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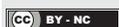
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# FUNCTIONS, SLEEP, FATIGUE AND QUALITY OF LIFE IN PATIENTS WITH SCLERODERMA DURING COVID-19: CROSS - SECTIONAL STUDY

## ORIGINAL ARTICLE

### ABSTRACT

**Purpose:** COVID-19, which has affected people in various ways, has also shown to cause various limitations on the lives of Scleroderma patients. The current study aims at evaluating the upper extremity functions, sleep quality, fatigue, and health-related quality of life in Scleroderma patients and to determine the factors affecting upper extremity functions.

**Methods:** A total of 83 participants were recruited in this study. Of the participants, 39 were Scleroderma patients (mean age 43.28±9.96 years) and 44 were healthy controls (mean age 40.05±8.89 years). The Disabilities of the Arm, Shoulder and Hand Questionnaire (DASH) and Michigan Hand Outcomes Questionnaire (MHQ) were applied to evaluate upper extremity functions of the participants. Pittsburgh Sleep Quality Index (PSQI), Fatigue Severity Scale (FSS), and the Scleroderma Health Assessment Questionnaire (SHAQ) were used to evaluate the sleep quality, fatigue, and health-related quality of life, respectively.

**Results:** Scleroderma patients had significantly lower scores in hand functions, sleep quality, fatigue, and health-related quality than the healthy group (p=0.001). The correlations between DASH and PSQI (r=0.559, p=0.001), FSS (r=0.496, p=0.001), SHAQ scores (r=0.754, p=0.001) were highly positive. Similarly, a high correlation was found between MHQ and SHAQ scores (r=-0.679, p=0.001).

**Conclusion:** Upper extremity functions and health-related quality of life were found to be affected in patients with Scleroderma. It was revealed that upper extremity functions were affected by sleep quality, fatigue, and health-related quality of life. Therefore, knowing all these effects and their relationships with each other allows to draw a systematic treatment plan on Scleroderma patients.

**Key Words:** Activities of Daily Living, Hand, Quality of Life, Systemic Sclerosis

## COVID-19 PANDEMİSİ SIRASINDA SKLERODERMALİ HASTALARDA FONKSİYON, UYKU, YORGUNLUK VE YAŞAM KALİTESİ: KESİTSEL ÇALIŞMA

### ARAŞTIRMA MAKALESİ

#### ÖZ

**Amaç:** İnsan sağlığını çeşitli şekillerde etkileyen COVID-19, Skleroderma hastalarının yaşamlarında da çeşitli etkilere ve kısıtlamalara neden olmuştur. Bu çalışmada Skleroderma hastalarında üst ekstremitte fonksiyonları, uyku kalitesi, yorgunluk ve sağlıklı ilgili yaşam kalitesinin değerlendirilmesi ve üst ekstremitte fonksiyonlarını etkileyen faktörlerin belirlenmesi amaçlandı.

**Yöntem:** Çalışmaya toplam 83 katılımcı dahil edildi. Katılımcıların 39'u Skleroderma hastası (ortalama yaş 43,28±9,96 yıl) ve 44'ü sağlıklı kontrol (ortalama yaş 40,05±8,89 yıl) idi. Katılımcıların üst ekstremitte fonksiyonlarını değerlendirmede Kol, Omuz ve El Sorunları Anketi ve Michigan El Sonuç Anketi uygulandı. Pittsburgh Uyku Kalitesi İndeksi, Yorgunluk Şiddet Ölçeği ve Skleroderma Sağlık Değerlendirme Anketi sırasıyla uyku kalitesini, yorgunluğu ve sağlıklı ilişkili yaşam kalitesini değerlendirmek için kullanıldı.

**Sonuçlar:** Skleroderma hastaları, el fonksiyonları, uyku kalitesi, yorgunluk ve sağlıklı ilgili kalite açısından sağlıklı gruba göre anlamlı olarak daha düşük puanlara sahipti (p=0,001). Kol, Omuz ve El Sorunları Anketi puanı ile Pittsburgh Uyku Kalitesi İndeksi puanı (r=0,559, p=0,001), Yorgunluk Şiddet Ölçeği puanı (r=0,496, p=0,001), Skleroderma Sağlık Değerlendirme Anketi puanı (r=0,754, p=0,001) arasında pozitif yönde yüksek korelasyon vardı. Benzer şekilde Michigan El Sonuç Anketi puanı ile Skleroderma Sağlık Değerlendirme Anketi puanı arasında da yüksek korelasyon bulundu (r=-0,679, p=0,001).

**Tartışma:** Sklerodermalı hastalarda üst ekstremitte fonksiyonlarının ve sağlıklı ilgili yaşam kalitesinin etkilendiği bulundu. Üst ekstremitte fonksiyonlarının uyku kalitesi, yorgunluk ve sağlıklı ilgili yaşam kalitesinden etkilendiği ortaya kondu. Dolayısıyla tüm bu etkileri ve birbirleriyle olan ilişkilerini bilmek Skleroderma hastalarında sistematik bir tedavi planı çizmeye olanak sağlar.

**Anahtar Kelimeler:** Günlük Yaşam Aktiviteleri, El, Yaşam Kalitesi, Sistemik Skleroz

## INTRODUCTION

Coronavirus Disease 2019 (COVID-19) was first detected in December 2019, with several cases of pneumonia in China (1). Dyspnea and pneumonia developed in a lot of the cases in the following days. In severe cases, acute respiratory distress syndrome developed rapidly (1-3). COVID-19, which affects the respiratory tract in various ways, has also caused various influences and limitations in the lives of Scleroderma (SSc) patients. Even the fear of contracting COVID-19 has affected the lives of individuals.

More than 25 million people in North America and more than 30 million people in Europe are affected by SSc which is a rare disease. In the only study conducted in Turkey, the prevalence of scleroderma 23.2/100.000, incidence was determined as 2.1/100.000 and it was found to be similar to Europe and the United States (4). Although the etiology is not fully known, it is chronic, progressive, autoimmune, connective tissue disease known to cause excessive collagen deposition and widespread microvascular damage in the internal organs and skin (5). In SSc patients, especially pulmonary arterial hypertension and interstitial lung disease are especially seen with lung involvement (6). Hypoxemia and limitation of exercise capacity are observed in patients. Lung involvement seriously affects the prognosis in scleroderma and is closely related to morbidity and mortality (7).

Since SSc is a multisystem disease, clinical manifestations and prognosis vary. The presence of joint, muscle, and bone involvement may cause a decrease in functional capacity and hindrance of activities of daily living (ADL) (8). Because of all these reasons, SSc draws attention with high levels of disability, severe disruptions to impaired health-related quality of life (HRQOL), and ADL (9). Sleep efficiency and rapid-eye movement sleep of the SSc patients decrease, and arousal index and slow-wave sleep increase. Despite this, the risk of sleep-diseased breathing does not increase (10). In the literature, the importance of limitation of hand functions as well as decrease in the ability to perform ADL, increase in fatigue and pain in SSc patients are emphasized. Accordingly, fatigue is considered to be a very important symptom in most

SSc patients (11).

There are some similarities between COVID-19 and SSc in terms of the pattern of organ involvement, the presence of significant vasculopathy, and cardiorespiratory complications (12). These similarities suggest that SSc patients may experience more severe symptoms if they are likely to have COVID-19. The current study aimed to evaluate the upper extremity functions and HRQOL of SSc patients and to compare them to the healthy controls (HC). In addition, we sought to clarify the factors associated with the influence of upper extremity functions and HRQOL. On the other hand, The COVID-19 process also affects healthy individuals. In terms of health status, we also aimed to investigate the differences between healthy individuals and individuals with SSc in this process.

## METHODS

### Design

The ethical approval for the research project has been granted by Cerrahpasa Medical Faculty Ethics Committee of Istanbul University-Cerrahpasa (A-18 05.01.2021). All procedures of the study are carried out in accordance with the Helsinki Declaration. All patients were clarified and they signed the informed consent form.

### Participants

A total of 83 participants (39 patients with SSc and 44 age- and sex-matched healthy controls) were recruited to the cross-sectional study conducted between March 2020 and February 2021, during COVID-19 pandemic. The patients were diagnosed with diffuse cutaneous SSc according to 2013 ACR/EULAR Classification Criteria for SSc, by a rheumatologist at Clinic of Cerrahpasa Medical Faculty. Patients aged 20-60 years who received routine medical treatment were included in the study. Patients diagnosed with juvenile onset SSc, and those with a history of neurological disease or trauma that may affect hand functions were excluded from the study.

### Outcome Measures

The participants were questioned about gender, age, body mass index, employment, presence of

rheumatic diseases in the family, smoking status and the disease duration. The disease duration was defined from the date of diagnosis.

### Primary Outcome Measurements

#### The Scleroderma Health Assessment Questionnaire (SHAQ)

SSc-related quality of life assessed with valid and reliable Turkish version of the SHAQ tool. SHAQ consists of five scleroderma specific items (Raynaud's phenomenon, overall disease severity, digital ulcers, respiratory and intestinal involvement). The effects of digital ulcers, Raynaud's phenomenon, lung respiratory symptoms, gastrointestinal symptoms and general SSc symptoms on ADL were questioned. The score ranges from 0 (minimum limitation) to 3 (max limitation). In addition, the functional ability level of the participants on the scale was questioned with Health Assessment Questionnaire-Disability Index (HAQ-DI). The higher SHAQ score [(5VAS scores+8HAQ-DI domains)/13] meant worse situation (13).

#### The Disabilities of the Arm, Shoulder and Hand Questionnaire (DASH)

The upper extremity functions and musculoskeletal conditions were assessed with the Turkish version of DASH. The participants were asked to answer the questions assessing difficulties during ADL, symptoms, social function, working, sleeping and self-confidence. Scores from 0 to 100 can be obtained for each module in DASH, and a high DASH score indicates severe disability (14).

### Secondary Outcome Measurements

#### Michigan Hand Outcomes Questionnaire (MHQ)

The MHQ is a standardized method for assessing patients with all types of hand disorders. The patients were asked to evaluate herself/himself with the MHQ containing six domains (pain, hand function, satisfaction with hand function, work performance, ADL, and aesthetics). A higher score [right hand score+left hand score)/2] indicates a better hand function (15,16).

#### Pittsburgh Sleep Quality Index (PSQI)

The Pittsburgh Sleep Quality Index (PSQI) is a

self-rated questionnaire and assesses sleep disturbances and sleep quality over 1-month time period. The participants were asked nine questions evaluating sleep quality, latency, duration, efficiency and disturbances, daytime dysfunction and usage of sleeping medication. Each component is evaluated over 0-3 points, and the total score of the scale is obtained with the total score of the 7 components. A global PSQI score equal to or greater than five means that sleep quality and patterns have worsened (17).

#### Fatigue Severity Scale (FSS)

The FSS is a nine-item self-report measure that assesses the effect of fatigue on functioning. The severity of fatigue symptoms during the past week were evaluated with FSS. Each item scored from 1 to 7. "1" indicates strong disagreement with the statement, while "7" indicates strong agreement. The total score is calculated by taking an arithmetic mean. A score of 4 or higher indicates severe fatigue. As the total score increases, the severity of fatigue symptom increases (18).

### Statistical Analysis

All variables showed normal distribution according to the Kolmogorov-Smirnov test ( $p=0.160$ ) and, therefore, a parametric analysis was conducted. The groups were compared using the Independent samples-t test in the case of numerical variables and Chi-square test when the variables were categorical. Pearson correlation coefficient was used to evaluate the associations between variables ( $r$ ). The data analysis was performed using IBM SPSS (Statistical Package for Social Sciences) version 21.00 software (IBM Corp., Armonk, NY, USA). Differences were considered statistically significant at  $p<0.05$ . Post-hoc power analyzes were calculated for SHAQ using the final sample size, at an alpha level of 0.05 and based on Independent samples-t test (G\*Power 3.1 software) and were found as 0.99.

## RESULTS

Demographic and clinical characteristics of the SSc patients and HC are presented in Table 1. There were no significant differences between groups ( $p>0.05$ ). The SSc group had a mean of disease duration over six years.

Comparison of SSc and HC in terms of upper ex-

**Table 1.** Descriptive Variables of SSc Patients and HC

	SSc (n = 39)	HC (n = 44)	p	t
<b>Age (years) mean ± SD</b>	43.28 ± 9.96	40.05 ± 8.89	0.122	-1.404
<b>BMI (kg/cm<sup>2</sup>) mean ± SD</b>	23.71 ± 5.23	24.83 ± 4.10	0.279	-1.089
<b>Disease duration (month) mean ± SD</b>	83.08 ± 64.31			
<b>Gender-Female n (%)</b>	34 (%87.2)	33 (%75.0)	0.160	
<b>Employment n (%)</b>	15 (%38.5)	33 (%75.0)	0.001	
<b>Family history n (%)</b>	18 (%46.2)	8 (%18.2)	0.006	
<b>Smoking status - Nonsmoker n (%)</b>	26 (%66.7)	21 (%47.7)	0.158	
<b>Smoking status - Smoker n (%)</b>	6 (%15.4)	14 (%31.8)		

SSc: Scleroderma, HC: Health Control, SD: Standard Deviation, BMI: Body mass index, kg: kilogram, cm: centimeter, Family history: Rheumatic diseases in family

\*p<0.05 (Independent samples t test, Chi-square test)

tremity functions, sleep quality, fatigue and HRQOL were specified in Table 2. The SSc group had significantly lower scores than the HC group in terms of DASH, MHQ-pain, MHQ-total, SHAQ and HAQ-DI. The differences between the two groups were significantly reflected in the statistics (p<0.001). However, there were no significant differences between the two groups in terms of PSQI (p=0.155) and FSS (p=0.152) scores.

Correlations between upper extremity functions and HRQOL for all patients were presented in Table 3. There was highly positive correlation between DASH and SHAQ, HAQ-DI, FSS, PSQI (p<0.001). While there was a moderate correlation between MHQ - Overall hand function and SHAQ, HAQ-DI, low correlation was found between MHQ - Overall hand function and FSS. Similarly, high correlation was found between MHQ-Total and SHAQ, HAQ-DI.

**Table 2.** Comparison of SSc and HC Groups in Terms of Upper Extremity Functions, Sleep Quality, Fatigue and Health-Related Quality of Life

	SSc (n = 39)		HC (n = 44)		t	p
	min-max	mean ± SD	min-max	mean ± SD		
<b>DASH</b>	0.83 - 86.67	36.43 ± 22.98	0 - 48.33	6.83 ± 10.35	7.708	<b>0.001*</b>
<b>MHQ - Pain</b>	10.00 - 125.00	53.07 ± 31.30	5.00 - 125.00	75.45 ± 53.64	-2.282	<b>0.025*</b>
<b>MHQ - Total</b>	27.92 - 96.94	56.61 ± 15.63	50.07-104.17	87.96 ± 13.60	-9.769	<b>0.001*</b>
<b>PSQI</b>	0 - 13.00	6.25 ± 3.17	0 - 16.00	5.18 ± 3.59	1.436	0.155
<b>FSS</b>	0 - 6.90	4.54 ± 1.95	1.00 - 6.70	3.97 ± 1.65	1.447	0.152
<b>SHAQ</b>	0 - 2.30	1.07 ± 0.56	0 - 1.00	0.25 ± 0.25	8.675	<b>0.001*</b>
<b>HAQ-DI</b>	0 - 3.00	1.05 ± 0.71	0 - 1.50	0.21 ± 0.35	6.841	<b>0.001*</b>

SSc: Scleroderma, HC: Health Control, DASH: Disabilities of the Arm, Shoulder and Hand Questionnaire, MHQ: Michigan Hand Outcomes Questionnaire, PSQI: Pittsburgh Sleep Quality Index, FSS: Fatigue Severity Scale, SHAQ: Scleroderma Health Assessment Questionnaire, HAQ-DI: Health Assessment Questionnaire Disability Index

\*p<0.05 (Independent samples t test)

**Table 3.** Relationship Between Upper Extremity Functions and Sleep Quality, Fatigue, Health-Related Quality of Life in Patients with SSc

	PSQI		FSS		SHAQ		HAQ-DI	
	r	p	r	p	r	p	r	p
<b>DASH</b>	0.559	<b>0.001*</b>	0.496	<b>0.001*</b>	0.754	<b>0.001*</b>	0.793	<b>0.001*</b>
<b>MHQ - Overall hand function</b>	-0.266	<b>0.101*</b>	-0.362	<b>0.024*</b>	-0.643	<b>0.001*</b>	-0.598	<b>0.001*</b>
<b>MHQ - ADL</b>	-0.148	0.368	-0.271	0.095	-0.721	<b>0.001*</b>	-0.711	<b>0.001*</b>
<b>MHQ - ADL Both hands</b>	-0.335	<b>0.037</b>	-0.306	0.058	-0.730	<b>0.001*</b>	-0.734	<b>0.001*</b>
<b>MHQ - ADL Total</b>	-0.255	0.117	-0.302	0.062	-0.758	<b>0.001*</b>	-0.755	<b>0.001*</b>
<b>MHQ - Work performance</b>	-0.362	<b>0.024*</b>	-0.335	<b>0.037*</b>	-0.596	<b>0.001*</b>	-0.597	<b>0.001*</b>
<b>MHQ - Pain</b>	0.264	0.104	0.158	0.337	0.128	0.436	0.194	0.235
<b>MHQ - Aesthetics</b>	-0.071	0.669	-0.119	0.471	-0.205	0.211	-0.167	0.309
<b>MHQ - Patient satisfaction</b>	-0.222	0.174	-0.290	<b>0.073*</b>	-0.536	<b>0.001*</b>	-0.517	<b>0.001*</b>
<b>MHQ - Total</b>	-0.200	0.223	-0.315	0.223	-0.679	<b>0.001*</b>	-0.628	<b>0.001*</b>

SSc: Scleroderma, HC: Health Control, DASH: Disabilities of the Arm, Shoulder and Hand Questionnaire, MHQ: Michigan Hand Outcomes Questionnaire, PSQI: Pittsburgh Sleep Quality Index, FSS: Fatigue Severity Scale, SHAQ: Scleroderma Health Assessment Questionnaire, HAQ-DI: Health Assessment Questionnaire Disability Index, ADL: Activities of daily living.

\*p<0.05 (Pearson correlation analysis)

Sleep quality and fatigue scores were not found to be highly correlated with other variables except for DASH.

## DISCUSSION

In this study, the SSc group had significantly lower scores in terms of DASH, MHQ-pain, MHQ-total, SHAQ and HAQ-DI compared to the healthy group. To our knowledge, this is the first study in the literature evaluating upper extremity functions and HRQOL together in patients with SSc during COVID-19 pandemic. The COVID-19 pandemic has had a huge impact on the health situation worldwide. This led to an increase in the usual disease burden in individuals with SSc as well, with unexpected results (12). However, severe outcomes are observed more frequently in individuals with SSc, especially those with cardiopulmonary involvement, than in the general population. On the other hand, one of the things that complicates the situation of individuals with SSc is the restriction of access to health institutions. This may prevent patients from receiving quality care during the COVID-19 period and affect their health status (19).

It has been reported in the literature that the most important risk factors complicating ADL are de-

creased grip strength and dexterity, stiffness and Raynaud’s phenomenon (20). There is also a relationship between hand mobility and skin score and difficulty in ADL. Similarly, in our study, we examined the relationship between upper extremity functions and HRQOL. There were highly positive correlations between upper extremity functions and HRQOL, sleep quality, and fatigue. We could also classify our patients according to the Rodnan skin scoring. On the other hand, Peytrignet et al. reported that pain, fatigue and impaired hand function are important contributors to overall disability in diffuse cutaneous SSc in their study with an average disease duration of 11.9 months (11). Being in the early period of the disease may have not affected the function much and may have even made it difficult to demonstrate its effects. SSc patients in our study were diagnosed more than six years ago on average. We think that this period is a suitable time to reveal the effects of the disease on function and HRQOL. Yakut et al., in their study with SSc patients and healthy control subjects, emphasize that the increase in fatigue may occur due to decrease in both respiratory and peripheral muscle strength, decrease in diffusion capacity, increase in dyspnea, and deterioration of functional

capacity (21). In addition, they reported that fatigue affected the ADL and HRQOL of the patient. On the other hand, Liem et al. compared the activity level of SSc patients with the general population (22). They noted that the total minutes of physical activity per week was markedly lower in SSc. In addition, according to this study, male gender, functional inability and lack of energy are factors that reduce physical activity level. Unlike the method of this study, we did not evaluate physical activity level. But in a similar vein, we compared SSc with HC in our study. Only the diffuse cutaneous SSc patients were included in the study. Because we thought that parameters such as pain, function, sleep quality, and fatigue could be affected more in these patients due to their involvement.

Nokes et al. reported that about a third of patients had sleep-disordered breathing in the study which they investigated the risk of sleep-disordered breathing in patients with SSc (10). Furthermore, this rate is approximately the same as the rate of interstitial lung disease, and the rate of pulmonary hypertension is half of this rate. Similarly, in Bassel et al.'s study to identify symptoms that make it difficult for SSc patients to perform ADL, they confirmed that symptoms such as pain, fatigue and limitations in hand function were the most important symptoms affecting HRQOL in SSc (23). In this study, it was emphasized that the number of studies focusing on the sleep problem, which has a very important role in limiting the ADL in SSc patients, should be increased. PSQI is a widely used scale for evaluating the sleep quality. According to the PSQI, a global score of five or more is defined as a poor sleeper (24). We also concluded that sleep quality was poor in both SSc patients and healthy individuals. Although SSc patients have more sleep problems as the mean value, there is no statistically significant difference when compared with healthy individuals. We think that, this result may be due to the fact that the COVID-19 pandemic may have caused changes in the sleep patterns of healthy people also.

As Odonwodo et al. wrote in their reviews, hardening of the skin and involvement of the musculoskeletal system in patients with SSc may affect their ability to use their hands functionally, especially (25). Similarly, in a study on 62 patients, 63%

of which were diffuse cutaneous SSc by Kallen et al., it was reported that 89% of SSc patients had problems with hand function and so that it could be said that the skin and tendon involvement of the hand was a generalizable problem in SSc patients (26). In another review article Thombs et al. emphasized that the level of pain in SSc was similar to other chronic pain and rheumatic diseases (5). It has been noted that the source of pain in SSc may be Raynaud's phenomenon, musculoskeletal, tightness, calcinosis, ulcers, gastrointestinal problems or depressive symptoms. Additionally, it has been stated that the association between pain and sleep disorder was strong. While the sleep-pain relationship was emphasized in this study, the relationship of many different parameters was revealed in our study. It can be said that sleep quality, fatigue and HRQOL are among the parameters that affect the functions of SSc patients. Similarly, most of the studies in the literature have focused on the hand problems. The superior aspect of our study is that we evaluated the overall upper extremity involvement.

### Limitations

In this study, we compared diffuse cutaneous SSc patients with healthy individuals. We did not make a classification according to the Rodnan skin scoring. However, this is the first study to evaluate upper extremity functions, sleep quality, fatigue and HRQOL together in SSc patients and to identify an association between these parameters. Our study is also limited by the fact that we did not evaluate physical activity level, although our results could be beneficial in the future studies that evaluate these factors.

### Conclusions

Since SSc is a multisystem disease, it is very important to know its effects on upper extremity functions and HRQOL, especially in pandemic conditions. Because the most important factors affecting the upper extremity functions in patients with SSc are fatigue, sleep quality, and health-related quality of life. Knowing all these influences and their interrelationships on SSc patients enables a systematic treatment plan. This study continues as a randomized controlled trial. Knowing these results will have an important place in the rehabil-

itation plans.

**Sources of Support:** None.

**Conflict of Interest:** There is no conflict of interest.

**Ethical Approval:** The ethical approval for the research project has been granted by Cerrahpasa Medical Faculty Ethics Committee of Istanbul University-Cerrahpasa (A-18 05.01.2021). All procedures of the study are carried out in accordance with the Helsinki Declaration.

**Informed Consent:** All patients were clarified and they signed the informed consent form.

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