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# ORIGINAL ARTICLE

# Evaluating sarcopenia prevalence and relationship with disease activity of primary Sjögren syndrome in females

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## ABSTRACT

**BACKGROUND**

Primary Sjögren's syndrome (pSS) leads to impaired muscle function and mass as well as pain and fatigue. Sarcopenia is the pathological reduction of skeletal muscle mass and strength. We aimed to investigate the prevalence of sarcopenia and determine its relationship with disease activity levels in females with primary Sjögren syndrome.

**METHODS**

This cross-sectional study was performed on 62 female patients diagnosed with pSS and 62 female age matched healthy controls. Disease activity was evaluated with the EULAR Sjögren's syndrome patient reported index (ESSPRI) and EULAR Sjögren's syndrome disease activity index (ESSDAI), fatigue severity scale (FSS), hospital anxiety and depression scale (HADS), and numerical rating scale (NRS). A simple questionnaire to rapidly diagnose sarcopenia (SARC-F) was used to screen for sarcopenia. Degree of sarcopenia was evaluated by handgrip strength, anterior thigh muscle thickness by USG, the 6-meter walk test (6MWT), and the five times sit-to-stand test (FTSST).

**RESULTS**

The prevalence of sarcopenia was found to be 36/62 (58.1%) in pSS and 6/62 (9.7%) in healthy controls ($p<0.001$). HADS anxiety and depression scores and SARC-F scores were significantly higher in pSS ($p<0.001$). There were significant differences in 6MWT, FTSST, and hand grip strength results in pSS ($p<0.001$). Anterior thigh muscle thickness was similar in both groups ($p=0.298$). A positive correlation was found between SARC-F on the one hand and ESSPRI and NRS on the other ($r=0.595$, $p=0.009$; $r=0.569$, $p=0.014$).

**CONCLUSION**

Sarcopenia prevalence was increased in female patients with pSS and there was a relationship of SARC-F scores with pain and disease activity levels.

**Keywords**: Sarcopenia, Sjögren's syndrome, disease activity, anxiety, depression, female

## INTRODUCTION

Sjögren's syndrome (SS) is a chronic, multi-systemic inflammatory disease characterized by decreased function of the exocrine glands, such as the lacrimal and salivary glands.[1] The kidneys, bladder, lymph nodes, liver, pancreas, gastrointestinal system, nervous system, and cardiovascular system can be affected in primary SS (pSS).[1] One of the most important features of Sjögren's syndrome is musculoskeletal system involvement. [1] In the literature, there are some clinical trials and case reports showing clinical and microscopic evidence of skeletal muscle involvement in patients with pSS. [2-5]

Sarcopenia is a musculoskeletal disorder that is characterized by a loss of skeletal muscle function and mass that increases with age. [6–8] Sarcopenia that is only age-related is called primary sarcopenia.[7] However, endocrine diseases or malignancies are known to be risk factors of sarcopenia. [9] Chronic inflammation can play an important role in sarcopenia [9,10] and in the literature, there are many studies about rheumatoid arthritis and sarcopenia.[11] The European Working Group on Sarcopenia in Older People (EWGSOP) published a consensus definition of sarcopenia with diagnostic criteria for clinical practice in 2010 and updated as EWGSOP2 in January 2019.[6] Under the umbrella of the International Society of Physical and Rehabilitation Medicine (ISPRM), Kara et al.[12] proposed a diagnostic algorithm for sarcopenia (ISarcoPRM) and used ultrasonographic evaluation criteria to determine the presence of sarcopenia based on features of the anterior thigh musculature. Several studies in the literature have explored the relationship between sarcopenia and Sjögren's syndrome. [13–15] Various methods, including dual-energy X-ray absorptiometry (DXA), magnetic resonance imaging (MRI), computed tomography (CT), and bioelectrical impedance analysis (BIA), are available for assessing muscle mass, though each has its limitations. For example, DXA cannot evaluate specific muscle groups and exposes patients to radiation. Although CT and MRI are considered gold standards for muscle mass assessment, they are expensive and time-intensive. Bioelectrical impedance analysis, on the other hand, is a more affordable option but lacks accuracy in measuring specific muscle groups. Previous studies have predominantly employed BIA and DXA for evaluating muscle mass.[16-17] We aimed to investigate the prevalence of sarcopenia according to ISarcoPRM and whether any relationship exists between disease activity levels in females and primary Sjögren syndrome.

## METHODS

### Research design

This cross-sectional study was conducted at Hitit University Physical Medicine and Rehabilitation outpatient clinic between July 2023 and July 2024.

### Research subjects

A total of 62 female patients were diagnosed with pSS according to the 2016 European Alliance of Associations for Rheumatology (EULAR)/American College of Rheumatology (ACR) classification criteria [18] and 62 age- and sex-matched healthy controls were included. According to a previous study, using the power analysis performed with the G* Power program (power=0.85; α=0.05; d (effect size) = 0.70) based on the handgrip strength test scores obtained from the study, the sample size for each group was calculated to be 62 patients.[19]

Female patients with pSS without exclusion criteria and age-matched healthy female controls were included in the study. Participants with a history of other concomitant rheumatic disease, peripheral or central nervous system diseases, myopathies, or other disorders that affect ambulation such as lower extremity operations, severe lung or heart failure, kidney or liver diseases, malignancy, pregnancy, breastfeeding, any psychiatric disorder, or diabetes mellitus and also male patients were excluded from our study. The physical activity level, nutritional status, smoking, and menopausal status of the patients in both the patient and the control groups were not subject to questioning. All evaluations were made by the same physician.

### Measurements

The clinical and demographic characteristics were recorded. Anthropometric measures of the patients, namely weight (kg), height (cm), and body mass index (BMI, $kg/m^2$) were recorded. All patients had used hydroxychloroquine.

### Disease activity assessment

In the pSS group, disease activity was evaluated with the EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) and EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI). ESSPRI is a patient-reported outcome

that measures the three cardinal symptoms of dryness, pain, and fatigue using 0-10 numerical scales (0: no symptoms and 10: worst possible symptoms), and the final score is the mean of the total score. ESSPRI score <5 is considered an acceptable disease condition, and a score of ≥5 is a sign of high activity.[20]

ESSDAI calculates with 12 domains, each domain being scored on a 4-point scale. Scores of 0–7 are defined as mild disease, whereas scores above seven are defined as active disease.[21]

Anxiety and depression symptom levels are assessed with the Hospital Anxiety and Depression Scale (HADS) questionnaire, having two subscales, i.e. HADS-A for anxiety and HADS-D for depression. There are seven questions in each subscale, each being scored on a 4-point (0-3) scale. The HADS questionnaire indicates that a score between 8 and 10 is possible, between 11 and 14 probable, and between 15 and 21 severe symptom levels of depression and anxiety.[22]

The Turkish version of the Fatigue Severity Scale (FSS) was used in the evaluation of fatigue levels, with the severity of fatigue on this scale being assessed with nine questions. Each question is scored between 1(I don't agree at all)- 7(I completely agree). The final FSS score is calculated by taking the mean score of the nine questions. Higher scores reflect more severe fatigue.[23]

Pain was assessed with the Numerical Rating Scale (NRS), in which the patients rated their pain from 0 which means no pain to 10 which means the worst pain.[24]

**Sarcopenia assessment**

All the participants were evaluated according to ISarcoPRM criteria. [12] The hand grip strength test was used for upper extremity muscle strength, the five times sit to stand test (FTSST) and 6-meter walk test were used to evaluate the physical performance, while anterior thigh muscle thickness was measured by ultrasonography. According to the ISarcoPRM diagnostic algorithm for sarcopenia, first the grip strength is measured. For females, results under 19kg are assessed as "probable sarcopenia", after which ultrasonography is performed for anterior thigh muscle thickness evaluation. A single physician, who had experience in musculoskeletal US and was blinded to the participant's group assignment, performed US examinations using a multi-frequency linear probe (6-12 MHz;6-12 MHz: Philips pure wave). While obtaining images, a generous amount of water-soluble gel was applied between the transducer and the skin to aid acoustic coupling and to avoid compression or deformation of the muscle fibers. For anterior thigh muscle measurement, participants lay supine with their legs extended and their muscles relaxed. Images were taken at 50% of the distance between the anterior superior iliac spine and the superior border of the patella. Muscle thickness was measured as the perpendicular distance between the deep and superficial aponeurosis **(Figure 1)**. This adjustment using BMI and the sonographic thigh adjustment ratio (STAR) has already been suggested for the diagnosis of sarcopenia. The correlation between anterior thigh muscle thickness and BMI was calculated, the cut-off point being 1.0 in females according to STAR. [12] After that, slow gait speed and longer duration for rising from a chair indicate severe sarcopenia. The presence and severity of sarcopenia was recorded.

The hand grip strength test with the Jamar dynamo meter (Saehan hydraulic hand dynamometer) expressed in kilograms, was used for the upper extremities. This test was performed while the participants were sitting upright with their backs touching the back of the chair and the elbows fully extended. Patients performed the test three times with each hand. Then the mean score was calculated from these three measurements. Low muscle strength is assessed by hand grip strength test below 19 kg according to the ISarcoPRM diagnostic algorithm for sarcopenia for females.[12]

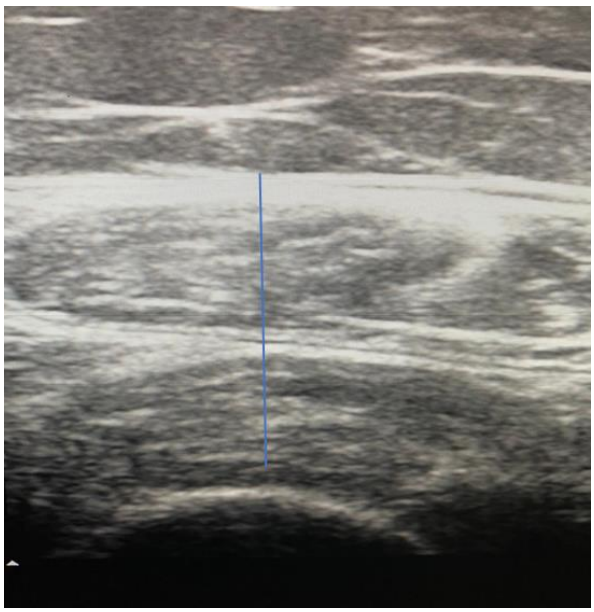

**Figure 1.** The measurement of anterior thigh muscle thickness

For the 6-meter walk test (6MWT), a 6-meter flat path is marked on the hospital corridor, then the participants walked on the path and walking time was measured in seconds.[25] According to EWGSOP2 gait speed under 0.8 m/s is called low physical performance.

The five times sit-to-stand test (FTSST) was measured while the participants sat down and stood up five times from the chair without touching the back and the arms of the chair, while trying to do it as fast as possible, and the total duration was recorded.[26] For the ISarcoPRM diagnostic algorithm for sarcopenia, above 15 seconds is accepted as disability.

A simple questionnaire to rapidly diagnose sarcopenia (SARC-F) was used to screen for sarcopenia.[27] The questionnaire is composed of five parameters, with each parameter scored from 0 to 2. The presence of sarcopenia should be considered with a score of 4 points or above.[28]

**Statistical analyses**

SPSS for Windows version 16.0 software (SPSS Inc., Chicago, IL, USA) was used for statistical analyses. The visual and analytical methods (Kolmogorov-Smirnov and Shapiro-Wilk tests) were used to determine whether the variables were normally distributed. Continuous data were expressed in mean ± standard deviation (SD) or median (interquartile range). Categorical data were expressed as number and frequency. The Student t-test was used for comparison of parametric data, and the Mann-Whitney U test was used for comparison of non-parametric data. The Spearman correlation coefficients were used to determine the correlation between the patient's characteristics and clinical parameters. A p-value of <0.05 was considered statistically significant.

**Ethical clearance**

The study was conducted in accordance with the principles of the Declaration of Helsinki. This study was approved by the Ethics Committee of the University, under no. 2023-84 and written informed consent was obtained from each participant.

## RESULTS

There was no significant difference in age, height, weight, smoking status, or body mass index between pSS and healthy subjects**.** In pSS, disease duration was 92.50 ± 71.69 months, the mean ESSDAI score was 2.10 ± 1.13,and the ESSPRI score was 19.13 ± 6.50. HADS anxiety and depression scores, and SARC-F scores were significantly higher in pSS (p<0.001). The results of the FTSST test, 6-meter walk test, and hand grip strength test were significantly different in pSS (Table 1). The prevalence of sarcopenia was found to be 36/62 (58.1%) in pSS and 6/62 (9.7%) in healthy controls (p<0.001).

Table 1. Demographic and clinical features of the participants

| | **Sjogren's syndrome (n=62)** | **Healthy controls (n=62)** | **p-value** |
|---|---|---|---|
| ** Age (years) | 45 (41-50) | 44 (40-51) | 0.682 |
| *Height (cm) | 158.51±6.55 | 159.72±6.48 | 0.468 |
| ** Weight(kg) | 70 (65.9-80) | 65.4 (60-74.3) | 0.113 |
| *BMI (kg/m$^2$) | 28.91±5.08 | 26.71±4.93 | 0.089 |
| #Smoking n (%) | 24 (38.7%) | 26 (41.9%) | 0.180 |
| ** NRS | 5 (5-8) | | |
| ** FSS | 50 (37-59) | 41 (22-54) | 0.116 |
| ** HADS anxiety score | 11 (9-15) | 7 (5-9) | <0.001 |
| ** HADS depression score | 9 (6-12) | 5 (3-7) | <0.001 |
| *SARC-F | 4.16±2.49 | 0.55±0.810 | <0.001 |
| ** 6MWT (s) | 9.13 (8.56-10.02) | 7.42 (7.18-7.52) | <0.001 |
| *FTSST (s) | 10.94±2.53 | 8.32±1.09 | <0.001 |
| *Hand grip strength (kg) | 17.81±5.82 | 24.52±5.24 | <0.001 |
| *Anterior thigh muscle thickness(mm) | 18.31±3.15 | 17.45±3.34 | 0.298 |
| #Presence of sarcopenia (n%) | 36 (58.1%) | 6 (9.7%) | <0.001 |

BMI: Body mass index, NRS: Numeric Rating Scale, FSS: Fatigue severity scale, HADS: Hospital anxiety depression score, SARC-F: A simple questionnaire to rapidly diagnose sarcopenia, 6MWT: 6-meter walk test, FTSST: five-times-sit- to-stand test. Numerical data are given as mean ± standard deviation or median (interquartile range) values. p values in bold indicate statistical significance. Statistical tests used: * Student t test, ** Mann-Whitney U test, #Chi-square test

Table 2. Clinical features of pSS patients with sarcopenia and pSS patients without sarcopenia

| | pSS patients with sarcopenia (n=36) | pSS patients without sarcopenia (n=26) | p value |
|---|---|---|---|
| **Age | 45.5 (43.25-49.75) | 45 (35-50.5) | 0.630 |
| **ESSDAI | 2 (1-3) | 2 (1-3) | 0.868 |
| **ESPPRI | 23 (13.75-24.25) | 18 (15.5-22.5) | 0.314 |
| **NRS | 7.5 (5-9.25) | 5 (4.5-8) | 0.115 |
| **FSS | 51 (32.25-59) | 46 (37-56.5) | 0.659 |
| **HADS anxiety score | 12 (8.75-15) | 9 (9-15) | 0.687 |
| **HADS depression score | 10 (6-12.25) | 9 (5.5-11.5) | 0.658 |
| *SARC-F | 4.83±2.45 | 3.23±2.31 | 0.075 |
| **6MWT (s) | 9.29 (8.7-10.39) | 8.92 (7.80-9.56) | 0.215 |
| *FTSST (s) | 11.29±3.08 | 10.46±1.45 | 0.326 |
| *Anterior thigh muscle thickness (mm) | 18.37±3.38 | 18.24±2.93 | 0.913 |
| *Hand grip strength (kg) | 13.89±3.59 | 23.23±3.41 | <0.001 |

ESSDAI: European League Against Rheumatism Sjögren's Syndrome Disease Activity Index, ESPPRI: EULAR Sjögren's Syndrome Patient Reported Index, NRS: Numeric Rating Scale, FSS: Fatigue severity scale score, HADS: Hospital anxiety depression score, SARC-F: A simple questionnaire to rapidly diagnose sarcopenia, 6MWT: 6-meter walk test, FTSST: five-times-sit- to-stand test. Numerical data are given as mean ± standard deviation or median (interquartile range) values. p values in bold indicate statistical significance. Statistical tests used: * Student t test, ** Mann Whitney U test

There was no difference in clinical features between pSS with sarcopenia and pSS without sarcopenia (Table 2). The hand grip strength was significantly higher among pSS subjects without sarcopenia compared to pSS subjects with sarcopenia ($p<0.001$) (Table 2). In pSS with sarcopenia, a positive correlation was found between SARC-F, 6MWT, and FTSST tests on the one hand and ESSPRI on the other. There also was a positive correlation between SARC-F and 6MWT on the one hand and NRS on the other in pSS with sarcopenia. Also, 6MWT and FTSST tests were each positively correlated with FSS in pSS with sarcopenia (Table 3).

**Table 3.** Correlation between sarcopenia criteria and clinical features in pSS patients with sarcopenia

| | SARC-F | 6MWT (s) | FTSST (s) | Right anterior thigh muscle thickness(mm) | Right hand grip strength (kg) |
|---|---|---|---|---|---|
| Age | r=0.313 | r=0.117 | r=0.295 | r=0.092 | r=-0.009 |
| | p=0.216 | p=0.644 | p=0.234 | p=0.717 | p=0.972 |
| ESSDAI | r=0.224 | r=0.392 | r=0.508 | r=0.163 | r=0.010 |
| | p=0.371 | p=0.107 | p=0.031 | p=0.519 | p=0.967 |
| ESPPRI | r=0.595 | r=0.660 | r=0.611 | r=0.519 | r=-0.288 |
| | p=0.009 | p=0.003 | p=0.007 | p=0.027 | p=0.247 |
| NRS | r=0.569 | r=0.617 | r=0.398 | r=0.650 | r=-0.126 |
| | p=0.014 | p=0.006 | p=0.102 | p=0.003 | p=0.618 |
| FSS | r=0.300 | r=0.785 | r=0.613 | r=0.115 | r=-0.200 |
| | p=0.227 | p=0.000 | p=0.007 | p=0.648 | p=0.425 |
| HADS anxiety score | r=0.336 | r=0.072 | r=0.366 | r=-0.106 | r=0.056 |
| | p=0.172 | p=0.778 | p=0.135 | p=0.676 | p=0.825 |
| HADS depression score | r=0.357 | r=0.018 | r=0.279 | r=0.002 | r=0.093 |
| | p=0.146 | p=0.945 | p=0.262 | p=0.995 | p=0.714 |

ESSDAI: European League Against Rheumatism Sjögren's Syndrome Disease Activity Index, ESPPRI: EULAR Sjögren's Syndrome Patient Reported Index, NRS: Numeric Rating Scale, FSS: Fatigue severity scale score, HADS: Hospital anxiety depression score, SARC-F: A simple questionnaire to rapidly diagnose sarcopenia, 6MWT: 6-meter walk test, FTSST: five-times-sit- to-stand test. p values in bold indicate statistical significance. Statistical test used: Spearman correlation test

## DISCUSSION

In this study, we found that the prevalence of sarcopenia was increased in patients with pSS. We did not find any difference in ESSDAI, ESSPRI, NRS (pain), and FSS (fatigue) levels between patients with sarcopenia and patients without sarcopenia. In patients with pSS and sarcopenia, the SARC-F score, 6MWT, and FTSST tests were found to be related with the ESSPRI score. Also, we found that SARC-F, 6MWT, and pain level were related. Fatigue level was related to 6MWT and FTSST tests in patients with pSS and sarcopenia.

We found that the presence of sarcopenia was 58.1% in pSS patients and 9.7% in healthy controls. Öztürk et al.[13] found the presence of pre-sarcopenia to be 28.5% in pSS and 6.1% in healthy controls. They used EWGSOP2 sarcopenia criteria but we used the ISarcoPRM diagnostic algorithm for sarcopenia. Similar to our study, they found that patients with pre-sarcopenia had decreased grip strength compared to patients without pre-sarcopenia.[13] Also, they found that the presence of pre-sarcopenia was associated with health-related quality of life.[13] We found that disease activity, pain, fatigue, anxiety, and depression levels were similar in pSS patients with and without sarcopenia. In our study, we found a relationship between sarcopenia screening test scores and disease activity rather than quality of life in pSS patients with sarcopenia.

A study showed low skeletal muscle mass index and appendicular lean mass in patients with pSS. [14] Especially, lean muscle tissue was found to be the main predictor of bone mineralization in pSS patients.· [14] In rheumatological disease, a high inflammatory load could be related to a higher prevalence of skeletal muscle loss.[29] In the previous studies, it was shown that the increased skeletal muscle loss was associated with high interleukin-6, tumor necrosis factor alpha, and CRP levels.[30] In SS these proinflammatory cytokines may cause sarcopenia. We found an increased risk of sarcopenia in pSS but we did not determine the skeletal muscle mass index or lean mass. Also, we did not evaluate bone mineralization in our study. A key feature of our study was the use of ultrasonography (US) for diagnosing sarcopenia. Compared to other methods, the US instrument is portable, cost-efficient, and user-friendly, making it the preferred choice for muscle mass evaluation in our research. We evaluated muscle mass with ultrasonography, although there are some other tools for evaluating muscle mass, such as DXA, MRI, CT, or BIA. However, ultrasonography can be easily applied under outpatient conditions, is more economical, and commonly available in hospitals. Also, the ISarcoPRM diagnostic algorithm for sarcopenia recommends ultrasonography to diagnose sarcopenia. In addition to the literature, anterior thigh muscle thickness was evaluated by ultrasonography in our study. The anterior thigh muscles, which are fundamental to mobility skills, are more commonly and severely affected in sarcopenia. It is difficult to diagnose sarcopenia in daily practice due to the lack of tools that can be easily applied to measure muscle thickness. According to a meta-analysis, ultrasonography is a reliable and valid diagnostic method for the quantitative assessment of appendicular muscle mass in sarcopenia in older people. The thickness and cross-sectional area of the rectus femoris or gastrocnemius seem to be proper ultrasonographic parameters to predict muscle mass in sarcopenia.[31] In a study, Tecer et al.[32] evaluated the muscle thickness, pennation angle, and fascicle length of lower extremity muscles (rectus femoris, vastus lateralis, vastus medialis, vastus intermedius, gastrocnemius, and soleus) in pSS patients. They did not find any difference in the thickness of these muscles in pSS compared to healthy controls. Also in isokinetic muscle strength measurement, they did not find any muscle strength differences between pSS and healthy controls. Similarly, we did not find any difference in anterior thigh muscle thickness between our study and theirs. They found that knee extension muscle strength was associated with ESSPRI.[32] We found a relationship between ESSPRI and SARC-F, 6MWT, and FTSST test scores in pSS patients with sarcopenia. The relationship we found between SARC-F, ESSPRI, and pain level suggests that in patients with high disease activity and pain level, SARC-F can be used as a screening tool for sarcopenia in patients with pSS. Similar to our study, Tecer et al.[32] found that anxiety, depression, and fatigue levels were increased in patients with pSS, but they found no correlation between muscle strength, anxiety, and depression levels. We did not evaluate muscle strength and we did not find any relationship between anxiety, depression levels, and sarcopenia criteria. In a meta-analysis there was a correlation between pain levels and sarcopenia, as was also the case in our study.[33] When we consider that musculoskeletal pain is common in patients with pSS and we suspect sarcopenia or screen for

sarcopenia in patients with high pain and disease activity levels, then when these patients with pSS follow exercise recommendations and precautions for sarcopenia, this may help improve their quality of life. This is also important because in daily practice if we screen for sarcopenia in painful pSS patients it helps us in establishing an early diagnosis and administering treatment before adverse complications occur. Sarcopenia in rheumatic diseases is due to a complex mechanism. There are many parameters that may be associated with sarcopenia. Age, gender, BMI, nutrition, smoking, joint damage, disease duration, pain, disease activity level, inflammatory parameters in the blood, medications and physical activity level are only some of these parameters. In addition, pain and disease activity are the most easily preventable factors that may be associated with sarcopenia in patients with pSS.

We think that ours is a valuable study for the literature and in daily practice, because it is the first study to investigate the prevalence of sarcopenia in pSS using the new sarcopenia criteria. In addition, this is a comprehensive study investigating the relationship between sarcopenia and disease activity, pain, fatigue, anxiety, and depression levels. There are some limitations in our study, in that ours was a cross-sectional study and we do not know how medical therapy (hydroxychloroquine) affected muscle strength. Also, the physical activity levels, nutritional status, or menopausal status of participants were unknown.

Future research should focus on validating the use of US for muscle mass evaluation in larger, more diverse cohorts. Additionally, longitudinal studies are needed to assess the predictive value of US measurements for clinical outcomes in sarcopenia. Investigating the role of interventions, such as nutritional and exercise programs, in preventing or reversing muscle loss in Sjögren's syndrome could also provide valuable insights for patient care.

## CONCLUSION

We found that the prevalence of sarcopenia, anxiety, and depression were increased in patients with pSS and there was a relationship of SARC-F scores with pain and disease activity levels in pSS patients with sarcopenia.

### Conflict of Interest

No relevant disclosure.

### Acknowledgement

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### Author Contributions

PÖB: Conceptualization, data curation, investigation, methodology, project administration, writing. DEB: formal analysis, software, supervision, writing - review and editing. Both authors have read and approved the final manuscript.

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### Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author

### Declaration of Use of AI in Scientific Writing

Authors declare that there was no use of generative AI and AI-assisted technologies in the writing process.

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