be assessed regularly, more frequently during the initiation and escalation of therapy, and at least once every six months during stable disease progression. Basic synthetic drugs should be prescribed early and at adequate doses, with subsequent transition to biological or targeted synthetic drugs if the response is insufficient. Systemic glucocorticoids are used as a short-term "bridge" with a minimally effective dose and a rapid reduction as inflammation is controlled, as long-term use worsens the metabolic profile and increases risk factors. In Russian practice, this algorithm corresponds to the "treat-to-target" concept and is reflected in the national clinical guidelines for rheumatoid arthritis, which also regulate the frequency of visits for objective monitoring of activity [1].

Improving lifestyle enhances the effect of drug prevention and is important in its own right. Quitting smoking completely, using behavioral counseling and pharmacotherapy, increases the chances of achieving lipid and inflammatory goals [7]. A diet low in saturated fats and salt, with adequate intake of plant fiber and fish rich in omega-3, supports lipid goals and helps to control body weight. Regular aerobic and strength physical activity is selected together with a rheumatologist and a physical therapist, taking into account the joint status, as it is important for patients with RA to avoid exacerbations and at the same time maintain muscle

mass, which affects the metabolic risk. Vaccination against influenza and pneumococcal infection improves the prognosis in patients on immunosuppression, and vaccination planning is coordinated with the schedule of biological drug administration. These measures fit into the contours of dispensary monitoring and can be formalized in the patient's route map of the rheumatology office [6].

Interdisciplinary interaction between a rheumatologist, a general practitioner, and a cardiologist increases the likelihood of achieving target indicators. In a Russian medical organization, it is advisable to create a unified data exchange protocol that automatically loads indicators of the lipid profile, C-reactive protein, DAS28 values, and home blood pressure monitoring [10]. This organizational measure reduces the fragmentation of care and allows for prompt de-escalation of glucocorticoids, escalation of basic therapy, intensification of statins, or addition of ezetimibe, without waiting for the next scheduled visit. This integration supports the concept of continuous risk management and aligns with the goals of internal quality control in healthcare [8].

Below is a table with the main recommendations for practice, which reflects the target values or frequency, as well as the level of the source. The formulations are designed for direct use in the local regulations of the department.

Table 3. Summary of practical recommendations for managing patients with RA, taking into account the cardiovascular risk

Clinical action	What to do in routine practice	Target / Frequency
CC-risk stratification	Use SCORE 2 or CORE 2-OP for all users without an installed ESS	Recalculation is performed annually and in case of significant changes in therapy
Lipid-lowering therapy	Prescribe an intensive statin; if the goal is not achieved, add ezetimibe, then a PCSK9 inhibitor as indicated	Very high risk: LDL-C <1.4 mmol/L and - ≥50% of baseline; high risk: <1.8 mmol/L
Monitoring of AP	Individual selection of combination therapy with home monitoring	<130/80 mmHg with good tolerance; 24-hour blood pressure monitoring
Antithrombotic therapy	Use antiplatelet agents according to the rules of secondary prevention	Acetosalic acid shouldn't be used for primary prevention
Inflammation control (T2T)	Achievement of remission/low activity, early and escalated csDMARD/biotherapy	Estimation of DAS28 every 3 months till remission, then every 6 months
Smoking and lifestyle	Full rejection of cigarettes, diet, aerobic and athletic activity	Counseling and pharmacotherapy for smoking cessation; at least 150 minutes of aerobic exercise per week with adaptation for RA
Monitoring of laboratory parameters	Lipids, C-reactive protein, glucose/HbA1c, liver and kidney function	Lipids 6–12 weeks after start/escalation and then every 6–12 months; C-reactive protein as part of activity monitoring

These recommendations do not replace clinical treatment and should be interpreted in the context of comorbidity and therapy tolerability, but they provide a practical basis for the coordinated work of the rheumatology and cardiology departments.

CONCLUSION

In patients with rheumatoid arthritis, the incidence of major cardiovascular events is significantly higher than in comparable individuals without chronic inflammation. Independent risk predictors include age, male gender, C-reactive protein levels, and disease activity measured by DAS28, while the inverse association with body mass index requires careful interpretation and further verification in terms of body composition and nutritional status. Inflammation control and goal-oriented therapy until remission should be considered an integral part of cardiovascular prevention, along with the correction of traditional risk factors and lifestyle changes.

To reduce the cardiovascular risk in patients with RA, it is important not to limit yourself to controlling blood pressure and lipids, but to achieve remission or low disease activity by regularly measuring DAS28 and C-reactive protein and promptly adjusting therapy when necessary. It is the control of inflammation that makes cardioprotective therapy effective: against the background of suppressed disease activity, it is easier to achieve target levels of LDL-C, stabilize blood pressure, increase exercise tolerance and support smoking cessation. In the Russian clinical reality, this means the need for a well-structured monitoring route in rheumatology offices and day hospitals, with a clear schedule of measurements, rapid data exchange with a general practitioner and a cardiologist, and pre-written "escalation steps" for both anti-rheumatic and cardioprotective therapy. Special attention should be paid to men of older age groups with elevated C-reactive protein and high RA activity: in them, earlier intensification of basic treatment in combination with aggressive correction of lipids and blood pressure is justified.

In sum, the study results support a simple and important thesis: in patients with rheumatoid arthritis, cardiovascular prevention works better when it is combined with inflammation control.

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