

Metabolic syndrome in patients with autoimmune inflammatory rheumatisms.

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Abstract

Background: Systemic inflammation has been associated with obesity, with elevated levels of triglycerides and reduced levels of HDL-cholesterol.

Aim: To determine the frequency of metabolic syndrome (MetS) in patients suffering of rheumatoid arthritis (RA), ankylosing spondylitis (AS) and psoriatic arthritis (PsA) and to compare the evolution of MetS parameters during DMARD (Disease-Modifying Anti-rheumatic Drugs) therapy *versus* combination of DMARDs and biologics.

Methods: The study was conducted on 277 RA patients, 115 AS patients and 103 PsA patients. Patients with inflammatory rheumatism and MetS were randomized into two groups per disease (RA, AS and PsA). Group 1 underwent DMARD therapy. Group 2 followed a combination of DMARDs and biologics. Patients were assessed for the inflammatory status (C-reactive protein) and MetS (triglycerides, HDL cholesterol and blood pressure) initially, after 1 y and after 2 y.

Results: 88 RA patients (31.7%), 16 AS patients (14%) and 35 PsA patients (34%) met the criteria for MetS. RA, AS and PsA patients with MetS who followed a combination of DMARDs and biologic therapy had significant improvement of triglycerides and HDL-cholesterol compared to patients who followed only DMARDs both at 1-y and 2-y assessments. There were no differences of the blood pressure in the two groups.

Conclusion: The frequency of MetS was higher in RA and AS patients than in PsA patients. Biologic therapy could influence the evolution of MetS in patients suffering of autoimmune inflammatory rheumatism.

Keywords: Metabolic syndrome, Rheumatoid arthritis, Ankylosing spondylitis, Psoriatic arthritis, Biologic therapy.

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Introduction

Metabolic syndrome (MetS) is a common clinical condition characterized by the clustering of cardiovascular risk factors related to insulin resistance, including central obesity, impaired glucose tolerance, hypertension and dyslipidaemia [1,2]. MetS and its components have been consistently associated with the presence of "low-grade" systemic inflammation [3,4]. Various studies have shown that the pathogenesis of MetS involves an inflammatory process. Pro-inflammatory cytokines, such as tumour necrosis factor alpha (TNF-alpha), reduce the activity of insulin, promoting thus insulin resistance [5]. Inflammation has also been associated with obesity, with elevated levels of triglycerides and reduced levels of High-Density Lipoprotein (HDL) cholesterol [6].

Patients with rheumatoid arthritis (RA) are at increased risk for cardiovascular disease independently of traditional vascular risk factors [7,8]. Cohort studies have demonstrated increased prevalence of metabolic syndrome in patients with RA, correlating with disease activity and markers of atherosclerosis

[9-11]. Observational studies suggest that anti-TNF therapy improves disease activity and may reduce cardiovascular events in RA patients [12,13]. This effect is thought to be mediated by reduction in insulin resistance and metabolic syndrome components demonstrated in patients treated with TNF blockade [14-18].

Duration and severity of ankylosing spondylitis (AS) and its typical cardiovascular (CV) complications such as aortic insufficiency, conduction disturbances, mitral valve disease, cardiomyopathy, and pericarditis have been implicated as risk factors in AS patients [19,20]. In the last years, a clear relationship between CV risk factors, obesity, and insulin-resistance allowed to propose the existence of MetS that was shown to promote an increase of CV mortality risk [21]. Moreover, some studies have pointed out a relationship among some CV risk factors or MetS and inflammation [22,23].

Patients with psoriasis (Ps) have an increased prevalence of obesity and MetS compared to that of matched healthy controls. It seems that Ps precedes the obesity and other

features of MetS in these patients. Although the underlying mechanisms for increased MetS in Ps patients are not well established, a link between inflammation and MetS seems likely [24].

The objectives of our study are to determine the frequency of Mets in patients suffering of inflammatory autoimmune rheumatism (RA, AS and psoriatic arthritis-PsA) and to compare the evolution of MetS parameters during the DMARD (Diseases-Modifying Anti-rheumatic Drug) therapy *versus* during the combination of DMARDs and biologics.

Materials and Methods

The study was approved by the Ethics Committee of Timisoara University of Medicine and Pharmacy, Romania. Written informed consent was obtained from all the participants.

The study was conducted on 277 RA patients, 115 AS patients and 103 PsA patients. The patients were investigated for the metabolic syndrome (MetS) defined according to the National Cholesterol Education Program [25]. For each rheumatic disease, patients who also had MetS were randomized into two groups. Group 1 underwent DMARD therapy, while group 2 followed a combination of DMARDs and biologic therapy (TNF inhibitors). In addition, some of group 2 patients with RA followed an anti-CD20 biologic therapy.

Data regarding MetS (triglycerides, HDL cholesterol and blood pressure) and inflammatory status (CRP: C-reactive protein)

Table 1. Demographic and clinical characteristics of the patients enrolled in the study.

	RA		AS		PsA	
	n ₁ (40)	n ₂ (48)	n ₁ (8)	n ₂ (8)	n ₁ (16)	n ₂ (19)
Age (y)	51.4 ± 11.3	49.1 ± 12.5	43.4 ± 15.6	44.9 ± 12.3	50.6 ± 15.7	52.1 ± 17.1
BMI (kg/m ²)	27.7 ± 8.8	29.1 ± 10.9	30.3 ± 8.5	29.9 ± 6.9	28.7 ± 8.2	27.6 ± 9.1
Gender						
Male	9 (22.5%)	11 (23%)	6 (75%)	6 (75%)	4 (25%)	5 (26%)
Female	31 (77.5%)	37 (77%)	2 (25%)	2 (25%)	12 (75%)	14 (74%)
Disease duration (y)	10.5 ± 2.2	9.4 ± 2.6	8.3 ± 1.9	8.5 ± 0.7	10.7 ± 1.1	9.1 ± 1.8

n₁: Group 1; n₂: Group 2; BMI: Body Mass Index.

16 AS patients (14%) also had the criteria for MetS, 11 women (69%) and 5 men (31%). 8 AS patients followed a DMARD therapy, while 8 AS patients followed a combination of DMARD and biologic therapy. The results regarding the MetS items (triglycerides, HDL-C, systolic and diastolic blood pressure), inflammatory parameters (CRP) and health status (HAQ) are presented in detail in Table 3.

35 PsA patients (34%) had also the criteria for MetS, 25 women (71%) and 10 men (29%). 16 PsA patients followed a DMARD therapy, while 19 PsA patients followed a combination of DMARD and biologic therapy. The results regarding the MetS items (triglycerides, HDL-C, systolic and

were recorded. The general health was evaluated by the Health Assessment Questionnaire (HAQ). For RA patients DAS28-CRP (Disease Activity Score in 28 Joints) was also calculated. These assessments were performed initially, after 1 y and after 2 y.

Statistical analysis of the obtained results was performed. Data were analysed using SPSS version 16 and STATA 10. Descriptive statistics were calculated (mean and standard deviation). Levene's test was applied to test the homogeneity of variances between groups. Comparisons between the two groups were done by Student's unpaired t-test. A p-value less than 0.05 were considered statistically significant.

Results

The demographic and clinical characteristics of the patients enrolled in the study are included in Table 1. The group patients were homogenous in terms of anthropometrical characteristics (Levene's test-p>0.05).

88 RA patients (31.7%) also had the criteria for MetS, 70 women (79.5%) and 18 men (20.5%). 40 RA patients followed a DMARD therapy, while 48 RA patients followed a combination of DMARD and biologic therapy. The results regarding the MetS items (triglycerides, HDL-C, systolic and diastolic blood pressure), inflammatory parameters (CRP) and disease activity (DAS28-CRP) are presented in detail in Table 2.

diastolic blood pressure), inflammatory parameters (CRP) and health status (HAQ) are presented in Table 4.

Table 2. MetS items, inflammatory parameters and disease activity in RA patients.

	Initially	1 y	2 y
	Group 1 (n ₁)	Group 1 (n ₁)	Group 1 (n ₁)
	Group 2 (n ₂)	Group 2 (n ₂)	Group 2 (n ₂)
Triglycerides (mg/dl)	217.78 ± 112.7	154.66 ± 52.5	138.93 ± 45.11
	225.45 ± 100.1	133.5 ± 33.79	108.13 ± 25.73

	p>0.05	p<0.01	p<0.001
HDL-C men (mg/dl)	34.56 ± 8.13	39.45 ± 3.33	45.9 ± 6.12
	32.66 ± 3.31	44.44 ± 5.48	50.22 ± 5.09
HDL-C women (mg/dl)	43.05 ± 4.23	48.34 ± 4.12	53.93 ± 6.21
	41.91 ± 5.02	52.94 ± 4.76	57.77 ± 5.54
Systolic blood pressure (mmHg)	151.44 ± 31.2	150 ± 21.5	142.3 ± 22
	153.5 ± 24	151 ± 19.5	140.5 ± 21.5
Diastolic blood pressure (mmHg)	85.5 ± 11.3	82 ± 12.5	78.3 ± 5.5
	87.3 ± 9.5	81.5 ± 9.3	79.5 ± 8.3
CRP (mg/dl)	3.42 ± 0.67	1.33 ± 0.23	0.82 ± 0.38
	3.66 ± 1.07	0.91 ± 0.59	0.47 ± 0.29
DAS28-CRP	6.82 ± 1.02	3.27 ± 0.41	2.71 ± 0.33
	7.06 ± 0.74	2.87 ± 0.53	2.35 ± 0.36

n₁=40 patients; n₂=48 patients; DAS28: Disease Activity Score in 28 joints.

Table 3. MetS items, inflammatory parameters and health status in AS patients.

	Initially	1 y	2 y
	Group 1 (n ₁)	Group 1 (n ₁)	Group 1 (n ₁)
	Group 2 (n ₂)	Group 2 (n ₂)	Group 2 (n ₂)
Triglycerides (mg/dl)	219.2 ± 103.6	157.2 ± 55.8	139.1 ± 48.7
	224.6 ± 101.7	138.1 ± 34.8	112.13 ± 26.1
HDL-C men (mg/dl)	33.51 ± 8.13	39.44 ± 3.22	47.9 ± 6.18
	34.66 ± 4.21	44.33 ± 5.48	51.22 ± 6.11
HDL-C women (mg/dl)	44.15 ± 4.93	47.34 ± 4.02	54.23 ± 6.6
	42.91 ± 6.02	53.01 ± 4.01	58.22 ± 5.03
Systolic blood pressure (mmHg)	152.5 ± 30.5	150 ± 21.5	142.3 ± 22
	154.5 ± 21	151 ± 19.5	140.5 ± 21.5
Diastolic blood pressure (mmHg)	86.5 ± 12.3	82 ± 12.3	78.3 ± 6
	88.3 ± 10.5	81.5 ± 9.5	79 ± 9
CRP (mg/dl)	2.42 ± 0.8	1.62 ± 0.43	0.78 ± 0.28
	2.46 ± 1.27	1.1 ± 0.29	0.45 ± 0.21

	1.22 ± 0.52	0.97 ± 0.22	0.43 ± 0.06
HAQ	1.24 ± 0.61	0.96 ± 0.38	0.31 ± 0.11
	p>0.05	p<0.05	p<0.001

n₁=8 patients; n₂=8 patients; HAQ: Health Assessment Questionnaire.

Table 4. MetS items, inflammatory parameters and health status in PsA patients.

	Initially	1 y	2 y
	Group 1 (n ₁)	Group 1 (n ₁)	Group 1 (n ₁)
	Group 2 (n ₂)	Group 2 (n ₂)	Group 2 (n ₂)
Triglycerides (mg/dl)	222.77 ± 112.8	159.66 ± 51.5	137.93 ± 45.04
	224.43 ± 101.9	138.5 ± 34.02	107.13 ± 25.13
HDL-C men (mg/dl)	35.26 ± 9.13	38.45 ± 2.33	44.9 ± 7.12
	32.77 ± 6.39	41.44 ± 6.48	50.08 ± 5.29
HDL-C women (mg/dl)	42.25 ± 4.13	47.34 ± 6.12	53.93 ± 6.21
	42.91 ± 5.02	51.94 ± 4.76	56.99 ± 5.54
Systolic blood pressure (mmHg)	152.5 ± 31.5	149.5 ± 21.3	144.5 ± 22
	154.5 ± 24	150.5 ± 19	142.5 ± 22.5
Diastolic blood pressure (mmHg)	86.5 ± 13.3	82.5 ± 12	79.3 ± 5
	86.3 ± 10	82.5 ± 9.3	79.5 ± 8.3
CRP (mg/dl)	3.44 ± 1.1	1.2 ± 0.41	0.52 ± 0.22
	3.56 ± 1.17	1.01 ± 0.7	0.41 ± 0.33
HAQ	1.32 ± 0.82	1.07 ± 0.92	0.41 ± 0.09
	1.34 ± 0.91	0.95 ± 0.66	0.41 ± 0.61

n₁=16 patients; n₂=19 patients; HAQ: Health Assessment Questionnaire.

Discussion

The study of Medina et al. reviewed the recent evidences of the interaction between MetS and autoimmune rheumatic diseases [26].

Our study showed that RA, AS and PsA patients with MetS who followed a combination of DMARDs and biologic therapy presented a significant improvement of triglycerides and HDL-cholesterol in comparison to patients who followed only DMARD therapy both at 1-y and 2-y assessments. There were no differences of the blood pressure in the 2 groups.

The frequency of MetS was higher in RA and AS patients than in PsA patients. Biologic therapy could influence the evolution

of MetS in patients suffering of autoimmune inflammatory rheumatisms.

Conflict of Interest

None.

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