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Relationship of Thenar and Hypothenar Muscle Thickness with Clinical Factors, Thigh Muscle Thickness and Physical Performance in Female Patients with Rheumatoid Arthritis

Romatoid Artritli Kadın Hastalarda Tenar ve Hipotenar Kas Kalınlıklarının Klinik Faktörler, Uyluk Kas Kalınlığı ve Fiziksel Performans ile İlişkisi

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Abstract

Objective: The aim of this study was to evaluate hand muscle thickness in patients with rheumatoid arthritis (RA) and to investigate the relationship between muscle thickness and clinical factors and physical performance indicators.
Materials and Methods: This cross-sectional study was conducted with 73 female participants between May 2022 and September 2022 (mean age: 60.83±9.73 years, range: 18-85). Among them, there were 37 RA patients (mean age: 60.8±9.9 years) diagnosed according to the 2010 American College of Rheumatology/European League Against Rheumatism RA classification criteria. The remaining 36 females were age- and sex-matched healthy subjects (mean age: 60.9±9.8 years). Thickness measurements of the thenar, hypothenar, and thigh muscles were obtained with ultrasound for all participants. In both groups, hand grip strength was measured using a hand dynamometer, and lower extremity performance assessments were made using 6-meter timed walk test (6MTWT) and a 5-time sit-to-stand test (5XSST). Disease activity score-28 (DAS-28), RA articular damage score (RA-ADS), and Duruöz Hand scale scores of RA patients were calculated.
Results: Compared with the control group, thenar (p=0.004), hypothenar (p=0.000), and thigh (p=0.006) muscle thickness values were lower in RA patients. The RA group showed lower mean hand grip strength, longer time to complete 5XSST, and slower gait speed on 6MTWT (all p<0.01). Hand muscle thickness was negatively correlated with disease duration, RA-ADS, Duruöz Hand scale, and positively correlated with hand grip strength. Thigh muscle thickness was negatively correlated with age and 5XSST and positively correlated with hand grip strength and gait speed. Thickness measurements from all three muscles were not correlated with DAS-28.
Conclusion: Hand muscle thickness of RA patients is affected by the disease regardless of age. Disease duration, articular damage, and decreased hand functions are closely related to muscle thickness. Low muscle thickness indicates reduced physical performance.
Keywords: Hand function, muscular atrophy, rheumatoid arthritis, sarcopenia, ultrasonography

Öz

Amaç: Bu çalışmada romatoid artritli (RA) hastalarda el kas kalınlıklarının değerlendirilmesi ve kas kalınlıkları ile klinik faktörler ve fiziksel performans göstergelerinin ilişkisinin araştırılması amaçlandı.
Gereç ve Yöntem: Bu kesitsel çalışma Mayıs 2022-Eylül 2022 tarihleri arasında 73 kadın katılımcı ile yapıldı (ortalama yaş: 60,83±9,73 yıl, aralık:18-85). Bunlardan 37'si 2010 American College of Rheumatology/European League Against Rheumatism RA sınıflama kriterlerine göre tanı konulan RA'lı hastalardı (ortalama yaş: 60,8±9,9 yıl). Otuz altı tanesi yaş ve cinsiyet olarak eşleştirilmiş sağlıklı kişiler idi (ortalama yaş: 60,9±9,8 yıl). Tüm katılımcıların ultrason ile tenar, hipotenar ve uyluk kas kalınlıkları ölçüldü. Her iki grupta el dinamometresi ile el grip gücü ölçümü, 6 metre yürüme testi (6MYT) ve 5 tekrarlı otur kalk testi (5XOKT) ile alt ekstremite performans değerlendirmeleri yapıldı. RA'lı hastaların hastalık aktivite skoru-28 (DAS-28), RA artiküler hasar skoru (RA-AHS) ve Duruöz El skalası skorları hesaplandı.
Bulgular: RA'lı hastaların tenar (p=0,004), hipotenar (p=0,000), ve uyluk (p=0,006) kas kalınlıklarının kontrol grubuna göre düşük olduğu görüldü. RA'lı grubun el sıkma güçleri ortalamasının düşük, 5XOKT sürelerinin uzun, 6MYT hızlarının düşük olduğu saptandı (tüm p<0,01). El kas kalınlıkları hastalık süresi, RA-AHS, Duruöz El skalası ile negatif, el grip gücü ile pozitif yönde ilişkili idi. Uyluk kas kalınlıkları ise yaş ve 5XOKT ile negatif, el sıkma gücü ve yürüme hızı ile pozitif yönde ilişkili bulundu. Her üç kas bölgesinden yapılan kalınlık ölçümleri de DAS-28 ile ilişkili değildi.

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Sonuç: RA'lı hastaların el kas kalınlıkları yaştan bağımsız olarak hastalıktan etkilenmektedir. Hastalık süresi, artiküler hasar ve azalmış el fonksiyonları kas kalınlıkları ile yakından ilişkilidir. Düşük kas kalınlıkları fiziksel performansta azalmaya işaret etmektedir.
Anahtar kelimeler: El fonksiyonu, kas atrofisi, romatoid artrit, sarkopeni, ultrasonografi

Introduction

Rheumatoid arthritis (RA) is a chronic, systemic, autoimmune disease characterized by synovial inflammation and bone erosions. RA negatively affects the quality of life by causing structural damage in the joints involved and surrounding tissues (1). Loss of muscle mass is known to occur in patients with RA (2). Elevated cytokine levels and associated inflammation have adverse effects on muscle structure and muscle mass (3). Decreased physical activity due to pain and loss of joint function contributes to considerable reductions in muscle mass and muscle function in RA patients (4,5).

In these patients, the occurrence of sarcopenia defined as generalized loss of skeletal muscle mass beyond critical limits was examined in various aspects. It was demonstrated that 37.1% of patients with RA have sarcopenia, and although some of them did not meet the criteria for sarcopenia, 49% had reduced muscle mass (2). It is known that ultrasound (US) is a very effective method in detecting changes in muscle structure and mass in sarcopenic RA patients. In these patients, US imaging revealed reductions in the thickness of the biceps, vastus medialis and rectus femoris muscles (4). It has been reported that muscle thickness measured by US shows a linear relationship with muscle volume (6). In RA patients, thigh muscle thickness as assessed by US was found to be lower in patients with sarcopenia than in those without sarcopenia. It has been shown that sarcopenia diagnosed using bioelectrical impedance analysis is correlated with muscle thickness values obtained by US (7).

It has been previously shown that vastus lateralis muscle thickness, lower extremity performance, and knee extensor strength are lower in RA patients versus controls (8). In another study, reduced functional surface cross-sectional area of the vastus lateralis muscle was shown in patients with RA compared to controls. In that study, lower limb physical performance and balance of the patients were also poor (9). Parameters such as gait speed, sit-to-stand test, and hand grip strength are among the criteria for the diagnosis of sarcopenia (10).

RA most commonly affects the joints of the hand. In the rheumatoid hand, loss of muscle mass occurs due to the effects of local inflammatory mechanisms as well as disuse as a result of joint pain. However, there are only a few studies examining the amount of muscle loss in the rheumatoid hand and its consequences. In a recent study in which muscle volume was measured with magnetic resonance imaging (MRI), lower hand muscle volume was demonstrated in patients with RA than in patients with psoriatic arthritis (PsA), irrespective of age (11).

A literature search conducted by the authors of the current study did not identify any study that reported on US-detected hand muscle loss in RA. In this study we aimed to examine possible reduction in muscle mass by measuring the thickness of thenar and hypothenar muscles in patients with RA by US, to determine changes in anterior mid-thigh muscle thickness, hand grip strength and lower extremity performance tests, which are also considered as indicators of sarcopenia, and to assess the relationship of hand muscle thickness with clinical parameters and indicators of functional capacity.

Materials and Methods

This cross-sectional, analytical study was conducted with 73 female participants (mean age: 60.83±9.73 years, range:18-85) between May 2022 and September 2022 at the outpatient clinics of the Department of Physical Medicine and Rehabilitation at İstanbul Medeniyet University Faculty of Medicine. Approval for the study was obtained from the Clinical Research Ethics Committee of the İstanbul Medeniyet University Göztepe Training and Research Hospital (decision no: 2022/0259, date: 27.04.2022). Signed written informed consent was obtained from all subjects prior to enrollment in the study. Among the participants, there were 37 patients (mean age: 60.8±9.9 years) diagnosed with RA who were being followed at the outpatient clinics and 36 age- and sex-matched healthy females (mean age: 60.9±9.8 years). Patients diagnosed with RA according to the 2010 American College of Rheumatology/European League Against Rheumatism RA classification criteria were included in the study (12).

Individuals with neurological, malignant, severe psychiatric and/or cardiac diseases, prior orthopedic surgery and those refusing to sign written informed consent were excluded from the study. Age, height, body weight, body mass index (BMI) and dominant hand of the patients were noted. Antirheumatic drug use and disease duration were questioned. The tender joint count and swollen joint count were obtained on physical examination. During the follow-up of the patients, erythrocyte sedimentation rate and C-reactive protein (CRP) values were retrieved from the most recent laboratory tests.

Visual Analog Scale (VAS): For all patients, the severity of pain on movement was assessed using a 0-10 cm VAS.

Disease Activity Score-28 (DAS-28): Disease activity was assessed on the basis of DAS-28 (DAS in 28 joints) scores. The DAS-28 CRP score was calculated using a formula that includes the number of tender joints, the number of swollen joints, patient's global assessment and CRP level (13).

Rheumatoid Arthritis Articular Damage Score (RA-ADS): The RA-ADS was developed to measure irreversible long-term joint damage due to RA. In this scale, 35 joints are individually examined and assigned a score between 0 and 70. Higher scores indicate greater joint damage (14).

Duruöz Hand Scale: Duruöz Hand scale consists of 18 questions used for the assessment of hand functions in patients with RA. It is a simple, useful and reliable tool that questions daily hand activities. Questions are scored on a Likert scale, with scores ranging from 0 to 5 points. Lower scores indicate better functional status (15).

Hand Grip Strength: Hand grip strength was measured on the dominant hand of the patients using the Baseline Hydraulic Hand Dynamometer (Irvington, NY 10533, USA) with 90-kilogram (kg) capacity.

6-meter Timed Walk Test (6MTWT): In order to evaluate the functional capacity of the lower extremities, gait speed was measured using the 6MTWT. For this test, the patient walked on a smooth surface, where 0, 2, 8 and 10 meters were previously marked. Time recording was started at the 2nd meter and ended at the 8th meter. The gait speed measured for 6 meters when the patient walked at a constant pace was taken into account. This way, the potentially confounding effect of acceleration and deceleration in the first 2 meters and last 2 meters was eliminated. Results were recorded in meters/second (m/s). The average of the two velocity values obtained with a 10-minute break between measurements was taken into consideration (16).

Five Times Sit-to-stand Test (5XSST): 5XSST was used to evaluate functional capacity of the lower extremities. This test measures the time in seconds taken to stand five times from a chair (17).

Ultrasonographic Assessment: Thenar and hypothenar muscle thickness and mid-thigh muscle thickness of the patients were measured using US on the dominant side. Measurements were obtained by a physiatrist with 10 years of experience in musculoskeletal US. DC-T6 (Mindray, China) US device with a 5-10 mHz linear probe were used for the measurements.

Hand muscle thickness measurements were performed with the patient in the supine position, forearm supinated, wrist and fingers in neutral position, and the back of the hand contacting the examination table. For the measurement of thenar muscle thickness, the probe was placed longitudinally over the thenar area to visualize the first metacarpal bone (18). The distance between the fascia and the metacarpal bone was recorded as the thenar muscle thickness (Figure 1). For the measurement of hypothenar muscle thickness, the probe was placed longitudinally over the hypothenar area, parallel to the fifth metacarpal bone. The distance between the fascia and the metacarpal bone was measured and recorded (Figure 2).

Thigh muscle thickness was measured with the patient lying in the supine position with the knee extended. The probe was placed in the transverse plane over the anterior thigh of the dominant side, at the midpoint between the spina iliaca anterior superior and the upper border of the patella (19). During muscle thickness measurements, care was taken not to apply pressure in order to avoid depression of the skin surface. The distance from the beginning of the fascia of the rectus femoris muscle to the femur was recorded as the mid-thigh muscle thickness (Figure 3).

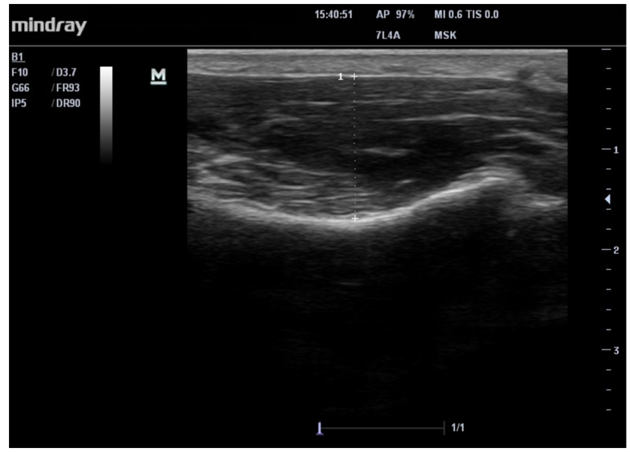

Figure 1. Thenar muscle thickness as measured by ultrasound

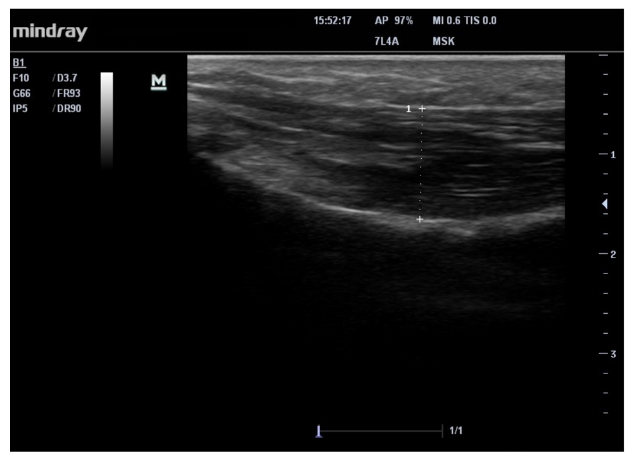

Figure 2. Hypothenar muscle thickness as measured by ultrasound

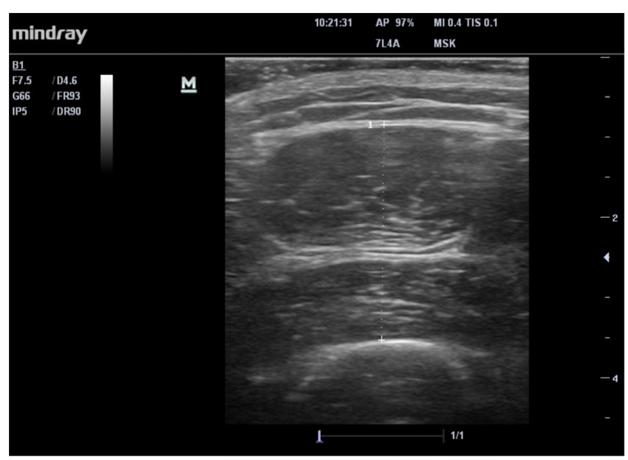

Figure 3. Anterior mid-thigh muscle thickness as measured by ultrasound

Statistical Analysis

SPSS (Statistical Package for Social Sciences) for Windows, version 22.0 was used for statistical analysis of the study data. In addition to descriptive statistics (mean, median, standard deviation, minimum-maximum), comparisons between the groups were made using Student's t-test for normally distributed numerical data, and Mann-Whitney U test for non-normally distributed numerical data. Relationships between muscle thickness and normally distributed variables were analyzed using Pearson correlation analysis, and correlations between non-normally distributed variables were examined with Spearman correlation analysis. The results were considered significant at the p<0.05 level with a 95% confidence interval. Power analysis was performed using the G*Power software to determine the sample size. The effect size for hypothenar muscle thickness was estimated at 0.79, based on preliminary data from 15 patients and 15 controls. Assuming alpha =0.05 and 1-beta =0.90, it was calculated that 35 individuals per group would be needed. Intraclass correlation coefficients were calculated to evaluate intra-rater reliability for US measurements of muscle thickness.

Results

The two groups did not differ in terms of mean age and BMI. The mean age was 60.8±9.9 years in the RA group and 60.9±9.8 years in the control group (p=0.964). The mean BMI of the RA patient group (29.2±4.5 kg/m^2) was similar to that of control group (28.3±4.6 kg/m^2) (p=0.368). Twenty four patients were receiving biological disease-modifying antirheumatic drugs (DMARDs) and 13 patients were using synthetic DMARDs. The median disease duration was 18 years (minimum: 3-maximum: 30). The mean hand grip strength of the RA group (15.8±4.7 kg) was significantly lower compared to the control group (20.0±3.7 kg) (p<0.001). Longer 5XSST times and slower gait speed (6MTWT) were observed in RA patients than in the control group (Table 1).

Table 1. Characteristics of rheumatoid arthritis and control groups

	RA group	Control group	p-value
Age (years, X±SD)	60.8±9.9	60.9±9.8	0.964
BMI (kg/m^2, X±SD)	29.2±4.5	28.3±4.6	0.368
Grip strength (kg, X±SD)	15.8±4.7	20.0±3.7	0.000**
5XSST (s, X±SD)	18.1±4.4	11.3±3.0	0.000**
6MTWT (m/s, X±SD)	0.8±0.2	1.1±0.5	0.002**
DAS-28 (X±SD)	3.8±1.2	-	-
Duruöz Hand scale	10 (0-72)[a]	-	-
RA-ADS	3 (0-33)[a]	-	-
Disease duration, years	18 (3-30)[a]	-	-
Treatment, n (%)			
Synthetic DMARDs	13 (35.1%)	-	-
Biological DMARDs	24 (64.9%)	-	-

**p<0.01, [a]Median (minimum-maximum). BMI: Body mass index, SD: Standard deviation, 5XSST: Five times Sit-to-stand test, 6MTWT: 6-meter timed walk test, DAS-28: Disease activity score-28, RA-ADS: Rheumatoid arthritis articular damage score, DMARDs: Disease-modifying antirheumatic drugs, RA: Rheumatoid arthritis

Comparisons of thenar, hypothenar and thigh muscle thickness values of the two groups are presented in Table 2. Measurements from all three regions showed reduced muscle thickness in the RA group compared to controls (Table 2).

In RA patients, a negative correlation was found between age and anterior mid-thigh muscle thickness (p=0.003). Hand muscle thickness measured from thenar and hypothenar areas was not correlated with age but showed a negative correlation with disease duration (Table 3). Thickness measurements from all three muscles were not correlated with disease activity indicators including VAS and DAS-28. On the other hand, the RA articular damage score was not correlated with thigh muscle thickness, but showed a significant negative correlation with thenar and hypothenar muscle thickness values (Table 3).

In patients with RA, there was a negative correlation between hand muscle thickness and Duruöz Hand index, which was more evident in hypothenar muscles (Table 4). Hand grip strength scores were positively correlated with all muscle thickness measurements. 5XSST times were negatively correlated with thenar and thigh muscle thickness (Table 4). 6MTWT scores showed a positively correlation only with thigh muscle thickness (p=0.005).

Discussion

Rheumatoid hand is one of the leading causes of functional loss in patients with RA. Although hand joints are most commonly affected by the disease, little information is available about the extent of hand muscle atrophy in patients with RA. The data from the present study show that there are significant losses in the thenar and hypothenar muscles in RA patients. Thigh muscle thickness of the patients was also found to be reduced when compared with the controls. As a remarkable finding, while thigh muscle thickness decreased with age, the reduction in hand muscle thickness was not correlated with age. In addition, although thinning of the hand muscles was associated with disease duration, there was no such correlation with the thickness of the thigh muscle. This suggests that the decrease in the hand muscles begins with the onset of the disease and in the early period, and the loss of thigh muscles becomes more pronounced with the effect of advancing age.

Table 2. Comparison of muscle thickness measurements between the groups

	RA group mean ± SD (mm)	Control group mean ± SD (mm)	p-value
Thenar	13.7±1.0	14.4±1.1	0.004**
Hypothenar	11.5±1.2	12.5±0.9	0.000**
Mid-thigh Mid-thigh	28.7±6.4	32.7±5.6	0.006**

**p<0.01. SD: Standard deviation, RA: Rheumatoid arthritis

Table 3. Relationships between muscle thickness and demographic and clinical parameters in RA patients

		Age	Disease duration	VAS	RA-ADS	DAS-28
Thenar	rho	-0.324	-0.375*	-0.112	-0.447**	-0.131
	p-value	0.050	0.022	0.510	0.005	0.440
Hypothenar	rho	-0.204	-0.383*	-0.256	-0.482**	-0.274
	p-value	0.225	0.019	0.126	0.003	0.101
Thigh	rho	-0.504**	-0.280	0.121	-0.260	0.126
	p-value	0.003	0.093	0.475	0.121	0.459

*Significant at the 0.05 level, **Significant at the 0.01 level; RA: Rheumatoid arthritis, RA-ADS: Rheumatoid arthritis articular damage score, DAS-28: Disease activity score-28, VAS: Visual analog scale

Table 4. Relationships between muscle thickness and physical function parameters in RA patients

		Duruoz index	Grip strength test	5XSST	6MTWT
Thenar	rho	-0.382*	0.525**	-0.384*	0.085
	p-value	0.020	0.001	0.019	0.617
Hypothenar	rho	-0.559**	0.592**	-0.240	0.038
	p-value	0.000	0.000	0.152	0.825
Thigh	rho	-0.303	0.325*	-0.350*	0.454**
	p-value	0.068	0.049	0.034	0.005

*Significant at the 0.05 level, **Significant at the 0.01 level; RA: Rheumatoid arthritis, 5XSST: Five times Sit-to-stand test, 6MTWT: 6-meter timed walk test

Although a limited number of studies are available on muscle atrophy in the rheumatoid hand, there are data supporting our findings. To the best of our knowledge, Friedberger et al.'s (11) study was the first study to objectively evaluate hand muscle wasting in RA patients using imaging modalities. In that study, it was reported that hand muscle volumes measured by MRI were lower in RA patients than in patients with psoriasis and PsA, after the age of 50. In the same study, it was shown that the difference among the three groups of patients disappeared in the 7th and 8th decades because the muscle volume of female patients with psoriasis and PsA decreased gradually with age (11).

In a study of Abe et al. (20), it was found that forearm muscle thickness in the general population decreased significantly after 70 years of age in males and 80 years of age in females compared to younger age groups. Although there is not much data on hand muscles, convincing data exists for lower extremity muscles, showing that muscle wasting starts at an earlier age in patients with RA compared to healthy controls (8). Farrow et al. (21) reported that the decrease in thigh muscle volume started in the early stages of the disease in patients with RA.

In the literature, there are also studies evaluating the reduction in lower limb muscle thickness irrespective of age. In a study by Blum et al. (8), age was found to be correlated with muscle thickness, pennation angle and muscle strength in the control group but not in RA patients. The authors suggested that muscle loss and associated problems occur due to the effects of the disease itself, independent of the aging process in patients with RA (8).

Our findings suggest that muscle thickness is not correlated with DAS-28 and VAS scores, which are indicators of current disease activity. A high articular damage score is associated with low thenar and hypothenar muscle thickness. This reveals the relationship of muscle thickness with the long-term outcomes of high disease activity that continues throughout the course of the disease, rather than current disease activity. Higher Sharp scores have been shown to be associated with lower calf muscle mass in patients with RA (22).

Our study demonstrated that low muscle thickness is associated with functional loss. Reduced hand muscle thickness in both thenar and hypothenar areas is correlated with a decrease in hand grip strength as well as impairment of hand functions as measured by the Duruöz Hand scale. There was no correlation between gait speed (6MTWT) and hand muscle thickness. Reduced thigh muscle thickness resulted in longer time to complete 5XSST, slower gait speed and a decrease in hand grip strength. Data from studies in the general population also demonstrate the relationship between upper and lower extremity muscle thickness and hand grip strength (23). It has been shown that there is a positive correlation between upper and lower limb muscle thickness measured by US and gait speed in patients with RA. This relationship is more pronounced in lower extremity muscles such as the rectus femoris than in the biceps (4). Matschke et al. (9) showed that functional surface cross-sectional area of the vastus lateralis and lower extremity physical performance were lower in RA patients compared to controls. It is known that low muscle mass results in decreased muscle strength in patients with RA (8,21,22).

In recent years, muscle involvement has been increasingly cited among the factors that cause a reduction in physical and functional capacity in RA patients. It has been demonstrated that intramuscular cytokine concentrations are very high in patients with RA and are not correlated with serum cytokine levels (24). Although exercise is generally recommended to patients with RA, there are many questions that remain to be answered, such as which exercise should be prescribed to which area, for how long and at what intensity (5). According to Farrow et al. (21), medical treatment does not affect the ongoing pathological process in the muscles in RA patients. As such, it was recommended that muscle strengthening interventions be included in the treatment approaches for RA (21). In patients with RA, it is important to objectively evaluate the hand, which is an area where physicians and patients mostly avoid exercise due to active joint involvement and pain. Our findings demonstrated that the loss of hand muscles in patients with RA can be evaluated with US. Detection and follow-up of muscle atrophy in patients with RA will contribute to the development of preventive and therapeutic strategies such as exercise, joint protection techniques and use of assistive devices.

Study Limitations

The strength of our study lies in the fact that it is the first study to reveal reduced hand muscle thickness with US and its relationship with functional loss in patients with RA. However, our study has a number of limitations. First, lower limb muscle performance was not evaluated with an objective method such as dynamometer. Secondly, since this was a cross-sectional study, we were not able to demonstrate the rate of muscle loss over a long-term.

Conclusion

The thenar and hypothenar muscle thickness of patients with RA are significantly reduced compared to healthy population. This decrease is correlated with disease duration, but not with age. It seems that muscle loss in the hand starts in the early period with the effect of the disease process. It is possible to detect decreases in muscle thickness with musculoskeletal US examination. Assessment of muscle thickness with US during follow-up of hand involvement, which is often neglected in exercise programs and is one of the leading causes of disability in RA patients, can enable timely intervention with individualized rehabilitation approaches before severe muscle loss occurs.

Ethics

Ethics Committee Approval: Approval for the study was obtained from the Clinical Research Ethics Committee of the İstanbul Medeniyet University Göztepe Training and Research Hospital (decision no: 2022/0259, date: 27.04.2022).

Informed Consent: Signed written informed consent was obtained from all subjects prior to enrollment in the study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: E.M., N.M., Design: E.M., Data Collection or Processing: E.M., N.M., Analysis or Interpretation: E.M., Literature Search: E.M., N.M., Writing: E.M., N.M.

Conflict of Interest: No conflict of interest was declared by the authors.

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