Muscle Architecture In Patients With Sjogren’s Syndrome

Duygu Tecer[1], Dilek Eker Buyuksireci,[2] Zafer Günendi[3] Jale Meray[4], Feride Gogus[3]

MS.DUYGU TECER

Adress: Rheumatology Clinic, Gülhane Education and Research Hospital, Ankara, Turkey

Telephone: 0905385136970

E-mail: duygu-tecer@hotmail.com

Orcıd: **0000-0002-8816-6181**

MS. DILEK EKER BUYUKSIRECI

Adress: Department of Physical Medicine and Rehabilitation, Hitit University Erol Olçok Education and Research Hospital, Çorum, Turkey

Telephone: 090543996253

E-mail: **dilekeker55@gmail.com**

Orcıd: **0000-0002-5420-7563**

MRS. ZAFER GUNENDI

Adress: Department of Physical Medicine and Rehabilitation, Division of Rheumatology, Gazi University Faculty of Medicine, Ankara, Turkey

Telephone: 0905323839153

E-mail: zafergunendi@yahoo.com

Orcid: **0000-0003-0696-5834**

MS. JALE MERAY

Adress: Department of Physical Medicine and Rehabilitation, Gazi University Faculty of Medicine, Ankara, Turkey

Telephone: 0905333219915

E-mail: jalem1959@gmail.com

Orcid: **0000-0002-6960-4676**

MS. FERIDE GOGUS

Adress: Department of Physical Medicine and Rehabilitation, division of Rheumatology, Gazi University Faculty of Medicine, Ankara, Turkey

Telephone: 090532250164

E-mail: feride_g@yahoo.com

Orcid: **0000-0003-0921-5991**

Corresponding author:

Dilek Eker Buyuksireci,MD Adress: Department of Physical Medicine and Rehabilitation, Hitit University Erol Olçok Education and Research Hospital, Çorum, Turkey

Telephone number: 0905439196253

Mail address: dilekeker55@gmail.com

Dear Editor,

We are sending you our article titled **“Muscle Architecture In Patients With Sjogren’s Syndrome**

’’ to evaluate its publication in your journal.

Disclosure: We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome. We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us. We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property.

Sincerely,

Dr. DİLEK EKER BÜYÜKŞİRECİ

Muscle Architecture In Patients With Sjogren's Syndrome

Aim: To investigate the effect of primary (pSS) on skeletal muscle architecture and strength.

Method: 19 pSS patients and 19 age, body mass index and sex matched healthy controls were included. Symptoms of subject's were assessed with ESSPRI (The EULAR Sjogren's Syndrome Patient Reported Index), anxiety and depression with the Hospital Anxiety and Depression Scale (HADS), fatigue with Multidimensional Assessment of Fatigue scale (MAF), functionality with HAQ. Ultrasonographic evaluations were performed with a multifrequency linear probe from quadriceps femoralis, gastrocnemius and soleus of the bilateral lower extremity. Muscle thickness, pennation angle and fascicle length were measured. Isokinetic knee muscle strength tests were performed at 60 and 180°/s. Isokinetic ankle muscle strenght tests were performed at 30 and 120°/s.

Result: In pSS group, mean ESSPRI was 7.70±1.17. Scores of depression (10.05 ± 3.09 vs 4.47 ± 2.29 $p<0.0001$), anxiety (8.26 ± 4.28 vs 3.79 ± 2.42 $p<0.0001$), functionality (0.94 ± 0.78 vs 0.22 ± 0.26, $p<0.0001$), fatigue (37.69 ± 5.47 vs 17.69 ± 5.26, $p<0.0001$) were significantly higher in patients with pSS than healthy controls. In dominant leg, pennation angle of vastus medialis was significantly greater in healthy controls than in patients with pSS ($p=0.049$). The other ultrasonographic measurements were similar between the two groups. Peak torque/body weight of knee and ankle muscle were found to be similar.

Conclusion: Although patients with pSS have some minor structural changes on ultrasonographic evaluation, isokinetic muscle strength were similar between groups. In patients with pSS, disease activity and fatigue level were negatively correlated with isokinetic muscle strength measurement.

Key words: primary sjogren's syndrome, muscle architecture, muscle strength, disease activity

Muscle Architecture In Patients With Sjogren's Syndrome

Aim: To investigate the effect of primary (pSS) on skeletal muscle architecture and strength.

Method: 19 pSS patients and 19 age, body mass index and sex matched healthy controls were included. Symptoms of subject's were assessed with ESSPRI (The EULAR Sjogren's Syndrome Patient Reported Index), anxiety and depression with the Hospital Anxiety and Depression Scale (HADS), fatigue with Multidimensional Assessment of Fatigue scale (MAF), functionality with HAQ. Ultrasonographic evaluations were performed with a multifrequency linear probe from quadriceps femoralis, gastrocnemius and soleus in bilateral lower extremity. Muscle thickness, pennation angle and fascicle length were measured. Isokinetic knee and ankle muscle strength tests were performed

at 60 and 180°/s and 30 and 120°/s respectly.

Result: In pSS group, mean ESSPRI was 7.70±1.17. Scores of depression (10.05 ± 3.09 vs 4.47 ± 2.29 $p<0.0001$), anxiety (8.26 ± 4.28 vs 3.79 ± 2.42 $p<0.0001$), functionality (0.94 ± 0.78 vs 0.22 ± 0.26, $p<0.0001$), fatigue (37.69 ± 5.47 vs 17.69 ± 5.26, $p<0.0001$) were significantly higher in patients with pSS than healthy controls. In dominant leg, pennation angle of vastus medialis was significantly greater in healthy controls than in patients with pSS ($p=0.049$). The other ultrasonographic measurements were similar between the two groups. Peak torque/body weight of knee and ankle muscle were found to be similar.

Conclusion: Although patients with pSS have some minor structural changes on ultrasonographic evaluation, isokinetic muscle strength were similar between groups. In patients with pSS, disease activity and fatigue level were negatively correlated with isokinetic muscle strength measurement.

Key words: primary sjogren's syndrome, muscle architecture, muscle strength, disease activity

Introduction:

Sjogren's syndrome (SS) is a systemic autoimmune disease with wide range of clinical manifestation. The spectrum of the disease extends form autoimmune exocrinopathy to a systemic process (1). Patients with pSS often complain of joint pain, myalgia, increased fatigue, impaired physical capacity and function (2), (3), (4). This may result in decreased ability to perform daily living activities, working disability and impaired health related quality of life (5), (6), (7). In fact, it has been reported that myositis is rarely seen in patients with primary sjogren's syndrome (8) (9).

Although there are clinical trials and case reports about clinical and microscopic evidence of skeletal muscle involvement in patients with pSS, there is no information about the macroscopic structure of skeletal muscle of patients with pSS (10), (11), (12), (13). Muscle architecture, arrangement of muscle fibers within a muscle relative to the axis of force generation, is the primary determinant of muscle function (14). The understanding of the relationship between structure and function is important for clarifying the physiology of force production and movement. Also it provides scientific basis for tendon transfer procedures, placement of electrode during electromyography and interpretation of muscle biopsies (15). Commonly used parameters in architectural muscle analysis are fascicle length, pennation angle, cross sectional area. Fascicle lenght represents the number of sarcomeres in series and longer fascicles are associated with higher peak shortening velocity (16), (17). Pennation angle is the angle of the insertion of muscle fascicles into the deep aponeurosis and positively correlated with muscle thickness (18). Lower leg muscle thickness is valuable predictor of the muscle cross sectional area and muscle volume and therefore muscle strength (19). The most common method of measuring muscle architecture is B-mode ultrasonography (US), which has been previously shown to be a reliable and valid method (20), (21).

To the best of our knowledge, no study has evaluated muscle architecture in pSS. Objective evidence on muscle architecture and strenght in pSS may lead to a better understanding of its role in health releated parameters in this disease. Therefore, the aim of this study was to asses the muscle architecture in pSS by comparing them with heathy control group. A second aim was to determine relationship between muscle architecture and strength and mood status, fatigue, disease activity in patients with pSS.

Material and Method:

19 patients who admitted to our clinic with a diagnosis of pSS according to 2016 ACR/EULAR classification criteria for primary Sjögren's syndrome were included to the study (21). Nineteen age and sex matched healthy controls were included (22). Patients with pSS and concomitant rheumatic disease, neurological disease, peripheral neuropathy; history of other systemic diseases such as hypothyroidism/hyperthyroidism, diabetes mellitus; previous history of myositis or overt trauma of the muscles, previous history of lower extremity surgery were excluded. Demographic and clinical characteristics were recorded. Anxiety and depression were assessed with the Hospital Anxiety and Depression Scale (HADS), fatigue with Multidimensional Assessment of Fatigue scale (MAF), functional disability with HAQ (23), (24).

In patient group, disease activity was evaluated with the EULAR Sjogren's Syndrome Patient Reported Index (ESSPRI). The ESSPRI is a self-evaluation index for measuring symptoms including pain, fatigue and dryness. Each symptom was measured with a single 0 (no symptoms) to 10 (severe symptoms) numerical scale and the final ESSPRI score is calculated by averaging these domains with a maximum severity score of 10. Scores of < 5 indicate low disease activity and scores of ≥ 5 indicate high disease activity (25), (26).

Anxiety and depression were assessed with the Hospital Anxiety and Depression Scale (HADS). This self-evaluation questionnaire consists of 2 subscales: anxiety (HADS-A) and depression (HADS-D). Both subscales contain 7 items and each item is scored from 0 to 3. HADS scores of 8–10 define possible, scores of 11–14 define probable and scores of 15–21 define extreme cases of depression and anxiety (23).

Fatigue was assessed using the Multidimensional Assessment of Fatigue scale (MAF). This self-reported questionnaire contains 16 items and measures four dimensions of fatigue: severity, distress, timing and degree of interference with daily living activities. The MAF score ranges from 0 to 50 and higher scores indicate higher levels of fatigue (24).

HAQ was used to evaluate how the disease affects some movements and activities in daily life over the past week. It consists of 20 questions in 8 categories including dressing, arising, eating, walking, hygiene, reach, grip and activities. Each question scored from 0 to 3 and a lower score represent a better outcome. In scoring the category, the highest score among the items was accepted as the category score. HAQ score was calculated by dividing the total score of categories into 8 (27).

Ultrasonographic assessment

A single rheumatologist, who had considerable experience on musculoskeletal ultrasonography and blinded to the participant's group assignment, performed ultrasonographic evaluation using a multi-frequency linear probe (6-12 MHz; MyLab 70 XV, EsaoteBiomedica, Genoa, Italy). 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 fibres. Measurement were done on quadriceps femoris, gastrocnemius and soleus of the bilaterally lower extremity. For quadriceps femoris measurement, participants lied supine with their legs extended and their muscles relaxed. Rectus femoris images were taken at 50% of the distance between the anterior superior iliac spine and the superior border of the patella. Vastus lateralis images were acquired at the middle of the thigh length (the distance between the most prominent portion of the greater trochanter and the lateral femoral epicondile). Vastus medialis images were taken at 30% the lenght of a reference line connecting the anterior superior iliac spine to the proximal edge of the patella; the probe was placed just medial to the border between vastus medialis and the rectus femuris, located using ultrasonography . For gastrocnemius and soleus measurement, participants lied prone with the feet hanging off the edge of the table and knees fully extended. Images were acquired at the level of the maximum girth of muscles.

Muscle thickness was measured as the perpendicular distance between the deep and superficial aponeurosis. Pennation angle was measured as the angle of the insertion of muscle fascicles selected for length measurement into the deep aponeurosis. Fascicle length is the linear fascicular path between the insertion into the deep and superficial aponeurosis. It was calculated as muscle thickness / sin (pennation angle) (28).

Isokinetic strength measurement

Isokinetic measurements of muscles were done by a calibrated isokinetic testing machine (Cybex-NORM isokinetic machine) with standard attachments. Isokinetic knee muscle strength tests were performed bilaterally at 60 and 180°/s and isokinetic ankle muscle strength tests were performed bilaterally at 30 and 120°/s as peak torque/body weight (Nm/kg) and work. Before performing the isokinetic test, all participants conducted the submaximal repetitions. When isokinetic knee muscle strength test was performing, the participants were sitting the chair as the knee is flexed 90 degrees and the ankle is in neutral position and when isokinetic ankle muscle strength test was performing, the participants were lying the table as the knee is in 0 degree extension and the ankle is in 90 degrees dorsiflexion.
Approval for the study was obtained from the Committee on Human Research Ethics of Zekai Tahir Burak Women's Health Education and Research Hospital (dated: 20.06.2017 decision number: 91/2017). A well written informed consent was obtained from all participants according to the principles of the Helsinki Declaration.

Statistical analysis:
Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA) 16.0 program for Windows. The variables were investigated using visual and analytical methods to determine whether or not they were normally distributed. Continuous values were expressed as mean ± standard deviation (SD). Student's *t*-test was used for comparison of normally distributed data, and the Mann-Whitney *U* test was used for comparison of non-normally distributed data. Spearman correlation coefficients was used to investigate correlation between patient's characteristics and clinical parameters. A value of $p < 0.05$ was considered statistically significant.

Results:
No significant differences between the pSS patients and healthy controls were seen for age, weights, heights and body mass index (table 1). In pSS group, mean disease duration was 27.68 ± 30.93 months and mean ESSPRI was 7.70±1.17. ANA positivity was seen in 11 (57.9%) of patients, anti-SSA 8(42.1%) and anti-SSB 3(15.3%). None of the parrticipants had any abnormalities in blood tests such as aspartate amino transferase, creatininee phosphokinase. All patients were taking only hydroxychloroquine 200mg/day. In the last 6 months, there were no patients who took drugs other than hydroxychloroquine. A significant differences were seen in the experience of anxiety and depression according to HADS between groups (table 1). In pSS group, 4(21.1%) subjects scored more than 10 on the anxiety scale and 11(57.9%) scored more than 10 on the depression scale. In the control group, no subject had a score of more than 10 on the depression scale and on the anxiety scale. The primary SS group had significantly higher levels of fatigue on the MAF scale than control group (table 1). Also, according to the HAQ, pSS patients had significantly decreased functional ability compared with healthy control (table 1).
In dominant leg, pennation angle of vastus medialis was significantly greater in healthy controls than that in patients with pSS (p=0.049). Except pennation angle of vastus medialis of dominant leg, the other ultrasonographic measurements were similar between the two groups (table 2). Peak torque/body weight of knee and ankle muscles were found to be similar (table 3). Correlation between disease activity, fatigue, anxiety, depression and isokinetic muscle strength measurement in patients with pSS were presented in table 4.

Discussion:

To our knowledge, this is the first study that assess the muscle architecture in patients with pSS.
According to our results, thicknesses and fascicle length of lower limb muscles were similar between groups. However, pennation angle of vastus medialis on dominant leg was significantly lower in pSS patients. We found similar pennation angles of the other muscles in both group in dominant and non-dominant leg. Additionally, peak torque/body weight of knee and ankle muscles were similar in both group. Some relationship was found between knee, ankle muscle strengths, ESSPRİ and fatigue in dominant and non-dominant leg.
We know that musculoskletal involvement in patients with pSS may not only be in the form of arthritis and arthralgia, but also rarely in the form of myositis (especially inclusion body myositis) (8) (9). Therefore in this study, we investigated whether muscle structure and strength of pSS patients were any different from the healthy subject. According to our results, thicknesses of lower limb muscles were similar between groups. Pennation angle of vastus medialis on dominant leg was significantly lower in pSS patients. On the other hand, pennation angle of other muscles were similar. Additionally fascicle length of other muscles were similar between groups.

Limited number of ultrasonography studies concerning muscle architectural changes in inflammatory diseases have been performed (29), (30). Kaya et al reported that although systemic lupus erythematosus (SLE) patients had significantly greater muscle thickness and pennation angle of vastus lateralis than healthy controls, fascicle length was similar. Authors attributed the increased pennation angle because of increased muscle thickness due to edema (30). Also, SLE patients had similar muscle thickness, pennation angle and fascicle length of gastrocnemius compared with healthy controls (30). Matschke et al reported that, when compared with their age-sex- and BMI-matched healthy subjects, sarcopenic patients with rheumatoid arthritis had significantly smaller vastus lateralis muscle volume, with no differences in fascicle length, physiological cross-sectional area, pennation angle of vastus lateralis.(29). Similar to these studies, we found some differences in pennation angle and fascicle lengths in some muscles compared to healthy controls. This may be due to muscle involvement in pSS, or due to low activity levels of patients. However, we did not question the activity levels of participants. Also, small sample size might have been effective in this result. Also all of the patients with pSS had used hydroxychloroquine. These small changes of muscle architecture in patients with pSS can be related with hydroxychloroquine usage. Because it is known that hydroxychloroquine can cause myopathy (31). Serum creatinine phosphokinase levels were normal in our patients.
In our study, the mean age was 54.11 ± 6.57 and 53.21 ± 6.74 years in pSS group and healthy controls respectively. So there were some participants with osteoporosis in both group. Increasing the probability of osteosarcopenia with aging (32), may have been effective in finding similar muscle architecture results in both groups.

In our study, we showed that the muscle strength was similar between groups. In another study, Strömbeck et al investigated isokinetic strength of the flexors and extensors of the knee at velocities of 60°/second in pSS patients. Similarly to our result, they showed that there was no difference in isokinetic muscle strength of the knee extensors between pSS patients and healthy controls. But they reported that pSS patients had significantly reduced isokinetic muscle strenght of the knee flexor, measured as peak torque at 60°/second than healthy controls (4). Also they reported that pSS patients had significantly reduced in isokinetic endurance of knee flexor, measured at 240°/second compared to healthy controls (4). Because of muscle endurance is dependent on oxygen uptake, they thought that patients with pSS had lower level of aerobic capacity or lower level of activity compared to healthy control (4). Since we did not know the aerobic capacities and activity levels of participants, we may have found the similar muscle strengths in both groups. But worsened isokinetic lower limb muscle strength was reported in another rheumatic diseases such as SLE, RA, ankylosing spondylitis and systemic sclerosis (30), (33), (34). Since the use of drugs such as corticosteroids and the active disease period will affect the measurement of muscle strength, in some of these studies, there are some limitations such as unknown use of drugs and disease activity.

Disease activity was assessed with ESSPRI. In pSS group, on both legs, ESSPRI was negatively correlated with isokinetic muscle strength of the knee extensors at velocities of 60°/second and 180°/second, ankle plantar flexors at velocities of 30°/second. In addition, on dominant leg, ESSPRI was negatively correlated with isokinetic muscle strength of the knee flexors at velocities of 60°/second. We concluded that isokinetic muscle strength decreases in some muscle as disease activity increases. To the best of our knowledge, our study is the first study that investigate the impact of disease activity on isokinetic muscle strength in pSS.

Fatigue is one of the most common extraglandular manifestation in pSS and is associated with decreased aerobic capacity, lower physical activity levels, functional impairment and impaired health releated quality of life in pSS (4), (35) (36), (37), (38). In the current study the fatigue score of pSS patients was significantly higher than the control group, similar to the literature. Additionally fatigue scores were correlated with some isokinetic muscle strength and work. Likewise, anxiety and depression is more prevalent in patients with pSS than healthy controls (39), (40). Similarly in our study, the prevalence of depression and anxiety was higher in the pSS group. But there was no correlation between scores of anxiety and depression and muscle strength.

There were several limitations of this study. Small sample size was an important limitation. Another limitation of the present study is that physical activity levels of participants were unknown. Due to the cross-sectional design of this study, the effects of medical therapy and change in disease activity on muscle architecture is unknown. New prospective studies including larger sample size should be undertaken to confirm the findings of the present study.

Conclusion:

Although patients with pSS have some minor structural changes on ultrasonographic evaluation, isokinetic muscle strength were similar between groups. In patients with pSS, disease activity and fatigue level were negatively correlated with isokinetic muscle strength measurement.

Acknowledgement: Not applicable.

Compliance with ethical standards: The study protocol was approved by the committee on Human and Research Ethics of Turkish Ministry of Health Zekai Tahir Burak Women's Health, Training and Research Hospital and all participants gave written informed consent to a protocol adhering to the 1964 Decleration of Helsinki.

Conflict of interest: Authors have no conflict of interest.

Funding: This study did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' contributions: All authors had contributions to the conception, design, acquisition, analysis, interpretation of the results, write of paper. All authors read and approved the final manuscript.

References:

1. Barone F, Colafrancesco S. Sjogren's syndrome: from pathogenesis to novel therapeutic targets. Clin Exp Rheumatol. 2016;34(4 Suppl 98):58-62.
2. Vivino FB. Sjogren's syndrome: Clinical aspects. Clin Immunol. 2017;182:48-54.
3. Dassouki T, Benatti FB, Pinto AJ, Roschel H, Lima FR, Augusto K, et al. Objectively measured physical activity and its influence on physical capacity and clinical parameters in patients with primary Sjogren's syndrome. Lupus. 2017;26(7):690-7.
4. Strombeck B, Ekdahl C, Manthorpe R, Jacobsson LT. Physical capacity in women with primary Sjogren's syndrome: a controlled study. Arthritis Rheum. 2003;49(5):681-8.
5. Westhoff G, Dorner T, Zink A. Fatigue and depression predict physician visits and work disability in women with primary Sjogren's syndrome: results from a cohort study. Rheumatology (Oxford). 2012;51(2):262-9.
6. Meijer JM, Meiners PM, Huddleston Slater JJ, Spijkervet FK, Kallenberg CG, Vissink A, et al. Health-related quality of life, employment and disability in patients with Sjogren's syndrome. Rheumatology (Oxford). 2009;48(9):1077-82.
7. Strombeck B, Ekdahl C, Manthorpe R, Wikstrom I, Jacobsson L. Health-related quality of life in primary Sjogren's syndrome, rheumatoid arthritis and fibromyalgia compared to normal population data using SF-36. Scand J Rheumatol. 2000;29(1):20-8.
8. Baer AN, Walitt B. Sjögren syndrome and other causes of sicca in older adults. Clinics in geriatric medicine. 2017;33(1):87-103.
9. Hom J, Marwaha S, Postolova A, Kittle J, Vasquez R, Davidson J, et al. A Patient with Sjogren's Syndrome and Subsequent Diagnosis of Inclusion Body Myositis and Light-Chain Amyloidosis. Journal of general internal medicine. 2019;34(6):1058-62.
10. Colafrancesco S, Priori R, Gattamelata A, Picarelli G, Minniti A, Brancatisano F, et al. Myositis in primary Sjogren's syndrome: data from a multicentre cohort. Clin Exp Rheumatol. 2015;33(4):457-64.
11. Aoki A, Ono S, Ueda A, Hagiwara E, Tsuji T, Misumi M, et al. Myositis in primary Sjogren's syndrome: clinical and pathological report. Mod Rheumatol. 2003;13(1):57-61.
12. Misterska-Skora M, Sebastian A, Dziegiel P, Sebastian M, Wiland P. Inclusion body myositis associated with Sjogren's syndrome. Rheumatol Int. 2013;33(12):3083-6.
13. Kanellopoulos P, Baltoyiannis C, Tzioufas AG. Primary Sjogren's syndrome associated with inclusion body myositis. Rheumatology (Oxford). 2002;41(4):440-4.
14. Lieber RL, Friden J. Functional and clinical significance of skeletal muscle architecture. Muscle Nerve. 2000;23(11):1647-66.
15. Lieber RL, Friden J. Clinical significance of skeletal muscle architecture. Clin Orthop Relat Res. 2001(383):140-51.
16. Ruiz-Cardenas JD, Rodriguez-Juan JJ, Rios-Diaz J. Relationship between jumping abilities and skeletal muscle architecture of lower limbs in humans: Systematic review and meta-analysis. Hum Mov Sci. 2018;58:10-20.
17. Abe T, Kumagai K, Brechue WF. Fascicle length of leg muscles is greater in sprinters than distance runners. Med Sci Sports Exerc. 2000;32(6):1125-9.
18. Kawakami Y, Abe T, Kanehisa H, Fukunaga T. Human skeletal muscle size and architecture: variability and interdependence. Am J Hum Biol. 2006;18(6):845-8.
19. Abe T, Loenneke JP, Thiebaud RS. Morphological and functional relationships with ultrasound measured muscle thickness of the lower extremity: a brief review. Ultrasound. 2015;23(3):166-73.
20. Kwah LK, Pinto RZ, Diong J, Herbert RD. Reliability and validity of ultrasound measurements of muscle fascicle length and pennation in humans: a systematic review. J Appl Physiol (1985). 2013;114(6):761-9.
21. Chiaramonte R, Bonfiglio M, Castorina EG, Antoci SAM. The primacy of ultrasound in the assessment of muscle architecture: precision, accuracy, reliability of ultrasonography. Physiatrist, radiologist, general internist, and family practitioner's experiences. Rev Assoc Med Bras (1992). 2019;65(2):165-70.
22. Shiboski CH, Shiboski SC, Seror R, Criswell LA, Labetoulle M, Lietman TM, et al. 2016 American College of Rheumatology/European League Against Rheumatism classification criteria for primary Sjogren's

syndrome: A consensus and data-driven methodology involving three international patient cohorts. Ann Rheum Dis. 2017;76(1):9-16.
23. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand. 1983;67(6):361-70.
24. Neuberger GB. Measures of fatigue: The Fatigue Questionnaire, Fatigue Severity Scale, Multidimensional Assessment of Fatigue Scale, and Short Form-36 Vitality (Energy/Fatigue) Subscale of the Short Form Health Survey. Arthritis Care & Research. 2003;49(S5):S175-S83.
25. Seror R, Ravaud P, Mariette X, Bootsma H, Theander E, Hansen A, et al. EULAR Sjogren's Syndrome Patient Reported Index (ESSPRI): development of a consensus patient index for primary Sjogren's syndrome. Ann Rheum Dis. 2011;70(6):968-72.
26. Seror R, Bootsma H, Saraux A, Bowman SJ, Theander E, Brun JG, et al. Defining disease activity states and clinically meaningful improvement in primary Sjogren's syndrome with EULAR primary Sjogren's syndrome disease activity (ESSDAI) and patient-reported indexes (ESSPRI). Ann Rheum Dis. 2016;75(2):382-9.
27. Fries JF, Spitz P, Kraines RG, Holman HR. Measurement of patient outcome in arthritis. Arthritis Rheum. 1980;23(2):137-45.
28. Franchi MV, Raiteri BJ, Longo S, Sinha S, Narici MV, Csapo R. Muscle Architecture Assessment: Strengths, Shortcomings and New Frontiers of in Vivo Imaging Techniques. Ultrasound Med Biol. 2018;44(12):2492-504.
29. Matschke V, Murphy P, Lemmey AB, Maddison PJ, Thom JM. Muscle quality, architecture, and activation in cachectic patients with rheumatoid arthritis. J Rheumatol. 2010;37(2):282-4.
30. Kaya A, Kara M, Tiftik T, Tezcan ME, Ozel S, Ersoz M, et al. Ultrasonographic evaluation of the muscle architecture in patients with systemic lupus erythematosus. Clin Rheumatol. 2013;32(8):1155-60.
31. Jafri K, Zahed H, Wysham KD, Patterson S, Nolan AL, Bucknor MD, et al. Antimalarial myopathy in a systemic lupus erythematosus patient with quadriparesis and seizures: a case-based review. Clinical Rheumatology. 2017;36(6):1437-44.
32. Paintin J, Cooper C, Dennison E. Osteosarcopenia. British journal of hospital medicine. 2018;79(5):253-8.
33. Oliveira SC, Oliveira LM, Jones A, Natour J. [Isokinetic assessment of ankles in patients with rheumatoid arthritis]. Rev Bras Reumatol. 2015;55(4):318-24.
34. Sahin N, Ozcan E, Baskent A, Karan A, Kasikcioglu E. Muscular kinetics and fatigue evaluation of knee using by isokinetic dynamometer in patients with ankylosing spondylitis. Acta Reumatol Port. 2011;36(3):252-9.
35. Segal B, Thomas W, Rogers T, Leon JM, Hughes P, Patel D, et al. Prevalence, severity, and predictors of fatigue in subjects with primary Sjogren's syndrome. Arthritis Rheum. 2008;59(12):1780-7.
36. Ng WF, Miller A, Bowman SJ, Price EJ, Kitas GD, Pease C, et al. Physical activity but not sedentary activity is reduced in primary Sjogren's syndrome. Rheumatol Int. 2017;37(4):623-31.
37. Hackett KL, Newton JL, Frith J, Elliott C, Lendrem D, Foggo H, et al. Impaired functional status in primary Sjogren's syndrome. Arthritis Care Res (Hoboken). 2012;64(11):1760-4.
38. Lackner A, Ficjan A, Stradner MH, Hermann J, Unger J, Stamm T, et al. It's more than dryness and fatigue: The patient perspective on health-related quality of life in Primary Sjogren's Syndrome - A qualitative study. PLoS One. 2017;12(2):e0172056.
39. Cui Y, Xia L, Li L, Zhao Q, Chen S, Gu Z. Anxiety and depression in primary Sjogren's syndrome: a cross-sectional study. BMC Psychiatry. 2018;18(1):131.
40. Cui Y, Li L, Yin R, Zhao Q, Chen S, Zhang Q, et al. Depression in primary Sjogren's syndrome: a systematic review and meta-analysis. Psychol Health Med. 2018;23(2):198-209.