Original paper

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Skeletal muscle status in patients with rheumatoid arthritis and its association with disease course

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Abstract

Introduction: Rheumatoid arthritis (RA) is a chronic autoimmune disease that leads to rapid disability. Increased systemic inflammation, limited physical activity, and frequent glucocorticosteroid use in patients with RA can lead to sarcopenia, which is the loss of muscle strength, mass, and sometimes physical performance, thereby worsening the course of the primary disease, reducing productivity, and lowering quality of life. The aim of our study was to assess the state of skeletal muscle in patients with RA and evaluate its relationship with the course of the disease.

Material and methods: The study included 120 patients with RA (women and men) and 30 control group participants. Skeletal muscle status was evaluated according to the criteria of the European Working Group on Sarcopenia in Older People (EWGSOP2), 2019. Skeletal muscle status was determined using dual-energy X-ray absorptiometry. Rheumatoid arthritis activity was evaluated using the Disease Activity Score (DAS28), Clinical Disease Activity Index, and Simplified Disease Activity Index indices. Laboratory studies included measurement of the erythrocyte sedimentation rate and C-reactive protein (CRP).

Results: The state of skeletal muscle was significantly worse in RA patients than in the control group. The most significant correlations were found between the risk of developing sarcopenia according to SARC-F score (which assesses strength, assistance with walking, rising from a chair, climbing stairs, and falls), handgrip strength, chair stand test and appendicular skeletal muscle mass (ASM) on the one hand, and DAS28 values on the other ($r = 0.57$, $r = –0.35$, $r = 0.44$, $r = –0.37$, respectively, $p < 0.05$). In contrast, a lower ASM index was significantly associated with higher CRP levels ($r = –0.37$, $p < 0.05$) and was not associated with patient age or disease duration.

Conclusions: The decrease in handgrip strength and skeletal muscle mass is not associated with the age of patients or disease duration. Instead, the values of all skeletal muscle parameters are associated with disease activity and the radiographic stage of RA.

Key words: rheumatoid arthritis, skeletal muscle, sarcopenia.

Introduction

It is known that the presence of comorbidities may worsen the course of rheumatoid arthritis (RA), increase the number of hospitalizations, and contribute to loss of work capacity [1]. One of the most common comorbid conditions in RA patients is sarcopenia. It is characterised by loss of strength and mass of skeletal muscles and, in severe cases, reduced physical performance [2]. In the general population, sarcopenia occurs mainly in older people, while in RA patients, it ranges from 10.1% to 45.1% regardless of age [2]. The pathogenetic mechanisms of sarcopenia development are complex and mainly related to the pathogenesis of RA. It is known that high levels of pro-inflammatory cytokines such as interleukin-1 (IL-1), interleukin-6 (IL-6), and tumour necrosis factor (TNF) negatively affect muscle metabolism, leading to skeletal muscle loss [3]. The most extensively studied mechanism involves cytokine-mediated activation of nuclear factor κB and the mitogen-activated protein kinase (MAPK)/

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p38 MAPK pathways, which influence the expression of the atrogenes atrogin-1 and muscle RING finger 1 – well-known inducers of muscle atrophy. These factors, in turn, activate proteolysis through the ubiquitin-proteasome system and enhance muscle catabolism [4]. Regarding RA patients, the role of age, acute phase reactant levels, the presence of rheumatoid factor (RF), and RA activity in the development of sarcopenia is known [5, 6]. It was reported that the use of disease-modifying antirheumatic drugs (DMARDs) in the treatment of patients with RA also had a positive effect on the state of skeletal muscles [7]. However, some studies have not found any association with these factors [8]. In addition, due to stiffness and pain, which are the main symptoms of RA, patients have limited ability to perform physical activities, which may further impair the state of the skeletal muscles [9]. According to some data, frequent use of glucocorticosteroids (GCs) may also negatively impact the muscular system, as GCs have a direct catabolic effect and cause muscle protein loss [10, 11].

Therefore, the purpose of our study was to examine the state of skeletal muscles in patients with RA and assess its relationship with the course of the disease.

Material and methods

The study involved 120 patients with RA (22 men and 98 women) with an average age of 55.2 ±11.8 years who were hospitalised at the Rheumatological Department of the University Clinic of the National Pirogov Memorial Medical University, Vinnytsya, Ukraine. The average duration of the disease was 12.0 ±8.3 years. The control group included 30 practically healthy individuals, representative in terms of age and sex. The diagnosis of RA was confirmed according to the criteria of the American College of Rheumatology and the European Alliance of Associations for Rheumatology 2010, as well as the Ukrainian Unified Clinical Protocol For Primary, Secondary (Specialized), and Tertiary (Highly Specialized) Medical Care and Medical Rehabilitation, "Rheumatoid Arthritis" [12]. All patients underwent a complete general clinical examination, which included collection of complaints, medical and life history, physical examination, and anthropometric measurements.

The assessment of inflammatory activity in RA patients was performed using the Disease Activity Score (DAS28: ≤ 2.6 – remission, > 2.6–3. 2 – low activity, > 3.2–5.1– moderate activity, > 5.1 – high activity), the Clinical Disease Activity Index (CDAI: ≤ 2.8 – remission, > 2.8–10 – low activity, > 10–22 – moderate activity > 22 – high activity), and the Simplified Disease Activity Index (SDAI: ≤ 3.3 – remission, > 3.3–11 – low activity, > 11–26 – moderate activity > 26 – high activity).

The radiographic stage of RA was determined using the radiographic method.

The level of C-reactive protein (CRP) was determined using the enzyme-linked immunosorbent assay with the "Ultrasensitive ELISA test system for C-reactive protein" kit (Monocent, Inc., USA, No. EL1-1049) following the manufacturer's instructions.

Skeletal muscle examination was performed in accordance with the recommendations of the European Working Group on Sarcopenia in Older People (EWGSOP2) 2019, which included a questionnaire on the presence of complaints typical of sarcopenia using the SARC-F questionnaire (strength, assistance with walking, rise from a chair, climb stairs, and falls), assessment of skeletal muscle strength, mass and physical performance. Skeletal muscle strength was determined using handgrip dynamometry of the dominant hand and the chair stand test. Decreased skeletal muscle strength was reported when handgrip strength was < 27 kg in men and < 16 kg in women, or when the chair stand test took >15 seconds for both sexes. Skeletal muscle mass was determined using dual-energy X-ray absorptiometry on a Hologic Discovery Wi device (S/N 87227), followed by assessment of appendicular skeletal mass (ASM) and ASM/height^2 (ASM index – ASMI). A decrease in skeletal muscle mass was established at ASM values < 20 kg in men and < 15 kg in women or ASMI values < 7 kg/m^2 in men and < 5.5 kg/m^2 in women. Physical performance was determined using a gait speed test. A decrease in physical performance was determined when the test values were ≤ 0.8 m/s [13].

Statistical analysis

Statistical analysis and data processing were performed using MS Excel and IBM SPSS Statistics 27.0. The results are presented as mean ± standard deviation (mean ± standard deviation). The normality of the distribution of samples was determined using the Shapiro-Wilk test. Two independent samples with normal distribution were compared using Student's *t*-test, and samples with abnormal distribution were compared using the Mann-Whitney *U*-test. Three independent samples were compared using analysis of variance (ANOVA) followed by Tukey's honestly significant difference *post hoc* test for multiple pairwise comparisons. Spearman's correlation analysis (*r*) was used to assess the relationship between variables. Results were considered statistically significant at $p < 0.05$.

Bioethical standards

The study was conducted in accordance with the recommendations of the Declaration of Helsinki and was

Table I. Skeletal muscle parameters in patients with rheumatoid arthritis by sex

	SARC-F (points)	Handgrip strength [kg]	Chair stand test [s]	ASM [g]	ASMI [kg/m^2]	Gait speed [m/s]
Women with RA (n = 98)	1.90 ±1.68*	12.51 ±6.91*	15.38 ±4.83*	18,226.48 ±2,904.20*	6.84 ±1.06*	0.97 ±0.19*
Men with RA (n = 22)	2.00 ±1.60*	23.36 ±10.65	14.25 ±2.41	23,375.73 ±2,747.71	7.80 ±0.72	1.00 ±0.13
All patients (n = 120)	1.92 ±1.66*	14.50 ±8.76*	15.17 ±4.50*	19,170.51 ±3,494.37*	7.02 ±1.07*	0.97 ±0.18*
Control group (n = 30)	0.17 ±0.59	21.37 ±5.89	11.73 ±2.53	21,262.71 ±3,269.27	7.79 ±0.85	1.07 ±0.14

**Significant differences compared to the control group, $p < 0.05$.*
ASM – appendicular skeletal muscle mass, ASMI – appendicular skeletal muscle mass index, RA – rheumatoid arthritis, SARC-F – strength, assistance with walking, rising from a chair, climbing stairs, and falls.

approved by the Ethics Committee of National Pirogov Memorial Medical University, Vinnytsya, Ukraine (protocol No. 2 dated 31 January 2024). All patients signed an informed consent form before any interventions.

Results

The study found that RA patients had significantly worse skeletal muscle status compared to the control group. In particular, the results of the SARC-F questionnaire were significantly higher in both men (2.00 ±1.60 points) and women (1.90 ±1.68 points) with RA compared to the control group (0.17 ±0.59 points, $p < 0.05$), suggesting a higher risk of developing sarcopenia. It was found that the handgrip strength of female patients with RA was 40% lower than in the control group (12.51 ±6.91 kg vs. 21.37 ±5.89 kg, respectively, $p < 0.05$). The results of the chair stand test and gait speed test showed similar trends. A significant difference in these parameters was observed only between female patients with RA and the control group. The densitometric parameters of ASM and ASMI were significantly lower in female RA patients compared to the control group (18,226.48 ±2,904.20 g vs. 21,262.71 ±3,269.27 g and 6.84 ±1.06 kg/m^2 vs. 7.79 ±0.85 kg/m^2, respectively, $p < 0.05$) (Table I).

The analysis of age characteristics showed that the parameters of strength, mass, and physical performance of the skeletal muscles deteriorated with increasing patient age. Thus, patients > 60 years old showed a significant decrease in the chair stand test, ASM, and the gait speed test compared to the groups of patients 45–59 years old and 18–44 years old ($p < 0.05$). The most significant difference was observed in the chair stand test, which was 47% worse in patients over 60 years old compared to those aged 18–44 years (17.53 ±5.18 s vs. 11.89 ±2.29 s, respectively, $p < 0.05$). In contrast, the SARC-F questionnaire points, handgrip strength, and ASMI showed no difference between patients of different age groups, but tended to deteriorate with increasing age.

The analysis of the impact of RA duration on muscle state showed that greater skeletal muscle loss was observed in patients with longer disease duration. Thus, the risk of developing sarcopenia according to the SARC-F questionnaire was 4 times higher in patients with RA duration > 10 years compared to patients with duration < 5 years (2.53 ±1.67 points vs. 0.61 ±0.84 points, $p < 0.05$). Handgrip strength, chair stand test, and gait speed test were the worst in patients with disease duration > 10 years ($p < 0.05$). However, densitometric parameters of skeletal muscle mass (ASM and ASMI) did not differ significantly between patients with different RA durations (Table II).

The study found that seropositive RA was characterised by a more severe decrease in skeletal muscle parameters compared to seronegative RA. Thus, seropositive patients had a 1.7 times higher risk of developing sarcopenia according to SARC-F results, and approximately 15% worse skeletal muscle strength. Moreover, seropositive RA patients had a significantly lower skeletal muscle mass (ASM and ASMI indicators) and physical performance (gait speed test) ($p < 0.05$) (Table III).

The study found that the progression of the radiographic stage of RA was accompanied by an increase in the symptoms of sarcopenia. In particular, patients with radiographic stage IV had the highest risk of developing sarcopenia according to SARC-F results. Handgrip strength and the chair stand test in patients with stage IV compared to patients with radiographic stage I of RA were 10.13 ±7.84 kg vs. 19.36 ±5.89 kg and 19.36 ±5.89 s vs. 11.61 ±2.01 s, respectively ($p < 0.05$), which showed a loss of skeletal muscle strength almost twice as great. Furthermore, in patients with radiographic stage IV compared to patients with stage I, it was found that ASM values were significantly lower by 17% (16,835.07 ±2,141.78 g vs. 20,148.60 ±3,328.45 g, $p < 0.05$), ASMI by 16% (6.27 ±1.04 kg/m^2 vs. 7.43 ±0.64 kg/m^2, $p < 0.05$), and gait speed test by 27% (0.86 ±0.19 m/s vs. 1.18 ±0.20 m/s, $p < 0.05$) (Table IV).

Table II. Skeletal muscle parameters in patients with rheumatoid arthritis by age and disease duration

	SARC-F (points)	Handgrip strength [kg]	Chair stand test [s]	ASM [g]	ASMI [kg/m^2]	Gait speed [m/s]
Depending on the age of the patients						
18–44 years old (n = 21)	1.71 ±1.52	16.62 ±7.40	11.89 ±2.29	19,993.44 ±3,640.81	6.99 ±1.03	1.07 ±0.18
45–59 years old (n = 51)	1.65 ±1.71	15.69 ±10.12	14.31 ±3.21	20,057.84 ±3,717.62	7.19 ±1.08	1.00 ±0.16
≥ 60 years old (n = 48)	2.29 ±1.62	12.31 ±7.33	17.53 ±5.18*#	17,867.68 ±2,771.71*#	6.85 ±1.06	0.97 ±0.18*#
**p < 0.05 – compared to the group aged 18–44 years* *#p < 0.05 – compared to the group aged 45–59 years*						
Depending on disease duration						
< 5 years (n = 23)	0.61 ±0.84	19.09 ±6.87	12.52 ±2.37	20,358.93 ±3,243.79	7.34 ±0.75	1.07 ±0.19
5–10 years (n = 38)	1.76 ±1.53*	13.89 ±8.24	14.54 ±3.97	19,521.57 ±3,387.55	7.00 ±0.96	1.01 ±0.17
> 10 years (n = 59)	2.53 ±1.67*#	13.10 ±9.25*	16.61 ±4.92*	18,481.11 ±3,552.02	6.90 ±1.22	0.91 ±0.17*#

**p < 0.05 – compared to the group aged <5 years*
#p < 0.05 – compared to the group aged 5–10 years
ASM – appendicular skeletal muscle mass, ASMI – appendicular skeletal muscle mass index, SARC-F – strength, assistance with walking, rising from a chair, climbing stairs, and falls.

Table III. Skeletal muscle parameters in patients with rheumatoid arthritis by serological status

Serological status	SARC-F (points)	Handgrip strength [kg]	Chair stand test [s]	ASM [g]	ASMI [kg/m^2]	Gait speed [m/s]
Seronegative (n = 52)	1.37 ±1.27	15.96 ±8.07	14.02 ±4.05	20,264.25 ±2,742.00	7.45 ±0.93	1.02 ±0.19
Seropositive (n = 68)	2.34 ±1.80*	13.38 ±9.16	16.05 ±4.66*	18,334.12 ±3,784.97*	6.69 ±1.06*	0.94 ±0.17*

**p < 0.05 – compared to the seronegative group.*
ASM – appendicular skeletal muscle mass, ASMI – appendicular skeletal muscle mass index, SARC-F – strength, assistance with walking, rising from a chair, climbing stairs, and falls.

The analysis of the relationship between inflammatory activity and skeletal muscle parameters (strength, mass, and physical performance) revealed strong associations.

In particular, RA patients with an erythrocyte sedimentation rate (ESR) level above the median (≥ 18 mm/hour) have a significantly higher risk of developing sarcopenia according to SARC-F, a 29% decrease in handgrip strength (12.20 ±8.80 kg vs. 17.13 ±8.01 kg, $p < 0.05$), and a significant reduction in skeletal muscle mass. The chair stand test and gait speed did not differ significantly, but showed a tendency to worsen at higher ESR levels. Similar changes were observed when assessing the symptoms of sarcopenia depending on the CRP levels. Thus, patients with CRP levels above the median (≥ 10.2 mg/l) had a 2.1 times higher risk of developing sarcopenia according to SARC-F, a 25% decrease in handgrip strength, and a 12% increase in the chair stand test. Moreover, patients with RA and CRP levels ≥ 10.2 mg/l showed a significant decrease in skeletal muscle mass and physical performance. A worse skeletal muscle state is closely associated with increased RA activity according to DAS28, CDAI, and SDAI. Indeed, in the group of patients with high DAS28 activity compared to those with low DAS28 activity, it was found that the risk of developing sarcopenia according to SARC-F was 4.4 times higher at 3.50 ±1.22 points vs. 0.79 ±0.99 points, $p < 0.05$; handgrip strength was half as strong at 9.93 ±11.23 kg vs. 18.91 ±7.16 kg, $p < 0.05$; and the time of the chair stand test was 39% longer at 17.48 ±4.52 s, $p < 0.05$. The ASM, ASMI, and gait speed test were lowest in patients with high DAS28 activity. Similar results were obtained when patients were classified according to CDAI. Thus, all skeletal muscle parameters, except handgrip strength, were significantly worse in patients with high activity compared to those with low activity. However, handgrip strength demonstrated a tendency to decrease

Table IV. Skeletal muscle parameters in patients with rheumatoid arthritis depending on radiographic stage

Stage	SARC-F (points)	Handgrip strength [kg]	Chair stand test [s]	ASM [g]	ASMI [kg/m^2]	Gait speed [m/s]
I (n = 11)	0.27 ±0.47	19.36 ±5.89	11.61 ±2.01	20,148.60 ±3,328.45	7.43 ±0.64	1.18 ±0.20
II (n = 58)	1.67 ±1.56*	16.66 ±8.70	13.69 ±2.76	19,792.70 ±3,629.96	7.10 ±1.06	1.01 ±0.15*
III (n = 35)	2.31 ±1.79*	11.40 ±8.37*#	16.13 ±3.61*#	18,899.67 ±3,428.22	7.09 ±1.09	0.90 ±0.15*#
IV (n = 16)	3.06 ±1.06*#	10.13 ±7.84*#	20.90 ±6.68*#†	16,835.07 ±2,141.78#	6.27 ±1.04*#	0.86 ±0.19*#

**$p < 0.05$ – compared to the stage I group.*
#$p < 0.05$ – compared to the stage II group.
†$p < 0.05$ – compared to the stage III group.
ASM – appendicular skeletal muscle mass, ASMI – appendicular skeletal muscle mass index, SARC-F – strength, assistance with walking, rising from a chair, climbing stairs, and falls.

with increasing CDAI activity. When the parameters were analysed based on activity level according to the SDAI, it was found that only the risk of developing sarcopenia, assessed by the SARC-F, differed significantly between patients with high and low activity levels. The risk of sarcopenia was 4.6 times higher in patients with high activity levels, with a score of 4.29 ±0.76 points compared to 0.92 ±1.04 points in patients with low activity ($p < 0.05$). ASM and ASMI were 21% lower in the group with high activity compared to low activity ($p < 0.05$). However, there was no significant difference in handgrip strength, chair stand test, and gait speed between groups with high and low activity, although there was a trend towards deterioration with increasing SDAI activity (Table V).

Correlation analysis revealed that SARC-F scores ($r = 0.21$), chair stand test performance ($r = 0.42$), ASM ($r = –0.24$), and gait speed ($r = –0.31$) correlated with age of RA patients. A similar trend was observed between disease duration and the results of the SARC-F questionnaire, chair stand test, and gait speed. It was also found that all parameters of skeletal muscle strength, mass, and physical performance correlated with the radiographic stage of RA ($r = –0.23$ to 0.42). In addition, a correlation was observed between skeletal muscle status and higher levels of ESR ($r = –0.28$ to 0.42) and CRP ($r = 0.22$ to 0.45). The strongest positive correlations were found between the disease activity indices (DAS28, CDAI, and SDAI) and SARC-F (from $r = 0.45$ to $r = 0.57$) and the chair stand test ($r = 0.37$–0.44), whereas negative correlations were observed with handgrip strength (r = –0.28–0.35), ASM ($r = –0.28$–0.37), ASMI (r = –0.26–0.36), and gait speed (r = –0.37–0.40) (Table VI).

Discussion

Therefore, this study has established that skeletal muscle parameters, such as strength, mass, and physical performance, were significantly worse in RA patients compared to the control group. In particular, a considerable decrease in skeletal muscle strength was found in RA patients, ranging from 30% to 33%, while the decrease in muscle mass and physical performance did not exceed 10%. Female RA patients showed a significant loss of skeletal muscle mass in all skeletal muscle parameters compared to the control group. In contrast, male RA patients had only a significantly higher risk of developing sarcopenia according to SARC-F compared to the control group. Similar patterns have been observed in the literature. Thus, a study by Doğan et al. [14] found that ASMI was lower in RA patients compared to the control group (5.83 ±0.80 kg/m^2 vs. 7.30 ±1.64 kg/m^2, $p < 0.05$), and according to an analysis by Su et al. [3], RA was associated with low handgrip strength (OR = 1.042, 95% CI: 1.013–1.072) and reduced ASM (OR = 0.979, 95% CI: 0.964–0.995), but was not associated with gait speed. Regarding sex characteristics, Giles et al. [8] found that a higher risk of sarcopenia was observed only in women with RA, but not in men. There are limited data about this topic, which may be the result of the greater prevalence of RA among women than men.

Our results showed that the status of skeletal muscles deteriorated with increasing age in RA patients. The worst results were observed in patients over 60 years old, although only the chair stand test, ASM, and gait speed test were significantly different. This trend is confirmed in numerous scientific studies. In particular, a study by Mochizuki et al. [15] involving 240 RA patients found that patient age was associated with sarcopenia ($p = 0.008$; odds ratio [OR] = 1.08), and a study by Lozada-Mellado et al. [16] involving 165 female RA patients showed that the median age of patients with sarcopenia was 59.5 years (49.8–65.3 years), compared to 50 years in RA patients without sarcopenia (43–59 years; $p = 0.001$). However, the study by Alkan Melikoğlu [17],

Table V. Skeletal muscle parameters in patients with rheumatoid arthritis depending on disease activity

	SARC-F (points)	Handgrip strength [kg]	Chair stand test [s]	ASM [g]	ASMI [kg/m^2]	Gait speed [m/s]
Depending on ESR levels						
ESR < 18 (*n* = 56)	1.36 ±1.46	17.13 ±8.01	14.95 ±5.15	20,108.45 ±3,412.38	7.32 ±0.98	1.01 ±0.18
ESR ≥ 18 (*n* = 64)	2.41 ±1.68*	12.20 ±8.80*	15.37 ±3.87	18,346.12 ±3,379.58*	6.76 ±1.07*	0.94 ±0.18
**p < 0.05 – compared to the ESR < 18 mm/hour group*						
Depending on CRB levels						
CRP < 10.2 (*n* = 59)	1.20 ±1.13	16.66 ±8.09	14.32 ±3.18	20,201.74 ±2,689.05	7.43 ±0.77	1.03 ±0.18
CRP ≥ 10.2 (*n* = 61)	2.61 ±1.80*	12.41 ±8.94*	16.00 ±5.39	18,169.64 ±3,893.50*	6.62 ±1.17*	0.92 ±0.17*
**p < 0.05 – compared to the CRP < 10.2 mg/l group*						
Depending on DAS28						
Low (*n* = 33)	0.79 ±0.99	18.91 ±7.16	12.55 ±2.73	21,093.45 ±2,812.20	7.72 ±0.78	1.07 ±0.20
Moderate (*n* = 73)	2.12 ±1.65*	13.38 ±8.19*	15.92 ±4.66*	18,761.61 ±3,442.14*	6.86 ±1.02*	0.95 ±0.16*
High (*n* = 14)	3.50 ±1.22*#	9.93 ±11.23*	17.48 ±4.52*	16,754.94 ±3,171.21*	6.20 ±1.01*	0.88 ±0.18*
Depending on CDAI						
Low (*n* = 40)	1.03 ±1.17	16.68 ±6.77	13.49 ±2.72	20,270.46 ±2,927.14	7.46 ±0.77	1.05 ±0.20
Moderate (*n* = 68)	2.13 ±1.67*	13.44 ±9.26	15.62 ±4.90*	18,926.29 ±3,605.59	6.87 ±1.10*	0.94 ±0.16*
High (*n* = 12)	3.67 ±1.15*#	13.25 ±10.92	18.22 ±5.00*	16,870.38 ±3,460.04*	6.37 ±1.21*	0.86 ±0.16*
Depending on SDAI						
Low (*n* = 37)	0.92 ±1.04	17.22 ±6.40	13.45 ±2.73	20,368.32 ±2,866.10	7.49 ±0.70	1.07 ±0.20
Moderate (*n* = 76)	2.18 ±1.65*	13.61 ±9.37	15.97 ±5.12*	18,875.81 ±3,608.91	6.89 ±1.14*	0.93 ±0.16*
High (*n* = 7)	4.29 ±0.76*#	9.86 ±9.92	15.66 ±1.72	16,008.76 ±2,904.13*	5.93 ±0.75*#	0.95 ±0.10
**p < 0.05 – compared to the Low group* *#p < 0.05 – compared to the Moderate group*						

ASM – appendicular skeletal muscle mass, ASMI – appendicular skeletal muscle mass index, CDAI – Clinical Disease Activity Index, CRP – C-reactive protein, DAS28 – Disease Activity Score 28, ESR – erythrocyte sedimentation rate, SARC-F – strength, assistance with walking, rising from a chair, climbing stairs, and falls, SDAI – Simplified Disease Activity Index.

which included 40 women with RA, found no association between skeletal muscle status and the age of patients.

The data obtained from our study regarding the association between disease duration and skeletal muscle status are quite different. It has been established that patients with the longest duration of RA have significantly worse skeletal muscle parameters, except for muscle mass. The information in the literature is also controversial. According to a meta-analysis by Beenakker et al. [18], which included data from 71 studies (a total of 10,529 patients with RA), disease duration was significantly associated with a decrease in handgrip strength, which was accompanied by an annual reduction of 0.34 kg at the age of 55.6 years (95% confidence interval, CI: from –0.58 to –0.10). Similar results were observed in the Torii et al. [19] study, among 388 RA patients, which found that disease duration was an independent factor in the development of sarcopenia (OR = 1.06; 95% CI: 1.04–1.09). Also, the study by Kulyk et al. [20] on 138 patients with inflammatory arthritis revealed that sarcopenia was more fre-

Table VI. Correlation between skeletal muscle parameters and the course of the disease

Variable	SARC-F (points)	Handgrip strength [kg]	Chair stand test [s]	ASM [g]	ASMI [kg/m^2]	Gait speed [m/s]
Age	0.21*	–0.19	0.42*	–0.24*	–0.06	–0.31*
Disease duration	0.47*	–0.16	0.33*	–0.16	–0.18	–0.38*
Radiographic stage	0.40*	–0.23*	0.42*	–0.26*	–0.23*	–0.37*
ESR	0.42*	–0.33*	0.29*	–0.35*	–0.31*	–0.28*
CRP	0.45*	–0.25*	0.22*	–0.30*	–0.37*	–0.30*
DAS28	0.57*	–0.35*	0.44*	–0.37*	–0.36*	–0.38*
CDAI	0.45*	–0.28*	0.37*	–0.28*	–0.26*	–0.37*
SDAI	0.48*	–0.30*	0.38*	–0.29*	–0.29*	–0.40*

**Significant correlation.*
ASM – appendicular skeletal muscle mass, ASMI – appendicular skeletal muscle mass index, CDAI – Clinical Disease Activity Index, CRP – C-reactive protein, DAS28 – Disease Activity Score 28, ESR – erythrocyte sedimentation rate, SARC-F – strength, assistance with walking, rising from a chair, climbing stairs, and falls, SDAI – Simplified Disease Activity Index.

quent in patients with earlier onset of disease (OR 0.95; 95% CI: 0.92–0.98, $p = 0.005$). However, according to a study by Bertelle et al. [21], disease duration was not a predictor of sarcopenia development.

We found that seropositive patients had significantly greater skeletal muscle loss than seronegative patients. Currently, there are limited data on the association between serological markers and sarcopenia in RA patients. Thus, a study by Guzmán-Guzmán et al. [22] showed that seropositivity for RF ($p = 0.05$) and anti-citrullinated protein antibodies ($p = 0.03$) was associated mainly with sarcopenic obesity. In contrast, the study by Bertelle et al. [21] found that the presence of RF was not a predictor of sarcopenia, but was associated with a numerically higher sarcopenia prevalence ($p = 0.092$). However, in the study by Müller et al. [23], low ASM was not associated with serological markers in patients with RA.

Various studies have reported the association between radiographic RA stage and sarcopenia, which confirmed our results. Thus, in the CHIKARA observational study, which included 100 RA patients, it was found that the radiographic stage of RA correlated with the presence of sarcopenia ($r = 0.206$, $p = 0.039$), but according to multiple regression analysis, it did not act as an independent predictor of sarcopenia development [24]. However, in a study by Lin et al. [25], among 457 patients with RA, multiple regression analysis showed that ASMI (OR = 0.633, 95% CI: 0.507–0.790, $p < 0.001$) and sarcopenia (OR = 2.154, 95% CI: 1.032–4.497, $p = 0.041$) were associated with the radiographic stage of RA.

Our study established that worse skeletal muscle status was closely associated with higher ESR and CRP levels, as well as higher inflammatory activity according to DAS28, CDAI, and SDAI indices. Other research has also demonstrated a relationship between higher RA activity and worse muscle status. Thus, a review article by Pardali et al. [26] mentioned that various pro-inflammatory markers (the non-specific marker ESR, the acute phase reactant CRP, and the pro-inflammatory cytokines IL-1β, IL-6, and TNF) contributed to muscle tissue loss by disrupting muscle metabolism. According to Munro et al. [27], women with RA showed a significant correlation between reduced ASM and acute phase parameters (ESR $p = 0.016$, CRP $p = 0.003$). In addition, a study by Müller et al. [23] involving 91 patients with early RA found that low ASM was associated with increased ESR (OR = 1.03, CI: 1.002–1.051, $p = 0.03$) and CRP (OR = 1.03, CI: 1.002–1.061, $p = 0.04$) levels. Similar results were obtained by Kulyk et al. [20], who observed that sarcopenia was more frequent in patients with higher ESR (OR = 1.04; 95% CI: 1.01–1.07, $p = 0.005$). An interesting study by van Atteveld et al. [28] showed that in older people without RA, an increased ESR was significantly associated with a decreased gait speed ($\beta = -0.005$; 95% CI: from –0.007 to –0.003), a more extended chair stand test (Ln$\beta = 0.005$; 95% CI: 0.002–0.008), lower handgrip strength ($\beta = -0.126$; 95% CI: from –0.189 to –0.063), and lower skeletal muscle mass ($\beta = -0.179$; 95% CI: from –0.274 to –0.084). In a study by Park et al. [29] involving 294 patients with RA, it was found that patients with comorbid sarcopenia had higher mean DAS28-ESR ($p = 0.014$) and DAS28-CRP ($p = 0.020$) values. Furthermore, multiple regression analysis confirmed a close association between sarcopenia and DAS28-ESR (OR = 4.477, 95% CI: 1.661–12.067, $p = 0.003$) [29]. In contrast, a study by Alkan Melikoğlu [17] showed that ASMI was not correlated with ESR or CRP values, and no association was found between skeletal muscle status and RA activity indices in other studies [5, 14, 30].

Study limitations

This study has some limitations. It was a single-centre study, and the sample size was relatively small. The ma-

jority of RA patients were female, which is explained by the higher prevalence of RA in women. More detailed analysis of sex characteristics requires the group of male patients to be increased. The next limitation is that we did not consider the role of various pharmacological strategies, including the use of GCs and DMARDs, during the statistical analysis.

Conclusions

Rheumatoid arthritis patients had worse skeletal muscle status compared to the control group. Moreover, handgrip strength and skeletal muscle mass were not significantly associated with patient age or disease duration; however, they were associated with radiographic stage of RA (from $r = -0.23$ to $r = 0.42$), activity of the inflammatory process according to DAS28 (from $r = -0.35$ to $r = 0.57$), CDAI (from $r = -0.26$ to $r = 0.45$) and SDAI (from $r = -0.29$ to $r = 0.48$).

Disclosures

Conflict of interest: The authors declare no conflict of interest.

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Data availability: The data that support the findings of this study are available on request from the corresponding author (A.P.).

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