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Examining the presence of sarcopenia in women with rheumatoid arthritis: Case-control study

BEGUM AKAR[1], BİLGE BASAKCİ CALİK[1], ELİF GUR KABUL[2], AYSE NUR BAYINDIR AKBAS[3], VELİ COBANKARA[3]

[1] Faculty of Physiotherapy and Rehabilitation, Pamukkale University, Denizli, Turkey
[2] Faculty of Health Sciences, Physiotherapy and Rehabilitation, Usak University, Usak, Turkey
[3] Department of Rheumatology, Medical Faculty, Pamukkale University, Denizli, Turkey

Abstract

Introduction: The aim of this study was to compare the frequency of sarcopenia, functional status, fear-avoidance behaviors, biopsychosocial status and quality of life in RA women with healthy controls.

Methods: 25 RA women and 25 healthy women were included in the study. Definition of sarcopenia was assessed using parameters recommended by the European Working Group on Sarcopenia (EWGSOP): Bioimpedance analysis for muscle mass (body fat ratio, skeletal muscle mass, skeletal muscle mass index); grip and knee extension strength for muscle strength and 4-m course gait speed test for physical performance was applied. Functional status was evaluated with the Health Assessment Questionnaire (HAQ), fear-avoidance behaviors with the Tampa Kinesiophobia Scale (TKS), biopsychosocial status with the Biopsychosocial Questionnaire (BETY-BQ), and quality of life with Short Form-36 (SF-36).

Results: While none of the healthy women had sarcopenia, severe sarcopenia was detected in 7 (28%) of the women with RA. When RA and healthy groups were compared; skeletal muscle mass (p: 0,004); skeletal muscle mass index (p: 0,011); grip strength-right (p:0.001) and left (p:0.001); knee extension strength-right (p:0.001) and left (p:0.001), 4-m course gait speed test (p:0.001), HAQ (p:0.001), TKS (p:0.001), BETY-BQ (p:0.001), SF-36 physical (p:0.001) ve mental component (p:0.001) results were significant in favor of the healthy group while there was no difference in body fat ratio (p>0.05).

Conclusion: In women with RA, the frequency of sarcopenia is higher, and functional status, fear-avoidance behaviors, biopsychosocial status and quality of life are worse than healthy.

Keywords: Rheumatoid arthritis, sarcopenia, quality of life, muscle, physical performance.

What is new? What is important?

- Considering that patients with RA with sarcopenia have a higher risk of CV disease than patients with RA without sarcopenia, it becomes very important to take precautions and intervene in sarcopenia in patients with RA.
- This is the first study to use The European Working Group on Sarcopenia (EWGSOP)'s sarcopenia diagnostic method in adults with RA.
- The frequency of sarcopenia was higher in RA patients than in healthy individuals.
- Functional status, biopsychosocial status and quality of life of RA patients were worse than healthy individuals, and fear-avoidance behaviors were higher than healthy individuals.

INTRODUCTION

Rheumatoid Arthritis (RA) is a chronic, systemic, inflammatory autoimmune disease that causes synovial inflammation, cartilage and bone destruction, and occurs in approximately 0.5–1% of the general population [1,2]. Although its etiology is not fully understood, researchers think that a combination of gender, environmental and hormonal factors influence the development of the disease. RA is 2–3 times more common in women than in men [3]. Clinical symptoms often have a latent onset. Typical symptoms are swelling, pain, tenderness in the joints and morning stiffness [4].

Metacarpophalangeal joint (MCF) and proximal interphalangeal (PIF) joint are the joints frequently involved. Synovitis occurring in these joints typically causes swelling and limited movement. Various deformities may develop in the later stages of the disease [5].

Sarcopenia is a progressive skeletal muscle disorder that causes adverse conditions such as functional loss, mortality and morbidity as a result of the decrease in skeletal muscle mass and strength [6]. Sarcopenia is considered a specific disease [7].

The European Working Group on Sarcopenia (EWGSOP) has proposed a conceptual staging as 'presarcopenia', 'sarcopenia' and 'severe sarcopenia' to guide the clinical management of sarcopenia. The 'presarcopenia' stage is characterized by low muscle mass with no impact on muscle strength or physical performance. The 'sarcopenia' stage is characterized by low muscle mass, as well as low muscle strength or low physical performance. The 'severe sarcopenia' stage is the stage that defines the presence of all three criteria (low muscle mass, low muscle strength and low physical performance) [8].

Proinflammatory cytokines such as Tumor Necrosis Factor-alpha (TNF-α), Interleukin-6 (IL-6) and Interleukin-1 (IL-1) are very important in the pathogenesis of RA [9]. As pro-inflammatory cytokine levels increase in patients with RA, the balance of the muscle damage cycle is disrupted and the risk of sarcopenia increases. For this reason, chronic inflammatory diseases such as RA are considered as an important cause in the etiopathogenesis of sarcopenia [10]. In patients with RA, decreased physical activity, as well as increased levels of IL-1β and TNF-α, increase the likelihood of developing sarcopenia [11].

Studies have shown that the risk of mortality due to cardiovascular (CV) disease is up to 50% higher in patients with RA. However, in the general population, sarcopenia is associated with a high risk of cardiovascular disease. Considering that patients with RA with sarcopenia have a higher risk of CV disease than patients with RA without sarcopenia, it becomes very important to take precautions and intervene in sarcopenia in patients with RA [12].

The aim of this study was to compare the frequency of sarcopenia, functional status, fear-avoidance behaviors, biopsychosocial status and quality of life in RA women with healthy controls.

MATERIALS AND METHODS

This study was planned as a case-control study and women with RA were compared with healthy controls.

PARTICIPANTS

25 healthy women and 25 women who were followed by Pamukkale University Rheumatology Clinic and diagnosed with RA by a rheumatologist according to the 2010 EULAR/ACR criteria were included in the study.

All consecutive patients and healthy individuals were assessed for meeting the following inclusion and exclusion criteria. Women in the healthy group were selected from companions who came to the clinic with the patient and met the inclusion and exclusion criteria and volunteered to participate in the study.

Inclusion Criteria: RA group:
- 18–65 age range,
- Diagnosed with RA according to EULAR/ACR 2010 classification criteria
- Volunteering to participate in the study
- Women gender.
- Healthy Group 18–65 age range,
- Volunteering to participate in the study
- Women gender.

Exclusion Criteria: RA group and healthy group:
- Having an additional rheumatic or neurological/orthopedic disease
- Being pregnant
- Using a walking aid
- Presence of malignancy.

Ethical approval for the study was received from the Pamukkale University Non-Interventional Clinical Research Ethics Committee at the board meeting dated 07.06.2022 and numbered 09. The study was conducted in accordance with the Principles of the Declaration of Helsinki. All participants of the study were informed about the study and all of them signed an informed consent form.

ASSESSMENT

After demographic data were recorded, definition of sarcopenia was evaluated using the parameters recommended by the EWGSOP: Bioimpedance analysis for muscle mass (body fat

ratio, skeletal muscle mass, skeletal muscle mass index); grip and knee extension strength for muscle strength and 4-m course gait speed test for physical performance was applied.

The presence and classification of sarcopenia (presarcopenia, sarcopenia or severe sarcopenia) was made according to the EWGSOP–suggested algorithm for sarcopenia (Figure 1) [8]. Functional status was evaluated with the Health Assessment Questionnaire (HAQ), fear-avoidance behaviors with the Tampa Kinesiophobia Scale (TKS), biopsychosocial status with the Biopsychosocial Questionnaire (BETY-BQ), and quality of life with Short Form-36 (SF-36). Data were collected by the same physiotherapist in a single session, approximately 40–45 minutes.

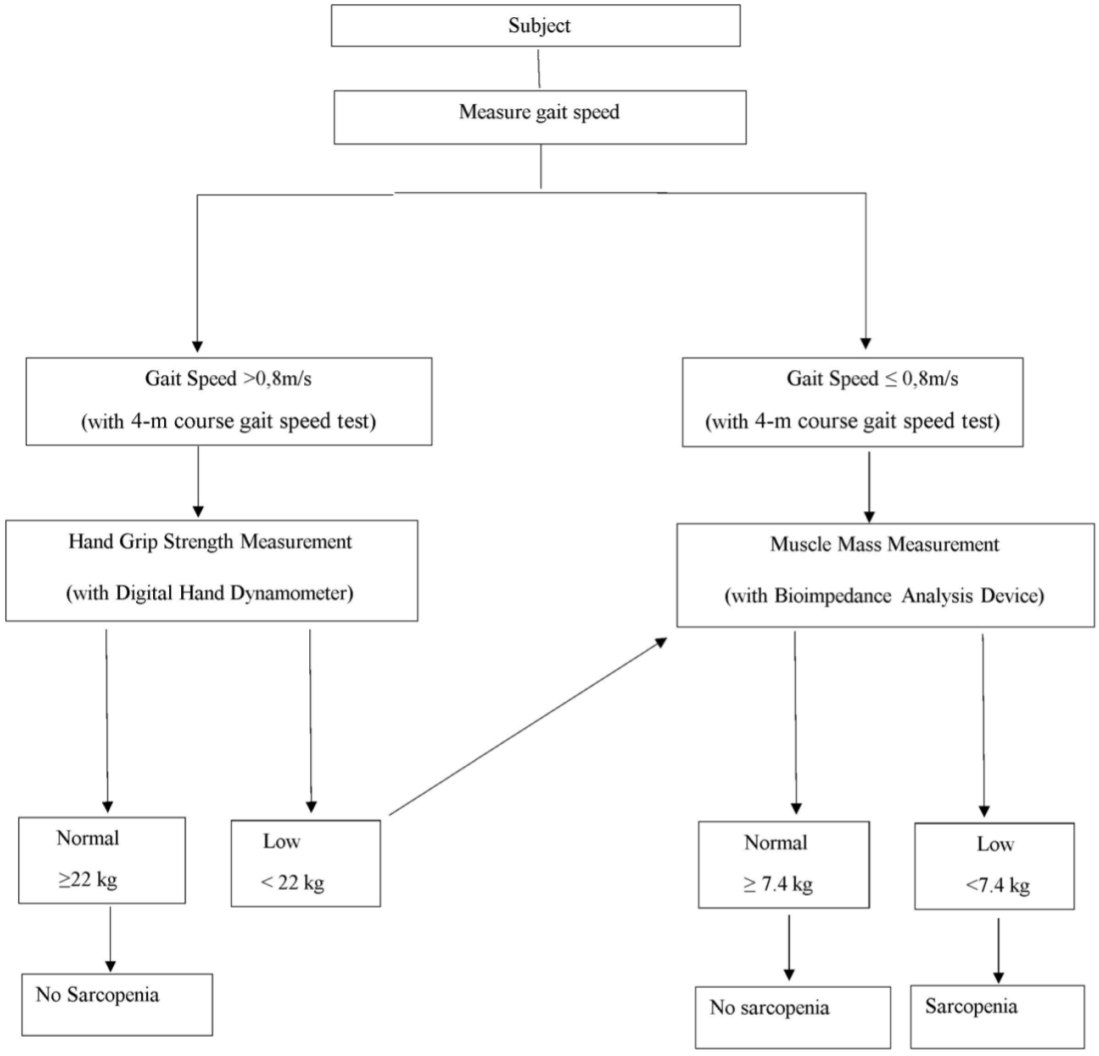


Figure 1. EWGSOP-suggested algorithm for sarcopenia (8)

DEFINITION OF SARCOPENIA

EWGSOP has developed practical clinical diagnostic criteria for sarcopenia. They propose an algorithm based on walking speed, grip strength and muscle mass measurements to determine sarcopenia. In line with what they recommend for muscle mass, strength and function measurements in research and practice; bioimpedance analysis for muscle mass (body fat ratio, skeletal muscle mass, skeletal muscle mass index); grip and knee extension strength for muscle strength and 4-m course gait speed test for physical performance was applied in the present study [8,13].

MUSCLE MASS

Bioimpedance (BIA) (Polosmart PSC12 Prolife) device was used for muscle mass measurements of the participants. Skeletal muscle

mass was calculated using the lean mass value obtained from the BIA device. The formula was Skeletal muscle mass=lean mass * 0.566. Skeletal muscle mass index was calculated by dividing the skeletal muscle mass value by the square of the individual's height. The cut-off point for skeletal muscle mass indexes was 7.4 kg/m² for women. Values below the cut-off point were considered as low muscle mass [8,13].

MUSCLE STRENGTH

Grip and knee extension strength were evaluated for muscle strength.

Baseline Digital Hand Dynanometer 198 LB/90 KG® was used to evaluate the participants' hand grip strength. In this evaluation, the participant was positioned in a sitting position on an upright chair without armrests, with her feet in contact with the floor. Then the participant was asked to grasp the dynamometer at a 90º angle from the body and the chair. Once the dynamometer position was adjusted, the participant was instructed to tighten the dynamometer as much as possible. Three measurements were made and a 30-second rest break was given between measurements. The device was reset after each measurement and the average of three measurements was recorded [13,14]. The cut-off point values for grip strength are 22 kg for women [13]. Values below this cut-off point were considered as a decrease in muscle strength.

Commander Echo™ Muscle Testing Dynamometer was used to measure knee extension (quadriceps) strength. The dynamometer is a portable tool with a digital display. For quadriceps strength measurement, participants were positioned sitting on a flat surface, with their hips and knees flexed at 90º, their feet free and unsupported. The participant was asked to resist resistance as much as possible. Muscle strength measurement was repeated 3 times, the average value was recorded in kilograms [15].

PHYSICAL PERFORMANCE

The physical performance was evaluated with the 4-m course gait speed test. The starting and ending points of the 4-meter distance were marked on the ground. Participants started walking with the "start" command and walked at their normal daily pace. They were informed that they should not stop until they heard the command "stop." When the test was completed, the time was recorded and walking speed was calculated with the distance/time formula. The test was performed 2 times, the best walking time was used in the calculation. In the 4-meter walking speed test, the cut-off point values for walking speed for physical performance were reported as 0.8 m/s. Walking speeds slower than this value were considered poor physical performance [8].

HEALTH ASSESSMENT QUESTIONNAIRE (HAQ)

HAQ is a questionnaire developed specifically for RA. It consists of 20 questions and 8 sections. Total score is between 0 and 3. High score means low functionality [16].

TAMPA KINESIOPHOBIA SCALE (TKS)

Tampa Kinesiophobia Scale is a 17-item scale that evaluates fear of movement/reinjury, developed by Miller *et al.* in 1991. The score varies between 17–68, and higher score indicates higher level of kinesiophobia [17].

BIOPSYCHOSOCIAL QUESTIONNAIRE (BETY-BQ)

This scale, developed to evaluate the biopsychosocial process related to the disease, has 30 items. The scale is scored with a 5-point likert system. The total score is obtained by adding up the scores for each item. High score indicates poor biopsychosocial situation [18].

SHORT FORM-36 (SF-36)

SF-36, one of the most widely used scales in assessing quality of life, was developed by Ware *et al.* in 1993. Physical and mental component scores can be obtained with 8 subdimensions consisting of 36 items. Each of the subdimensions is scored between 0–100. 100 score indicate good health status, 0 score indicate poor health status [19].

STATISTICAL ANALYSIS

The GPower V.3.1.9.4 (University of Kiel, Kiel, Germany) was used to determine the appropriate sample size. Depending on the gait speed test parameter based on the reference study results [20], it was found that 24 of the subjects for each group must have been enrolled to have 95% power with 5% type 1 error level. The data were analyzed with the SPSS 21.0 package program. Continuous variables are given as mean ± standard

deviation and categorical variables are given as number and percentage. Kolmogorov Smirnov Test was used to determine whether the tested values had a normal distribution. Independent Sample T Test was used to compare independent group differences according to the suitability of the data for normal distribution. Chi square test was used for categorical data. Statistical significance value was accepted as $p<0.05$.

RESULTS

The study was completed with 25 RA women and 25 healthy women. The flow diagram of the study shown in Figure 2. No injuries were reported during the asssessment.

Data on the demographic and physical characteristics of the participants were given in Table 1. There was no difference between RA group and the healthy group in age, height, weight, and body mass index ($p>0.05$). While the exercise habit of the healthy group was 48% higher, the weight loss of the RA group in the last 3 months was 28% higher ($p<0.05$).

Disease-related data of RA women were given in Table 2. The average disease duration of RA women was 14.68 ± 8.45 years and the Disease Activity Score-28 score was 5.72 ± 0.82.

While 18 (72%) of the RA women had no sarcopenia, 7 (28%) had severe sarcopenia. None of the healthy women had sarcopenia (Table 3).

COMPARISON BETWEEN RA AND HEALTHY GROUP

When RA and healthy groups were compared; skeletal muscle mass (p: 0.004); skeletal muscle mass index (p: 0.011); grip strength-right (p:0.001) and left (p:0.001); knee extension strength-right (p:0.001) and left (p:0.001), 4-m course gait speed test (p:0.001), HAQ (p:0.001), TKS (p:0.001), BETY-BQ (p:0.001), SF-36 physical (p:0.001) ve mental component (p:0.001) results were significant in favor of the healthy group while there was no difference in body fat ratio (Table 3).

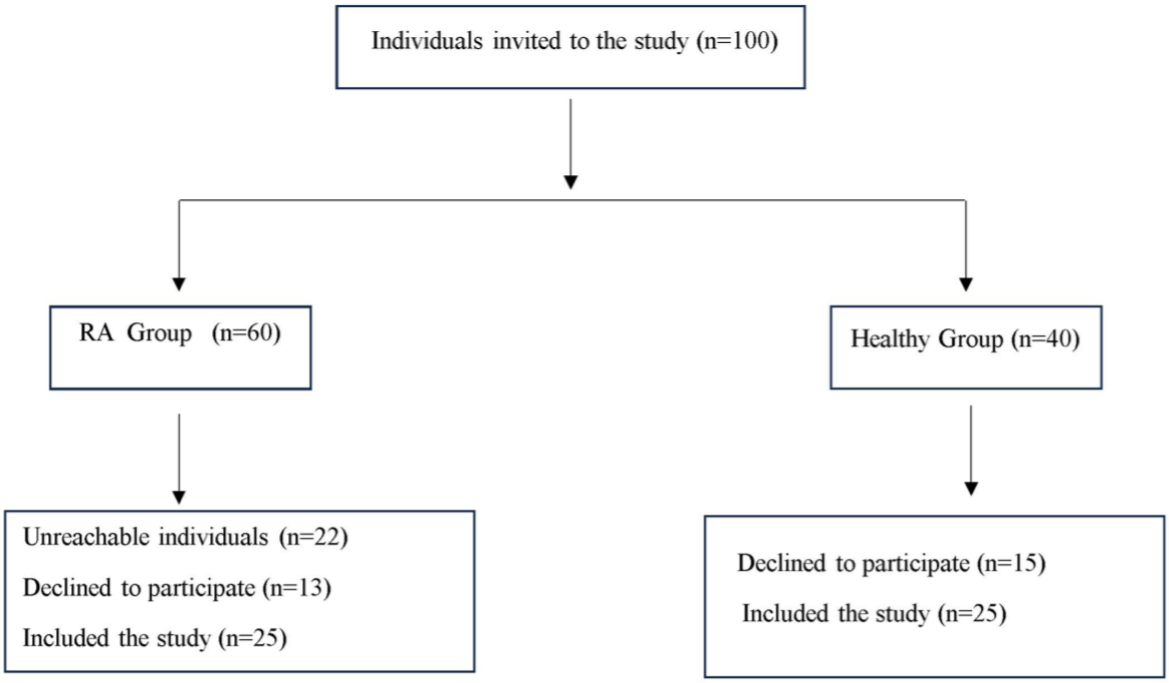


Figure 2. The flow diagram of the study.

Table 1

Demographic data of participants

	RA Group (n:25) Mean±SD	**Healthy Group (n:25) Mean±SD**	**p**
Age (years)	54.88±7.55	53.92±7.66	0.653*
Height (cm)	160.08±2.84	161.72±5.28	0.180*
Weight (kg)	64.80±12.68	70.04±10.66	0.120*
Body Mass Index (kg/m^2)	25.74±5.51	26.85±4.23	0.431*
	n (%)	**n (%)**	
Exercise Habitual -Yes	0(0)	12(48)	**0.001****
-No	25(100)	13(52)	
Have you lost any weight in the last 3 months? -Yes	7(28)	1(4)	**0.022****
-No	18(72)	24(96)	
SD: Standard Deviation, p: Significance Level, * Independent Sample T Test, ** Chi-Square Test			

Table 2

Disease-related data of women with RA

Variables	**RA Group (n:25)**	
Disease duration (year) **(**Mean±SD)	14.68 ±8.45	
Erythrocyte sedimentation rate **(**Mean±SD)	23.02±11.85	
C-Reactive Protein (Median (Min/Max))	3.49 (0.22/30.70)	
Disease Activity Score-28 **(**Mean±SD)	5.72±0.82	
Morning stiffness (minutes) (Median (Min/Max))	15(0/120)	
	n	%
Disease Activity Score-28		
-Moderate	6	24
-High	19	76
Rheumatoid Factor (RF)		
- Positive	16	64
- Negative	9	36
Anti-Cyclic Citrullinated Peptide -Positive	13	52
-Negative	12	48
Pharmacological treatment-Biological	3	12
-Steroid+csDMARD	7	28
-Steroid+csDMARD+ Biological	4	16
-csDMARD+ Biological +other	3	12
-other	2	8

Table 3

Comparison results of healthy and RA groups

	RA Group (n:25) Mean±SD	**Healthy Group (n:25) Mean±SD**	**p**
Definition of Sarcopenia			
- Body Fat Ratio (%)	34.71±8.98	35.29±5.18	0.781*
- Skeletal Muscle Mass (kg)	22.60±4.20	25.82±3.27	**0.004***
- Skeletal Muscle Mass Index (kg/ m²)	8.71±1.77	9.83±1.13	**0.011***
- 4-m course gait speed test (m/s)	0.74±0.21	1.16±0.22	**0.001***
- Grip Strength- Right (kg)	13.17±2.59	17.05±1.67	**0.001***
- Grip Strength- Left (kg)	12.41±2.83	16.33±1.78	**0.001***
- Right knee extension strength (kg)	10.48±1.82	13.20±3.15	**0.001***
- Left knee extension strength (kg)	10.20±2.18	13.55±2.75	**0.001***
	n (%)	**n (%)**	
Sarcopenia status -No sarcopenia	18 (72)	25 (100)	**0.04****
-Sarcopenia severe	7 (28)	0 (0)	
	Mean±SD	**Mean±SD**	
HAQ	1.53± 0.59	0.25±0.37	**0.001***
Tampa Kinesiophobia Scale	51.44±5.75	30.16±5.00	**0.001***
BETY-BQ	81.48±14.25	19.78±6.91	**0.001***
Short Form 36- physical component	30.72±11.66	81.90±7.81	**0.001***
Short Form 36- mental component	39.47±11.24	77.41±9.50	**0.001***

SD: Standard Deviation, p: Significance Level, * Independent Sample T Test, ** Chi-Square Test, HAQ: Health Assessment Questionnaire, BETY-BQ:Biopsychosocial Questionnaire, Bold values means p<0.05

DISCUSSION

In the present study, the frequency of sarcopenia was higher in RA women than in healthy women. Functional status, biopsychosocial status and quality of life of RA women were worse than healthy women, and fear-avoidance behaviors were higher.

In the literature, sarcopenia and sarcopenia parameters in RA were evaluated according to different criteria. In studies, sarcopenia status was mostly evaluated by dual energy x-ray absorptiometry (DXA). In these studies, the incidence of sarcopenia in RA patienst was reported as 25% by Aminov, 44% by Reina *et al.*, 19% by Dao *et al.*, 43.3% by Doğan *et al.*, 39.8% by Ngeuleu *et al.* [12,21–24]. Additionally, skeletal muscle mass and skeletal muscle mass index were observed to be lower in women with RA than in healthy women [22,24,25]. Women with RA had higher total fat mass and lower lean muscle mass than healthy women [26]. Dogan *et al.* stated that RA women with a low body mass index are almost twice as likely to develop sarcopenia [24]. Alkan-Melikoğlu expressed presarcopenia at a rate of 20% [25].

Similar to the present study, the only study reporting prevalence using all EWGSOP sarcopenia parameters was made by Tada *et al.* The authors measured muscle mass with BIA, walking speed with the 3-meter walk test, and grip strength with an isokinetic dynamometer in RA patients (mean age: 66.1 years). As a result of the study, the prevalence of sarcopenia was found to be 28%. Low body mass index and high fat mass are associated with sarcopenia [26]. The difference between the present study and this study was that the skeletal muscle index was lower than the present study. This may be due to the age of the participants in this study being older than the present study. Since the skeletal muscle mass index score will decrease with increasing muscle loss with advancing age, a lower skeletal muscle mass index than the present study may have been found.

In line with the literature, the presence of sarcopenia was determined to be 28% in the present study. Skeletal muscle mass index, 4-m course gait speed, grip strength, knee extension

strength were worse in women with RA compared to healthy controls. Body fat ratio was similar in both groups. The fact that the BMIs of RA women in the present study were not much above normal limits may explain the fact that their body fat ratios were not significantly higher than the healthy control. In the present study, different from other studies, the knee extension muscle strength of RA and healthy participants was evaluated and knee extension strength (quadriceps muscle strength) of RA was lower than healthy controls. We think that the reason for this is not only that RA causes loss of muscle strength, but also that the RA women in the present study did not have exercise habits.

DXA is considered the gold standard in detecting sarcopenia due to its high sensitivity. However, the high cost of this method is a disadvantage. Although the sarcopenia diagnosis method of EWGSOP used in the present study can detect the frequency of sarcopenia at a relatively low level, it is advantageous due to its ease of application and not requiring costly equipment.

The pain and inflammation process in RA patients not only causes physical disability, but also serious psychological and social problems [27]. In addition, it is known that the quality of life and physical activity levels of RA patients are lower than healthy individuals [28]. In the present study, the functional levels, biopsychosocial status and quality of life of RA women were worse than healthy controls, and they exhibited more fear-avoidance behaviors.

The strength of the present study is that it is the first study to use EWGSOP's sarcopenia diagnostic method (all EWGSOP sarcopenia parameters) in adults with RA. Also, there was no difference between the groups in age, height and weight. The limitation is that the data were obtained from a single hospital. If data had been collected as a multicenter, this population could have been better represented. Moreover, although a power analysis was performed, we recommend that studies be conducted in larger sample groups to obtain clearer information about the frequency of sarcopenia in RA.

Considering the breadth of causal factors associated with the development of sarcopenia in RA patients, a multidisciplinary management should be planned to prevent or treat sarcopenia. The use of glucocorticoids in the pharmacological treatment of RA symptoms is associated with muscle atrophy, and its negative effects on skeletal muscle may cause sarcopenia. More specifically, glucocorticoids can induce muscle atrophy (steroid myopathy) and lead to protein catabolism through activation of the transcription factor FOXO or suppression of mTOR signaling [29–30]. Yamada *et al.* showed that an average glucocorticoid dose of $\geq$ 3.25 mg/day for 1 year is an independent risk factor for the development of sarcopenia in individuals with RA. As a result of the study, they stated that reducing or discontinuing glucocorticoids could prevent the development of sarcopenia [31]. However, glucocorticoid-induced skeletal muscle atrophy easily causes fatigue in daily physical activities such as climbing stairs and fast walking, and thus causes sarcopenia to occur with decreased physical activity [32]. Strategies to increase physical activity/ exercise in the sarcopenia treatment approach may provide positive clinical benefits in RA patients. Physical activity/exercise approaches can improve not only sarcopenia, but also the functional levels, fears of avoiding movement, psychosocial status and quality of life of RA patients.

In future studies, we recommend collecting multicenter data to determine risk factors that may have an impact on sarcopenia in patients with RA. However, we also recommend investigating the effectiveness of physical activity/exercise approaches to prevent and reduce sarcopenia in RA patients.

CONCLUSION

In women with RA, the frequency of sarcopenia is higher, and functional status, fear-avoidance behaviors, biopsychosocial status and quality of life are worse than in healthy controls.

Introducere: *Scopul acestui studiu a fost de a compara frecvența sarcopeniei, starea funcțională, comportamentele de evitare a fricii, statutul biopsihosocial și calitatea vieții la femeile cu RA (artrita reumatoida) comparativ cu martori sănătoși.*

Metode: *25 de femei RA și 25 de femei sănătoase au fost incluse în studiu. Definiția sarcopeniei a fost evaluată folosind parametrii recomandați de Grupul de Lucru European pentru Sarcopenie (EWGSOP): Analiza de bioimpedanță pentru masa musculară (raportul de grăsime corporală, masa musculară scheletică, indicele de masă musculară scheletică); A fost evaluata forța de prindere și extensie a genunchiului pentru evaluarea forței*

musculare și testul de viteză a mersului de 4 m pentru evaluarea performanței fizice. Starea funcțională a fost evaluată cu Chestionarul de Evaluare a Sănătății (HAQ), comportamentele de evitare a fricii cu Scala Tampa Kinesiophobia (TKS), statutul biopsihosocial cu Chestionarul Biopsihosocial (BETY-BQ) și calitatea vieții cu Short Form-36 (SF- 36).

Rezultate: *În timp ce niciuna dintre femeile sănătoase nu a avut sarcopenie, sarcopenia severă a fost detectată la 7 (28%) dintre femeile cu RA. Când RA și grupurile sănătoase au fost comparate; masa musculară scheletică (p: 0,004); indicele de masă musculară scheletică (p: 0,011); puterea de prindere-dreapta (p:0.001) și stânga (p:0.001); puterea extensiei genunchiului-dreapta (p:0.001) și stânga (p:0.001), test de viteză a mersului de 4 m (p:0.001), HAQ (p:0.001), TKS (p:0.001), BETY-BQ (p. :0,001), rezultatele SF-36 fizice (p:0,001) cu componenta mentală (p:0,001) au fost semnificative în favoarea grupului de martori sănătosi, în timp ce nu a existat nicio diferență în raportul de grăsime corporală (p>0,05).*

Concluzie: *La femeile cu RA, frecvența sarcopeniei este mai mare, iar starea funcțională, comportamentele de evitare a fricii, statutul biopsihosocial și calitatea vieții sunt mai proaste decât la martorii sănătosi.*

Correspondence to: Elif Gur Kabul, P.T.
Faculty of Health Sciences, Physiotherapy and Rehabilitation, Usak University, Usak, Turkey.
E-mail: elifgur1988@hotmail.com
Phone: 00.90.2762213086/ Fax: 00.90.2762212145

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