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Muscle ultrasound in Spondyloarthritis patients receiving biologic disease-modifying anti-rheumatic drugs early in treatment

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ABSTRACT

Objective: This study evaluated muscle ultrasound in spondyloarthritis (SpA) patients receiving biologic disease-modifying anti-rheumatic drugs (b-DMARDs) early in treatment.

Methods: A prospective study was conducted with 110 b-DMARD-naive SpA patients. The baseline and control muscle strength, physical performance tests, ultrasonographic muscle parameters, and disease activity scores of 67 controlled patients were examined.

Results: During the follow-up period, there were significant improvements in the thickness of the gastrocnemius medialis (GM) muscle ($p<0.001$), the length of the GM fascicle ($p=0.031$), the thickness of the rectus femoris (RF) muscle ($p<0.001$), the cross-sectional area of the RF (RFCSA) muscle ($p<0.001$), the thickness of the rectus abdominis (RA) muscle ($p<0.001$), the thickness of the transverse abdominis (TA) muscle ($p=0.004$), and the thickness of the external oblique (EO) muscle ($p=0.042$). Besides, ASDAS-CRP scores were related to GM muscle thickness, RFCSA, and TA muscle thickness percent changes in patients whose disease activity regressed from high to moderate (respectively; $p=0.030$, $p=0.040$, $p=0.002$).

Conclusion: Muscle ultrasound examination can show muscle mass improvement in SpA patients during treatment.

Keywords: DMARDs, muscle ultrasonography, outcome measures, spondyloarthritis

INTRODUCTION

Spondyloarthritis (SpA) is a group of chronic inflammatory disorders that includes ankylosing spondylitis (AS), reactive arthritis, psoriasis-related arthritis (PsA), and inflammatory bowel disease-related arthritis.[1] The prevalence of sarcopenia, a condition characterized by decreased muscle strength, muscle mass, and physical performance, ranges from 13.7% to 34.3% in patients with SpA.[2,3] The major reason for muscle strength and mass loss is proinflammatory cytokines such as Interleukin-6 (IL-6), Interleukin-1B (IL-1B), and tumor necrosis factor-a (TNF-a), which increase in the case of chronic inflammation, and this results in reduced physical performance. In particular, TNF-a causes decreased protein synthesis, inhibition of muscle regeneration, and apoptosis of type I and type II muscle fibers.[4,5] The risk of sarcopenia in SpA patients increases with the addition of decreased physical activity to the chronic inflammation state, and it is related to a poor prognosis.[6] It has been shown that the higher the disease activity, the greater the muscle loss.[7] But it is still unclear whether this muscle decrease is regional or systemic and the time of onset of muscle loss.

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Muscle evaluation with ultrasonography (USG) is a current issue, and since it does not cause radiation exposure, it provides superiority to other methods.[8] According to the guidelines, USG is among the methods that can be used in the diagnosis of sarcopenia in various chronic diseases.[9] However, the use of USG in studies aimed at evaluating muscle in rheumatological diseases is very scarce.

The present study aimed to assess changes in muscle strength, physical performance, and muscle quantity as measured by USG in SpA patients receiving biologic disease-modifying anti-rheumatic drugs (b-DMARDs) in the early stages of treatment.

METHODS

Study design

A prospective study was conducted in a tertiary care center.

Study Population

The study included 110 b-DMARD-naive patients. Patients were started on b-DMARD because they had active SpA (BASDAI score >5 or expert judgement). The b-DMARD treatment was started in patients deemed necessary by the physician according to disease activity and the assesment of spondyloarthritis international society (ASAS) criteria.[10] The number of patients on the control visit was 67. A flow-chart of reasons for failing to perform a second assessment was shown in Figure 1.

Disease Activity Assessments

The data was collected from patients who entered the TReasure database.[11] TReasure methodolgy was previously defined in short, these data are recorded at the beginning of treatment and on the first check-up visit. The clinical activity and severity of the disease were evaluated by, the Bath AS Disease Activity Index (BASDAI)[12,13], Bath AS Functional Index (BASFI)[14,15], Bath Ankylosing Spondylitis Metrology Index (BASMI)[16], VAS (visual analog scale) global-physician assessment, VAS global-patient assessment, VAS for global pain, VAS fatigue[17], Health Assessment Questionnaire-Disability Index (HAQ-DI)[18], Ankylosing Spondylitis Disease Activity Score-ESR (ASDAS-ESR), Ankylosing Spondylitis Disease Activity Score-CRP (ASDAS-CRP) before treatment initiation and at the first visit.[19] ASDAS-CRP cut-offs for clinically important improvement scores were a change of ≥1.1 units or a control ASDAS-CRP score <2.[20]

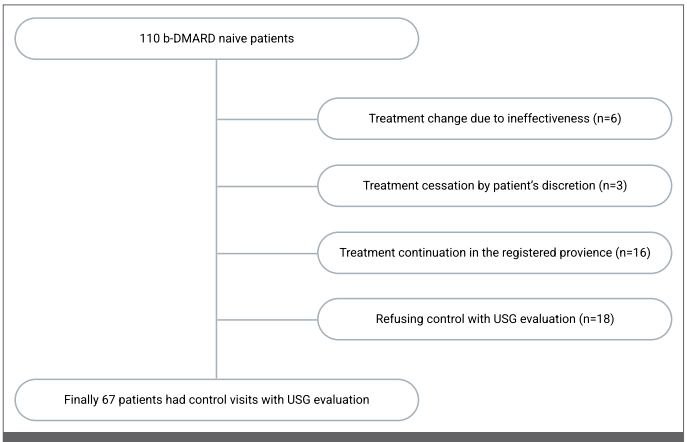

Figure 1. Flow-chart of reasons for failing to perform a second assessment
b-DMARD: Biologic disease-modifying antirheumatic drugs, USG: Ultrasound

Physical Parameters

Physical parameters were assessed by body mass index (BMI), waist circumference, and hip circumference. Height and weight measurements were made with the same calibrated device. The waist circumference was measured at the umbilicus, while the hip circumference was measured at the anterior superior iliac spine.

Muscle strength and physical performance tests

The handgrip strength test (HGST), and sit-to-stand test (SST) were performed for muscle strength evaluation. Physical performance was evaluated with the 4-meter walking test, gait speed, and timed up and go test (TUG). Sarcopenia was screened with the SARC-F test. The HGST was performed via the Takei (TKK-5401) digital hand grip strength dynamometer with the patient in a sitting position with the elbow at 90 degrees.[9] The SST is performed with the patient's arms crossed in front of his/her chest and his/her back supported by the back of the chair, sitting and standing five times as quickly as he/she can.[9] Gait speed was measured using the 4-meter usual gait speed (m/s).[9] The TUG test was evaluated as standing up, walking for 3 m, turning around, and sitting back.[21] For the SARC-F test, the patient was asked 5 questions, such as difficulty carrying a weight of 5 kg for lack of strength, difficulty walking across a room, difficulty getting up from a chair, difficulty climbing 10 flights of

Main Points

- Muscle evaluation is crucial as it closely concerns the physical capacity, and physical dependency in spondyloarthritis patients.
- Muscle improvement can be followed by a non-invasive method such as ultrasonography during the course of treatment.
- Controlling inflammatory activity in SpA patients with b-DMARD treatment may also have a positive effect on muscle mass.

stairs, and experiencing a fall in the last year. Each of the self-reported parameters was given a minimum and a maximum score of 0 and 2 (0=none, 2=a lot, use aids, or be unable), and the highest was evaluated as 10. Scores of 4 and above were considered significant for sarcopenia screening.[22,23] For evaluating muscle strength and physical performance test improvement, the difference between control and baseline assessments was examined.

Ultrasonographic assessments

For ultrasonographic assessments, gastrocnemius medialis (GM) muscle thickness, gastrocinemius medialis (GM) fascicle length, gastrocinemius medialis (GM) pennation angle, rectus femoris (RF) muscle thickness, rectus femoris cross-sectional area (RFCSA), rectus abdominis (RA) muscle thickness, transverse abdominis (TA) muscle thickness, internal oblique (IO) muscle thickness, and external oblique (EO) muscle thickness were measured by the same 3-years experienced physician by using a 8–10 MHz linear probe of 5 cm width (LOG˙ IQ 200 PRO, General Electrics Medical Systems). For muscle thickness, transversal images of the distance between the superficial and deep fascia at the widest distance were captured for the RF thickness from the midpoint between the anterior superior iliac spine and the proximal edge of the patella in the neutral, supine position, and the most bulky area of the medial head for GM in the prone position. In the longitudinal ultrasound image, the pennation angle (PA) was determined between muscle fibers and the deep fascia of the muscle. The length of the fascicular path between the fascicle's insertions into the superficial and deep aponeuroses was characterized as fascicle length (FL). The RF cross-sectional area was defined as the area of a muscle's cross-section perpendicular to its longitudinal axis. The images of the abdomen muscles were obtained at the end of a normal expiration while the patient was supine, at 2 cm lateral to the umbilicus for the RA, and at the midpoint between the iliac crest and the 12th costal cartilage for the EO, IO, and TA.[24-26]

Intervention

All patients were treated according to their doctor's orders, and therapies were continued or discontinued in accordance with our rheumatology department's standard operating procedures. Patients were treated with adalimumab (40 mg every 2 weeks), certolizumab (400 mg every 2 weeks (maintenance dose 200 mg every 2 weeks), etanercept (50 mg weekly), infliximab (3 or 5 mg/kg/infusion at weeks 0, 2, 6, and then infusions every 6 or 8 weeks), and secukinumab (300 mg weekly (maintenance dose 300 mg monthly)).

Statistical analyses

Statistical analyses were also performed on 67 patients with control visits. SPSS software version 25 was used for statistical analysis. Histograms, probability plots, and analytic procedures (Kolmogorov-Simirnov/Shapiro-Wilk's test) were used to evaluate if the variables were normally distributed. For normally distributed data, descriptive analyses were given using mean±standard deviation, and for non-normally distributed variables, median (IQR). The paired sample student T test was used to compare normally distributed variables before and after treatment; the Wilcoxon test was used for non-normally distributed variables. Physical parameters, muscle strength, physical performance tests, and ultrasonographic parameter changes were defined as differences between baseline values and control values. Besides, muscle improvement was evaluated as a percent change. Partial correlation analyses were performed to investigate the associations between baseline disease activity scores and physical parameters, muscle strength, physical performance tests. Correlation analyses were adjusted according to baseline BMI. A 5% type-1 error level was used to infer statistical significance.

Ethical approval

The clinical research ethics committee and TİTCK (Turkish pharmaceutical and medical device agency) (2023/04-05 (KA-21150)) approved the study. All participants provided verbal and written informed consent. The Helsinki Declaration was followed by the study protocol.

RESULTS

Patient characteristics

Of the total 110 patients included in the study, 67 had control visits. The mean age of the study population was 43.8±11.1 years, and 68 (61.8%) of them were female. The median disease duration was 3.8 (1.5) years. The median follow-up time was 3.9 (1.6) months. The demographic characteristics and disease activity scores of patients with and without control visits were shown in Table 1.

Laboratory parameters before and after b-DMARD treatment

Erythrocyte sedimentation rate (ESR) (11 (18.5) mm/h vs 5 (10.7) mm/h), CRP levels (0.91 (2.20) mg/dl vs 0.40 (0.49) mg/dl), lymphocyte percentage (31.0±7.0 vs 35.2±9.1), and neutrophil percentage (58.9±8.0 vs 53.5±11.2) were significantly different ($p<0.001$). The white blood cell (WBC) count, hemoglobin level, and platelet count were not statistically different.

Physical parameters before and after b-DMARD treatment

The baseline BMI of 67 patients was 25.4±4.3 kg/m², waist circumference was 88.5±9.9 cm, and hip circumference was 100.3±11.6 cm. In the control visits, there was only

Table 1. Baseline characteristics of participants

Characteristics	All participants (n=110)	Patients with control visits (n=67)	Patients without control visits (n=43)	p value
Age (years)	43.8±11.1	44.8±10.6	42.1±11.8	0.223
Female gender (n (%))	68 (61.8)	43 (64.1)	25 (58.1)	0.521
Disease duration (years)	3.8 (1.5)	3.9 (1.6)	3.7 (0.9)	0.880
Spondyloarthritis subgroup (n (%))				
Axial involvement	68 (61.8)	39 (58.2)	29 (67.4)	0.330
Peripheral involvement	42 (38.1)	28 (41.7)	14 (32.5)	0.330
Previous or current cs-DMARD treatments (n (%))				
Sulfasalazine	57 (51.8)	35 (52.2)	22 (51.1)	0.571
Methotrexate	32 (29)	20 (29.8)	12 (27.9)	0.782
b-DMARD treatments (n (%))				
Anti-TNFs				
Adalimumab	69 (62.7)	44 (65.6)	25 (58.1)	0.743
Certolizumab	21 (19)	9 (13.4)	12 (27.9)	0.010
Etanercept	7 (6.3)	6 (8.9)	1 (2.3)	0.240
Infliximab	2 (1.8)	2 (2.9)	-	N/A
Anti-IL17				
Secukinumab	10 (9)	8 (11.9)	2 (4.6)	0.290
Disease activity parameters				
BASDAI	5.5±2.0	5.5±2.1	5.4±1.7	0.871
BASFI	5.0 (3.6)	5.0 (3.9)	4.8 (3.5)	0.500
BASMI	1.7 (0.9)	1.8 (1.0)	1.4 (1.1)	**0.010**
VAS_global_physician	60 (20)	60 (20)	60 (20)	0.830
VAS_global_patient	70 (22.5)	70 (25)	70 (20)	0.852
VAS_pain	80 (20)	80 (20)	80 (10)	**0.040**
VAS_fatigue	70 (30)	70 (30)	70 (30)	0.760
HAQ-DI	0.7 (0.7)	0.8 (0.7)	0.5 (0.7)	0.233
ASDAS_ESR	2.7 (1.2)	2.9 (1.3)	2.6 (0.8)	0.261
ASDAS_CRP	3.1 (1.2)	3.2 (1.2)	3.1 (1.0)	0.380

ASDAS-CRP: Ankylosing Spondylitis Disease Activity Score-CRP, ASDAS-ESR: Ankylosing Spondylitis Disease Activity Score-ESR, BASDAI: Bath AS Disease Activity Index, BASFI: Bath AS Functional Index, BASMI: Bath Ankylosing Spondylitis Metrology Index, b-DMARD: Biologic disease-modifying antirheumatic drugs, cs-DMARD: Conventional synthetic disease-modifying antirheumatic drugs, HAQ-DI: Health Assessment Questionnaire-Disability Index, VAS: Visual analog scale.
Bold values indicate statistical significance.

a significant decrease in hip circumference, with a mean value of 98.3±9.9 cm (p=0.007).

Muscle strength and physical performance tests before and after b-DMARD treatment

The HGST, 4-m walking test, gait speed, and TUG test were not statistically different (respectively; p=0.210, p=0.700, p=0.880, p=0.820). The SST and SARC-F scores were significantly different (respectively; p=0.001, p<0.001) (Table 2).

Muscle changes before and after b-DMARD treatment

There were significant differences in terms of GM muscle thickness (p<0.001), GM fascicle length (p=0.031), RF muscle thickness (p<0.001), RFCSA (p<0.001), RA muscle thickness (p<0.001), TA muscle thickness (p=0.004), EO muscle thickness (p=0.042) (Table 2).

Correlations between baseline disease activity scores and muscle strength, physical parameters, and physical performance tests

The SARC-F score change was correlated with BASFI (r=-0.48), VAS-pain (r=-0.72), and HAQ-DI scores (r=-0.46) (Table 3).

Table 2. Baseline and control muscle strength and physical performance tests and ultrasonographic parameters

	Baseline	Control	p value
Muscle strength and physical performance tests			
HGST (kg)	23.7 (13.1)	26.8 (16.8)	0.210
4-m walking test (sec)	3.41 (0.52)	3.48 (0.88)	0.700
Gait Speed (m/sec)	1.17 (0.17)	1.14 (0.30)	0.880
TUG (sec)	7.89 (2.39)	7.53 (1.99)	0.820
SST (sec)	12.57 (6.47)	11.66 (3.65)	**0.001**
SARC-F scores	3 (4)	0 (2)	**<0.001**
Ultrasonographic parameters			
GM MT (mm)	14.02±3.06	17.87±3.10	**<0.001**
GM FL (mm)	28.53±5.32	31.20 (5.53)	**0.031**
GM PA (°)	25±3.31	25.5±4.80	0.251
RF MT (mm)	17.42±3.30	20.22±3.42	**<0.001**
RFCSA (cm^2)	6.64 (2.44)	8.47±2.30	**<0.001**
RA MT (mm)	8.54±1.48	9.07±1.93	**<0.001**
TA MT (mm)	2.80 (1.20)	3.50 (1.23)	**0.004**
IO MT (mm)	6.87±1.26	7.25 (2.40)	0.612
EO MT (mm)	3.39±1.00	3.40 (1.55)	**0.042**

EO MT: External Oblique Muscle Thickness, GM FL: Gastrocnemius Medialis Fascicle Length, GM MT: Gastrocnemius Medialis Muscle Thickness, GM PA: Gastrocnemius Medialis Pennation Angle, HGST: Hand Grip Strength test, IO MT: Internal Oblique Muscle Thickness, RA MT: Rectus Abdominis Muscle Thickness, RFCSA: Rectus Femoris Cross Sectional Area, RF MT: Rectus Femoris Muscle Thickness, SST:Sit-to-stand test, TA MT: Transverse Abdominis Muscle Thickness, TUG: Time up and Go.
Bold values indicate statistical significance.

Table 3. Spearman's correlation coefficients of baseline disease activity scores and muscle strength and physical performance tests differences after treatment with adjustment of BMI

	HGST	4-m walking test	Gait speed	TUG	SST	SARC-F scores
BASDAI	-0.29	0.19	-0.16	0.05	-0.12	-0.40
BASFI	-0.34	-0.06	0.05	0.02	-0.15	-0.48*
BASMI	-0.43	-0.15	-0.009	0.10	-0.26	-0.35
VAS_global_physician	-0.37	-0.01	-0.06	0.07	-0.17	-0.27
VAS_global_patient	-0.26	0.01	-0.07	-0.11	-0.28	-0.22
VAS_pain	-0.13	0.16	-0.24	0.09	-0.01	-0.72**
VAS_fatigue	-0.28	-0.01	0.05	-0.01	-0.24	0.02
HAQ-DI	-0.19	-0.22	0.26	-0.03	-0.02	-0.46*
ASDAS_ESR	-0.12	-0.04	0.10	0.10	-0.01	-0.08
ASDAS_CRP	0.01	0.02	0.02	0.06	-0.01	0.02

ASDAS-CRP: Ankylosing Spondylitis Disease Activity Score-CRP, ASDAS-ESR: Ankylosing Spondylitis Disease Activity Score-ESR, BASDAI: Bath AS Disease Activity Index, BASFI: Bath AS Functional Index, BASMI: Bath Ankylosing Spondylitis Metrology Index, HAQ-DI: Health Assessment Questionnaire-Disability Index, HGST: Hand Grip Strength test, SST:Sit-to-stand test, TUG: Time up and Go, VAS: Visual analog scale.
BMI adjusted partial correlations, *indicates $p<0.05$, ** indicates $p<0.001$

Comparison of physical performance test differences, percent changes of ultrasonographic measurements, and treatment responses according to ASDAS-CRP scores

When the patients were grouped according to a decrease of more than 1.1 units in ASDAS-CRP scores, there was no difference between the change in muscle strength and physical performance tests, whereas the percent change of only the transverse abdominis muscle thickness in ultrasonographic measurements was greater in the treatment-responsive group (p=0.030). When the patients were grouped as control ASDAS-CRP values below 2, there was no difference in the change in muscle strength and physical performance tests, whereas there was a significant difference in terms of the percent change of GM muscle thickness, RFCSA, and TA muscle thickness (respectively; p=0.030, p=0.040, p=0.002) (Table 4).

DISCUSSION

In this prospective study of SpA patients receiving b-DMARD, we found that GM muscle thickness, GM fascicle length, RF muscle thickness, RFCSA, RA muscle thickness, TA muscle thickness, and EO muscle thickness all increased significantly in the early stages of treatment. Besides, significant improvement was observed in the disease activity scores, SST, and SARC-F scores during treatment. We also showed the correlation between basal disease activity scores (BASDAI, VAS_global, ASDAS-ESR, and ASDAS-CRP) and the change in SARC-F scores. When the treatment response was evaluated according to the ASDAS-CRP scores, we found that the percentage changes in GM muscle thickness, RFCSA, and TA muscle thickness were better in the treatment-responsive group.

Sarcopenia is defined as low muscle mass associated with low skeletal muscle strength and/or low physical performance by the European Working Group on Sarcopenia in Older People (EWGSOP) criteria.[9] Although sarcopenia was previously considered to be only an age-related condition, it has been shown in the current approach that chronic inflammation, nutritional deficiency, or physical inactivity may also cause sarcopenia. This condition is related to physical dependence, poor

Table 4. Comparison of muscle strength and physical performance tests differences, percent changes of ultrasonographic measurements and treatment responses according to ASDAS-CRP scores

	ASDAS-CRP minimal clinical improvement (≥1.1 decline)			Moderate and/or low disease activity regarding to ASDAS-CRP score (< 2)		
	Yes (n=26)	No (n=38)	p value	Yes (n=24)	No (n=40)	p value
Difference between baseline assessments and control assessments						
HGST (kg)	1.6 (8.5)	0.5 (8.6)	0.570	0.00 (9.5)	0.8 (6.7)	N/A
4-m walking test (sec)	0.05 (0.83)	0.17 (1.11)	0.120	-0.11 (0.74)	0.17 (1.13)	0.353
Gait Speed (m/sec)	0.00 (0.25)	-0.03 (0.38)	N/A	0.02 (0.23)	-0.02 (0.35)	0.351
TUG (sec)	-0.37 (2.13)	0.58 (2.15)	0.300	-0.37 (2.13)	0.71 (2.40)	0.491
SST (sec)	-1.30 (3.00)	-1.28 (5.89)	0.900	-1.68 (3.06)	-1.13 (5.70)	0.612
SARC-F scores	-2.0 (3.0)	-1.0 (1.0)	0.160	-1.0 (3.0)	-1.0 (2.0)	0.340
Percent changes of muscle measurements						
GM MT (mm)	17.83 (23.43)	13.55 (18.53)	0.670	27.08 (23.51)	13.17 (15.20)	**0.030**
GM FL (mm)	6.04 (29.92)	6.63 (40.00)	0.630	13.84 (44.75)	0.97 (27.35)	0.343
GM PA (°)	7.29 (22.40)	1.66 (30.70)	0.180	3.83 (28.60)	3.70 (23.53)	0.811
RF MT (mm)	8.97 (11.74)	5.75 (18.31)	0.210	7.91 (8.92)	7.08 (21.49)	0.550
RFCSA (cm²)	16.12 (29.99)	11.79 (27.99)	0.180	18.25 (22.01)	7.73 (25.02)	**0.040**
RA MT (mm)	2.92 (19.21)	8.21 (17.70)	0.190	3.17 (24.3)	7.61 (16.1)	0.911
TA MT (mm)	29.98 (43.90)	8.57 (47.22)	0.030	42.85 (49.08)	6.16 (43.01)	**0.002**
IO MT (mm)	0.00 (23.15)	0.72 (37.80)	N/A	0.75 (25.29)	0.00 (36.01)	N/A
EO MT (mm)	13.63 (46.62)	6.05 (77.23)	0.880	15.15 (61.02)	2.43 (65.96)	0.540

EO MT: External Oblique Muscle Thickness, GM FL: Gastrocnemius Medialis Fascicle Length, GM MT: Gastrocnemius Medialis Muscle Thickness, GM PA: Gastrocnemius Medialis Pennation Angle, HGST: Hand Grip Strength test, IO MT: Internal Oblique Muscle Thickness, RA MT: Rectus Abdominis Muscle Thickness, RFCSA: Rectus Femoris Cross Sectional Area, RF MT: Rectus Femoris Muscle Thickness, TA MT: Transverse Abdominis Muscle Thickness, TUG: Time up and Go, SST:Sit-to-stand test.
* ≥1.1 decline in ASDAS-CRP scores **Control ASDAS-CRP score <2
Bold values indicate statistical significance.

prognosis in many diseases, and an increased risk of mortality.[6] Merle et al. showed that SpA patients with probable sarcopenia had significantly higher BASDAI scores and lower quality of life scores.[27] However, Neto et al. could not show a significant difference between SpA patients and healthy controls in terms of sarcopenia. But they showed reduced physical performance and lower strength in SpA patients.[28] This supports the theory that chronic inflammation causes muscle dysfunction. Although many studies have examined total lean mass (TLM) to define sarcopenia, there are opinions that extremity muscles better reflect total muscle mass in SpA patients. Tekaya et al. emphasized the importance of assessing appendicular lean mass in SpA patients.[29] The fact that 74% of the total muscle mass is in the extremities supports this view. Besides, the presence of syndesmophyte and ankylosis may cause faulty results, especially in total muscle mass measurements made with BIA and DXA.[30] Therefore, regional measurements to be performed with USG in SpA patients seem logical in terms of reflecting total muscle mass.

In studies examining the effect of b-DMARD therapy on muscle mass in rheumatological diseases, the results are inconsistent. The fact that the definition of sarcopenia is not homogenous among the studies (some include only muscle strength and mass, while others include physical performance additionally), body composition analysis using different methods (such as DXA and BIA), and the absence of a control group in most studies are among the reasons for the controversial results. Although a positive effect could not be demonstrated in studies conducted with RA patients until 2020, it was observed that more positive results were obtained in patients followed up with SpA.[31,32] Recent meta-analyses have shown that b-DMARDs significantly improve muscle mass in 64% of SpA patients and 49.3% of RA patients.[29]

Studies evaluating outcomes on muscle strength and physical performance in SpA patients after b-DMARD therapy are very scarce. However, there are few studies on RA patients with conflicting results. Vial et al. demonstrated a significant increase in HGST and a 6-minute walking test in TNFi-receiving RA patients.[33] In another study investigating the efficacy of etanercept in RA patients, no significant improvement was obtained in HGST, gait speed, or SST.[34] Also, no significant HGST change was found in the study of Santo et al. in b-DMARD-receiving RA patients.[35] In our study, significant improvement was observed in the SST and SARC-F tests. Although it did not reach statistical significance, there was an improvement in the HGST and gait speed. This may be due to the short follow-up period.

There are more studies in the literature on muscle quantity measurement in this regard. Briot et al. showed a significant increase in TLM after 1 year in SpA patients receiving infliximab and etanercept with DXA, and they confirmed this result with a larger population and longer follow-up.[36,37] Durnez et al. evaluated the 6-year results with a retrospective observation and showed that adalimumab, etanercept, and infliximab treatment led to a significant increase in TLM measurements made with DXA.[38] In a more recent study, it was shown that TNFi treatment led to a significant increase in fat-free mass index (FFMI) and appendicular skeletal mass (ASM) in 6-month follow-up in SpA patients evaluated with BIA.[32] Hmamouchi et al. followed up on SpA patients treated with TNFi for 2 years and showed an increase in TLM with DXA in the first 6 months, but this increase did not continue in the follow-up.[39] In our study, a significant increase was also observed in GM muscle thickness, GM fascicle length, RF muscle thickness, RFCSA, RA muscle thickness, TA, and EO muscle thickness.

Tekaya et al. showed that skeletal mass index (SMI) and muscle strength or performance were not investigated in SpA patients as sarcopenia outcomes after treatment, and they suggested a comparison of sarcopenia outcomes with disease activity.[29] Santo et al. showed that b-DMARD caused a more significant FFMI and ASM increase in low disease activity in RA patients.[35] In our study, we showed a negative correlation between basal disease activity scores and the change in the SARC-F scores. When evaluated according to ASDAS-CRP responses, significant increases in GM muscle thickness, RFCSA, and TA muscle thickness percent changes were detected in patients whose disease activity regressed from high to moderate.

The strengths of our study are the evaluation of three parameters of sarcopenia: muscle strength and physical performance, in addition to muscle quantity. As recommended in the literature, the evaluation of extremity muscles and examining the relationship between these values and disease activity scores are the advantages of our study. To the best of our knowledge, this is the first study conducted in SpA patients receiving b-DMARD that shows an early and significant increase in muscle quantity in the lower extremities measured by USG.

The limitations of the present study include the absence of a control group. In addition, more precise results can be obtained with analyses with a larger population and longer follow-up in muscle strength and physical performance in the same study design. The short follow-up time and the excessive number of patients dropping out are among the other limitations. The fact that the study period coincides

with the COVID-19 pandemic is one of the major reasons for this. We also failed to identify the term of sarcopenia in the study population because there were no exact cut-off values in this age group in a Turkish population for muscle measurements with USG. Additionally, not examining the effects of nutrition and exercise on muscle parameters is among the limitations of the study.

CONCLUSION

In conclusion, our study showed improvement in muscle mass by ultrasound in SpA patients under b-DMARD treatment. We also showed that this improvement was better in the treatment-responsive group. This emphasizes the importance of controlling inflammatory activity in preventing sarcopenia. However, in order to reach a definite conclusion, this opinion should be supported by longer follow-up in a larger population..

Ethical approval: The study was approved by the Hacettepe University Department of Medicine Clinical Research Ethics Committee (KA-21150 / 4 May, 2023).

Informed consent: Written informed consent was obtained from all patients who participated in this study.

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