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Prevalence of metabolic syndrome patients with systemic sclerosis

Sistemik skleroz hastalarında metabolik sendrom sıklığı

Ümit Özmen[1] Elif Er Gülbezer[2] Burcu Barutçuoğlu[3]
Figen Yargucu Zihni[4]

[1] Karkamış Şehit Fuat Oğuzcan State Hospital, Department of Internal Medicine, Gaziantep, Türkiye
[2] Koç University Faculty of Medicine Department of Internal Medicine, Istanbul, Türkiye
[3] Ege University Faculty of Medicine Department of Clinical Biochemistry, Izmir, Türkiye
[4] Ege University Faculty of Medicine Department of Internal Medicine Division of Rheumatology, Izmir, Türkiye

ABSTRACT

Aim: To determine the prevalence of metabolic syndrome (MetS) in Turkish systemic sclerosis (SSc) patients.

Materials and Methods: In this cross-sectional, single-centre study, 76 SSc patients admitted to the outpatient clinic of our tertiary care hospital between July and September 2021 were included. The National Cholesterol Education Programme's Adult Treatment Panel (NCEP-ATP III) criteria were used to define metabolic syndrome (MetS). The relationship between MetS and SSc organ involvement and disease characteristics was investigated.

Results: According to the ATP III criteria, 37 cases (48.7%) were identified as having MetS. The prevalance of MetS increased with advancing age (40-45 years: 25%, 46-60 years: 48.4%, >60 years: 62.9%). The cases were divided into two groups according to the presence or absence of MetS. Patients with MetS had higher mean age (58.2±9.4 vs. 51.6±13.5, p=0.015) and lower modified Rodnan skin scores (14 vs. 22, p=0.019). The groups were comparable regarding disease subtype, duration and activity, organs/systems involved and disease-related damage.

Conclusion: Although the prevalence of MetS in SSc patients in our study was higher than that observed in the general population of our country, the prevalence of MetS did not increase when compared to the similar age group. MetS was thought to be related to age and gender predominance rather than the disease itself. Although mRSS was found to be significantly lower in patients with MetS, its sensitivity to predict MetS was found to be low. Nevertheless, our data suggest that the risk of MetS should be considered in SSc patients.

Keywords: Systemic sclerosis, metabolic syndrome, prevalence, insulin resistance.

ÖZ

Amaç: *Türk sistemik skleroz (SSc) hastalarında metabolik sendrom (MetS) prevalansının saptanması amaçlamıştır.*

Gereç ve Yöntem: *Kesitsel ve tek merkezli çalışmaya, Temmuz-Eylül 2021 tarihleri arasında üçüncü basamak hastanemizin polikliniğinde başvuran 76 SSc olgusu alındı. MetS, National Cholesterol Education Program's Adult Treatment Panel (NCEP-ATP III) kriterlerine göre tanımlandı. MetS'in SSc organ tutulumu ve hastalık özellikleri ile ilişkisi incelendi.*

Corresponding author: Ümit Özmen
Karkamış Şehit Fuat Oğuzcan State Hospital, Gaziantep, Türkiye
E-mail: *umidozmen@gmail.com*
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Bulgular: *ATP III kriterlerine göre MetS, 37 olguda (%48.7) saptandı. MetS sıklığının ilerleyen yaşla birlikte arttığı (40-45 yaşta: %25, 46-60 yaşta: %48.4, >60 yaşta: %62.9) görüldü. Olgular MetS olup olmamasına göre 2 gruba ayrılarak karşılaştırıldı. MetS olan olguların yaşlarının daha yüksek (58.2±9.4'e karşı 51.6±13.5, p=0.015) ve modifiye Rodnan deri skorlarının daha düşük olduğu görüldü. (14'e karşı 22, p=0,019). Hastalık tipi, süresi, aktivitesi, tutulan organlar/sistemler ve hastalık ilişkili hasar bakımından da grupların benzer nitelikte oldukları görüldü.*

Sonuç: *Çalışmamızda SSc hastalarında saptanan Mets sıklığı ülkemiz genel popülasyonuna göre daha yüksek olsa da benzer yaş grubuna göre değerlendirildiğinde MetS sıklığının artmamış olduğu görülmektedir. MetS'in hastalığın kendisinden ziyade yaş ve cinsiyet baskınlığına bağlı olduğu düşünülmüştür. MetS'li hastalarda mRSS anlamlı olarak düşük saptanmasına rağmen, MetS'i öngörme duyarlılığı düşük bulunmuştur. Yine de verilerimiz SSc hastalarında MetS riskinin dikkate alınması gerektiğini ve daha geniş hasta gruplarında ileri çalışmalara ihtiyaç olduğunu ortaya koymaktadır.*

Anahtar Sözcükler: *Sistemik skleroz, metabolik sendrom, prevalans, insulin direnci.*

INTRODUCTION

Systemic sclerosis (SSc), also known as scleroderma, is a chronic autoimmune disease that affects both the skin and internal organs (1). The disease is characterised by vascular dysfunction and progressive fibrosis (1). The aetiology of this disease remains unclear, and it is associated with high mortality and morbidity rates (2, 3).

Metabolic syndrome (MetS) is a condition characterised by a cluster of metabolic disorders, including insulin resistance, obesity, dyslipidaemia and hypertension. The National Cholesterol Education Programme Adult Treatment Panel III (NCEP ATP III) criteria are used to define MetS. The aforementioned criteria encompass abdominal obesity, elevated triglyceride levels, diminished HDL cholesterol levels, elevated blood pressure, and elevated fasting plasma glucose levels (4). It is established that MetS is a significant risk factor for the development of cardiovascular disease and diabetes.

An increased prevalence of MetS has been reported in numerous rheumatological disorders, including gout, systemic lupus erythematosus (SLE), ankylosing spondylitis, rheumatoid arthritis, and antiphospholipid antibody syndrome (5). The prevalence of MetS in patients with SSc and the relationship between these two conditions remain a topic of debate in the scientific community (6-8). Systemic sclerosis (SSc) is characterised by microvascular changes and fibrosis, which are associated with systemic inflammation and autoimmune reactions. It can therefore be postulated that the inflammatory and vascular damage observed in SSc patients may predispose them to the development of MetS. Conversely, both diseases have some common pathological pathways, including oxidative stress associated with increased leptin and reactive oxygen radicals (ROS) and decreased adipokine levels (9-15). Furthermore, there are reports indicating that SSc fibrosis interacts with metabolic pathways via connective tissue growth factor (CTGF) and peroxisome proliferator-activated receptor gamma (PPARG) (16-19). It has been demonstrated that the enhanced sensitivity of SSc fibroblasts to CTGF-mediated collagen synthesis is mediated by insulin (16). Furthermore, it is established that reduced PPARG expression, which is closely associated with insulin resistance, is also a contributing factor in SSc fibrosis (17). While decreased PPARG expression is linked to fibrosis, PPARG activation with rosiglitazone has been observed to mitigate SSc fibrosis in mouse models (18, 19).

The existing literature on the prevalence of MetS in patients with SSc is limited, and there is a paucity of data on the relationship between these two conditions. Additionally, there is evidence indicating that the prevalence of MetS varies across different racial groups (20). The objective of this study was to investigate the prevalence of MetS according to the Adult Treatment Panel III (ATPIII) criteria in patients with SSc in the Turkish population. To this end, the prevalence of MetS in patients with SSc was calculated according to the ATPIII criteria, and the relationship between the presence of MetS and disease characteristics was analysed.

MATERIALS and METHODS

Patient Selection

A single-centre, cross-sectional study was conducted on consecutive patients who had applied to the internal medicine-rheumatology outpatient clinic of Ege University Faculty of Medicine Hospital between July 2021 and September 2021. Patients who met the diagnosis of SSc according to the 2013 European League Against Rheumatism (EULAR) / American College of Rheumatology (ACR) classification criteria (21) and who were aged 18 years or over were included in the study, provided that they had given written consent to participate. Patients with other concomitant rheumatological diseases, active treatment for any malignancy, and pregnancy were excluded from the study. The study was approved by the Clinical Research Ethics Committee of Ege University Faculty of Medicine (29.07.2021, Decision no:21-7.1T/19) and conducted in accordance with the principles of the Declaration of Helsinki. No support was received from any institution/organisation in the conduct of the study.

Demographic and Anthropometric Characteristics

The follow-up files were consulted in order to obtain information pertaining to the age, number of pregnancies, menstrual status and smoking status of the subjects. The weight and height of all patients were measured by the same researcher (UO) using a scale with a calibrated height measuring stand. Body mass index (BMI) was calculated as weight in kilograms divided by height in square metres. The waist circumference of all patients was measured by the same researcher (UO) using a non-flexible measuring tape. The midpoint between the anterior superior iliac crest and the lowest rib was identified as the measurement point. The measurement was conducted at the end of normal expiration with the patient in an upright position. Blood pressure readings for all patients were recorded by the same individual using a calibrated manual sphygmomanometer in the sitting position after a 30-minute rest period.

Laboratory Parameters

The total cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL), low-density lipoprotein (LDL), C-reactive protein (CRP) and fasting blood glucose (FBS) results were retrospectively obtained from the Patient Information Management System (PIMS) of Ege University Hospital. Given that the lipid parameters of the patients had already been screened on an annual basis in accordance with the recommendations set forth by the Dyslipidaemia Guideline of the Turkish Society of Endocrinology and Metabolism (annual dyslipidaemia follow-up in chronic inflammatory diseases), no further tests were deemed necessary. The results of the samples obtained between 08:00 and 10:00 a.m., following at least eight hours of fasting, during a patient visit within the past year were taken into consideration.

Characteristics of the Disease

The patients were divided into two groups, namely limited and diffuse cutaneous, on the basis of the extent of skin involvement and other clinical features (22). The current modified Rodnan skin score (mRSS) (range 0-51) was determined by physical examination by the same experienced rheumatologist (23). The disease activity was calculated with the Revised European Scleroderma Therapy (EUSTAR) Activity Index (RAI) score (24), while the disease burden/damage level was determined with the Scleroderma Clinical Trials Consortium Damage Index (SCTC-DI) score (25), both of which were calculated by the same rheumatologist (FYZ). A RAI score of 2.5 or greater was considered indicative of active disease. The maximum SCTC-DI score was 55, which was interpreted as indicating a low damage score (less than 5), a medium damage score (between 6 and 12), and a high damage score (equal to or greater than 13). The dates of onset of Raynaud's phenomenon and disease diagnosis, the presence of digital ulcers, the organs and systems involved, the presence of comorbidities and the current treatment information (including the duration of corticosteroid use and the cumulative corticosteroid dose) were obtained from the patient follow-up files.

In the evaluation of the involved organs and systems, a diagnosis of interstitial lung disease (ILD) was made based on the presence of characteristic pulmonary function tests and high-

resolution computed tomography (HRCT) findings. A diagnosis of pulmonary arterial hypertension (PAH) was made on the basis of right heart catheterisation, with a mean pulmonary arterial pressure (mPAP) of greater than 25 mmHg and a pulmonary capillary wedge pressure (PCWP) of less than 15 mmHg. Left ventricular diastolic dysfunction, myocarditis, pericarditis, pleural effusion exceeding 1 cm on echocardiogram, and arrhythmia requiring treatment were deemed to represent cardiac involvement. Gastroesophageal reflux disease necessitating the use of proton pump inhibitors and dysphagia with manometry evidence were deemed to represent oesophageal involvement, whereas constipation not attributable to any other cause for a period exceeding six months and diarrhoea attacks necessitating the administration of antibiotics were considered to indicate intestinal involvement. Renal failure accompanied by malignant hypertension was defined as scleroderma renal crisis. Tendon rubbing sound, arthritis and myositis were defined as locomotor system involvement. The data related to the involved organs and systems were obtained from the patient follow-up files.

Statistical Analysis

The statistical analyses of the data were conducted using the SPSS (IBM Statistics for Windows, Version 25.0, Armonk, NY: IBM Corp.) programme. The conformity of the data to a normal distribution was evaluated using the Shapiro-Wilk test. The Mann-Whitney U test was employed for the comparison of data that do not present a normal distribution, while the Chi-square test was used for the comparison of categorical variables. The correlations of continuous variables were evaluated by Spearman correlation analysis. The cut-off value for the presence of MetS was determined by ROC analysis using the Youden J index, and the data were presented as mean ± standard deviation (SD) and n (%). A p-value of less than 0.05 was considered statistically significant.

RESULTS

The study cohort comprised 76 individuals with SSc, 70 of whom were females (92.1%) and 6 males. The mean age of the participants was 54.8 ± 12.0 years, with a median disease duration of 10 (5-13.5) years. The median Rodnan skin score was 19 (10-26), with 57.9% of patients presenting with limited and 42.1% with diffuse cutaneous systemic sclerosis. According to the RAI score, 49.3% of the patients exhibited evidence of active disease. According to HRCT, 54 patients (71.1%) exhibited interstitial lung disease, 7 patients (92%) demonstrated pulmonary hypertension, as confirmed by right heart catheterisation, and 32 patients (42.1%) exhibited involvement of the locomotor system. All patients exhibited oesophageal involvement, while intestinal involvement was observed in 25 patients (32.9%).

According to the ATP III criteria, MetS was identified in 37 patients, representing a prevalence of 48.7%. When analysed according to age groups, no patients below the age of 40 years were found to have MetS. However, the frequency of MetS increased with advancing age, with 25% of patients aged 40-45 years, 48.4% of patients aged 46-60 years, and 62.9% of patients aged over 60 years having MetS.

The patients were divided into two groups according to the presence or absence of the MetS and compared in terms of patient and disease characteristics. The age of patients in the MetS group was found to be significantly higher than that of patients without MetS (58.2 ± 9.4 vs. 51.6 ± 13.5, p = 0.015). In contrast, no significant differences were observed between the groups with regard to patient characteristics, including gender, smoking status, number of pregnancies, and postmenopausal status. Additionally, the groups exhibited comparable disease types, durations, activities, and disease-related damage. The distribution of demographic and disease characteristics according to the presence of MetS is summarized in Table-1.

Table-2 illustrates the distribution of subjects according to their metabolic profiles. As expected, the subjects with MetS exhibited higher blood pressure, waist circumference, body mass index (BMI), and lipid levels, as well as lower high-density lipoprotein (HDL) levels, compared to those without MetS. The prevalence of diabetes mellitus (DM) and hypertension (HT) was higher in subjects with MetS, whereas the

prevalence of other diseases, including coronary artery disease (CAD), hyperlipidaemia and hypothyroidism, was similar.

A comparison was also conducted between patients with and without MetS in order to determine whether there were any differences in the organs and systems involved. When the involvement of the skin was categorised as limited or diffuse, no significant difference was observed between the groups. However, when mRSS, a quantitative assessment of skin involvement, was used, it was noted that the median mRSS was lower in those with MetS. The median mRSS was 14 (6-24) in those with MetS and 22 (14-28) in those without MetS (p=0.019). Nevertheless, no significant difference was observed between the two groups with respect to organ involvement. Table-3 presents a comparison of organ involvement in patients with SSc according to the presence of MetS.

Table-1. Descriptive characteristics of the patients and the disease.

Feature	MetS (+) (n=37)	MetS (-) (n=39)	All group (n=76)	*p* value
Age*	58.21±9.36	51.58±13.46	54.81±12.04	**0.015**
Gender (F:M)	35:2	35:4	70:6	0.675
Current smokers n(%)	10 (27.0)	12 (30.8)	22 (28.9)	0.719
Gestation†	3 (2-4)	2 (1.5-3)	2 (2-4)	0.182
Menopause n(%)	31 (83.8)	25 (64.1)	56 (73.7)	0.073
Disease subtype n(%)				
Limited cutaneous	24 (64.9)	20 (51.3)	44 (57.9)	0.231
Diffuse cutaneous	13 (35.1)	19 (48.7)	32 (42.1)	
Disease duration†	10 (5-13)	10 (5-14)	10 (5-13.5)	0.815
Active disease (RAI ≥2.5) n(%)	16 (43.2)	20 (51.3)	36 (47.4)	0.412
SCTC-DI score†	8 (5-12)	8 (5-12)	8 (5-12)	0.613
Autoantibodies				
Anti-centromere n (%)	8 (21.6)	6 (15.4)	14 (18.4)	0.160
Anti-Scl70 n (%)	21 (56.8)	23 (59.0)	44 (57.9)	
Anti-nucleolar n(%)	3 (8.1)	3 (7.7)	6 (7.9)	
Anti-Ro n (%)	5 (13.5)	2 (5.1)	7 (9.2)	
Anti-RNP n (%)	0	5 (12.8)	5 (6.6)	
Steroid exposure (months) †	24 (0-60)	8 (0-60)	12 (0-60)	0.543
Cumulative steroid dose (mg) †	2880 (300-10710)	1440 (0-9360)	2070 (0-10035)	0.514

MetS: Metabolic syndrome**; F**: female; **M**: male; **RAI**: Revised activity score; **SCTC-DI**: Scleroderma clinical trials consortium damage index; **Anti-Scl70**: Anti-topoisomerase antiboides; **Anti-RNP**: anti-ribonucleoprotein antibodies; * mean±SD, †median (d interquartile range)

Table-2. Comparison of metabolic features in systemic sclerosis patients with and without metabolic syndrome.

Feature	MetS (+) (n=37)	MetS (-) (n=39)	All group (n=76)	p value
Systolic BP (mmHg) *	124.02±17.17	111.64±15.24	117.67±17.26	**0.001**
Diastolic BP (mmHg) *	75.27±10.36	70.56±9.25	72.85±10.02	**0.040**
Waist circumference (cm)*	97.50 (92-103)	92 (82-100)	93 (88-102)	**0.015**
Weight (kg) †	68.80 (58.60-74.40)	61.90 (54.20;72.40)	65.30 (55.85-74.30)	0.262
Height (cm)*	155.16±8.51	159.25±7.13	157.26±8.05	**0.026**
BMI (kg/m^2) †	28.20 (24.70-30.30)	24.30 (21-29.30)	26.80 (22.90-30.10)	**0.026**
TC (mg/dL)*	204.54±47.15	187.87±35.16	195.98±42	0.084
LDL (mg/dL)*	123.67±38.65	107.53±28.29	115.39±34.48	**0.041**
HDL (mg/dL) †	47 (39-54)	57 (53-64)	54 (44.50-61)	**<0.001**
TG (mg/dL) †	155 (109-218)	92 (68-122)	114.5 (80-158.5)	**<0.001**
Serum glucose (mg/dL) †	92 (86-105)	87 (82-91)	88.50 (83.50-94.50)	**0.003**
Comorbid diseases n(%)				
DM	10 (27.0)	0	10 (13.2)	**0.001**
Hyperlipidaemia	2 (5.4)	1 (2.6)	3 (3.9)	-
CHD	3 (8.1)	1 (2.6)	4 (5.3)	0.294
Hypothyroidism	3 (8.1)	5 (12.8)	8 (10.5)	1.000
Malignancy	6 (16.2)	2 (5.1)	8 (10.5)	0.115
Hypertension	19 (51.4)	11 (28.2)	30 (39.4)	**0.048**

MetS: metabolic syndrome, **BP:** blood pressure, **BMI:** body mass index**, TC:** total cholesterol; **LDL:** low density lipoprotein, **HDL:** high density lipoprotein, **TG:** Triglyceride; **DM**: diabetes mellitus, **CHD:** coronary heart disease, ***** mean ±SD, **†**median (interquartile range).

Tablo-3. Distribution of organ involvement in patients with systemic sclerosis according to the presence of metabolic syndrome.

Feature	MetS (+) (n=37)	MetS (-) (n=39)	All group (n=76)	p value
mRSS†	14(6-24)	22 (14-28)	19 (10-26)	**0.019**
ILD n(%)	27 (73.0)	27 (69.2)	57 (75)	0.719
% FVC*	84.47±21.56	90.92±21.90	87.8±21.8	0.206
DCLO*, mLCO/min/mm	58.55±18.57	64.47±17.05	61.5±17.9	0.164
PAH	4 (10.8)	3 (7.7)	7 (9.2)	0.708
Cardiac involvement n (%)	11 (29.7)	6 (15.4)	17 (22.4)	0.134
Renal involvement n (%)	2 (5.4)	1 (2.6)	3 (3.9)	0.610
Locomotor involvement n(%)	16 (43.2)	16 (41.0)	32 (42.1)	0.845
Digital ulcers n(%)	21 (56.8)	27 (69.2)	48 (63.2)	0.260
Active digital ulcers n(%)	2 (5.4)	3 (7.7)	5 (6.6)	0.190
GIT involvement				
Oesophageal n(%)	37 (100)	39 (100)	76(100)	0.567
Intestinal n(%)	11 (29.7)	14 (35.9)	25 (32.9)	

MetS: metabolic syndrome; **mRSS**: modified Rodnan skin score; **ILD:** interstitial lung disease; **FVC**: forced vital capacity; **DLCO**: diffusing capacity of the lung for carbon monoxide; **PAH**: pulmonary arterial hypertension; **GIT**: gastrointestinal tract.

Given that the median mRSS was observed to be lower in patients with MetS, a ROC analysis was conducted to determine the mRSS cut-off point predictive of the presence of MetS. The specificity and sensitivity of the mRSS≤11 cut-off value in predicting MetS were calculated to be 84.62% and 45.95%, respectively (AUC: 0.656, 95% CI 29.5-63.1, p=0.014), as illustrated in Figure-1. However, the relationship was weak, and no statistically significant difference was found when the subjects were divided into two groups according to the mRSS predictive value and compared in terms of demographic factors, comorbid diseases and MetS risk factors (age, smoking, number of pregnancies, presence of menopause, cumulative steroid dose, blood pressure, waist circumference, height and weight, BMI, TC, HDL, LDL, TG, ACS and DM, HT, CAD).

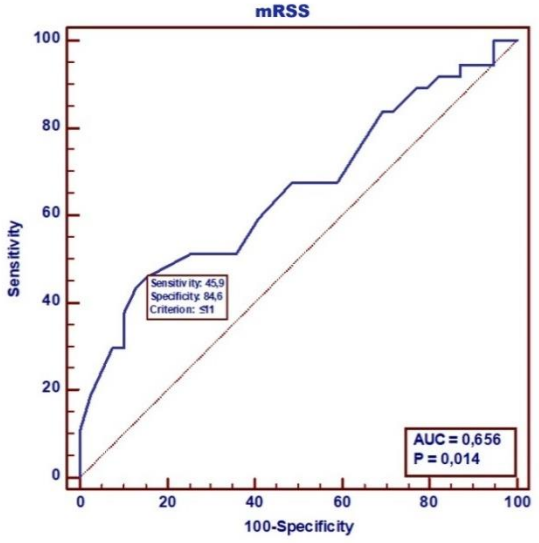

Figure-1. ROC analysis for the relationship between mRSS and MetS.

AUC: Area under curve; mRSS: Modified Rodnan Skin Score; MetS: Metabolik sendrom; ROC: Receiver Operating Characteristic

DISCUSSION

The aim of this study was to investigate the prevalence of metabolic syndrome in Turkish patients with systemic sclerosis. The prevalence of MetS in patients with SSc was found to be 48.7% in the present study. In accordance with the ATP III definition, the prevalence of MetS in the general population of Turkey is estimated to be between 32.9 and 33.9 percent (26-27). In this regard, the 48.7% prevalence of MetS observed in SSc patients suggests a higher prevalence compared to the general population. On the other hand, it is widely acknowledged that gender is a significant determinant of the prevalence of metabolic syndrome. Kozan et al. demonstrated that the prevalence of MetS was significantly lower in men (28%) than in women (39.6%) (27). In the TEKHARF2012 study, it was reported that the prevalence of MetS was 45.1% in men and 54.5% in women (28). Similarly, Abacı A. et al. (26) revealed that the prevalence of MetS was 26.8% in men and 38.3% in women in their meta-analysis. It was therefore considered that the high prevalence of MetS in SSc may be attributed to the dominant female gender, given that the female population ranged between 50-55% in all MetS prevalence studies in Turkey, whereas the female population in our study was 92.1%.

The prevalence of MetS is also influenced by age. A number of studies have demonstrated that the prevalence of MetS increases with age in both sexes (26-28). In the study by Kozan O. et al., the prevalence of MetS was reported as 10.7% in men and 9.6% in women in the 20-29 age group, while it was 49% in men and 68.6% in women over the age of 70 (27). In the TEKHARF 2012 study, the prevalence of MetS was reported as 36.5% in men and 36.7% in women in the <50 age group, 48% in men and 52% in women in the 50-59 age group, and 54.3% in men and 68.1% in women in the 60-69 age group (28). Upon evaluating the results according to age groups, we observed that MetS was not present in any patients below the age of 40 years. However, with advancing age, there was a notable increase in the frequency of MetS (40-45 years: 25%, 46-60 years: 48.4%, >60 years: 62.9%). The high prevalence of MetS, reaching 62.9%, particularly among patients over 60 years of age, serves to reinforce the pivotal role of age as a risk factor. In conclusion, given that the majority of our patients (92.1% of whom were women) were over 40 years of age (and under 70 years of age), it can be concluded that the prevalence of MetS in SSc is consistent with the data for our country and similar to that observed in the general population.

Given the absence of a comparable study conducted in our country examining the prevalence of MetS in patients with SSc, it is not feasible to conduct a disease-specific analysis of our findings. Nevertheless, two studies conducted in patients with rheumatoid arthritis, another inflammatory rheumatological disease, have reported a prevalence of MetS between

17.3 and 27%, which is comparable to that observed in healthy controls (29–30). Furthermore, the international literature on this topic is also limited (6-8, 31). In studies conducted in Italy, the prevalence of MetS in patients with SSc was reported to be between 10.6% and 19.3% (6, 7). Similarly, a prevalence of 20% was reported in a Korean study (31). Compared to the prevalence we found; these rates are quite low. On the other hand, when the healthy Turkish population was considered, it was reported that the prevalence of MetS was higher compared to Americans, Koreans, Chinese, Japanese and Mongolians, and comparable to those of Mexican, South Asian and Iranian origin (27). Similarly, a study conducted in 2015 in 55 SSc cases from a single centre in Mexico showed that the prevalence of MetS in SSc was 36.4% (8). Therefore, considering that the prevalence of MetS has gradually increased over the years in our country and probably in the whole world, it can be assumed that the results obtained in our study are compatible with the literature. Nevertheless, it is obvious that further studies should be carried out with a larger number of patients in regions with different demographic and geographical characteristics, both in our country and in the world.

In our study, we did not find an association between disease subtype (limited or diffuse SSc) and MetS. Many studies in the literature have not shown an association between MetS and disease subtypes (6-7, 31). On the contrary, Peralto-Amaro et al. suggested that limited SSc was associated with insulin resistance and MetS (8). This may be due to the fact that the criteria they used to diagnose MetS were different from those used in other studies. In general, data from our study and the literature support that the development of MetS may occur independently of scleroderma subtypes. Apart from disease subtypes, we did not find any differences between the groups in terms of disease duration, activity and disease-related damage. Similar to our study, previous studies have not shown a significant association between disease characteristics and the frequency of MetS (6-7, 31). On the other hand, when we analysed mRSS, one of the disease characteristics, we found that patients with MetS had lower mRSS (p:0.019), contrary to other reports (7,31). When ROC analysis was performed, we found that the mRSS cut-off point predicting the presence of MetS was ≤11 (specificity: 84%, sensitivity: 45.95%, AUC: 0.656, p:0.014). Considering that mRSS is an important marker associated with visceral organ involvement and mortality in diffuse SSc, we believe that our data should be confirmed in more patients and in different ethnic groups (32).

As expected, we found that blood pressure, waist circumference, BMI, lipid levels and blood glucose levels were higher, and HDL levels were lower in patients with MetS. In addition, the higher prevalence of DM and HT in patients with MetS suggests that these diseases may be associated with MetS. However, there was no difference between the groups in the prevalence of other diseases such as coronary heart disease, hyperlipidaemia and hypothyroidism, suggesting that MetS is more specifically associated with some metabolic factors.

Our study has some limitations. First, the number of patients with SSc was small. Therefore, multivariate analyses to investigate risk factors for the presence of MetS could not be performed. Therefore, the causality between clinical characteristics and MetS in SSc patients could not be fully assessed. Secondly, only cases attending a single tertiary centre were included in this study, which may lead to selection bias. The majority of cases reside in the coastal regions of the Aegean Sea, and different lifestyles may influence the prevalence of MetS. Therefore, the study population in our study may differ from the general population and SSc patients in other centres. Thirdly, our study did not include a control group of healthy individuals, and the interpretations regarding the prevalence of MetS were based on the results obtained from the country in previous years. Finally, our study did not include the physical activity of the subjects, which may influence the presence of MetS.

CONCLUSION

The prevalence of MetS in patients with SSc is higher than in the general population. However, when analysed according to age and gender, the results are comparable. It has been demonstrated that age is an important risk factor in the development of MetS, and the degree of skin involvement may also be effective. These findings emphasise that MetS should not be ignored in scleroderma patients, and cardiovascular risk management of these patients should be considered. Further studies in larger patient populations are needed, as MetS is

affected by factors such as age, gender, ethnicity, nutrition and exercise habits.

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