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Sarcopenia-Related Factors and the Diagnostic Role of Ultrasonography in Rheumatoid Arthritis

ABSTRACT

Background/Aims: Sarcopenia is a common condition in patients with chronic inflammatory diseases, including rheumatoid arthritis (RA). The present study was designed to investigate the factors related to sarcopenia in patients with RA and to evaluate the diagnostic performance of ultrasonography (USG) in sarcopenia.

Materials and Methods: Fifty-one patients with RA (aged 18-65 years), diagnosed according to the 2010 American College of Rheumatology/European Alliance of Associations for Rheumatology criteria, and 51 age-and sex-matched healthy controls were included. Participants were assessed for Disease Activity Score 28, muscle strength, muscle mass, anthropometric data, functional status, physical performance, balance, and quality of life (QoL). Sarcopenia was diagnosed by handgrip strength and calculating the skeletal muscle mass index value with dual-energy x-ray absorptiometry. Quadriceps muscle mass was measured by USG.

Results: Among RA patients, 41 were female, with a mean age of 45.59 ± 9.85 years. In the control group, 37 were female, with a mean age of 47.41 ± 8.90 years. The mean disease duration was 15.12 ± 9.36 years. Sarcopenia prevalence was significantly higher in the RA group (37.3%) than controls (17.6%, P = .027). Sarcopenia was associated with disease duration, history of falls, reduced function, lower physical performance, anthropometric parameters, and decreased ultrasound muscle mass. Diagnostic cut-off values for quadriceps muscle thickness were 1.72 cm (right) and 1.71 cm (left) on ultrasound.

Conclusion: Sarcopenia in RA patients is significantly associated with disease duration, falls, functional status, physical performance, anthropometric measures, muscle mass assessed by ultrasound, and QoL. Ultrasonography may be a useful screening tool for sarcopenia, with defined cut-off values for quadriceps muscle thickness.

Keywords: Physical performance, quality of life, rheumatoid arthritis, sarcopenia, ultrasonography

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Introduction

Sarcopenia is a progressive skeletal muscle disease characterized by reductions in muscle mass, muscle strength, and physical performance. Age-related decline in skeletal muscle fibers typically begins after the fifth decade of life, with muscle mass and strength decreasing by approximately 20%-40% after the age of 70 years.[1,2] Multiple mechanisms, including age-associated hormonal alterations, immune system dysregulation, chronic low-grade inflammation, and insulin resistance, are involved in the development of

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sarcopenia.[3,4] The pathogenesis of sarcopenia is primarily driven by increased pro-inflammatory cytokines, enhanced apoptosis, mitochondrial dysfunction, and abnormal myokine production.[3,5,6] Sarcopenia is associated with impaired posture and balance, increased risk of falls and fractures, deterioration in quality of life (QoL), and higher rates of physical disability and mortality.[4,5]

Various studies have demonstrated that chronic inflammatory diseases contribute to sarcopenia.[7-10] Among the strongest inflammatory markers associated with sarcopenia are C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α), while IL-1 and IL-18 play a role in inflammatory aging and sarcopenia progression.[11,12] These cytokines may disrupt intercellular signaling pathways, promote adipose tissue accumulation, and interfere with insulin-like growth factor-1 (IGF-1) activity within skeletal muscle tissue, thereby contributing to muscle degeneration.[13] Rheumatoid arthritis (RA)-related sarcopenia appears to involve additional disease-specific molecular pathways. Activation of the ubiquitin–proteasome system mediated by TNF-α promotes muscle protein catabolism, while impaired satellite cell activity compromises muscle regeneration.[14-16] Moreover, RA is characterized by a distinct inflammatory profile involving elevated leptin and resistin levels together with reduced concentrations of myokines such as irisin and meteorin-like protein.[14-16] Inflammatory activity may also reduce the number and proliferative capacity of satellite cells located between the basal lamina and sarcolemma, which are normally activated in response to exercise, injury, or mechanical loading.[17,18] Disease activity is considered an important determinant of rheumatoid sarcopenia. Previous studies have demonstrated that higher Disease Activity Score-28 (DAS28) values are associated with both the presence and severity of sarcopenia in patients with RA.[19,20]In addition, pharmacological agents used in RA management may exert variable effects on muscle metabolism. Although corticosteroids effectively suppress inflammation during short-term treatment, prolonged use may accelerate muscle wasting through enhanced proteolysis via the ubiquitin–proteasome pathway, inhibition of satellite cell proliferation, and suppression of IGF-1 signaling.[21] Conversely, biologic therapies, particularly anti-TNF agents, may help preserve or improve muscle mass and function by reducing systemic inflammatory burden.[22,23] In addition to cellular changes in RA, factors such as age, disease duration, history of fractures, and medication use are known risk factors for sarcopenia.[24] Muscle loss in RA should be considered a dynamic process shaped by the inflammatory burden of the disease, the effects of therapeutic interventions, and individual patient-specific factors.

Identifying the prevalence and risks of sarcopenia in individuals with RA is crucial for mitigating secondary complications associated with muscle loss. Several techniques are currently available for the evaluation of muscle mass in sarcopenia, including dual-energy x-ray absorptiometry (DXA), bioelectrical impedance analysis, and ultrasonography (USG). Among these modalities, USG enables direct visualization of muscle architecture and provides quantitative information regarding muscle thickness, cross-sectional area, and echogenicity, thereby allowing assessment of both muscle quantity and quality. In addition, USG has several practical advantages, including its non-invasive nature, absence of radiation exposure, relatively low cost, and suitability for bedside use in routine clinical settings. Consequently, USG has increasingly been recognized as a complementary and alternative imaging method for the early evaluation and follow-up of muscle involvement in RA.

Accordingly, the present study was designed to investigate the prevalence of sarcopenia and associated clinical factors in Turkish patients with RA and to assess the diagnostic performance of USG in the detection of sarcopenia.

MAIN POINTS

- *The prevalence of sarcopenia was significantly higher in patients with rheumatoid arthritis (RA) (37.3%) compared with healthy controls (17.6%).*
- *In patients with RA, sarcopenia is particularly associated with longer disease duration, a history of falls, reduced physical performance, and poorer functional status.*
- *In patients with RA, sarcopenia exhibit significantly decreased muscle strength, balance, quality of life, and lower extremity muscle thickness.*
- *Ultrasound measurements of rectus femoris, vastus intermedius, and overall quadriceps muscle thickness demonstrated moderate diagnostic accuracy for detecting sarcopenia.*
- *Ultrasonography is a rapid, safe, and low-cost method that may serve as a potential alternative to dual-energy x-ray absorptiometry for assessing muscle mass in RA patients.*

Materials and Methods

The cross-sectional study included 51 patients diagnosed with RA based on the 2010 American College of Rheumatology/European Alliance of Associations for Rheumatology criteria[25] and 51 healthy controls aged between 18 and 65 years. The study was conducted between September 2021 and October 2024. Demographic characteristics, laboratory analyses, and comorbid diseases of the participants were recorded. Individuals with neurological disorders, primary muscle diseases, malignancy, hepatic or renal failure, or a history of immobilization longer than 3 months, dementia, hip dislocation, limb deformities, or joint arthroplasty were excluded.

The disease activity in RA patients was assessed using the Disease Activity Score 28-CRP (DAS28-CRP) and the Rheumatoid Arthritis Disease Activity Index-5 (RADAI-5)

scales.[26,27] Muscle strength was measured using a Jamar hydraulic hand dynamometer (FEI®, 5030J1 model, USA). Functional status was evaluated using the Health Assessment Questionnaire (HAQ). Physical performance was assessed with the Short Physical Performance Battery,[30] balance was measured using the Tinetti Scale, and quality of life was evaluated with the Rheumatoid Arthritis Quality of Life Questionnaire and the Sarcopenia Quality of Life Questionnaire (SARQoL).[31,32]

For anthropometric measurements, arm and thigh circumferences were measured. Upper arm circumference was measured at the midpoint of both upper extremities, whereas thigh circumference was measured at the thickest part of both thighs using a measuring tape.

Muscle mass was assessed using both DXA and USG. The DXA measurements were performed using Lunar iDEXA (GE Healthcare, 3030 Ohmeda Drive, Madison, WI 53718, USA). Appendicular skeletal muscle mass (ASM) was calculated, and the skeletal muscle mass index (SMMI) was derived using the formula ASM/height^2. Ultrasound measurements were performed using a Logiq 9 (GE, USA) ultrasound device with a 7-12 MHz high-frequency linear probe. The bilateral distance between the anterior superior iliac spine and the upper border of the patella was measured, and the distal 1/3 was marked. Measurements were taken in a seated position without applying compression to the subcutaneous fat or muscle.[33]

Axial images were recorded, and the thickness of subcutaneous fat, vastus intermedius, rectus femoris, and total quadriceps muscle was measured (Figure 1). All ultrasonographic measurements were performed by the same blinded investigator, ensuring intraobserver reliability.

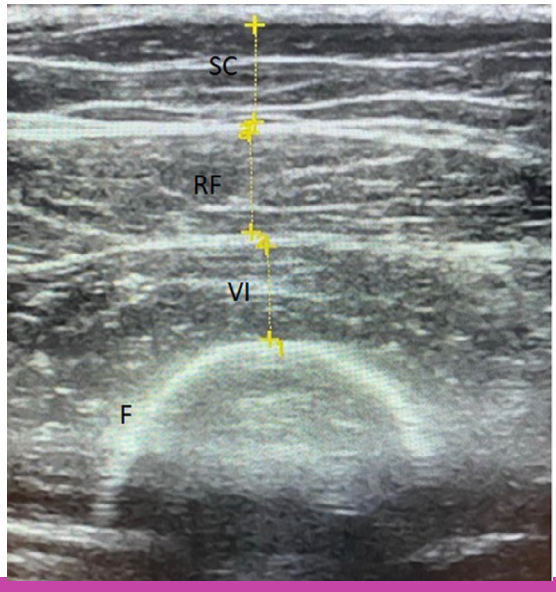


Figure 1. Measurement of subcutaneous tissue and quadriceps muscle thickness with USG. F, femur; RF, rectus femoris; SC, subcutaneous tissue; VI, vastus intermedius.

The diagnosis of sarcopenia was determined based on the European Working Group on Sarcopenia in Older People diagnostic criteria.[5] For probable sarcopenia diagnosis, handgrip strength values were first determined. A cut-off value of less than 32 in men and 22 in women was considered as decreased handgrip strength.[28] Sarcopenia was diagnosed in those with low hand grip strength and SMMI scores below 7.4 in women and 9.2 in men.[28]

This study was approved by the Ankara City Hospital No. 2 Clinical Research Ethics Committee (Approval No: E2-21-312, Date: March 24, 2021) and conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants. All study steps were performed following Strengthening the Reporting of Observational Studies in Epidemiology guidelines.

Statistical Analysis

A priori power analysis was performed using G*Power 3.1.9.4 software (Heinrich Heine University Düsseldorf; Düsseldorf, Germany). To achieve a statistical power of 0.80 with a significance level of $\alpha = 0.05$ and a type II error rate ($\beta = 0.20$), the minimum required sample size was calculated as 98 participants (49 patients and 49 controls). The effect size (0.51) was derived from a previous study conducted by Tada et al.[34]

Statistical analyses were performed using IBM Statistical Package for the Social Sciences Statistics for Windows, version 23.0 (IBM Corp., Armonk, NY, USA). Continuous variables are expressed as mean, standard deviation, median, minimum, and maximum values, while categorical variables are presented as frequencies and percentages. The normality of data distribution was assessed using the Kolmogorov–Smirnov and Shapiro–Wilk tests.

For group comparisons, the chi-square test or Fisher's exact test was used for categorical variables, whereas Student's *t*-test or Mann–Whitney *U*-test was applied for continuous variables, depending on data distribution. Correlation analyses were performed using Pearson or Spearman correlation coefficients according to the distribution characteristics of the variables. Correlation values close to 0 were considered weak, whereas values approaching 1 indicated strong correlations.

Receiver operating characteristic (ROC) curve analysis was conducted to determine optimal cut-off values for rectus femoris, vastus intermedius, and quadriceps muscle thickness in the diagnosis of sarcopenia. Statistical significance was defined as $P < .05$, and a 95% CI was used throughout the analyses.

Results

Among the RA patients included in the study, 41 were female, while 37 participants in the healthy control group were female. The mean age was 45.59 ± 9.85 years in RA patients and 47.41 ± 8.90 years in the control group. Comorbidities were identified in 43.1% of RA patients and in 39.2% of healthy controls. Detailed demographic and anthropometric characteristics are summarized in Table 1.

Table 1. Demographic and Anthropometric Data of Patients with Rheumatoid Arthritis and the Control Group

	RA	Conrol	*P*
Age (mean ± SD)	45.59 ± 9.85	47.41 ± 8.90	
Median	57	54	.163
Min-Max	36-77	37-74	
Gender (n)			
Female	41	37	,350
Male	10	14	.687
Comorbid disease (n, %)	29 (43.1)	31 (39.2)	
History of falls			
Yes	44	51	**.006**
No	7	0	
BMI (mean ± SD)	28.61 ± 5.83	28.60 ± 3.99	.583
CRP (mean ± SD) (mg/L)	26.50 ± 23,.5	5.35 ± 2.68	**<.001**
Right arm circumference (mean ± SD) (cm)	29.71 ± 4.67	31.27 ± 3.45	.79
Left arm circumference (mean ± SD) (cm)	29.90 ± 4.72	31.33 ± 3.44	.69
Right thigh circumference (mean ± SD) (cm)	36.24 ± 5.82	40.78 ± 6.79	**.002**
Left Thigh Circumference (mean ± SD) (cm)	36.29 ± 6.03	40.92 ± 6.73	**.001**

BMI, body mass index; CRP, C-reactive protein; RA, rheumatoid arthritis.
P < .05 is considered statistically significant.

Based on DXA measurements, sarcopenia was diagnosed in 19 RA patients (37.3%) and 9 control subjects (17.6%, *P* = .027).

Compared to the control group, patients with RA demonstrated significantly reduced muscle strength, physical performance, sarcopenia-specific QoL, balance, and ultrasound-based muscle mass measurements. These parameters are detailed in Table 2.

In RA patients with sarcopenia, disease duration was significantly longer, whereas functional capacity, balance,

Table 2. Functional Assessment, USG, and DXA Measurement Results of Patients with Rheumatoid Arthritis and the Control Group

	RA	Control	*P*
Muscle strength (hand grip strength)			
Dominant hand (mean ± SD)	25.35 ± 10.53	30.53 ± 10.52	.071
Non-dominant hand (mean ± SD)	20.80 ± 9.63	27.69 ± 9.29	**.002**
SPPB	10.27 ± 2.58	11.65 ± 0.68	**.002**
SARQoL (mean ± SD)	62.07 ± 10.78	76.50 ± 12.73	**<.001**
Tinetti balance test (mean ± SD)	20.39 ± 5.47	25.53 ± 0.86	**<.001**
Right subcutaneous tissue (mean ± SD) cm	0.94 ± 0.52	0.87 ± 0.30	.963
Left subcutaneous tissue (mean ± SD) cm	0.91 ± 0.49	0.83 ± 0.26	.738
Right rectus femoris (mean ± SD) cm	1.03 ± 1.31	1.09 ± 0.38	**.003**
Left rectus femoris (mean ± SD) cm	0.81 ± 0.34	1.09 ± 0.37	**<.001**
Right vastus intermedius (mean ± SD) cm	0.74 ± 0.30	1.11 ± 0.34	**<.001**
Left vastus intermedius (mean ± SD) cm	0.68 ± 0.31	1.11 ± 0.35	**<.001**
Total right quadriceps (mean ± SD) cm	1.77 ± 1.40	2.19 ± 2.68	**<.001**
Total left quadriceps (mean ± SD) cm	1.49 ± 0.63	2.20 ± 0.66	**<.001**
ASM (mean ± SD)	18.78 ± 4.89	21.01 ± 4.88	.056
SMMI (mean ± SD)	7.17 ± 1.74	7.75 ± 1.30	.08
Sarcopenia (n, %)	19 (37.3)	9 (17.6)	**.027**

ASM, appendicular skeletal muscle mass; SARQoL, Sarcopenia Quality of Life Questionnaire; SMMI, skeletal muscle mass index; SPPB, Short Physical Performance Battery.
P < .05 is considered statistically significant.

physical performance, quality of life, lower limb anthropometric parameters, and ultrasound-measured muscle mass were significantly reduced. The comparison between sarcopenic and non-sarcopenic RA patients is presented in Table 3.

In RA patients, SMMI showed significant correlations with BMI, anthropometric measurements, muscle strength, ultrasound-based muscle mass measurements, sarcopenia-related QoL, and physical performance levels. Variables associated with sarcopenia in the RA cohort are summarized in Table 4.

In the sarcopenia group, the thickness values for the right/left rectus femoris, right/left vastus intermedius, and right/left quadriceps muscles were significantly

Table 3. Variables Associated with Sarcopenia in Rheumatoid Arthritis Patients

	Sarcopenic	Non-Sarcopenic	*P*
Gender, n (%)			
Female	14 (73.7)	27 (84.4)	.353
Male	5 (26.3)	5 (15.6)	
Age (years)	57.47 ± 11.10	57.28 ± 9.22	.969
Comorbid disease, n (%)			
Yes	9 (47.4)	13 (40.6)	.638
No	10 (52.6)	19 (59.4)	
History of fall, n (%)	14 (73.7)	5 (26.3)	**.044**
Disease duration			
Mean ± SD (years)	20.11 ± 7.98	12.16 ± 8.95	**.003**
Median (min-max)	18 (7-35)	11 (1-32)	
RADAI	4.05 ± 1.78	3.80 ± 1.73	.591
DAS 28	3.35 ± 1.32	3.70 ± 1.67	.861
CRP	33.32 ± 24.41	22.45 ± 22.09	.155
RAQoL	20.68 ± 8.06	15.31 ± 6.12	**.017**
HAQ	1.16 ± 0.72	0.53 ± 0.39	**.002**
Tinetti balance test	17.42 ± 6.35	22.16 ± 4.03	**.007**
SPPB	8.42 ± 3.34	11.38 ± 0.94	**<.001**
SARQoL	49.34 ± 16.56	69.63 ± 9.16	**<.001**
Right arm circumference (mean ± SD) cm	27.79 ± 4.53	30.84 ± 4.43	.054
Left arm circumference (mean ± SD) cm	27.89 ± 0.67	31.09 ± 4.40	.051
Right thigh circumference (mean ± SD) cm	32.79 ± 4.53	38.28 ± 5.59	**.002**
Left thigh circumference (mean ± SD) cm	33.16 ± 4.80	38.16 ± 5.97	**.008**
Right rectus femoris (mean ± SD) cm	0.69 ± 0.40	0.95 ± 0.28	**.002**
Left rectus femoris (mean ± SD) cm	0.65 ± 0.43	0.90 ± 0.23	**.001**
Right vastus intermedius (mean ± SD) cm	0.60 ± 0.37	0.82 ± 0.22	**.001**
Left vastus intermedius (mean ± SD) cm	0.56 ± 0.39	0.76 ± 0.22	**.001**
Total right quadriceps (mean ± SD) cm	1.77 ± 2.24	1.78 ± 0.48	**.004**
Total left quadriceps (mean ± SD) cm	1.21 ± 0.81	1.66 ± 0.42	**<.001**
Right subcutaneous tissue (mean ± SD) cm	0.75 ± 0.32	1.05 ± 0.58	**.019**
Left subcutaneous tissue (mean ± SD) cm	0.71 ± 0.32	1.03 ± 0.54	**.009**
SMMI (mean ± SD)	6.02 ± 1.73	7.86 ± 1.35	**<.001**
csDMARD n (%)	15 (78.9)	4 (12.5)	.945
bDMARD n (%)	4 (21.1)	15 (78.9)	.417
NSAİD n (%)	2 (10.5)	17 (89.5)	.832
Steroid n (%)	10 (52.6)	9 (47.4)	.539

bDMARD, biologic disease-modifying antirheumatic drug; CRP, C-reactive protein; csDMARD, conventional disease-modifying antirheumatic drugs; DAS28, Disease Activity Score 28; HAQ, Health Assessment Questionnaire; NSAID, nonsteroidal anti-inflammatory drug; RADAI, Rheumatoid Arthritis Disease Activity Index; RAQoL, Rheumatoid Arthritis Quality of Life Questionnaire; SARQoL, Sarcopenia Quality of Life Questionnaire; SD, standard deviation; SMMI, skeletal muscle mass index; SPPB, Short Physical Performance Battery.
P < .05 indicates statistical significance.

Table 4. Correlation of SMMI with Various Parameters

	SMMI	
	Correlation Coefficient	*P*
BMI	0.566	**<.001**
HAQ	0.289	.039
Right arm circumference	0.607	**<.001**
Left arm circumference	0.616	**<.001**
Right tight circumference	0.595	**<.001**
Left tight circumference	0.566	**<.001**
Dominant hand muscle strength	0.611	**<.001**
Non-Dominant hand muscle strength	0.563	**<.001**
Left rectus femoris	0.524	**<.001**
Right vastus intermedius	0.524	**<.001**
Left vastus intermedius	0.511	**<.001**
Total right quadriceps	0.530	**<.001**
Right subcutaneous tissue	0.515	**<.001**
Left subcutaneous tissue	0.514	**<.001**
SAQoL	0.639	**<.001**
Tinetti balance test	0.391	.005
SPPB	0.550	**<.001**

BMI, body mass index; HAQ, Health Assessment Questionnaire; SAR-QoL, Sarcopenia Quality of Life Questionnaire; SMMI, skeletal muscle mass index; SPPB, Short Physical Performance Battery.
P < .05 indicates statistical significance.

lower compared with non-sarcopenic patients (*P* values: .005/.001; .001/.001; .004/<.001, respectively). To evaluate the diagnostic value of these muscle thickness measurements in sarcopenia, a ROC curve analysis was performed, and optimal threshold values were determined. The area under the curve (AUC) values were 0.718 ± 0.070 for the right rectus femoris (*P* = .001), 0.740 ± 0.069 for the left rectus femoris (*P* < .001), 0.722 ± 0.067 for the right vastus intermedius (*P* = .001), 0.714 ± 0.068 for the left vastus intermedius (*P* = .001), 0.699 ± 0.070 for the right quadriceps muscle (*P* = .002), and 0.725 ± 0.069 for the left quadriceps muscle (*P* < .001). The optimal cut-off values and their corresponding sensitivity and specificity values were determined as follows: right rectus femoris muscle thickness 0.85 cm (sensitivity: 59%, specificity: 61%), left rectus femoris muscle thickness 0.84 cm (sensitivity: 65%, specificity: 71%), right vastus intermedius muscle thickness 0.89 cm (sensitivity: 57%, specificity: 68%), left vastus intermedius muscle thickness 0.85 cm (sensitivity: 60%, specificity: 68%), right quadriceps muscle thickness 1.72 cm (sensitivity: 57%, specificity: 57%), left quadriceps muscle thickness 1.71 cm (sensitivity: 61%, specificity: 68%).

The intra-observer reproducibility of ultrasonographic measurements for rectus femoris and vastus intermedius muscle thickness was evaluated using intraclass correlation coefficient (ICC) analysis. The ICC value for the rectus femoris was 0.956 (95% CI: 0.779-0.991; *P* < .001), while the ICC for the vastus intermedius was 0.873 (95% CI: 0.664-0.975; *P* = .007).

Best Youden indexes were reported as: 0.20 for right rectus femoris muscle; 0.36 for left rectus femoris muscle; 0.25 for right vastus intermedius muscle; 0.28 for left vastus intermedius muscle; 0.14 for right quadriceps muscle; 0.29 for left quadriceps muscle.

The ROC analysis result for the optimal threshold of muscle thickness is shown in Figure 2 and Table 5.

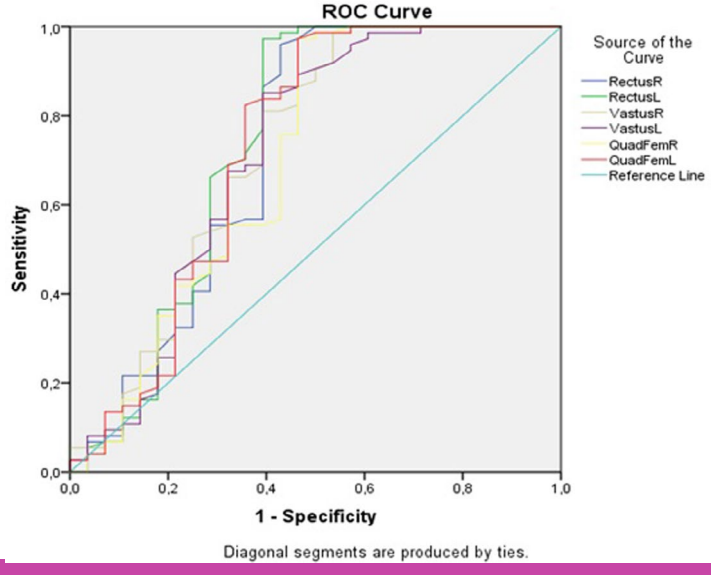


Figure 2. Receiver operating curve curve demonstrating the optimal threshold of muscle thickness in sarcopenia.

Table 5. ROC Analyses Results for Ultrasonographic Muscle Thickness

	AUC	95% CI	*P*
Right rectus femoris (mean ± SE)	0.718 ± 0.070	0.581-0.855	.001
Left rectus femoris (mean ± SE)	0.740 ± 0.069	0.604-0.876	<.001
Right vastus intermedius (mean ± SE)	0.722 ± 0.067	0.591-0.852	.001
Left vastus intermedius (mean ± SE)	0.714 ± 0.068	0.581-0.847	.001
Total right quadriceps (mean ± SE)	0.699 ± 0.070	0.562-0.835	.002
Total left quadriceps (mean ± SE)	0.725 ± 0.069	0.590-0.861	.001

AUC, area under the curve; ROC, receiver operating characteristic; SE, standard error.
P < .05 indicates statistical significance.

Discussion

In this study, the prevalence of sarcopenia and related clinical factors were investigated in patients with RA, and the optimal threshold of ultrasound in this population was evaluated. The findings demonstrated that sarcopenia was significantly more common in patients with RA than in healthy controls. Longer disease duration was also associated with the presence of sarcopenia in RA. Ultrasonographic muscle thickness significantly decreased in patients with sarcopenia. Optimum cut-off values of ultrasonographic muscle thickness in the diagnosis of sarcopenia were determined by ROC analysis.

In the present study, sarcopenia was identified in 19 patients with RA (37.3%) and in 9 participants from the control group (17.6%). Previous studies have reported that the prevalence of sarcopenia in patients with RA varies between 4.5% and 39.85%.[19,35-38] The prevalence of sarcopenia varies widely. In studies investigating the related factors with sarcopenia in RA, differences in age, gender, disease duration, joint deformity, and malnutrition have been shown to be associated with sarcopenia. The findings are in agreement with previous reports in the literature. Differences in sarcopenia prevalence among studies may be related to variations in demographic and clinical characteristics across patient populations.

A significant association was observed between sarcopenia and prolonged disease duration, decreased physical performance, poorer functional status, impaired balance, increased fall frequency, reduced quality of life, and ultrasound measurements of both thighs. The mean disease duration in the patients with RA was 20.11 ± 7.98 years, and it was significantly associated with sarcopenia. Gumtorntip et al[39] reported a significant correlation between disease duration and sarcopenia in their study. A cross-sectional study conducted in patients with RA similarly reported a relationship between disease duration and sarcopenia.[40] The IORRA cohort study in Japan also reported a significant relationship between disease duration and sarcopenia.[24] Other studies have also linked sarcopenia to disease duration in patients with RA.[37,41,42] However, Ngeuleu et al[19] and Mochizuki et al[43] did not find a significant association between disease duration and sarcopenia. Although different findings have been reported, the literature provides stronger evidence supporting the association between disease duration and sarcopenia. In RA, the long duration of the disease leads to an increased cumulative inflammatory load due to the accumulation of recurrent and persistent inflammatory attacks over time. This chronic inflammatory environment increases muscle protein breakdown through the continuous activation of catabolic cytokines, primarily TNF-α and IL-6, while suppressing anabolic processes. Therefore, prolonged disease duration can be considered a significant determinant in the development and progression of sarcopenia specific to RA.[44]

The relationship between sarcopenia and functional status in patients with RA has been explored in various studies. Gumtorntip et al[39] found that sarcopenic RA patients had higher HAQ scores than those without sarcopenia. Li et al[37] suggested that the HAQ score is an important parameter in predicting sarcopenia. Dietzel et al[38] also linked sarcopenia in RA patients to poor functional status (HAQ). Likewise, Akar et al[45] demonstrated a significant relationship between sarcopenia and HAQ scores. Consistent with these findings, patients with RA and sarcopenia in this study exhibited significantly higher HAQ scores compared with non-sarcopenic patients. Poor functional status negatively impacts mobility and independence in daily living activities. It is proposed that poor functional status, along with prolonged disease duration, contributes to the increased risk of sarcopenia.

Previous studies have reported impaired balance both in patients with RA and in individuals with sarcopenia.[45,46] Furthermore, studies examining sarcopenia-related factors in RA have shown that balance disorders, falls, and fracture risk occur more frequently in this patient population. Wiegmann et al[49] followed patients with RA for 1 year and found that 20.2% of the patients experienced at least 1 fall during the observation period. However, they did not find a significant relationship between sarcopenia and falls; instead, they reported that older age, poor functional status, and low balance scores were significantly associated with falls.[45] Studies found a higher incidence of falls in sarcopenic patients with RA.[40,47,48] In this study, the number of patients with a history of falls was significantly higher among those with sarcopenia. It is proposed that prolonged disease duration, poor functional

status, low physical performance, and impaired balance contribute to an increased fall risk.

Physical performance was assessed using KFPB tests. Physical performance was significantly worse in patients with sarcopenic RA. Li et al[37] found an association between sarcopenia and reduced functional capacity in patients with RA. Another study reported a decrease in the physical function domain of the SF-36 in patients with sarcopenic RA.[30] Akar et al[45] also found significant reductions in functional test performance among sarcopenic patients.[49] The decline in physical performance may be due to reduced mobility over the course of the disease, as well as the interplay between poor functional status, balance impairment, and sarcopenia. These factors may contribute to each other's progression.

Rheumatoid arthritis negatively impacts quality of life, and the presence of sarcopenia further exacerbates this effect. In this study, both RA-related and sarcopenia-related quality of life were significantly lower in RA patients with sarcopenia. Previous studies have reported that sarcopenia adversely affects quality of life in RA patients.[40,45] The 2020 ESCEO update recommendations highlight the importance of subjective patient-reported measures, in addition to objective criteria, in evaluating physical performance in sarcopenia.[50] Studies have reported a linear relationship between physical performance and health-related quality of life in older adults. The SARQoL questionnaire is highly sensitive in detecting even minor changes and is the most widely used questionnaire in sarcopenia. In the sarcopenic patient group, quality of life was negatively affected along with functional performance.

In this study, there were no significant differences between the RA patients with and without sarcopenia in terms of age, gender, comorbid systemic diseases, disease activity, or medication use. Katchamart et al[36] found that older age and high disease activity were associated with sarcopenia. However, Ngeuleu et al. reported no relationship between disease activity and sarcopenia.[19] While Li et al[37] found an association between DAS28 and sarcopenia, Gumtorntip et al[39] did not find such a correlation. The data on the relationship between disease activity and sarcopenia remain inconsistent. The lack of clear information on when long-term medication use was initiated, steroid usage history, and inflammatory markers in many studies limits the ability to establish definitive conclusions.

The limitation of this study is that the daily mobility and exercise habits of patients were not assessed, which may have influenced the results. Another limitation of the present study is that corticosteroid exposure was not analyzed with respect to treatment dose, duration, or cumulative dosage. The sample size was insufficient to subdivide patients according to disease stage or remission status while maintaining statistical power; therefore, this analysis was not performed. One limitation of this study is the lack of evaluation of muscle echogenicity or elastography in addition to muscle thickness. Combining these qualitative measurements with thickness data in future studies would be groundbreaking. In this study, only patients with RA of more than 1 year's duration were evaluated; therefore, the findings cannot be generalized to patients with early RA. However, its strengths include the presence of a control group and the assessment of RA patients using ultrasonographic muscle mass measurements. The sensitivity and specificity values obtained from the ROC analysis indicate a modest level of diagnostic performance, suggesting limited discriminative ability.

In conclusion, sarcopenia was detected in 37.3% of RA patients and 17.6% of the control group. Variables associated with sarcopenia in patients with RA were disease duration, history of falls, functional status, anthropometric measurements, ultrasound muscle mass measurements, QoL, and physical performance levels. The analysis demonstrated that quadriceps muscle thickness measured by ultrasound was significantly lower in patients with sarcopenia. Based on the findings, ultrasound muscle thickness measurements were evaluated for their optimal threshold in sarcopenia using ROC analysis. Diagnostic cut-off values for sarcopenia were calculated for the thickness of the examined muscles using the ROC curve. For ultrasonographic quadriceps muscle thickness, the optimal cut-off value was 1.72 cm for the right side, with a sensitivity of 57% and a specificity of 57%. For the left quadriceps muscle, the cut-off value was determined as 1.71 cm, yielding a sensitivity of 61% and a specificity of 68%.

Recently, the use of ultrasound to support sarcopenia diagnosis in rheumatologic diseases has become more widespread. Muscle USG is a rapid, safe, and low-cost method used to measure muscle mass and evaluate its architecture. The results suggest that USG may represent a potential alternative to DXA for evaluating muscle mass in patients with RA; however, its diagnostic performance needs to be supported by future studies.

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