

# STRUCTURAL AND FUNCTIONAL INDICATORS OF THE CARDIOVASCULAR SYSTEM OF PATIENTS WITH RHEUMATOID ARTHRITIS

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## ABSTRACT

This scientific research studies clinical and instrumental data, including the assessment of systolic and diastolic heart function, intraventricular hemodynamics, structural parameters of the heart in patients with rheumatoid arthritis (RA).

102 patients with RA were examined based on the classification criteria proposed by ARA 2001. The control group consisted of 20 healthy middle-aged individuals. In addition to standard laboratory and instrumental studies, all patients underwent echocardiographic examination (Echo-KG) using a MEDISON 8000 LIGHT ultrasound machine (South Korea) with a 2.4 MHz cardiac transducer, in accordance with the recommendations of the American Echocardiography Association according to the standard method.

In RA patients, cardiovascular risk was associated with disease duration over five years, disease activity (DAS 28), and systemic lesion. In RA patients, the morphofunctional indices of the left chambers of the heart and diastolic functions of the left ventricle were comparatively more often disturbed. They indicate the maladaptive nature of the remodelling of the left heart.

**Key words:** *rheumatoid arthritis, cardiovascular system, echocardiography, diagnostics.*

## I. INTRODUCTION

Rheumatoid arthritis (RA) is a severe, chronic disease manifested mainly by inflammatory arthritis of the peripheral joints, usually symmetrical. Systemic manifestations are possible, including damage to the hematopoietic, cardiovascular and nervous systems, lungs, eyes, and salivary glands. [4,7,23].

Several circumstances determine the extremely high medical and social importance of RA. First, its cardinal feature is almost constant pain and progressive dysfunction of the joints, leading to a decrease in patients' quality of life and early disability. Secondly, a chronic inflammatory process increases the risk of developing concomitant diseases (atherosclerotic vascular lesions, hypersensitivity to intercurrent infections, osteoporotic fractures of the skeletal bones), and the toxic effects of non-steroidal anti-inflammatory drugs (NSAIDs) - gastrointestinal tract damage, renal dysfunction. Moreover, complications of inadequate glucocorticoid therapy lead to a decrease in life expectancy.

Damage to the cardiovascular system (CVS) is usually considered an extra-articular manifestation of RA. It includes pericarditis, valvular lesions, myocarditis, coronary arteritis, conduction system abnormalities, aortitis,

and pulmonary hypertension. Nevertheless, cardiac pathology in RA patients is often not diagnosed, receding into the background compared to the severe articular syndrome.

Despite the high incidence of cardiovascular pathology developing in RA, the presence of prerequisites for the appearance of structural and functional impairments has not been sufficiently studied.

## II. MATERIAL AND METHODS

We examined 102 patients with RA who received inpatient treatment in the rheumatology department of the 1st clinic of the TMA. The RA diagnosis was verified based on the classification criteria proposed by the American Rheumatological Association (ARA 2001). The control group consisted of 20 healthy middle-aged individuals.

Among the examined patients, there were 10 men (9.8%), 92 women (90.2%). Patients of young age under 30 years old accounted for more than half of the examined patients (54% of cases). The rest were of middle age - 46%. Patients with a disease duration of 1 to 5 years accounted for 38.3%, with a disease duration of 5 to 10 years - 34%.

Patients underwent a study of the CBC (complete blood count), determination of RF (rheumatoid factor), CRP (C-reactive protein), and biochemical blood test.

All 102 patients included in the study underwent echocardiographic examination (Echo-KG) using a MEDISON 8000 LIGHT ultrasound machine (South Korea) with a 2.4 MHz cardiac transducer, in accordance with the recommendations of the American Echocardiography Association according to the standard method.

## III. RESULTS

According to the rheumatoid factor (RF), the study of seroprevalence showed that the seropositive course of RA with the definition of RF was established in 67 patients (65.7%). Among women, this indicator was about 63%, men - more than 70%. The rest - 35 patients (34.3%) had a seronegative course with the absence of RF.

It is known that in the aggregate of clinical and laboratory changes, the total activity of inflammation is determined; among the examined patients with RA, the II degree of activity of the inflammatory process prevailed - in 67.6% of the examined. In 19.6% of patients, there was a moderate - I degree. In 18.3% of patients, a high - III degree of activity of the inflammatory process was revealed.

Systemic manifestations of RA were found in 21 RA patients, which corresponds to 20.6%, and in all cases in women.

In studying the structural and functional parameters of the heart, as can be seen from Table 1, in comparison with the control, in the group of patients, there is an increase in the parameters of EDV (end-diastolic volume) ( $P < 0.01$ ). This can be assumed that patients with RA have an eccentric type of myocardial hypertrophy.

Table 1

### Structural and functional indicators of the left heart in patients with rheumatoid arthritis during treatment with methotrexate

(M±m)

Indicators	Control (n=20)	RA patients, age (years)		
		Up to 20 (n=6)	20-30 (n=47)	30-40 (n=49)
EDD (cm)	4,50±0,26	4,99±0,25*	5,32±0,162*	5,68±0,126* <sup>+</sup>
EDV (ml/m <sup>2</sup> )	48,07±1,32	56,71±1,33 <sup>^</sup>	62,92±1,440 <sup>•</sup>	65,03±1,410 <sup>•</sup>
ESV (ml/m <sup>2</sup> )	16,81±0,51	16,90±0,48	17,00±0,330	17,91±0,390 <sup>+</sup>
IVSthickness (cm)	0,84±0,01	0,88±0,03*	1,05±0,034 <sup>•</sup>	1,21±0,044* <sup>•</sup>
LVPWthickness (cm)	0,80±0,02	0,90±0,00	1,02±0,021	1,19±0,035 <sup>•</sup>
OTC	0,36±0,02	0,39±0,20	0,41±0,011	0,44±0,110 <sup>•</sup>
EF (%)	73,11±0,58	70,04±0,29*	67,90±0,550*	65,14±0,320 <sup>•</sup>

SV (ml/m <sup>2</sup> )	30,82±0,78	34,09±0,48 <sup>^</sup>	36,09±0,530 <sup>^•</sup>	40,40±0,910 <sup>^+•</sup>
LVM (g)	140,53±2,34	149,10±2,11	155,10±1,550	159,20±3,410 <sup>*+•</sup>
LVM index (g/m <sup>2</sup> )	84,41±2,02	88,41±1,09	97,72±2,320 <sup>^•</sup>	104,31±1,780 <sup>^•</sup>
EDV/LVM index (ml/g)	0,57±0,01	0,64±0,032	0,68±0,021	0,72±0,031 <sup>^•</sup>

Note: \* P <0.05 significant difference with the control group

<sup>^</sup> P <0.01 significant difference with the control group

• P <0.01 significant difference with the group of RA patients under 20 years of age

+ P <0.01 significant difference with the group of patients with RA aged 20-30 years

This is also confirmed by the results of assessing the EDV / LVMI (left ventricular myocardial mass index), which in RA patients was higher than in control, and this difference increases with age, which in turn indicates the predominance of dilatation of the left ventricular cavity over the thickening of its walls. This type of remodelling eventually leads to the development of systolic, then diastolic myocardial dysfunction.

In the age range, the analysis of echocardiographic indicators established a more stable significant change towards the deterioration of almost all indicators of EDD, EDV, ESV, IVST, LVPWT, EF, SV, LVMI (P <0.05) compared with the data of patients under 20 years old, regardless of the time the onset of the disease. Less striking but also significant changes were observed in the group of patients aged 20 to 30 years. Interestingly, there was a significant (P <0.05) difference in almost many indicators in the groups of 20-30 and 30-40 years old. This indicates age indicators and the inadequacy of treatment with basic drugs that block autoimmune visceral and vascular changes.

The development of left ventricular hypertrophy in RA patients is primarily associated with volume overload as a result of activation of the renin-angiotensin-aldosterone system. This situation may also be due to the drugs used for long-term use, such as non-steroidal anti-inflammatory drugs and glucocorticoids. It should be noted that the anaemia accompanying RA may contribute to the development of preload.

There was a statistically significant increase in the indicators of EDV, EF and SV (P <0.01), which indicates the presence of systemic vasculitis and an increase in total peripheral resistance, followed by the tension of compensatory mechanisms. Here it is necessary to remember the importance of the tone of the sympathetic division of the autonomic nervous system, which is often found in patients with RA.

It is of interest to study the leading indicators of cardio hemodynamics in the context of RA history. So, table 2 provides data concerning the limitation of RA.

Table 2

**Some echocardiographic indicators of patients with rheumatoid arthritis, depending on the duration of the disease (M±m)**

Indicators	Control (n=20)	давность болезни (лет)			
		Up to one year (n=17)	1 to 5 years (n=39)	5 to 10 years (n=34)	Over 10 years (n=12)
EDD(cm)	4,50±0,260	4,77±0,551	4,52±0,178*	4,45±0,168	4,62±0,290
ESD (cm)	3,34±0,150	2,87±0,360	2,59±0,171 <sup>^</sup>	2,73±0,123 <sup>^</sup>	2,98±0,196
IVS thickness (cm)	0,84±0,010	0,95±0,121	1,04±0,042 <sup>^</sup>	1,18±0,033 <sup>^•</sup>	1,24±0,062 <sup>^•</sup>
LVPWthickness (cm)	0,80±0,020	0,89±0,034*	0,99±0,048 <sup>^</sup>	1,15±0,033 <sup>+•</sup>	1,25±0,037 <sup>+•</sup>

Note: \* P <0.05 significant difference with the control group

<sup>^</sup> P <0.01 significant difference with the control group

+ P <0.05 significant difference with the group of patients with RA duration of less than one year

- P <0.05 significant difference with the group of patients with RA duration of 1-5 years

As indicated by the study results, the main indicators of echocardiography, such as EDD, ESD were associated with the duration of the disease, especially reliable when the age was from 1 to 5 years (P <0.05; P <0.01). From the side of ESD indices, a significant decrease was noted in patients with a disease duration of 5 to 10 years (P <0.01). During these periods, the disease usually proceeds intensively and, accordingly, treatment with glucocorticoids, cytostatics are intensively carried out. Later, apparently, due to the stabilization of pathological processes, changes in ESD were unreliable. IVS thickness in RA patients tended to increase, especially when the disease was more than ten years, reaching  $1.24 \pm 0.062$ , which was 9.7% (P <0.05).

Of particular interest is the patients' age, although the surveyed contingent and the control group consisted of young people aged 17 to 40 years. Nevertheless, based on the fact that the ongoing therapy and the disease itself with immune-inflammatory shifts can have a particular effect on the cardiovascular system. We have studied some of the main indicators of echocardiography in the age aspect (Table 3).

Table 3

**Some echocardiographic parameters of patients with rheumatoid arthritis depending on age (M±m)**

Indicators	Control (n=20)	age (years)		
		Up to 20 (n=30)	20-30 (n=60)	30-40 (n=12)
EDD (cm)	4,50±0,260	4,99±0,250	4,62±0,162 <sup>^</sup>	4,88±0,126 <sup>^•+</sup>
ESD (cm)	3,34±0,150	3,10±0,101 <sup>^</sup>	2,94±0,106 <sup>^</sup>	3,10±0,134 <sup>•+</sup>
IVST(cm)	0,84±0,010	0,88±0,034 <sup>*</sup>	0,95±0,034 <sup>^</sup>	1,14±0,044 <sup>^•</sup>
LVPWT (cm)	0,80±0,020	0,90±0,000	0,99±0,021	1,21±0,035 <sup>*</sup>

Note: \* P <0.05 significant difference with the control group

<sup>^</sup> P <0.01 significant difference with the control group

• P <0.01 significant difference with the group of RA patients under 20 years of age

+ P <0.01 significant difference with the group of patients with RA aged 20-30 years

LVPWT, after one year from the onset of the disease, began to increase, reaching 1.21 cm (P <0.05) after ten years of duration.

Morphostructural and morphometric changes indicate an increase in pressure growth in the left ventricle and myocardial stiffness, causing interstitial fibrosis development.

Doppler ultrasonography of diastolic transmitral blood flow revealed a significant decrease in the maximum rate of early LV filling (E) and an increase in the maximum rate of the atrial filling (A) (p <0.01 for both parameters) (Table 4).

Table 4

**Indicators of left ventricular diastolic function in patients with rheumatoid arthritis(M±m)**

Indicators	RA patients(n=68)	Control group (n=20)
Rate E, m/s	0,51 ± 0,10	0,71±0,07
Rate A, m/s	0,57±0,11	0,46±0,11
E/A	0,87±0,26 <sup>*</sup>	1,58±0,03
Rate of changem/s	84,51±1,34 <sup>*</sup>	66,14±0,87
Moderation timeE, m/s	167,16±2,23 <sup>*</sup>	149,0±2,45

Note: \* P <0.01 significant difference with the control group

In our study, 27 (26.6%) patients showed changes in transmitral Doppler blood flow (E / A coefficient <1.0), which indicates the presence of LV diastolic dysfunction (LVDDF) in them with normal EF values.

DDF was associated with a high activity of the process, with the age of the patients, and the seropositivity of the disease (Table 5).

Table 5

**Diastolic dysfunction in RA patients depending on clinical manifestations**

Clinical characteristics of patients with RA		LV diastolic dysfunction			
		Patients with DDF n=27		Patients without DDF n=75	
		Abc. numb er	%	Abc. number	%
Course	Rapidly progressive	1	3,7	3	4
	Slowly progressive	26	96,3	72	96
Seropositivity in rheumatoid factor	Seropositive	22	81,5	34	45,33
	Seronegative	5	18,5	41	54,66
Activity, stage	1	7	25,9	9	12
	2	18	66,66	57	76
	3	2	7,4	9	12
Patients` age, years	Up to 20 years	8	29,6	22	29,33
	20-30 years	12	44,4	48	64
	30-40 years	7	25,9	5	6,66
Duration of the disease, years	1-5 years	6	22,2	30	40
	5-10 years	11	40,7	32	42,66
	>10 years	10	37,03	3	4
Extra-articular manifestations	Present	9	33,33	10	13,33
	Absent	18	66,66	65	86,66

#### IV. CONCLUSIONS

Patients with RA have features of cardiovascular complications - a high incidence without painful myocardial ischemia, asymptomatic myocardial infarction and sudden cardiac death, and increased mortality after the first MI. Histological examination of the vessels showed a low percentage of "critical" stenoses of the coronary arteries, but more pronounced signs of inflammation of the vascular wall were recorded.

It should be noted that, despite the high incidence of cardiovascular pathology that develops in RA, the presence of prerequisites for the appearance of a violation of the structural and functional parameters of intracardiac hemodynamics, the information available in the literature is contradictory and extremely few. Based on this, research on this topic should be continued.

#### Outputs:

1. In young patients with rheumatoid arthritis, cardiovascular risk is associated with the duration of the disease for more than 5 years, the activity of the disease, and the systemic nature of the lesion.
2. Cardiac pathology often proceeds subclinically - while clinical changes in the heart are usually minimal and rarely come to the fore in the overall picture of the disease.
3. In RA patients, the morphofunctional indices of the left chambers of the heart and the diastolic functions of the left ventricle are disturbed comparatively more often, which indicate the maladaptive nature of the remodelling of the left heart.

#### CONFLICT OF INTERESTS AND CONTRIBUTION OF AUTHORS

The authors declare the absence of obvious and potential conflicts of interest related to the publication of this article and report on the contribution of each author.

#### SOURCE OF FINANCING

No funding was required for this research.

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