

Metabolic syndrome in a cohort of rheumatoid arthritis patients

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ABSTRACT

Objectives. We aimed to assess the presence of MetS and traditional CV risk factors in a group of RA patients, compared to controls and their possible inter-relation with disease activity variables.

Methods. We performed an observational study on 38 consecutive patients diagnosed with RA in Rheumatology Department of the Emergency County Hospital Craiova, based on ACR/EULAR criteria, in a one-year interval between 2019-2020, and a control group including 30 subjects. Patients' data were obtained from each subject according to the study protocol and included demographic, clinical, laboratory parameters. The presence of MetS was assessed according to the National Cholesterol Education Program Adult Treatment Panel (NCPATP) III.

Results. Regarding the components of metabolic syndrome, as defined by NCPATP III, the differences established for the RA vs control groups were: increased waist circumference in 21 (52.25%) vs 13 (43.33%) subjects ($p = 0.002$); high triglycerides (or under treatment) in 10 (26.31%) vs 6 (20%) subjects, $p = 0.004$; low HDL cholesterol in 15 (39.47%) vs 7 (23.33%) subjects, $p = 0.002$; high blood pressure (or under treatment) in 25 (65.79%) vs 12 (40%) subjects, $p < 0.0001$; high blood glucose (or under treatment) in 7 (18.42%) vs 8 (26.66%) subjects, $p = 0.08$. Our data revealed a positive correlation between disease activity index and smoking ($r = 0.432$, $p = 0.02$), as well as between DAS 28-CRP and LDL-cholesterol ($r = 0.454$, $p = 0.004$), or triglycerides ($r = 0.337$, $p = 0.03$). We also observed a strong, positive correlation between the presence of MetS and disease activity score ($r = 0.645$, $p < 0.0001$).

Conclusions. Metabolic syndrome is associated with a high cardiovascular risk, the main cause of mortality in RA patients. Due to the chronic inflammatory state and the intervention of both traditional and non-traditional cardiovascular risk factors, each patient should undergo periodic evaluations, in order to apply an adequate and early therapeutic intervention and reduce further cardiovascular morbidity and mortality rates.

Keywords: metabolic syndrome, rheumatoid arthritis, disease activity

INTRODUCTION

Metabolic syndrome (MetS), a worldwide health problem, represents an association of several risk factors with important impact on atherosclerosis process, the main cause of cardiovascular pathology [1,2]. There are eight commonly used definitions for MetS, but the National Cholesterol Education Pro-

gram Adult Treatment Panel III (NCEP ATP III) is the most commonly used [3].

Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune pathology that frequently associates several traditional cardiovascular risk factors, which complexly interplay with the chronic inflammatory status, inducing an increased morbidity and mortality from cardiovascular disease [4-6]. High

frequencies MetS have been reported in patients with RA, in different percentages, statistically significant, data that require an accurate risk determination, in order to adopt a proper preventive diagnostic and therapeutic algorithm [7-9].

AIM

We aimed to assess the presence of MetS and traditional CV risk factors in a group of RA patients, compared to controls and their possible inter-relationship with disease activity variables.

MATERIAL AND METHOD

We performed an observational study on 38 consecutive patients diagnosed with RA in Rheumatology Department of the Emergency County Hospital Craiova, based on ACR/EULAR criteria [10], in a one-year interval between 2019-2020, and a control group including 30 subjects, with similar demographic characteristics, without inflammatory immune-mediated diseases.

The study was performed in accordance with the ethics and deontology principles of the Helsinki Human Right’s Declaration and the study was approved by the local Ethics Committee. All patients provided their written informed consent, after receiving a standard form which mentioned that the results would be used for research purposes.

Patients’ data were obtained from each subject according to the study protocol and included demographic, clinical, laboratory parameters.

The presence of MetS was assessed according to the National Cholesterol Education Program (NCP) Adult Treatment Panel (ATP) III by the presence of three or more of the following: reduced serum concentrations of high density lipoprotein cholesterol (HDL-C) (<40 mg/dl in men and <50 mg/dl in women); increased triglycerides levels (TG ≥150 mg/dl); hypertension (systolic/diastolic blood pressure ≥130/85 mmHg); impaired glucose tolerance (fasting blood glucose levels ≥100 mg/dl) and abdominal obesity (waist circumference (WC) >102 cm in men and >88 cm in women) [3].

For statistical analysis we used GraphPad Prism 5.5 and the results are presented as mean ± SD; in order to compare groups we used t-test and one-way ANOVA, and for evaluating correlations Pearson/Spearman’s coefficient. A level of p <0.05 was considered statistically significant.

RESULTS

Analyzing the two groups of patients regarding the general characteristics, we found no significant differences regarding age (54.34±10.02 vs 51.22±9.02

years), sex (women 97.7% vs 93.33%), weight or height. Smoking status was revealed for 10 of the 38 patients, and 9 of controls.

TABLE 1. General characteristics of RA patients

Patients (N)	38
Women (N; %)	37 (97.37%)
Age (years)	54.34 ± 10.02
Disease duration (years)	6.63 ± 4.26
CRP (mg/dl)	4.71 ± 5.91
ESR (mm/h)	20.82 ± 15.10
DAS28(4v) CRP	2.54 ± 0.66
SDAI	5.07 + 4.09
HAQ-DI	0.51 + 0.30
BMI (kg/m ²)	27.44 ± 6.35
Diabetes (yes/no)	8/30
Blood glucose (mg/dl)	94 + 13
Smoking (yes/no)	10/28
Therapeutic regimen	
csDMARD (N; %)	38 (100 %) MTX (N; 64.41%) LEF (13; 31.07%) SSZ (2; 4.87%)
bDMARD (N; %)	38 (100 %)

The general characteristics of the study group are presented in Table 1.

Regarding the components of metabolic syndrome, as defined by National Cholesterol Education Program (NCP) Adult Treatment Panel (ATP) III, the differences established for the RA vs control groups were: 21 (52.25%) vs 13 (43.33%) subjects with a waist circumference >102/88 cm (p = 0.002), triglycerides >150 mg/dl (or under treatment): 10 (26.31%) vs 6 (20%) subjects, p = 0.004, HDL cholesterol <40mg/dl men/50 women (or under treatment): 15 (39.47%) vs 7 (23.33%), p = 0.002, systolic pressure >130mm Hg or diastolic pressure >85 mmHg (or under treatment) 25 (65.79%) vs 12 (40%), p <0.0001, blood glucose >100 mg/dl (or under treatment) 7 (18.42%) vs 8 (26.66%), p = 0.08 (Figure 1).

The mean values of biologic and clinical parameters are presented in Table 2. Statistically significant differences were observed for total cholesterol (204.4 + 37.71 mg/dl vs 187.8 + 28, p = 0.005) and for waist circumference 92.34 +13.51 vs 81.53 + 12.07 cm, p = 0.003). The criteria for metabolic syndrome were established for 12 of the patients (31.57%) vs 11 of the controls (36.66%), p = 0.325.

An objective of the study was to analyze the possible relationship between the clinical and biological parameters defining metabolic syndrome, as well as between other cardiovascular traditional risk fac-

tors, and disease activity or inflammatory markers, results presented in Table 3.

Our data revealed a positive correlation between disease activity index and smoking ($r = 0.470$, $p < 0.0001$), as well as between DAS 28-CRP and LDL-cholesterol ($r = 0.454$, $p = 0.004$), or triglycerides ($r = 0.337$, $p = 0.03$). We also observed a strong, positive correlation between the presence of MetS and disease activity score ($r = 0.645$, $p < 0.0001$). No other significant correlations were observed (Table 3).

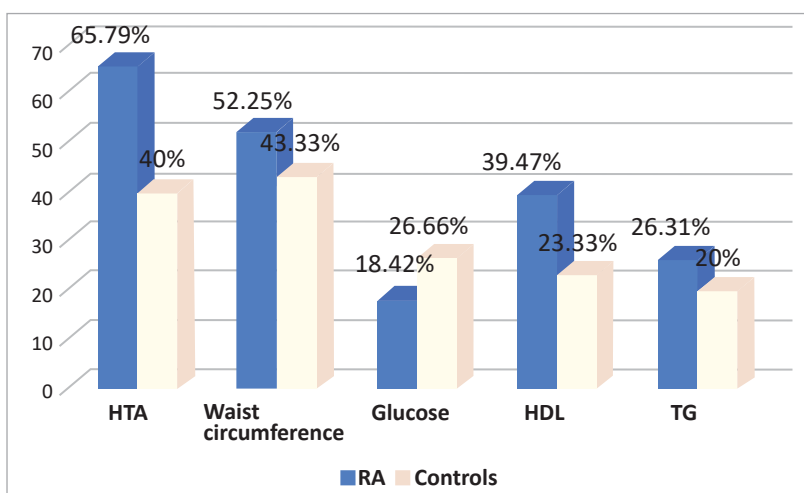


FIGURE 1. Prevalence of criteria for metabolic syndrome parameters in rheumatoid arthritis (RA) patients and controls

TABLE 2. Clinical and biologic parameters of metabolic syndrome for RA and controls

	RA	Controls	p
Total cholesterol (mg/dl)	204.4 + 37.71	187.8 + 28	0.005
LDL-cholesterol (mg/dl)	114.5 + 19.62	116.6 + 14.3	0.38
HDL-cholesterol (mg/dl)	62.15 + 15.48	68.15 + 22.3	0.03
Triglycerides (mg/dl)	126.9 + 108.2	134.3 + 118	0.88
Blood glucose	102.9 + 36.35	95.43 + 23.62	0.18
BMI (kg/m ² sc)	27.18 + 6.21	26.62 6.15	0.94
Waist circumference (cm)	92.34 +13.51	81.53 + 12.07	0.003
Systolic blood pressure (mmHg)	130.4 + 15.44	128 + 13.49	0.196
Diastolic blood pressure (mmHg)	81.18 + 10.49	80 + 7.31	0.342

TABLE 3. Correlations between inflammatory markers, disease activity and metabolic syndrome components in RA patients

	DAS28-CRP		ESR		CRP	
	r	p	r	p	r	p
Age	0.025	0.87	0.2524	0.12	0.1626	0.32
BMI	0.2045	0.21	0.02338	0.88	0.2952	0.003
Waist circumference	0.05686	0.73	0.02431	0.88	0.09783	0.55
Smoking	0.470	<0.0001	0.287	0.08	0.195	0.01
Diabetes	0.1873	0.32	0.2520	0.17	-0.04016	0.81
Total Cholesterol	0.04499	0.78	-0.1069	0.52	-0.06380	0.71
LDL-Cholesterol	0.4546	0.004	0.2149	0.19	0.09108	0.58
HDL-Cholesterol	0.1785	0.28	0.2614	0.11	-0.01298	0.93
Triglycerides	0.3376	0.03	0.09817	0.55	0.1455	0.38
Systolic blood pressure	-0.1967	0.23	0.03453	0.83	-0.2277	0.16
Diastolic blood pressure	-0.2652	0.12	0.1465	0.38	-0.1214	0.46
MetS	0.6450	<0.0001	0.345	0.004	0.398	0.001

DISCUSSION

Rheumatoid arthritis is a condition associated with systemic inflammation and increased cardiovascular mortality and morbidity, directly related to metabolic syndrome, a cluster of traditional cardiovascular risk factors, characterized by a systemic pro-inflammatory state, which represents a worldwide health problem [6,11,12]. Evaluating the prevalence of MetS and its components in RA patients it is imperative, in order to establish early and proper preventive diagnostic algorithms that can help the

clinicians prevent future complications and apply an individualized, multifaced, optimal therapeutic management [12].

The association between MetS and RA has been analyzed in several studies, with variable data regarding MetS prevalence. Our results showed a percentage of 31.57% of the patients meeting MetS criteria. A meta-analysis published by Hallajzadeh J et al., that included 113 studies, reported an overall percentage of 30.65%, that varied between 10.6% and 55.5% in the included studies [13]. The reported percentages were between 14.32% to 37.83%, based

upon the diagnostic criteria used; according to NCEP/ATP III definition, also used in our analysis, the percentage of MetS was 31.55%. Moreover, the prevalence rates varied between men - 31.94% (95% CI: 24.37–39.51) and women - 33.03% (95% CI: 28.09–37.97), data accordingly to our results, obtained from a majority of 97.7% female patients. Similar prevalence was reported by Zhang et al., in a meta-analysis that included 12 observational studies involving 2,283 RA cases [14], or Karvounaris SA et al. [15]. An increased percentage, of 53.4%, based on NCEP/ATP III definition criteria, was reported by Oliviera et al., in a cohort of South American RA patients [16].

There are studies that reported lower prevalence of MetS among RA patients, compared to controls, mentioning the report published by Parra-Salcedo F et al., that analyzed a group of 139 RA patients, reported a percentage of 24% for MetS, according to the definition used in our analysis, lower than the control group [17]. Similar data were published by Karimi M et al. [18].

The controversial results may be possibly due to the variability of the groups (disease duration, age, age at diagnosis, socioeconomic differences or geographical distribution).

Regarding MetS components, the reported percentages found by our analysis were similar to the ones reported by the previously mentioned meta-analysis performed by Hallajzadeh J et al. [13]. The most common prevalent MetS component in different published studies remains high waist circumference, found in more than half of our patients [15,16, 19, 20].

The inflammatory markers or disease activity of RA did not show any significant differences according to the presence or absence of MetS, data accordingly to the one revealed in a recent report, by García-Chagollán M et al. [21]. We can consider this

finding to suggest that MetS can be an initiator for events that further influence disease activity.

When analyzing the possible relationship between the clinical and biological parameters defining metabolic syndrome, as well as between other cardiovascular traditional risk factors, and disease activity or inflammatory markers, our data revealed a positive correlation between DAS28-CRP and smoking, as well as between DAS 28 CRP and LDL-cholesterol or triglycerides. The association between smoking status and DAS28-CRP score was also noted by García-Chagollán M et al. [21].

We also observed a correlation between the presence of MetS and disease activity score, result also reported by Karvounaris et al. [15]. It is also worth mentioning that several studies have not reported any association between RA and MetS [22,23].

A possible limitation of our study is represented by the relative low number of subjects, which implies its extension, with multicentric involvement. Another point to be taken under consideration is that all of our patients are currently undergoing DMARD therapy, both synthetic and biologic, with an efficient control of inflammation and disease activity.

CONCLUSIONS

Metabolic syndrome is an important health problem not only in rheumatic inflammatory pathology, but also in the general population, which inputs first of all a high cardiovascular risk, the main cause of mortality in RA patients. Due to the chronic inflammatory state and the intervention of both traditional and non-traditional cardiovascular risk factors, each patient should benefit from a periodic proper evaluation, in order to approach an adequate and early therapeutic intervention and reduce further cardiovascular morbidity and mortality rates.

Conflict of interest: none declared

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