

## A COMPARATIVE STUDY OF THE FIVE-REPETITION SIT-TO-STAND TEST AND THE ONE MINUTE SIT-TO-STAND TEST TO ASSESS EXERCISE TOLERANCE IN SARCOIDOSIS PATIENTS

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**ABSTRACT.** *Background and aim:* In this study, we aimed to investigate the exercise tolerance in Sarcoidosis patients with sit-to-stand method. *Methods:* In our cross-sectional study 49 consecutive Sarcoidosis patients included in the study. Patients with Sarcoidosis performed 5 repeated sit-to-stand, 1 minute sit-to-stand test (1MSTS) and the 6-minute walking test (6MWT). Moreover, we collected pulmonary function test, sarcoidosis stage, treatment status, body mass index, quadriceps muscle strength. A receiver operating characteristic curve analysis of the 5STS and 1MSTS results was used to predict 6-minute walk distance (6MWD). We evaluated their feelings about the two end STST modes by Borg dyspnea score. *Results:* The average age of the patients was  $49 \pm 19$ . Four patients had stage 3 sarcoidosis, while the others had stage 1 sarcoidosis. The average 6MWD result of all patients was  $410 \pm 153$  meters. When we looked at the correlations between 5RSTS and 1MSTS in 6MWT, significant correlations were observed ( $r=0.454$ ,  $p=0.00$ ) ( $r=0.373$ ,  $p=0.08$ ). A significant correlation was observed between 1MRSTS and 5RSTS with quadriceps muscle strength ( $r=0.677$ ,  $p=0.00$ ) ( $r=0.48$ ,  $p=0.00$ ). *Conclusions:* Based on the results of our study, 1MSTS, 5RSTS, and 6MWT have similar correlations. Both are reasonable tests that can replace the 6MWT in sarcoidosis patients. As a primary screening test for predicting poor 6MWD, the 5STS is similar to the 1MSTS in terms of sensitivity and specificity, but the 5STS provides a better patient experience.

**KEY WORDS:** sarcoidosis, sit-to-stand test, five-repetition sit-to-stand, one-minute sit-to-stand, quadriceps muscle strength, sarcoidosis exercise tests, sarcoidosis functional capacity

### INTRODUCTION

Sarcoidosis is a disease characterized by the differentiation and uncontrolled proliferation of immune system structures. Following changes in the immune system, granuloma formation and granulomatous inflammation occur in tissues. This disease

is a multisystem inflammatory disorder (1,2). Sarcoidosis can affect the entire body system, primarily the lungs and lymph nodes. Parenchymal involvement and fibrosis can occur in the lungs. Excessive secretion of inflammatory mediators leads to uncontrolled oxidative stress. Mitochondrial function is impaired at the cellular level. Pathological effects manifest on lipid profiles and amino acid metabolism in myocytes (3,4). As a result of this pathophysiology, myopathy develops in myocytes. Consequently, according to the results of many literatures to date, regardless of the stage of the disease in sarcoidosis patients, there are complaints of muscle fatigue and general malaise, the cause of which is myocyte hyperinflammation (5-7). This situation results in

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muscle weakness, fatigue, decreased quality of life, and reduced exercise capacity in patients. In chronic pulmonary diseases, physical activity and performance are measured with the 6-minute walking test (6MWT) (8,9). As in all chronic diseases, exercise capacity in chronic pulmonary diseases is also related to the prognosis, mortality, and morbidity of the disease (10). Recently, alternative tests for the 6MWT have been introduced, with the sit-to-stand test being a primary consideration. Variants of this test include the five-repeated sit-to-stand test (5RSTS), one-minute sit-to-stand test (1MSTS), and the 30-second repeated sit-to-stand test (30srsts) (11). The studies looked at the correlation of 6MWT and sit-to-stand test and the differences between sit-to-stand tests in different diseases; (Chronic obstructive pulmonary disease) COPD, heart failure, muscle diseases. No study has evaluated physical performance in sarcoidosis patients using the sit-to-stand test. In sarcoidosis patients with myositis, femoral muscle strength is anticipated to decline. Can the STS test provide insights regarding femoral muscle strength? Is the STS test a practical method for assessing both performance and muscle strength? We evaluated patients' subjective perceptions of the two modes of STST to determine which mode is more suitable for assessing sarcoidosis.

## PATIENTS AND METHODS

### *Study subjects*

Our study was designed as a single-center, cross-sectional, observational clinical trial. At the Faculty of Medicine, Afyonkarahisar Health Sciences University, 49 out of 72 patients diagnosed with sarcoidosis based on the ATS/ERS/JRS criteria and undergoing regular monitoring and check-ups were included in the study after meeting the specified criteria. Diagnoses of the patients and their organ involvement were determined. Inclusion criteria were as follows: diffusion capacity for carbon monoxide (DLCO)  $\geq$  30% predicted, forced vital capacity (FVC)  $\geq$  50% predicted, six-minute walk test distance (6MWT)  $\geq$  150 m, clinical stability in the past six months, and being at least 18 years of age.

### *Exclusion criteria*

Rheumatic symptoms of sarcoidosis include inflammatory arthritis, periarticular soft tissue swelling,

tenosynovitis, dactylitis, bone involvement and myopathy (12-14). Since sarcoidosis may have symptoms of arthritis and arthralgia, we consulted the physical therapy and rehabilitation clinic for all our patients for arthritis and arthralgia. We excluded patients with arthritis and arthralgia that would inhibit knee joint movement. Included having suffered a lung infection in the past month, any condition hindering the act of walking, sitting, or standing (such as hemiplegia or injuries/pathologies of the lower extremity). Having undergone surgical operations for lower extremity joint diseases or other conditions in the past three months, having an unstable cardiac condition within the last four months, having a psychiatric pathology, and being unable to complete the walking or STS test. Who used supplemental oxygen during the 6MWT transported the cylinder on their own using a trolley or wheeled walker. Given the absence of data demonstrating the safety profile of desaturation to  $<$  80% at the facility during exercise testing, participants who desaturated to  $<$  80% were instructed to stop and rest and were permitted to recommence once their SpO<sub>2</sub> was  $\geq$  85 (15,16).

### *Lung function and subjective perception*

Pulmonary function tests of the patients were measured using spirometry. Each patient underwent the respiratory function test three times, with the best result recorded. Borg scale was applied to measure the effort of the participants during physical exercise. The Borg scale is a scale used to assess the severity of exertional dyspnea and resting dyspnea. It consists of ten items describing the degree of dyspnea (17). After performing the exercise test on the patients, we applied the Borg scale test. We measured how difficult they were doing the exercise. After the patients performed the 1MSTS, 5RSTS and 6MWD tests, their Borg scales were measured and written. Participants' BMI was measured. The BMI (Body Mass Index) of the participants was calculated, which is derived by dividing the body mass by the square of their height (in meters). Treatments received by the patients for sarcoidosis (such as oral corticosteroids) were documented. Patients were classified according to the sarcoidosis staging system.

### *Ethics approval and consent to participate*

This study was conducted in accordance of the Declaration of Helsinki and approved by the

Research Ethics Committee of the Medical University of Afyonkarahisar, Turkey (2011-KAEK-2). Informed consent was obtained from all patients.

### *6MWT*

The test was conducted in a flat corridor measured in meters. Under physician supervision, before the patient started from the starting line, their oxygen saturation from a fingertip using a pulse oximeter (Pulsebraun yk-81ceu pulse and oxygen meter pulse oximeter), heart rate, and systolic/diastolic blood pressure were measured. Subsequently, they were instructed to walk at their maximum speed from the starting line to the finish line of the corridor and then return. The track we applied the test on is 30 meters, and it's a quiet area designated for our patients. While the patient was walking, he was encouraged to finish the test with sentences that would encourage him. The patient was encouraged with sentences such as "Almost there, let's go on, you are doing very well". The overtired patient was allowed to rest or slow down for a short time. At the end of 6 minutes, the patients were immediately stopped and pulse, blood pressure and oxygen saturation were measured again at their place. The distance they walked was measured in meters.

### *5RSTS and 1MRSTS*

A chair with a firm seat, 48 cm in height, and without arms was positioned against a wall. Participants were seated in the chair with their backs resting against it. Under the guidance of a physician, patients were instructed to fully sit down and then stand up from the chair. Patients were asked to do this action as fast as possible for a total of 5 times. The total time it took for them to complete the sit-stand actions was recorded. The same patients, after a 30-minute interval, were asked to sit and stand as quickly as possible for 30 seconds. At the end of this period, the total number of sit-stand repetitions was recorded. The average of three attempts of the 5RSTS test was recorded. The 1MSTS test was repeated twice, and their averages were taken. Patients were allowed a 30-minute rest between each test. The 6MWT was first performed on patients, followed by the STS tests 30 minutes later. Before and after each test, patients' heart rate, blood pressure, and oxygen saturation with a pulse were measured.

### *Quadriceps muscle strength*

The maximal isometric muscle strength (QMS) of the quadriceps femoris muscle was measured using the Powertrak Hand-Held Dynamometer (JTech Medical, Utah, USA). The device was calibrated before starting the measurements. The Muscle Test Protocol was measured in both legs. Participants were seated prior to the measurements on a bed with their hips and knees in 90° flexion, feet free, arms crossed on the chest, and without taking any support. Each participant was verbally informed about the technique of the test before starting. Also, before starting the test to ensure the correct motion, participants were asked to perform a sub-maximal contraction against the evaluator's hand (18). During the test, after the participant completed maximum knee extension, the measurer stabilized the applied thigh with one hand. With the other hand, the dynamometer was placed perpendicularly to the leg, located 1-2 cm above the level of the malleoli. A thin towel was placed between the dynamometer and the leg during the measurement to avoid causing pain to the leg. The "make test" technique, which requires isometric contraction, was applied during the test. (The make test is a protocol where the measurer holds the dynamometer steady while the person being measured applies maximum force to the device). After completing the knee extension, the participant was asked to continue the maximum isometric contraction for 5 seconds. The average of 3 consecutive maximum contraction measurements, taken at 30-second intervals, was taken (19-21).

### *Statistical analyses*

In the study, a power analysis was conducted using the G\*Power program, and the sample size was determined as 42 based on  $\alpha = 0.05$ , (power of the test)  $1-\beta = 0.80$ , with an effect size of 0.8. Within the scope and limitations of the study, out of 72 people diagnosed with Sarcoidosis, 49 who met the criteria were included in the study. The data compiled in the study were analyzed through SPSS software. Besides the descriptive statistics given as mean and standard deviation, Correlation analysis and ROC Analysis are also applied to determine the correlations among 1MSTS, 5RSTS and 6MWD and AUC coefficients for evaluating the performances and prediction powers of alternative approaches for 6MWD. The significance level of the statistical analyses was considered as 0.05.

## RESULTS

### Patient characteristics

A total of 57 consecutive patients were intended to be included in the study, but only 49 who completed the tests were included. The average age of the patients was  $49 \pm 19$ . Only 5 of the patients were receiving medication. The average time for patients to perform the 5RSTS test was  $13 \pm 3$  seconds. 4 patients had stage 3 Sarcoidosis, while the rest had stage 1 Sarcoidosis. The average 6MWD result for all patients was  $410 \pm 153$  meters (Table 1).

### Completion rates of different STSTs and subjective feelings of patients

The results of the 1MSTS test were  $22 \pm 5$  repetitions (Table 1). Pre- and post-test pulse, saturation

**Table 1.** Demographic data of participants (mean  $\pm$  std)

	Total sample (N=49)
Age (years)	$49 \pm 19$
Sex, male (%)	13 (26)
BMI (mean $\pm$ SD)	$29 \pm 5$
FEV <sub>1</sub> , L	$2.1 \pm 0.6$
FVC, L	$2.4 \pm 0.7$
FEV <sub>1</sub> , %	$78 \pm 18$
FVC, %	$77 \pm 17$
FEV <sub>1</sub> /FVC, %	$86 \pm 9,7$
Saturation, %	$95 \pm 2$
Pulse (mean $\pm$ SD)	$88 \pm 11$
Drug Treatment (%)	5 (10.2)
5RSTS score, seconds	$13.1 \pm 3.1$
6MWD, m	$410 \pm 153$
1MSTS score, repetitions	$22 \pm 5$
Borg 5RSTS	$4.1 \pm 1.9$
Borg 1MSTS	$8 \pm 1.4$
Borg 6MWD	$5.8 \pm 2.2$
QMS <sup>a</sup> , kg	$12.68 \pm 3.4$

No significant difference was observed between the maximal isometric force generated on each side of the lower limb ( $P=0.865$ ).  
**Abbreviations:** BMI, body mass index; FEV, Functional Expiratory Volume; FVC, Functional Vital Capacity, FEV1 % pred, FEV1 percentage predicted; 5RSTS, five-repetition sit-to-stand test; 6MWD, 6-minute walk distance; 1MSTS, 1 minute sit to stand.

**Table 2.** Evaluation of 5RSTS and 1MSTS in terms of oxygen saturation difference, pulse difference, borg scale

	5RSTS	1MSTS	P
$\Delta\text{SpO}_2$	$3 \pm 0.5$	$2.3 \pm 0.4$	0.37
$\Delta\text{Pulse}$	$25.1 \pm 2.6$	$26.3 \pm 2.1$	0.72
Borg Scale after Sit to Stand test	$4.1 \pm 1.9$	$8 \pm 1.4$	0.2

**Abbreviations:** The difference between oxygen saturation before exercise and oxygen saturation as soon as exercise ends;  $\Delta\text{Pulse}$ , The difference between the heart rate before the exercise and the heart rate after the exercise ends.

were examined for the 5RSTS and 1MSTS tests. Also, post-exercise Borg scale values were examined for the 5RSTS and 1MSTS tests. Borg values after 2 tests were not significant between the two tests. ( $P < 0.05$ ) (Table 2).

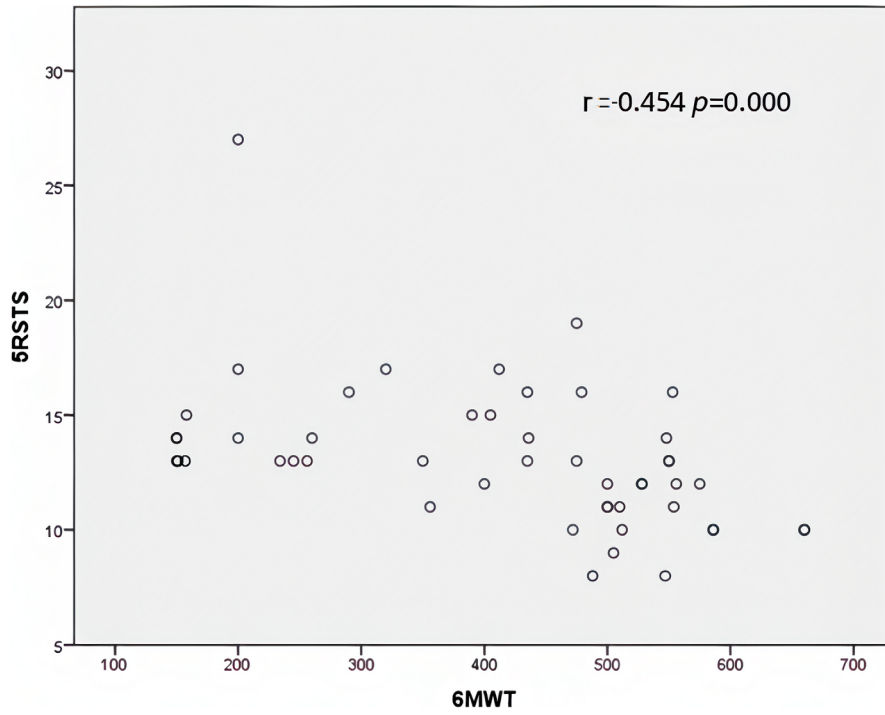
In our study comparing the correlations between 5RSTS and 1MSTS with 6MWT; a significant correlation was observed between 5RSTS and 6MWT ( $r=0.454$ ,  $p=0.00$ ). A significant correlation was also seen between 1MSTS and 6MWT ( $r=0.677$ ,  $p=0.00$ ) (Figure 1A and 1B). Significant correlations were observed between patients' QMS and both the 5RSTS test and the 1MSTS test ( $r=0.373$ ,  $p=0.08$ ), ( $r=0.48$ ,  $p=0.00$ ).

### Different STSTs predict a poor 6MWD

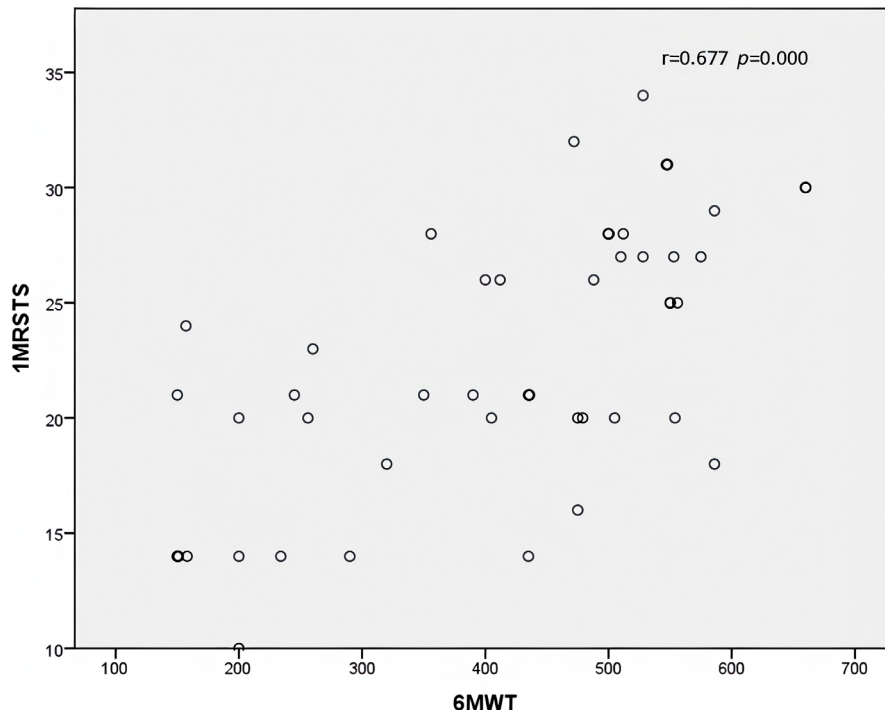
The specificities and sensitivities of the 1MSTS and 5RSTS tests in predicting 6MWD were evaluated using ROC analysis. Of the 49 patients, 15 (30%) performed a 6MWT of less than 350 meters, while the rest were able to walk more than 350 meters. The value of 350 meters has been determined as the normal value in previous studies. In the ROC analysis, 350 meters was accepted as the cut-off value. The AUC value obtained from the ROC analysis was 0.872 for 1MSTS and 0.770 for 5RSTS (Figure 2A2B). Comparing these two values, since the test with the higher AUC value will predict the standard 6MWD test better, it can be said that the predictive power of the 1MSTS test is better than that of the 5RSTS test.

## DISCUSSION

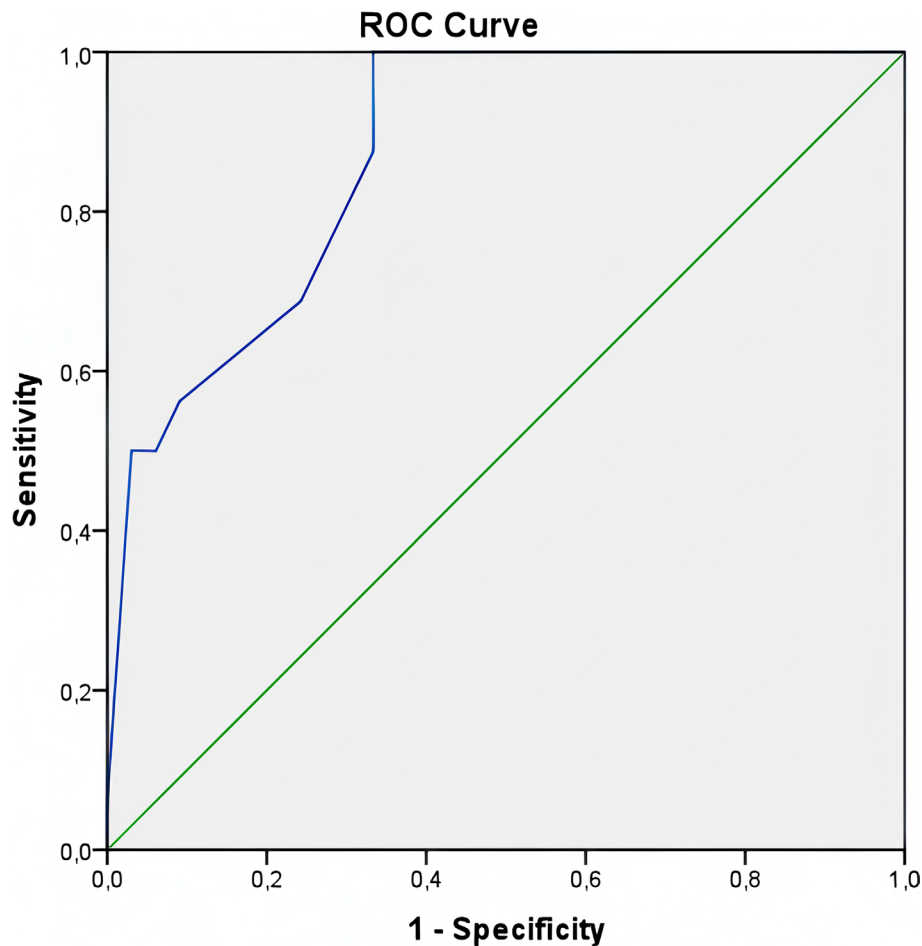
In recent years, STST has begun to be used instead of the 6MWT to evaluate exercise tolerance and assess muscle strength in patients with chronic lung conditions such as interstitial lung diseases and



**Figure 1A.** Relationship between the 5RSTS score and the 6MWD, N=49.  
*Abbreviations:* STST, sit-to-stand test; 5RSTS, five-repetition sit-to-stand test



**Figure 1B.** Relationship between the 1MRSTS score and the 6MWD, N=49.  
*Abbreviations:* STST, sit-to-stand test; 1MRSTS, one minute-repetition sit-to-stand test; 6MWD, 6-minute walk distance.



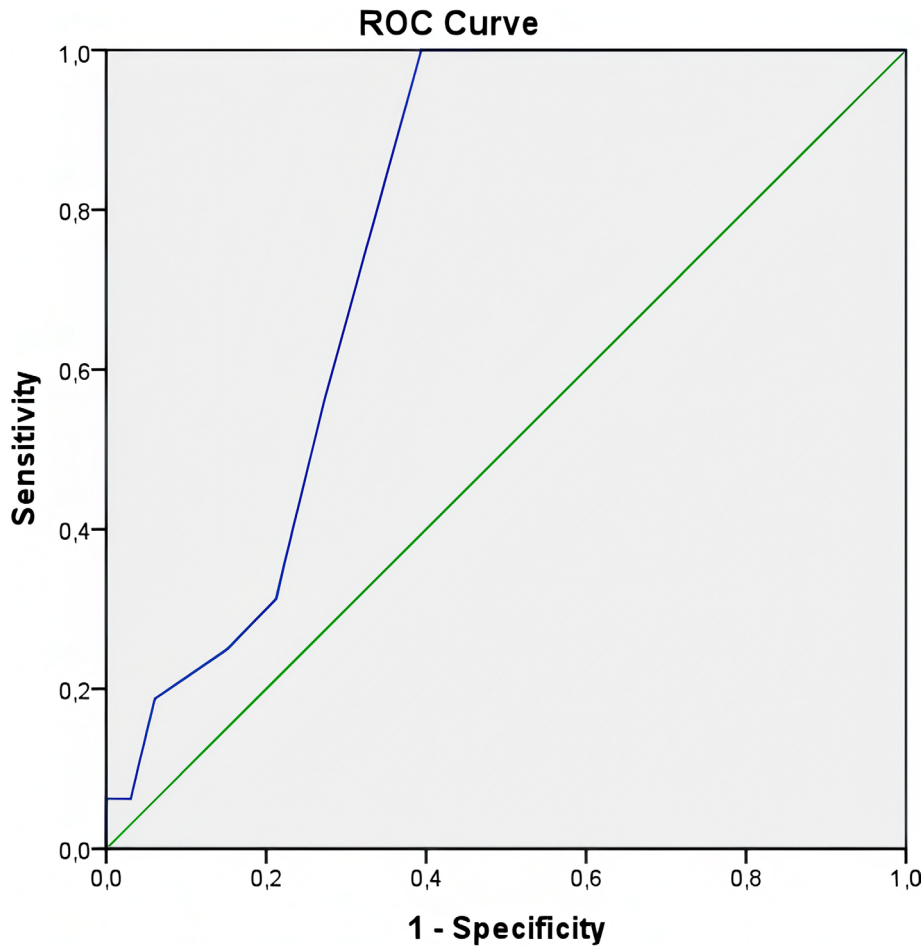
Diagonal segments are produced by ties.

**Figure 2A.** ROC curve analysis of the 5RSTS score for predicting 6MWD, 350 m. AUC = 0.770.

*Abbreviations:* ROC, receiver operating characteristic; 5RSTS, five-repetition sit-to-stand test; AUC, area under the curve.

COPD. There are many studies showing that the STS test can be used instead of the 6MWT. In fact, research has advanced a step further to find different types of STS tests and investigate which one would be better to use in place of the 6MWT (17-21). In this study, our aim was to investigate whether a simple application like the STS test, similar to what is used in COPD, could be used in place of the 6MWT in sarcoidosis patients. For the 6MWT, a special walking course is needed, and it is required to accompany the patient from the examination room to the course, continue evaluating the patient on the course, and spend a long time with the patient. The STS test only requires a chair, does not require special equipment,

is easy to apply, and is quick. This makes it an ideal exercise test for use in the clinic. Studies related to interstitial lung disease and the STS test have increased recently, but there is no study specifically with Sarcoidosis in the literature. In our study, we found that the STS test can be used in place of the 6MWT in Sarcoidosis patients. We experimented with different versions of STS tests to research which one is more suitable than the 6MWT. We evaluated the 1MSTS and 5RSTS tests separately and found that we can use both in Sarcoidosis. In our clinic, 49 patients who we followed in the last 3 years and completed the test were included in the study. When we examine the demographic findings, we observe that the



Diagonal segments are produced by ties.

**Figure 2B.** ROC curve analysis of the 1MRSTS score for predicting 6MWD, 350 m. AUC = 0.872. Abbreviations: ROC, receiver operating characteristic; 1MRSTS, One minute -repetition sit-to-stand test; AUC, area under the curve.

average oxygen saturation of the patients is  $95 \pm 2$ . Since there are few stages 3 and 4 sarcoidosis patients and we follow a few patients with widespread fibrosis, we worked with cases with good saturation (%93-%97). This situation offered us the opportunity to work with a more homogeneous population. Patients with approximately similar pulmonary involvement were included in the study. The 5RSTS test results and 1MRSTS test results of the patients were an average of  $13.1 \pm 3.1$  and  $22 \pm 5$ . When we compare with the values from different studies; In the study published by Justine Briand and colleagues in 2018, the 1MSTS test was applied to all interstitial lung patients. In this study, 31 out of 107 patients

have a diagnosis of sarcoidosis. The 1MRSTS test results in sarcoidosis patients were  $23 \pm 7$ , and they did not look at the 5RSTS test. However, in our study, the results of the two STSTs were lower than this study in many European and American studies, which ranged from  $13.1 \pm 3.1$  similar difference was also observed in body mass index and fat-free mass index. These differences may result from different studies' inclusion of different ethnicities (22). In our study, the Borg scale was evaluated in 2 STS end tests. Also, we evaluated scale after 6MWT. In our study, we evaluated the patients only by looking at their post-exercise Borg scales. In similar studies, we also observed that the post-exercise Borg value was

examined, or the difference was evaluated both before and after exercise. While we expected a significant decrease in these two tests used in place of the 6MWT, we surprisingly observed that there was no difference. When we look at different studies, Trembley and colleagues compared the 1MSTS test with the 6MWT in interstitial lung diseases in 2020, and contrary to expectations, they did not see a difference in the Borg value (23). We believed that the sit-to-stand test could be performed more easily than the 6MWT. We expected a significant decrease in the post-test Borg value in the patients. There was no difference between them. The patients' perception of effort strain was the same in all tests. In the literature, the correlation between the 6MWT and STS tests has been examined by measuring leg muscle strength. They found a significant correlation between muscle strength and STS. (25,26). A meta-analysis says that while leg muscle strength can be assessed with rapid STS, exercise strength can be assessed with a long exercise test (1MSTS, 6MWT). Some studies say that all STS and 6MWT are sufficient for evaluating exercise strength (24-27). There were similar correlations of the 5RSTS and 1MSTS scores with the QMS, meaning that there was no significant difference in the capacity of the two STST tests to indirectly assess lower extremity skeletal muscle strength.

However, there were several limitations in the present study. Firstly, the sample size of this study was relatively small, and the participants were limited to the Turkey population. Further investigations should be undertaken in different countries to identify differences in various ethnicities. Second, this study was cross-sectional, and data for the 1-minute STST, which have been reported to be a good predictor of increased long-term mortality, were lacking in this study, which should be evaluated in future studies. In this study, we did not look at the correlation between STS test and FVC capacity change. In fact, many studies have stated that the STS test can predict a decrease in FVC capacity (28-30). We did not make an evaluation in this direction. Will the patients be followed in the long term and there will be a decrease in the STS test along with the decrease in FVC? Will there be a correlation? We could look.

## CONCLUSION

As a result in this study; STS tests are a practical way to measure muscle strength and exercise capacity,

especially in Sarcoidosis and all pulmonary diseases. 6MWT; It is the main test with proven effectiveness to evaluate exercise capacity. We evaluated whether we could include STS tests, which are easy, practical and can be performed without the need for a different area, into our clinical routines. STS tests have low time, space and material requirements, making them an excellent choice for implementation in large cohort studies and clinical settings.

**Conflict of Interest:** Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

**Author Contribution:** SC: Planning, designing, literature survey, interpretation of the results, active intellectual support, submission; IGC: Planning, designing, literature survey, interpretation of the results, active intellectual support; AB: Planning, designing, literature survey, interpretation of the results, active intellectual support; SG: Planning, designing, literature survey, performing the study, interpretation of the results, active intellectual support, English editing; SS: Statistical analysis; EG: Designing, literature survey, interpretation of the results, active intellectual support.

**Ethic Approval:** This study was conducted in accordance of the Declaration of Helsinki and approved by the Research Ethics Committee of the Medical University of Afyonkarahisar, Turkey (2011-KAEK-2). Informed consent was obtained from all patients.

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