SUBCLINICAL ATHEROSCLEROSIS AND TYPES OF ATHEROSCLEROTIC PLAQUES IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Abstract: Sonographic evaluation of cIMT and the presence of atherosclerotic plaques is an easy and affordable method to evaluate the different cohorts of patients in our daily practice. In addition to diagnostic screening, it is also a therapeutic control method that can be used to detect vessel occlusions, to assess the vascular wall, atherosclerotic changes, to follow their patency, to assess CV risk (cIMT), etc. The general pathogenetic mechanisms
between joint and vascular inflammation are the unifying factor of these conditions. 69 patients were examined, of which: 34 patients had seropositive RA (average age: 38.74±7 years), 35 were healthy individuals (control group) – (average age: 36.93±5.93 years). It was found that 32% of patients with RA (seropositive rheumatoid arthritis) have subclinical atherosclerosis, which is asymptomatic. In addition, atherosclerotic plaques, mostly of the 1st, 2nd and 3rd types, are present, not occluding the ECS (extracranial vessels).
Keywords: cIMT (carotid intima-media ratio), CV risk (cardiovascular risk), ECS (extracranial vessels), RA (seropositive rheumatoid arthritis), CA (common carotid artery)
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1. INTRODUCTION

The participation of the same proinflammatory cells in the autoimmune inflammation of the synovium in inflammatory joint diseases and the local vascular inflammation in acute coronary syndromes cover common pathogenetic mechanisms, as well as the systemic manifestations induced by the synthesized cytokines. These processes are common to these diseases. [1, 6, 7] In the pathogenetic similarity of the two conditions, the main role is played by: activated macrophages and mast cells, the activation of collagen-degrading enzymes in the atheromatous plaques in the vessels are of the same type as in the patients' synovial tissue with RA. The similarity of the activated adhesion molecules - VCAM-1, ICAM-1, E- and P-selectins, the presence of neoangiogenesis - in both conditions, the role of activated T-cells and overexpression of IL2 R [11] also play a role. . Of special interest is the population of CD4+/ 28 + T Ly- in 65% of patients with RA and unstable angina pectoris, while in healthy people it is only 1%, as well as the increased synthesis of INF□ by T cells, the activation of vacrophages and the inhibition of collagen synthesis [13]. Thus, the two processes of systemic and local inflammation in RA and ACS mutually potentiate each other. Active rheumatoid arthritis is associated with accelerated atherosclerosis, high CV risk, higher incidence of CV mortality and earlier onset of ACS. Over 10 years, the death rate rose from 1.36 to 1.93 Odds Ratio. [2]. More than 50% of patients with RA die from CV diseases, and CV morbidity is 48% higher compared to the rest of the population, with the risk being the same for both sexes [3,4]. The increased mortality from two CV diseases in RA patients is 68%, and from MI and vascular events - 41%, affecting men and women equally [4, 6, 8, 9]. Mortality is higher in patients with a history of illness over 10 years, seropositive (RF and ACPA positive Ab), presence of extra-articular manifestations. Patients with RA have a 1.7 higher risk of AMI. [10] The assessment of patients at risk is easy and convenient in daily practice and, according to the latest updated consensus of EULAR 2015/2016, it is the responsibility of the rheumatologist. It evaluates the carotid vessels - the presence of plaques, their type and the cIMT ratio are the main parameters of this assessment.[12,14]

Sonographic examination of extracranial vessels in patients with active rheumatoid arthritis and assessment of the future risk of ACS/acute coronary syndrome/

2. MATERIALS AND METHODS

69 patients were studied, of which: 34 patients were seropositive RA (mean age: 38.74±7 years) with high activity DAS 28 > 5.1, 35 were healthy individuals (control group) – (mean (age: 36.93±5.93 years) Sonographic examination of carotid arteries was performed on all patients, evaluating the following parameters:

1. Type and presence of atherosclerotic plaques
2. How many of them are significant - with occlusion over 50%

• cIMT on the contralateral side during diastole, as the level of cIMT marker for subclinical atherosclerosis in patients with RA is assumed to be >0.6 mm (and in the normal population ≥ 0.90 mm)

3. GRACE and Raynoulds risk scale is used to assess CV risk

Essaote My Lab XS 7 apparatus is used, linear transducer 7.5 - 10 MHz in B-mode in longitudinal and transverse projection, optimal depth of focus at 30-40 mm, color doppler is in 5 MHz mode, consensus is used (Mannheim, 2006-2011) and the national consensus on ultrasound diagnosis of extracranial arteries

Type and presence of atherosclerotic plaques. Atherosclerotic plaques are divided into symptomatic and asymptomatic. Their characteristics are quantitative and qualitative parameters, respectively. Quantitatively important are: the size and degree of stenosis, maximum thickness, area, volume, and qualitatively – ulceration, which is defined as an indentation over 2 mm and echogenicity. According to these parameters, we distinguish type 1- uniform echotransparent (black), < 15% of the plaque area is occupied by colored areas, i.e. with gray scale pixels of no more than 25. If the fibrous cap is not visible, the plaque can only be detected using Color and Power Doppler.

Type 2. mainly echotransparent - colored areas occupy 15–50% of the plaque area.

Type 3. Mainly echogenic - colored areas occupy 50–85% of the plaque area

Type 4 and 5. uniformly echogenic - stained areas occupy more than 85% of the plaque area

3. RESULTS

The types of atherosclerotic plaques It was established that 32% of patients with RA (seropositive rheumatoid arthritis) have subclinical atherosclerosis, which is asymptomatic. In addition, atherosclerotic plaques, mostly of the 1st, 2nd and 3rd types, are present, not occluding the ECS (extracranial vessels).

Regarding the degree of stenosis, patients with rheumatoid arthritis arthritis do not have significant stenosis of the OCC (common carotid artery) - lack of linear dependence and low levels of correlation without statistical significance. They are distinguished by the presence of plaques.

Only GRACE risk scale – shows a statistically significant correlation in patients with rheumatoid arthritis, Ranoulds risk scale does not show significant statistical significance between the two groups of patients.

The results are presented in Tables 1 and 2

Table 1. Correlation analysis between CIMT, presence of plaques, degree of stenosis, GRACE Score and Reynolds Score

Corelation of Spearman's cIMT	plaques	Degree of stenosis	GRACE risk scale	Raynoulds risk scale
Coefficients	.183	.059	.066	.014
significance	.078	.579	.535	.900
Pacients	34	34	34	34

Table 2. Comparative analysis of ACS patients regarding carotid plaques, degree of stenosis, GRACE Score and Reynolds ScoreGroup Number (N)

	Group	Number (N)	Mean $\bar{X}$	Standard Deviation (SD)	Mann-Whitney U	Significance p
Plaques	with RA	34	.75	.43	1060.00	.640
	healthy	35	.69	.46		
Degree of	with RA	34	76.75	17.53	1017.00	.518

stenosis	**healthy**	**35**	**76.95**	**20.66**		
GRACE Score	**with RA**	**34**	**140.45**	**28.58**	**781.00**	**.030***
	healthy	35	**125.50**	**27.24**		
Reynolds Score	**with RA**	**34**	**24.60**	**16.10**	**831.00**	**.341**
	healthy	**35**	**20.76**	**11.31**		

3. CONCLUSIONS

Endothelial dysfunction leads to vascular dysfunction and a gradual[15] onset from subclinical to clinically manifest atherosclerotic lesions. In RA patients, it is important to detect subclinical atherosclerosis and monitor the risk of vascular events. The use of CIMT differentiates patients with active rheumatoid arthritis from healthy controls, and this assessment should be performed annually in high-risk patients and every 2-5 years in lower-risk patients. The presence of plaques is an indirect marker for future vascular manifestations in patients with RA, and the unstable plaques are mainly the soft ones of type 1 and 2. Also, the association of with the GRACE Risk Score in the RA group makes it applicable for assessing the risk of acute coronary events.

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