

Cardiovascular Disease Risk Factors and the Frequency of Metabolic Syndrome in Patients with Rheumatoid Arthritis and Ankylosing Spondylitis Compared with Healthy Controls: A Cross-Sectional Study

Sağlıklı Kontrollere Kıyasla Romatoid Artrit ve Ankilozan Spondilit Hastalarında Kardiyovasküler Hastalık Risk Faktörleri ve Metabolik Sendrom Sıklığı: Kesitsel Bir Çalışma

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ABSTRACT Objective: The purpose of this study to determine the presence of cardiovascular risk factors and metabolic syndrome (MetS) compared to healthy controls in patients with ankylosing spondylitis (AS) and rheumatoid arthritis (RA), and to determine the relationship between the disease activity scores of these rheumatic diseases and the risk of cardiovascular disease. **Material and Methods:** In this cross-sectional study, 52 patients with a diagnosis of RA, 49 patients with a diagnosis of AS, and 49 healthy controls were included in the study. Glucose levels, lipid profile, and inflammatory markers were registered. The Framingham risk score (FRS) and waist-to-height ratio (WHtR) were calculated, the presence of MetS was detected. **Results:** The prevalence of MetS was higher among patients with AS and RA than in the controls. We found significantly higher WHtR values in both the RA and AS groups compared with the control group. Also, WHtR values were significantly higher in patients with MetS than in the non-MetS group. FRS values in the RA and AS groups with MetS were statistically higher than in the control group with MetS ($p=0.019$). FRS values were significantly higher in patients with RA with high disease activity scores than in patients with RA with low disease activity ($p=0.030$). **Conclusion:** MetS was more common in patients with RA and AS than in controls. Predictors of cardiovascular risk were stronger in patients with MetS than in patients without MetS and were stronger in patients with RA with high disease activity scores than in those with low disease activity.

Keywords: Rheumatoid arthritis; ankylosing spondylitis; cardiovascular risk; metabolic syndrome

ÖZET Amaç: Bu çalışmanın amacı, ankilozan spondilit (AS) ve romatoid artritli (RA) hastalarda kardiyovasküler risk faktörleri ve metabolik sendrom (MetS) varlığını sağlıklı kontrollere karşılaştırmak ve hastalık aktivite skorları ile arasındaki ilişkiyi belirlemektir. **Gereç ve Yöntemler:** Bu kesitsel çalışmada, RA tanısı almış 52 hasta, AS tanısı almış 49 hasta ve 49 sağlıklı kontrol çalışmaya alındı. Her hastanın açlık glukoz seviyeleri, lipid profili ve inflamatuvar belirteçlerine bakıldı. Framingham risk skoru (FRS) ve bel-boy oranı [waist-to-height ratio (WHtR)] hesaplandı, MetS varlığı saptandı. **Bulgular:** MetS prevalansı, AS ve RA hastalarında kontrollere göre daha yüksekti. Hem RA hem de AS hasta gruplarında kontrol grubuna göre anlamlı olarak daha yüksek WHtR değerleri bulundu; ayrıca WHtR değerleri MetS'li hastalarda, MetS olmayan hasta grubuna göre anlamlı olarak daha yüksek bulundu. MetS'li RA ve AS hasta gruplarında FRS'ler, MetS'li kontrol grubuna göre istatistiksel olarak daha yüksekti ($p=0,019$). FRS'ler, hastalık aktivitesi yüksek olan RA hastalarında, hastalık aktivitesi düşük RA hastalarına göre anlamlı olarak daha yüksekti ($p=0,030$). **Sonuç:** MetS, RA ve AS hastalarında kontrollere göre daha yaygındı. Kardiyovasküler risk skorları, MetS hastalarında MetS olmayan hastalara göre daha güçlüydü ve ayrıca hastalık aktivitesi yüksek olan RA hastalarında kardiyovasküler risk, düşük hastalık aktivitesi olan RA hastalarına göre daha yüksekti.

Anahtar Kelimeler: Romatoid artrit; ankilozan spondilit; kardiyovasküler risk; metabolik sendrom

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Compared with the general population, chronic inflammatory rheumatic diseases such as rheumatoid arthritis (RA) and ankylosing spondylitis (AS) are associated with significant cardiovascular morbidity and mortality.¹⁻³ This increased cardiovascular risk is attributed to a combination of systemic inflammation and a high prevalence of traditional risk factors such as hypertension (HT) and hyperlipidemia.⁴ In previous studies, it was mentioned that traditional cardiovascular risk factors were quite common in this patient population, but the diagnosis was less and treatment was inadequate.⁵

The metabolic syndrome (MetS) has received increased attention in the past few years. This statement from the American Heart Association and the National Heart, Lung, and Blood Institute is intended to provide up-to-date guidance for professionals on the diagnosis and management of the MetS in adults. MetS was defined as the presence 3 or more of the following; waist circumferences ≥ 88 cm in women and ≥ 102 cm in men, triglyceride (TG) level ≥ 150 mg/dL, high-density lipoprotein cholesterol (HDL-C) < 40 mg/dL men and < 50 mg/dL in women, fasting glucose ≥ 100 mg/dL, and systolic or diastolic blood pressure $\geq 130/85$ mmHg.⁶

The predominant underlying risk factors for the syndrome appear to be abdominal obesity and insulin resistance; other associated conditions can be physical inactivity, aging and hormonal imbalance. Regardless of the relative contributions of visceral fat and abdominal subcutaneous fat to insulin resistance, a pattern of abdominal (or upper-body) obesity correlates more strongly with insulin resistance and the MetS than does lower-body obesity. Weight reduction deserves first priority in individuals with abdominal obesity and the MetS. In individuals with diabetes, the coexistence of other MetS factors denotes a higher risk for future development of atherosclerotic cardiovascular disease (CVD).⁶⁻⁸

The detection, prevention, and treatment of underlying risk factors in people with MetS is important in reducing the burden of CVD.⁹ Recent studies have shown that there is a high rate of MetS in patients with RA and systemic lupus erythematosus, and this has linked it to the inflammatory burden.^{10,11}

Despite this, data on MetS prevalence in patients with AS are limited, but in a study of 24 patients with AS, the presence of MetS was examined and found high.¹²

The Framingham CVD risk score (including age, sex, total cholesterol, HDL-C, systemic blood pressure, smoking, and presence of diabetes) is a scoring system used to measure the risk of CVD in the general population. It is also used in the risk assessment of people with RA and other inflammatory diseases.¹³ The risk management recommendations of RA and other inflammatory joint diseases guide of the The European Alliance of Associations for Rheumatology (EULAR), which was updated in 2016, suggested that the patients with RA and other inflammatory diseases who have 2 features such as a disease duration of more than 10 years, seropositive and extra-articular involvement should be multiplied by 1.5 in CVD risk score calculations and the CVD risk should be evaluated in this way.¹⁴

The purposes of this study were to determine the presence of cardiovascular risk factors and MetS compared to healthy controls in patients with AS and RA who were admitted to the physical medicine and rehabilitation-rheumatology outpatient clinic and to determine the relationship between the disease activity scores of these rheumatic diseases and the risk of CVD.

MATERIAL AND METHODS

PARTICIPANTS

The study design was prospective and observational. The participants included in the study were being followed by the Akdeniz University Physical Medicine and Rehabilitation-Rheumatology Outpatient Clinic with no history of cardiovascular events. The study comprised 49 AS patients who were diagnosed according to the 1984 modified New York criteria, 52 patients with RA aged 35-75 years who fulfilled the 2010 American College of Rheumatology/EULAR classification criteria for RA, and 49 randomly recruited sex and age matched healthy individuals with no history of cardiovascular events. The study was approved by the Akdeniz University Faculty of Medicine Clinical Research Ethics Committee (date: July 5, 2017, no: 396). All participants gave written in-

formed consent and the study was performed in accordance with the 1964 Declaration of Helsinki.

SPSS for Windows 22.0 (IBM SPSS Statistics, ABD) program was used for statistical analysis of the data obtained in the study. For the quantitative variables of the study determined by measurement, mean and standard deviation are shown as descriptive statistics, and for qualitative variables determined by counting, descriptive statistics are shown as numbers and percentages. First of all, the conformity tests of the data used for normal distribution were made with the Shapiro-Wilk test. As a result of the tests, it was understood that the data did not show normal distribution and non-parametric tests were used in the statistical analysis. In pairwise comparisons between variables with 2 categories such as gender, the Mann-Whitney U test and Kruskal-Wallis analysis of variance were applied to find the differences between variables with 3 or more categories such as diagnosis. Chi-square was used to reveal the relationship between dependent qualitative variables and correlation analysis was performed for the relationship between quantitative variables. A value of 0.05 was accepted as the level of significance in the entire study.

CLINICAL EXAMINATION AND LABORATORY TESTS

Comprehensive clinical assessments were performed including demographic variables (age, sex, duration of illness) and presence of HT, diabetes mellitus (DM) and smoking. A physical examination of all patients was conducted. Each person's height, weight, and abdominal circumference were measured. Each person's erythrocyte sedimentation rate, C-reactive protein (CRP) values, HDL-C, total cholesterol, TG, and fasting glucose values were evaluated. Daily life activity assessments of the patients were performed using the Bath Ankylosing Spondylitis Functional Index in patients with AS and the Health Assessment Questionnaire (HAQ) in patients with RA.

Disease activity scores were evaluated using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Ankylosing Spondylitis Disease Activity Score with CRP (ASDAS-CRP) in patients with AS and the Disease Activity Score 28 (DAS-28-CRP) in patients with RA. In patients with RA, patients with DAS-28-CRP values of 3.2 and below

were evaluated as having low disease activity, and patients with DAS-28-CRP values of >3.2 were considered as having high disease activity. In patients with AS, BASDAI scores of 4 and below and, ASDAS-CRP values of 2.1 and below were considered as having low disease activity, and BASDAI scores of >4 and ASDAS-CRP values of >2.1 were accepted as having high disease activity.

MetS was defined according to the modified National Cholesterol Education Program Adult Treatment Panel III criteria, which require the presence three or more of the following: waist circumferences ≥ 88 cm in women and ≥ 102 cm in men, TG level ≥ 150 mg/dL, HDL-C <40 mg/dL men and <50 mg/dL in women, fasting glucose ≥ 100 mg/dL, and systolic or diastolic blood pressure $\geq 130/85$ mmHg.^{6,15}

The blood pressure of each person was measured using an auscultatory method based on Korotkoff sounds with a mercury sphygmomanometer and the results were recorded.¹⁵

The Framingham Risk Score (FRS) is a sex-specific algorithm used to estimate the 10-year cardiovascular risk of an individual. The FRS was first developed based on data obtained from the Framingham Heart Study, to estimate the 10-year risk of developing coronary heart disease. This scoring system is calculated by evaluating age, sex, systolic and diastolic blood pressure, serum TG and HDL-C values, the presence of DM, and smoking.¹⁶

A person's waist-to-height ratio (WHtR), used for obesity determination, is defined as their waist circumference divided by their height, both measured in the same units. The WHtR is a measure of the distribution of body fat. Higher values of WHtR indicate a higher risk of obesity-related CVDs; it is correlated with abdominal obesity.¹⁷

RESULTS

The present study comprised 52 (45 females, 7 males) patients with RA, 49 (8 females, 41 males) with AS and 49 (25 females, 24 males) healthy controls. The mean disease duration of the patients with RA and AS was 13 years and 11 years, respectively. The demographic and clinical data of the patients are given in Table 1. There was no significant difference be-

tween the patients with RA, AS and the controls in terms of the presence of HT and DM, when the systolic and diastolic blood pressure values of the patients were compared however, the systolic and diastolic blood pressure values were significantly higher in the RA and AS groups compared with the control group ($p<0.001$) (Table 1, Table 2).

In the current study, as it was shown in Table 2, among the 3 groups, HDL-C levels were significantly higher in patients with RA, and mean 10-year FRS and WHtR values were found to be higher significantly in the RA group compared with the control group ($p<0.001$, $p=0.027$, and $p<0.001$, respectively). There was no statistically significant difference in the mean 10-year FRS values between the AS group and the control group. HDL-C levels were significantly lower in patients with AS and WHtR values were found to be significantly higher in the AS group compared with the control group. There was no statistically significant difference between fasting blood glucose values and TG values between all 3 groups (Table 2). In recent years, WHtR values calculated

for CVD risk and obesity assessment were significantly higher in the patients with RA and AS compared with controls ($p<0.001$) (Table 2).

When the patients and control groups with MetS were compared, the mean HDL-C values of patients with RA were significantly higher than in the AS and control groups ($p=0.002$) (Table 3). The mean systolic and diastolic blood pressure values in the RA and AS groups were statistically significantly higher than in the control group ($p=0.025$ and $p=0.00$ respectively). FRS values in the RA and AS groups were statistically higher than in the control group with MetS ($p=0.019$). There was no difference in mean fasting glucose and TG values between all 3 groups (Table 3).

When patients with RA with and without MetS were compared, although no statistically significant differences were found in CRP, DAS-28 and HAQ scores ($p>0.05$), WHtR values were higher in the RA group with MetS ($p<0.05$).

The mean 10-year FRS was higher in the group with MetS, but no significant difference was found.

TABLE 1: Demographic characteristics of the patients and controls.

	Diagnosis								p value
	RA		AS		C		All		
	n	%	n	%	n	%	n	%	
Sex									
Female	45	86.54	8	16.33	25	51.02	78	52.00	
Male	7	13.46	41	83.67	24	48.98	72	48.00	<0.001
Smoking									
Yes	8	15.38	16	32.65	5	10.20	29	19.33	
No	44	84.62	33	67.35	44	89.80	121	80.67	0.013
HT									
Yes	16	30.77	12	24.49	17	34.69	45	30.00	
No	36	69.23	37	75.51	32	65.31	105	70.00	0.539
DM									
Yes	3	5.77	6	12.24	4	8.16	13	8.67	
No	49	94.23	43	87.76	45	91.84	137	91.33	0.507
CAD									
No	52	100.00	49	100.00	49	100.00	150	100.00	
MetS									
Yes	22	42.31	20	40.82	8	16.33	50	33.33	
No	30	57.69	29	59.18	41	83.67	100	66.67	0.009

RA: Rheumatoid arthritis; AS: Ankylosing spondylitis; C: Control; HT: Hypertension; DM: Diabetes mellitus; CAD: Coronary artery disease; MetS: Metabolic syndrome.

TABLE 2: Comparison of data between the groups.

	Diagnosis									p value	Comparison
	RA ¹			AS ²			C ³				
	n	Mean	SD	n	Mean	SD	n	Mean	SD		
Age	52	56.13	7.74	49	44.02	6.38	49	56.94	9.92	<0.001	1, 3>2
Di	52	13.79	8.06	49	11.53	6.56	0	-	-	0.203	
CRP	52	1.51	1.77	49	1.26	2.34	0	-	-	0.148	
Triglyceride	52	145.88	76.53	49	170.47	127.66	49	162.51	85.65	0.583	
HDL-C	52	53.29	13.42	49	42.90	14.62	49	47.78	11.38	<0.001	1>3>2
Systolic BP	52	132.60	19.19	49	126.33	19.41	49	115.51	12.43	<0.001	1, 2>3
Diastolic BP	52	86.63	11.91	49	83.47	12.21	49	72.65	8.84	<0.001	1, 2>3
Fasting glucose	52	93.13	24.06	49	94.22	25.06	49	96.59	18.88	0.321	
FRS	52	9.25	5.34	49	7.47	5.72	49	6.88	4.85	0.027	1>2, 3
WHtR	52	0.60	0.07	49	0.59	0.07	49	0.56	0.06	<0.001	1, 2>3

Kruskal-Wallis variance analysis; RA: Rheumatoid arthritis; AS: Ankylosing spondylitis; C: Control; SD: Standard deviation; Di: Duration of illness; CRP: C-reactive protein; HDL-C: High-density lipoprotein cholesterol; BP: Blood pressure; FRS: Framingham risk score; WHtR: Weight to height ratio.

TABLE 3: Comparison of groups with metabolic syndrome.

	Diagnosis									p value	Comparison
	RA ¹			AS ²			C ³				
	n	Mean	SD	n	Mean	SD	n	Mean	SD		
Age	22	54.50	7.37	20	43.85	6.97	8	55.63	11.04	<0.001	1, 3>2
Di	22	10.64	6.85	20	9.25	6.33	0	-	-	0.324	
Triglyceride	22	177.59	94.43	20	211.15	79.20	8	173.75	73.86	0.126	
HDL	22	46.55	9.03	20	38.45	11.87	8	40.38	3.74	0.002	1>2, 3
Systolic BP	22	139.32	17.61	20	133.25	21.29	8	118.75	12.46	0.025	1, 2>3
Diastolic BP	22	90.91	13.42	20	86.00	12.73	8	72.50	8.86	0.003	1, 2>3
Fasting glucose	22	104.36	31.77	20	105.00	32.86	8	104.63	14.99	0.573	
FRS	22	10.32	4.51	20	8.95	6.99	8	5.38	3.16	0.019	1, 2>3
WHtR	22	0.63	0.05	20	0.61	0.07	8	0.59	0.04	0.242	

Kruskal-Wallis variance analysis; RA: Rheumatoid arthritis; AS: Ankylosing spondylitis; C: Control; SD: Standard deviation; Di: Duration of illness; HDL: High-density lipoprotein; BP: Blood pressure; FRS: Framingham risk score; WHtR: Waist-to-height ratio.

When we compared patients with AS with and without MetS, WHtR values were significantly higher in the AS group with MetS ($p < 0.05$). Although the mean 10-year FRS was higher, no significant difference was found ($p > 0.05$).

When the relationship between disease activity scores and CVD risk was evaluated, patients with RA with high disease activity (DAS-28-CRP > 3.2) had longer disease duration ($p = 0.033$), higher CRP values ($p = 0.020$), and higher HAQ scores ($p < 0.0010$) FRS values were significantly higher in patients with RA with high disease activity scores than in patients with

RA patients with RA with low disease activity ($p = 0.030$). WHtR values were higher in the group with high disease activity scores, but were not statistically significant (Table 4).

No significant result was found in the comparison of disease activity scores and CVD risk in the AS group ($p > 0.05$) (Table 5).

DISCUSSION

In this study, we assessed the presence of cardiovascular risk factors and MetS according to healthy con-

TABLE 4: Comparison with disease activity (RA).

		Diagnosis RA		
		n	Mean	p value
Age	DAS-28-CRP			
	≤3.2	27	54.33	
	>3.2	25	58.08	0.088
Di	DAS-28-CRP			
	≤3.2	27	11.33	
	>3.2	25	16.44	0.033
CRP	DAS-28-CRP			
	≤3.2	27	1.31	
	>3.2	25	1.73	0.020
HAQ	DAS-28-CRP			
	≤3.2	27	0.73	
	>3.2	25	1.38	<0.001
TG	DAS-28-CRP			
	≤3.2	27	164.56	
	>3.2	25	125.72	0.181
HDL-C	DAS-28-CRP			
	≤3.2	27	55.93	
	>3.2	25	50.44	0.404
Systolic BP	DAS-28-CRP			
	≤3.2	27	126.11	
	>3.2	25	139.60	0.009
Diastolic BP	DAS-28-CRP			
	≤3.2	27	84.44	
	>3.2	25	89.00	0.189
Fasting glucose	DAS-28-CRP			
	≤3.2	27	90.70	
	>3.2	25	95.76	0.119
FRS	DAS-28-CRP			
	≤3.2	27	7.67	
	>3.2	25	10.96	0.030
WHtR	DAS-28-CRP			
	≤3.2	27	0.59	
	>3.2	25	0.61	0.263

Mann-Whitney U test; RA: Rheumatoid arthritis; Di: Duration of illness; CRP: C-reactive protein; HAQ: Health Assessment Questionnaire; TG: Triglyceride; HDL-C: High-density lipoprotein cholesterol; BP: Blood pressure; FRS: Framingham risk score; WHtR: Waist-to-height ratio; DAS: Disease Activity Score.

trols in patients with AS and RA and also the relationship between the disease activity scores of these rheumatic diseases and the risk of CVD.

We found that MetS was more common in patients with RA and AS than in controls (Table 1). Predictors of cardiovascular risk were (systolic and

diastolic blood pressure values) stronger in patients (both AS and RA) than controls.

Compared with the normal population, patients with AS and RA have increased CVD risk and CVD mortality. In these patients, besides the risk of in-

TABLE 5: Comparison with disease activity , BASDAI (AS).

		Diagnosis RA		
		n	Mean	p value
Age	BASDAI			
	≤4	34	44.68	
	>4	15	42.53	0.163
Di	BASDAI			
	≤4	34	12.50	
	>4	15	9.33	0.123
CRP	BASDAI			
	≤4	34	0.97	
	>4	15	1.93	0.965
BASFI	BASDAI			
	≤4	34	1.69	
	>4	15	3.32	0.079
TG	BASDAI			
	≤4	34	172.50	
	>4	15	165.87	0.625
HDL-C	BASDAI			
	≤4	34	42.29	
	>4	15	44.27	0.522
Systolic BP	BASDAI			
	≤4	34	128.53	
	>4	15	121.33	0.244
Diastolic BP	BASDAI			
	≤4	34	83.97	
	>4	15	82.33	0.694
Fasting glucose	BASDAI			
	≤4	34	92.50	
	>4	15	98.13	0.508
FRS	BASDAI			
	≤4	34	8.15	
	>4	15	5.93	0.315
WHtR	BASDAI			
	≤4	34	0.58	
	>4	15	0.61	0.427

Mann-Whitney U test; AS: Ankylosing spondylitis; Di: Duration of illness; CRP: C-reactive protein; BASFI: Bath Ankylosing Spondylitis Functional Index; TG: Triglyceride; HDL-C: High-density lipoprotein cholesterol; BP: Blood pressure; FRS: Framingham risk score; WHtR: Waist-to-height ratio; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index.

flammatory burden, the frequency of traditional CVD risk factors such as dyslipidemia, HT and MetS are at a considerable level.^{2,3} However in the current study, there was no significant difference in the presence of HT in the history of the patient and control groups, the higher systolic and diastolic blood pressures and the presence of MetS in the patient group supports the literature (Table 1, Table 2).

Epidemiologic data show that RA is an independent risk factor for MetS. The presence of MetS may be responsible for the development of atherosclerosis and increased risk of CVD in patients with RA.^{18,19} The relationship between the inflammatory activity of RA and MetS has been mentioned in some studies. For example, studies on the relationship between RA and MetS have been conducted to determine the effect of the presence MetS on disease activity and CVD risk. In studies comparing the relationship between RA and MetS with healthy controls, the prevalence of MetS in patients with RA was found to be higher compared with healthy controls, and the DAS-28 of patients with RA with MetS were significantly higher than those of patients without MetS.^{11,20} In our study, the frequency of MetS was significantly higher in both the RA and AS groups than in the healthy controls (Table 1). Also, the FRS and disease activity score of patients with RA with MetS were higher than in those with RA without MetS, but there was no statistical difference.

In the study conducted by da Cunha et al., increased waist circumference, blood pressure values, and fasting glucose were (which are components of the MetS) detected in patients with RA compared with the control group.²⁰ In our study, increased WHtR values and increased blood pressures were detected in both the RA and AS groups compared with the control group (Table 2). Whereas there was no significant difference in fasting glucose values.

The FRS values we looked at for CVD risk were significantly higher in the RA group than in healthy controls (Table 2). Considering that patients with RA with risk factors (seropositivity, disease duration of more than 10 years, extraarticular involvement) are recommended to be multiplied by 1.5 according to the recommendations of EULAR, the risk of CVD,

which is already high in RA, will increase even more in such cases. The FRS values of the AS group were higher than in the control group, but no statistically significant difference was found. This result was associated with the lower mean age (which used in FRS calculation) of the AS group compared to the RA and control groups.

Patients with RA with high disease activity (DAS-28-CRP>3.2) had longer disease duration, higher CRP values, and higher HAQ scores. FRS values were significantly higher in patients with RA with high disease activity scores than those with low disease activity (Table 4). Based on these data, it may be considered that high disease activity scores are associated with an increased risk of CVD.

HDL-C was the highest in the RA group and, lowest in the AS group (Table 2). The high HDL-C values in the RA group were attributed to the fact that the majority of the patients were female, and the low values in the AS group were related to the high rate of male sex and smoking. In addition, although dyslipidemia is an important risk factor for CVD in the general population, it is a little more complicated when it comes to patients with RA. Studies are showing that serum lipid levels increase with decreasing inflammation whereas they decrease in patients with untreated active RA. These changes are considered to be a lipid paradox, and their effect on the risk of CVD is unclear.²¹

Both systolic and diastolic blood pressures were higher in the RA and AS groups compared with the control group (Table 2). Although there were no differences regarding the presence of HT in the patient and control groups in the present study, it was remarkable that the blood pressure values were higher in both patient groups than in the control group (Table 1, Table 2). Blood pressure is a component in both the calculation of FRS and among the MetS diagnostic criteria, so we wanted to draw attention to the addition of blood pressure checks the routine follow up of patients who are followed up for rheumatologic diseases.

For other inflammatory rheumatic diseases, patients with AS have an increased risk for CVD.²² Considering previous studies investigating the re-

relationship between MetS and AS, Malesci et al. found an increased MetS prevalence (46% vs. 11%) in AS in their study of 24 patients with AS.¹² Similarly, in our study, we found an increased frequency of MetS in the AS group compared with the control group (40% vs 16%) (Table 1).

Lower HDL-C values, and higher diastolic and systolic blood pressure were detected in the AS group compared with the control group. Due to these factors, which are also components of the MetS, MetS was observed more frequently in patients with AS than in the control group. Despite the negative risk factors (low HDL-C and high blood pressure) and presence of MetS, there was no statistically significant difference between the FRS values between the AS group and the control group, which was attributed to the mean age of the AS group (Table 2). When the relationship between disease activity and FRS was evaluated, we found no significant result (Table 5, Table 6).

In studies on lipid profiles in patients with AS, HDL-C levels were shown to be low.^{12,23} In Rossner’s study, normal HDL-C levels were determined.²⁴ In our study, the HDL-C values of patients with AS were significantly lower than in both the RA group and the control group (Table 2). This finding was compatible with studies with low HDL-C levels in patients with AS.

We evaluated the WHtR value (waist circumference/height-cm), which was used in recent studies for cardiometabolic risk and obesity, both in the patient group and in the control group.^{17,25} We found significantly higher WHtR values in both the RA and AS groups compared with the control group. We found significantly higher WHtR values in patients with MetS than in those without MetS. We found a significant correlation between FRS values and WHtR. Referring to these results, we concluded that WHtR was a fast, reliable, and inexpensive method to evaluate the presence of MetS in outpatient conditions.

This study has some limitations. First, the small sample size and the research’s being a cross-sectional study may have prevented the detection of a signifi-

TABLE 6: Comparison with disease activity ASDAS-CRP (AS).

		Diagnosis		
		RA		
		n	Mean	p value
Age	ASDAS-CRP			
	≤2.1	20	45.20	
	>2.1	29	43.21	0.385
Di	ASDAS-CRP			
	≤2.1	20	13.30	
	>2.1	29	10.31	0.179
CRP	ASDAS-CRP			
	≤2.1	20	0.66	
	>2.1	29	1.68	0.087
BASFI	ASDAS-CRP			
	≤2.1	20	1.46	
	>2.1	29	2.69	0.136
TG	ASDAS-CRP			
	≤2.1	20	196.40	
	>2.1	29	152.59	0.633
HDL-C	ASDAS-CRP			
	≤2.1	20	39.10	
	>2.1	29	45.52	0.318
Systolic BP	ASDAS-CRP			
	≤2.1	20	123.75	
	>2.1	29	128.10	0.318
Diastolic BP	ASDAS-CRP			
	≤2.1	20	82.25	
	>2.1	29	84.31	0.720
Fasting glucose	ASDAS-CRP			
	≤2.1	20	89.60	
	>2.1	29	97.41	0.319
FRS	ASDAS-CRP			
	≤2.1	20	9.85	
	>2.1	29	5.83	0.125
WHtR	ASDAS-CRP			
	≤2.1	20	0.59	
	>2.1	29	0.59	0.540

Mann-Whitney U test; AS: Ankylosing spondylitis; Di: Duration of illness; CRP: C-reactive protein; BASFI: Bath Ankylosing Spondylitis Functional Index; TG: Triglyceride; HDL-C: High-density lipoprotein cholesterol; BP: Blood pressure; FRS: Framingham risk score; WHtR: waist-to-height ratio. ASDAS: Ankylosing Spondylitis Disease Activity Score.

cant increase in CVD risk. Secondly, the observational design does not permit concluding causal relationships, only clinical associations.

Despite these, this study investigated the prevalence of MetS in patients with AS and RA, and sought to detect the relationship between the disease activity

scores of these rheumatic diseases and the risk of CVD, so we think it is important in this respect.

CONCLUSION

As a result, the frequency of MetS was found high in the RA and AS groups, also the Framingham scores were found high in these patients. In addition, the presence of MetS in the patient group was found to be correlated with both negative disease outcomes and an

increased risk of CVD. Considering the data of our study, the evaluation of these patients in terms of blood pressure, obesity, and MetS, as well as primary inflammatory diseases, will help in both risk assessment and early treatment in terms of cardiometabolic disease.

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REFERENCES

- Haskard DO. Accelerated atherosclerosis in inflammatory rheumatic diseases. *Scand J Rheumatol.* 2004;33:281-92. [[Crossref](#)] [[PubMed](#)]
- Han C, Robinson DW Jr, Hackett MV, et al. Cardiovascular disease and risk factors in patients with rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis. *J Rheumatol.* 2006;33:2167-72. [[PubMed](#)]
- Avina-Zubieta JA, Thomas J, Sadatsafavi M, et al. Risk of incident cardiovascular events in patients with rheumatoid arthritis: a meta-analysis of observational studies. *Ann Rheum Dis.* 2012;71:1524-9. [[Crossref](#)] [[PubMed](#)]
- Primdahl J, Clausen J, Hørslev-Petersen K. Results from systematic screening for cardiovascular risk in outpatients with rheumatoid arthritis in accordance with the EULAR recommendations. *Ann Rheum Dis.* 2013;72:1771-6. [[Crossref](#)] [[PubMed](#)]
- Bartels CM, Johnson H, Voelker K, et al. Impact of rheumatoid arthritis on receiving a diagnosis of hypertension among patients with regular primary care. *Arthritis Care Res (Hoboken).* 2014;66:1281-8. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
- Grundy SM, Cleeman JI, Daniels SR, et al; American Heart Association; National Heart, Lung, and Blood Institute. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation.* 2005;112:2735-52. Erratum in: *Circulation.* 2005;112:e297. Erratum in: *Circulation.* 2005;112:e298. [[Crossref](#)] [[PubMed](#)]
- Daskalopoulou SS, Mikhailidis DP, Elisaf M. Prevention and treatment of the metabolic syndrome. *Angiology.* 2004;55:589-612. [[Crossref](#)] [[PubMed](#)]
- Laaksonen DE, Lakka HM, Niskanen LK, et al. Metabolic syndrome and development of diabetes mellitus: application and validation of recently suggested definitions of the metabolic syndrome in a prospective cohort study. *Am J Epidemiol.* 2002;156:1070-7. [[Crossref](#)] [[PubMed](#)]
- Galassi A, Reynolds K, He J. Metabolic syndrome and risk of cardiovascular disease: a meta-analysis. *Am J Med.* 2006;119:812-9. [[Crossref](#)] [[PubMed](#)]
- Chung CP, Avalos I, Oeser A, et al. High prevalence of the metabolic syndrome in patients with systemic lupus erythematosus: association with disease characteristics and cardiovascular risk factors. *Ann Rheum Dis.* 2007;66:208-14. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
- Karvounaris SA, Sidiropoulos PI, Papadakis JA, et al. Metabolic syndrome is common among middle-to-older aged Mediterranean patients with rheumatoid arthritis and correlates with disease activity: a retrospective, cross-sectional, controlled, study. *Ann Rheum Dis.* 2007;66:28-33. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
- Malesci D, Niglio A, Mennillo Ga, Buono R, Valentini G, La Montagna G: High prevalence of metabolic syndrome in AS men, *Clin Rheumatol* 2007;26(5):710-4. [[Crossref](#)] [[PubMed](#)]
- Kawai VK, Chung CP, Solus JF, et al. The ability of the 2013 American College of Cardiology/American Heart Association cardiovascular risk score to identify rheumatoid arthritis patients with high coronary artery calcification scores. *Arthritis Rheumatol.* 2015;67:381-5. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
- Agca R, Heslinga SC, Rollefstad S, et al. EULAR recommendations for cardiovascular disease risk management in patients with rheumatoid arthritis and other forms of inflammatory joint disorders: 2015/2016 update. *Ann Rheum Dis.* 2017;76:17-28. [[Crossref](#)] [[PubMed](#)]
- Pressbooks [Internet]. [Cited: november 2018]. Manual Blood Pressure Measurement. Available from: [[Link](#)]
- Anderson KM, Wilson PW, Odell PM, et al. An updated coronary risk profile. A statement for health professionals. *Circulation.* 1991;83:356-62. [[Crossref](#)] [[PubMed](#)]
- Vikram NK, Latifi AN, Misra A, et al. Waist-to-height ratio compared to standard obesity measures as predictor of cardiometabolic risk factors in Asian Indians in North India. *Metab Syndr Relat Disord.* 2016;14:492-9. [[Crossref](#)] [[PubMed](#)]
- Avina-Zubieta JA, Choi HK, Sadatsafavi M, et al. Risk of cardiovascular mortality in patients with rheumatoid arthritis: a meta-analysis of observational studies. *Arthritis Rheum.* 2008;59:1690-7. [[Crossref](#)] [[PubMed](#)]
- Cavagna L, Boffini N, Cagnotto G, et al. Atherosclerosis and rheumatoid arthritis: more than a simple association. *Mediators Inflamm.* 2012;2012:147354. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
- Cunha VR, Brenol CV, Brenol JC, et al. Metabolic syndrome prevalence is increased in rheumatoid arthritis patients and is associated with disease activity. *Scand J Rheumatol.* 2012;41:186-91. [[Crossref](#)] [[PubMed](#)]
- Myasoedova E, Crowson CS, Kremers HM, et al. Lipid paradox in rheumatoid arthritis: the impact of serum lipid measures and systemic inflammation on the risk of cardiovascular disease. *Ann Rheum Dis.* 2011;70:482-7. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
- Peters MJ, van der Horst-Bruinsma IE, Dijkmans BA, et al. Cardiovascular risk profile of patients with spondylarthropathies, particularly ankylosing spondylitis and psoriatic arthritis. *Semin Arthritis Rheum.* 2004;34:585-92. [[Crossref](#)] [[PubMed](#)]
- Divecha H, Sattar N, Rumley A, et al. Cardiovascular risk parameters in men with ankylosing spondylitis in comparison with non-inflammatory control subjects: relevance of systemic inflammation. *Clin Sci (Lond).* 2005;109:171-6. [[Crossref](#)] [[PubMed](#)]
- Rossner S. Further studies on serum lipoproteins in connective tissue diseases. *Atherosclerosis.* 1978;31:93-9. [[Crossref](#)]
- Zhu Q, Shen F, Ye T, et al. Waist-to-height ratio is an appropriate index for identifying cardiometabolic risk in Chinese individuals with normal body mass index and waist circumference. *J Diabetes.* 2014;6:527-34. [[Crossref](#)] [[PubMed](#)]