ORIGINAL ARTICLE

Assessment of sarcopenia in female patients with sarcoidosis upon initial diagnosis

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ABSTRACT

Background and aim: There is a substantial body of literature that discusses the potential relationship between sarcopenia and sarcoidosis. This study aimed to evaluate the muscle mass of sarcoidosis patients without any treatment at the time of diagnosis using computed tomography (CT) images.

Methods: This retrospective study included only female patients, as the vast majority of sarcoidosis cases in our dataset were female, and this approach allowed us to minimize gender-related confounding. The sarcoidosis group consisted of newly diagnosed, untreated female patients who underwent abdominal CT as part of their diagnostic work-up. The control group comprised female patients with a comparable age distribution to the sarcoidosis cohort, who presented to the emergency department with non-chronic, unrelated conditions and had no history of chronic illness or medication use known to affect muscle mass. Total skeletal muscle (TSM), skeletal muscle index (SMI), and psoas muscle index (PMI) at the L3 vertebral level were measured using manual segmentation. SMI-based sex-, age-, and BMI-specific thresholds from the literature were used to define sarcopenia.

Results: A total of 168 female patients were evaluated. Sarcoidosis patients were significantly older and shorter than controls. TPM ($p = 0.003$), TSM ($p = 0.027$), SMI ($p = 0.037$), and PMI ($p = 0.001$) values were significantly lower in the sarcoidosis group. However, the prevalence of sarcopenia based on SMI criteria did not significantly differ between groups. Notably, significant muscle mass differences were most evident in the 50–60 age group.

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Conclusions: Our findings suggest that muscle loss may already be present at the time of diagnosis in female sarcoidosis patients, becoming more apparent with age. Further studies with broader populations and prospective designs are needed to clarify the association between sarcoidosis and sarcopenia.

Key words: sarcoidosis, sarcopenia, computed tomography, skeletal muscle index, cross-sectional study

Introduction

Sarcoidosis is a multisystemic disease of unknown etiology, which is characterized by inflammatory activity with the formation of noncaseating granulomas in various organ systems (1). While the precise cause remains unidentified, there are several factors that are believed to potentially contribute to the development of the disease, such as immunological, genetic, and environmental factors and oxidative stress (2, 3). In severe cases, the release of inflammatory mediators causes the derangement of organ physiology and functional impairment. The disease often stabilizes or shows improvement during the first two years, but in some instances, it can worsen and become chronic (4). Due to its potential to affect any organ and system, patients may present with a wide variety of symptoms. The clinical impact of sarcoidosis may vary from an asymptomatic state to a life-threatening condition (5). Most patients typically present with pulmonary, ocular, or cutaneous involvement. Additionally, patients may experience a wide spectrum of general disease symptoms, including fatigue, fever, arthralgia, muscle pain, and general weakness (6, 7). Recent studies have also highlighted the role of small fiber neuropathy in contributing to fatigue, pain, restless legs syndrome, and cognitive dysfunction in sarcoidosis patients (8). Moreover, the presence of circulating autoantibodies has been suggested as a potential biomarker for extrapulmonary involvement and disease activity, further supporting the immunological complexity of the disease (9). In other chronic inflammatory diseases such as inflammatory bowel disease (IBD) and rheumatoid arthritis (RA), skeletal muscle weakness resulting from muscle atrophy (sarcopenia) is recognized as one of the most important causes of these symptoms (10). However, comprehensive data on sarcoidosis patients are currently lacking. Sarcopenia is defined by low levels in three key parameters: muscle strength, muscle quantity/quality, and physical performance. These parameters can serve as severity indicators and may be influenced by systemic diseases with chronic inflammatory processes, such as sarcoidosis (11). Computed tomography (CT)-measured skeletal muscle index (SMI, cm2/m2) and psoas muscle index (PMI, cm2/m2) at the level of the third lumbar vertebrae (L3) have been established as precise and effective indicators of whole-body muscle mass (12). In a study, it was implicated that the prevalence of sarcopenia in the Dutch population with sarcoidosis was 25% (13). Considering that sarcoidosis is a chronic inflammatory disease and corticosteroids are used in its treatment, when necessary, the possibility that muscle loss in patients with sarcoidosis may be a result of chronic inflammatory processes as well as corticosteroid use comes to the fore. This situation brings to mind the question of whether sarcopenia occurs at the time of diagnosis or as a result of treatment. To the best of our knowledge, no study has made this specific distinction. While previous studies have examined muscle mass in sarcoidosis using indirect methods or in later disease stages, our study is the first to assess skeletal muscle volume directly through CT imaging at the time of diagnosis. By doing so, we aimed to explore whether measurable muscle loss is already present in untreated patients, and to examine how age may influence this effect.

Material and Methods

Study population

We conducted a retrospective study and included 86 female patients aged 21-74 who were newly diagnosed

with sarcoidosis. Since our sarcoidosis patient group consists almost entirely of female patients, we excluded 7 male sarcoidosis patients and selected the control group from the female population in order to minimize possible bias. As part of the diagnostic evaluation for suspected sarcoidosis, all patients underwent thoracic and abdominal CT imaging due to presenting clinical symptoms. Only those with available non-contrast abdominal CT scans were included in the study. All patients in the study group were histologically confirmed with sarcoidosis in our affiliated institutions between 2015 and 2022. The control group consisted of female patients with a broadly comparable age distribution to the sarcoidosis cohort, who underwent non-contrast abdominal CT in the emergency department for unrelated clinical indications, using the same imaging protocol and scanner. We chose the control group from emergency patients without any previous medical disease history to minimize people with chronic diseases that could affect muscle mass, as an alternative to sarcoidosis. To minimize confounding, control patients were selected from individuals presenting to the emergency department for non-chronic, non-inflammatory complaints such as renal colic or abdominal pain of unknown origin. Patients with any chronic disease, medication use affecting muscle mass, or acute inflammatory conditions were excluded. In both groups, we excluded patients with various medical conditions that could independently cause changes in muscle mass. Upon evaluation of clinical records, patients with the following conditions were excluded from the study group: medication use [statins (n=9), hormonal therapy (n=4), angiotensin inhibitors (n=12)], advanced orthopedic imbalance and scoliosis (n=13), corticosteroid use for any reason (n=9), spinal disc herniation (n=8), malignancy (n=5), abdominal hernia (n=2) and the presence of neuromuscular and metabolic muscle diseases (n=2) (Figure 1).

This study was approved by the institutional ethics committee. The requirement for informed consent was waived due to the retrospective design and anonymization of patient data.

Biochemical data collection

Serum parameters including WBC, RBC, HGB, MCV, CRP, ESR, neutrophils, lymphocytes, and N/L ratio were retrospectively extracted from electronic medical records and analyzed accordingly.

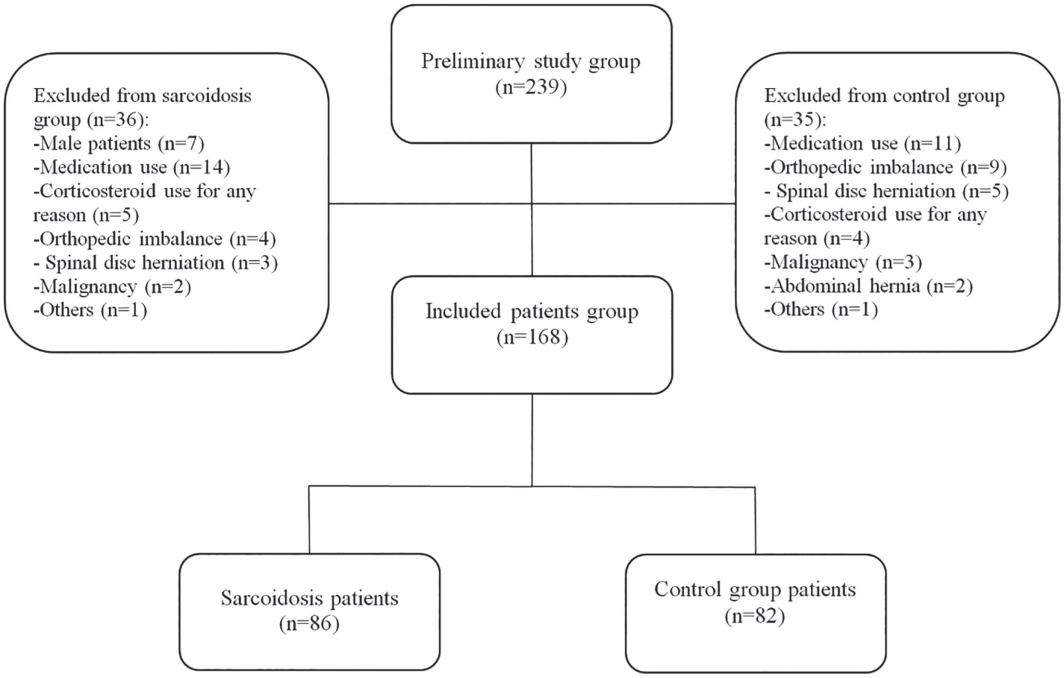

Figure 1. Flow chart illustrating the selection process of study participants. After applying exclusion criteria (e.g., chronic illness, corticosteroid use, incomplete imaging), 86 sarcoidosis patients and 82 controls were included in the final analysis.

Imaging study and analyses

CT scans were obtained using a 128-slice scanner (GE Revolution EVO, GE Healthcare, Waukesha, WI). Sarcoidosis patients underwent non-contrast-enhanced abdominal CT scans as part of their diagnostic work-up with the following parameters: 120 kV, automatic tube current modulation, 0.5-second rotation time, 1.375 pitch, and 2.5 mm slice thickness. Control patients underwent standard-dose abdominal CT scans without intravenous contrast. All images were reviewed at the L3 level. Manual segmentation of skeletal muscles was performed on axial sections by two radiologists with 13 and 8 years of experience in abdominal imaging, respectively, in a double-blind fashion. The average of both measurements was used for further analysis. Muscle areas were measured using attenuation values between -29 and +150 Hounsfield Units. Intermuscular adipose tissue (IMAT) was excluded through manual contouring. The Picture Archiving and Communication System (Extreme PACS, Ankara, Turkey) was used to calculate muscle area (Figure 2).

Total skeletal muscle area (TSM) was obtained by the sum of the areas of both psoas, erector spinae, quadratus lumborum, transversus abdominis, external and internal oblique muscles, as well as rectus abdominis muscles visualized in the L3 vertebral plane. Total Psoas Muscle area (TPM) was obtained only by the sum of both psoas muscle areas in the same plane. SMI was obtained by dividing the TSM data in cm^2 by the square of the height in m^2. Similarly, PMI was obtained by dividing the TPM data in cm^2 by the square of the height in m^2. Sarcopenia thresholds were defined based on similar previous study, using 5th percentile (p^5) reference values adjusted for age and BMI in a healthy Caucasian population (12). This study classified TSM and SMI p^5 values based on age groups and BMI. The threshold values in the referenced study are shown in Table 1.

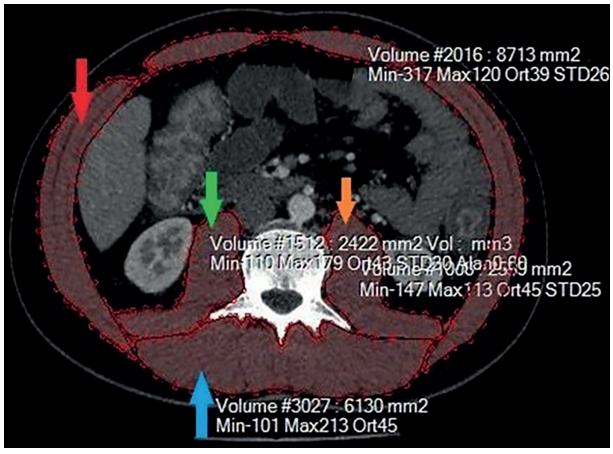

Figure 2. Axial non-contrast CT image at the L3 vertebral level illustrating manual segmentation of total skeletal muscle area (TSM) of the abdominal wall in a female sarcoidosis patient. Muscle boundaries were manually delineated, and the segmentation included psoas, paraspinal, and abdominal wall muscles. Abdominal wall muscle (Red Arrow), Erector Muscle (Blue Arrow), Right Psoas Muscle (Green Arrow), Left Psoas Muscle (Orange Arrow).

Statistical analysis

Continuous variables are described as mean and standard deviation (SD). Prior to intergroup comparisons, normal distribution of data was checked. Values with p>0.05 in the Kolmogorov-Smirnov normality test were considered normal, and parametric tests were applied in subsequent stages. Interobserver variability

Table 1. Predicted p5 values for SMI and TSM across different age and BMI categories in women;

BMI (kg/ m^2) / Age (years)	SMI (cm^2/ m^2)			
	17–20	**21–25**	**26–30**	**31–35**
All ages	28.6	31.3	34.5	37.5
20–29	28.5	33.7	39.6	45.1
30–39	28.7	32.8	37.6	42.2
40–49	28.8	31.8	35.6	39.2
50–59	28.7	30.9	33.5	36.1
60–69	28.5	29.9	31.4	32.9
70–79	28.2	28.8	29.3	29.5
*	TSM(cm^2)			
All ages	83.6	90.5	98.5	105.9
20–29	88.2	102.7	119.4	134.7
30–39	86.8	97.9	111.2	123.7
40–49	85.1	93.1	102.9	112.3
50–59	83.0	88.2	94.4	100.6
60–69	80.7	83.1	85.9	88.4
70–79	78.0	78.0	77.3	75.9

Abbreviations: BMI: Body Mass Index, SMI: Skelatal Muscle Index, TSM: Total Skelatal Muscle area.

was assessed using the intraclass correlation coefficient (ICC). Independent Samples t-Test was used for normally distributed data, while Mann-Whitney U test was employed for non-normally distributed data. Categorical variables are presented as percentages and associations between these variables were determined using Fisher's exact test. Correlation between SMI, PMI, TPM and TSM was determined by Pearson's correlation coefficient (r) analysis. Correlation between other continuous parameters was determined by Spearman's correlation coefficient (r) analysis. The compatibility between two different variables was assessed using the Pearson Chi-square goodness-of-fit test. All results were assessed at a 95% confidence interval and a significance level of $p<0.05$. Statistical analyses were performed using SPSS (SPSS for Windows, version 22.0, SPSS, Chicago, IL, USA), and a difference was considered statistically significant at a p-value of < 0.05.

Results

In our study, we examined a total of 168 female patients. The mean age of the patients was 45.8 years. The mean age of 86 (51.2%) patients diagnosed with sarcoidosis was 48.53 years, while the average age of 82 (48.8%) patients in the control group was 42.93 years. Sarcoidosis patients were observed to be significantly older compared to the control group. ($p = 0.004$) The median height of all patients was 165 cm, and the body mass index (BMI) was 25 kg/cm^2. The median height for patients with sarcoidosis was 164 cm, while the median height for the control group without sarcoidosis was 167 cm. The heights of the control group without sarcoidosis were significantly greater than the heights of patients with sarcoidosis ($p = 0.001$) (Table 2).

Interobserver agreement for muscle segmentation was excellent (ICC = 0.93). The mean total psoas muscle area (TPM) of all subjects in the study population

Table 2. Data from sarcoidosis patients and non-sarcoid patients are shown as means±standard deviations/median (min-max) and frequency.

Variables	Sarcoidosis Patient n=86 (%51.2)	Non-Sarcoidosis Controls n=82(%48.8)	Total n=168	p-Value
Age	48.53 ± 11.11	42.93 ± 12.72	45.8 ± 12.21	**0.004**
Height	1.64 (1.55-1.70)	1.67 (1.56-1.76)	1.65 (1.55-1.76)	**<0.001**
BMI	26 (20-32)	25 (19-32)	25 (19-32)	0.593
TPM (cm^2)	11.06 ± 3.31	13.16 ± 4.45	12.08 ± 4.03	**0.001***
TSM (cm^2)	115.0 ± 18.87	125.75 ± 25.76	120.25 ± 23.07	**0.002***
PMI (cm^2/m^2)	4.08 ± 1.20	4.63 ± 1.52	4.35 ± 1.39	**0.010***
SMI (cm^2/m^2)	42.42 ± 6.05	44.19 ± 7.42	43.28 ± 6.79	0.092*
CRP	7.0 (0.1-60)	4.18 (0.18-278)	5.49 (0.1-278)	0.308
ESR	20.0 (1.0-100)	20.24 (2-114)	20.24 (1-114)	0.073
WBC	7.00 (1.7-41)	7.8 (1.7-23)	7.3 (1.7-41)	**0.014**
RBC	4.52 (1.8-5.5)	4.5 (1.7-5.9)	4.5 (1.7-5.9)	0.263
HGB	12.40 (5.7-15)	12.5 (1-17.7)	12.5 (1-17.7)	0.257
MCV	83.0 (56.7-98)	85.5 (60-116.9)	83.4 (56.7-116.9)	**0.020**
Neutrophil	4.25 (0.9-10.3)	4.6 (0.6-31.1)	4.42 (0.6-31.1)	0.063
Lymphocyte	1.6 (0.3-35)	2.1 (0.3-4.5)	1.9 (0.3-35)	**0.009**
N/L Index	2.55 (0.11-17.0)	2.39 (0.54-16.33)	2.50 (0.11-17.0)	0.374
SMI-Sarcopenia	7 (%4.1)	6 (%3.6)	13 (%7.7)	1.000**
TSM-Sarcopenia	17 (%10.1)	9 (%5.3)	26 (%15.4)	0.138**

Abbreviations: BMI: Body Mass Index, TPM: Total Psoas Muscle area, TSM: Total Skelatal Muscle area, PMI:Psoas Msucle Index. SMI: Skeletal Muscle Index, N/L: Neutrophil/Lymphocyte; *T-independent test , **Fischer exact test, *The values written in bold font indicate statistically significant differences at the 0.05 level.*

was 12.08 cm^2, and the total skeletal muscle area (TSM) was 120.25 cm^2. While the mean total psoas muscle area of control group subjects in the study population was 13.16 cm^2, and the total skeletal muscle area was 125.75 cm^2. The mean total psoas muscle area of sarcoidosis patients in the study population was 11.06 cm^2, and the total skeletal muscle area was 115.0 cm^2. The total psoas muscle area (p = 0.001), total skeletal muscle area (p = 0.002) and PMI values (p = 0.010) of patients diagnosed with sarcoidosis were found to be significantly lower compared to the control group without sarcoidosis. There was no significant difference between sarcoidosis patients and the control group in SMI (p = 0.092) values. The total psoas muscle areas, total skeletal muscle areas, PMI, and SMI values according to age groups are summarized in Table 3.

SMI-based sarcopenia was identified in 7 (4.1%) sarcoidosis patients and 6 (3.6%) controls (p = 1.000). Based on TSM-based thresholds, 17 (10.2%) sarcoidosis patients and 9 (5.4%) controls were classified as sarcopenic (p = 0.138) (Table 4). There was moderate agreement between the two criteria (κ = 0.628, p<0.001). Subgroup analysis indicated that significant reductions in TPM, TSM, PMI, and SMI were mainly observed in the 50–60 age group. In addition, TSM values were significantly lower in the sarcoidosis group within the 40–50 age range (p = 0.023). No statistically significant differences were detected in other decades. Table 4 summarizes sarcopenia prevalence according to both SMI and TSM thresholds across age groups. Descriptive lab and muscle parameter data are detailed in Tables 2 and 3.

Table 3. The averages of total psoas muscle area, total skeletal muscle, psoas muscle index and skeletal muscle index according to ages are shown.

Variables	Age Groups (y)	Sarcoidosis Patient ±SD (n=86)	Non-Sarcoidosis Controls ±SD (n=82)	p-Value
Total Psoas Muscle Area (cm^2)	20-30	9.58 ± 4.36 (6)	12.48 ± 4.23 (16)	0.238
	30-40	11.61 ± 3.70 (11)	14.30 ± 5.13 (15)	0.152*
	40-50	11.66 ± 2.48 (28)	13.02 ± 4.89 (27)	0.197*
	50-60	10.35 ± 3.97 (26)	14.32 ± 3.23 (13)	**0.003***
	60-70	11.38 ± 2.74 (15)	11.61 ± 3.62 (11)	0.856*
Total Skelatal Muscle Area (cm^2)	20-30	94.08 ± 13.62 (6)	108.96 ± 21.17 (16)	0.210
	30-40	108.12 ± 10.64 (11)	123.63 ± 32.91 (15)	0.169
	40-50	117.93 ± 15.45 (28)	129.71 ± 21.59 (27)	**0.023***
	50-60	115.88 ± 21.67 (26)	141.54 ± 19.97 (13)	**0.027***
	60-70	121.43 ± 20.70 (15)	124.73 ± 25.94 (11)	0.916*
PMI (cm^2/m^2)	20-30	3.56 ± 1.26 (6)	4.51 ± 1.53 (16)	0.210
	30-40	4.33 ± 1.39 (11)	5.11 ± 1.61 (15)	0.206*
	40-50	4.32 ± 0.96 (28)	4.57 ± 1.73 (27)	0.513*
	50-60	3.79 ± 1.38 (26)	4.81 ± 1.12 (13)	**0.001***
	60-70	4.16 ± 0.96 (15)	4.11 ± 1.30 (11)	0.722*
SMI (cm^2/m^2)	20-30	35.06 ± 4.30 (6)	39.26 ± 5.92 (16)	0.140
	30-40	40.27 ± 3.39 (11)	44.32 ± 9.35 (15)	0.126
	40-50	43.62 ± 4.79 (28)	45.58 ± 6.73 (27)	0.217*
	50-60	42.60 ± 6.94 (26)	47.43 ± 5.78 (13)	**0.037***
	60-70	44.42 ± 6.62 (15)	43.97 ± 7.50 (11)	0.875*

Abbreviations: PMI: Psoas Msucle Index, SMI: Skeletal Muscle Index, *Independent-t test, The values written in dark font indicate statistically significant differences at the 0.05 level.

Table 4. The numbers of sarcoidosis and non-sarcoid patients are shown according to SMI-based and TSM-based sarcopenia classification.

Variables	Age Groups (y)	Sarcoidosis Patient (%) n=86	Non-Sarcoidosis Controls (%) n=82	p-Value
SMI-Based Sarcopenia	20-30	2 (%1.2)	3 (%1.8)	0.585
	30-40	2 (%1.2)	2 (%1.2)	1.000
	40-50	1 (%0.6)	1 (%0.6)	1.000
	50-60	2 (%1.2)	0 (%0)	0.544
	60-70	0 (%0)	0 (%0)	-
TSM-Based Sarcopenia	20-30	4 (%2.4)	4 (%2.4)	0.137
	30-40	5 (%3)	2 (%1.2)	0.095
	40-50	3 (%1.8)	3 (%1.8)	1.000
	50-60	5 (%3)	0 (%0)	0.149
	60-70	0 (%0)	0 (%0)	-

Abbreviations: SMI: Skeletal Muscle Index, TSM: Total Skelatal Muscle area.

The WBC (p = 0.014), MCV (p = 0.020), and Lymphocyte (p = 0.009) values of sarcoidosis patients were found to be significantly lower than those of the control group. No significant differences were observed between sarcoidosis patients and the control group in terms of other blood parameters and N/L (p = 0.616) ratios. The age and BMI of all patients showed a moderately positive correlation (r = 0.212, p = 0.006). Additionally, there was a moderate positive correlation between height and TPM in all patients (r = 0.356, p<0.001). However, a strong positive correlation was observed between height and TSM (r = 0.713, p<0.001).

Discussion

Sarcoidosis is a chronic, multisystem inflammatory disease (14) that has been associated with various extrapulmonary manifestations, including potential alterations in muscle metabolism and composition. Emerging evidence suggests that patients with sarcoidosis may be at increased risk for sarcopenia, a progressive loss of skeletal muscle mass and function (15). Previous studies investigating this relationship have predominantly utilized indirect methods such as bioelectrical impedance analysis (BIA) and sonography, focusing largely on fat-free mass index or regional muscle thickness (13, 16). While these approaches provide valuable insights, they are limited in their ability to directly quantify muscle volume. In this context, muscle atrophy and myopathy have been well-documented as adverse effects of corticosteroid therapy, which remains a cornerstone in the treatment of sarcoidosis (17, 18). However, it remains unclear whether sarcopenic changes are already present at the time of diagnosis — prior to the initiation of such therapies. This question formed the basis of our investigation. Previous studies have suggested an increased risk of muscle loss and sarcopenia in patients with sarcoidosis, particularly in those with chronic disease and advanced pulmonary involvement (13, 15). However, most of these investigations used indirect methods such as bioelectrical impedance analysis (BIA) or ultrasound to estimate muscle mass, and often focused on patients who had already initiated treatment. To date, few studies have examined muscle status in treatment-naïve sarcoidosis patients at the time of diagnosis using objective imaging methods. This study aimed to fill this gap by directly evaluating skeletal and psoas muscle volume using CT images in a well-defined, female-only sarcoidosis cohort. Our goal was to

determine whether sarcopenic changes were already detectable prior to therapy and to explore whether these changes vary by age group. We assessed muscle mass using abdominal CT images obtained from 168 female patients, focusing on parameters such as total skeletal muscle volume of the abdominal wall and total psoas muscle volume. To minimize potential bias arising from threshold variability in sarcopenia classification, we adopted reference values from a previously published study conducted in a demographically similar population (12). Our findings suggest that muscle mass was lower in sarcoidosis patients compared to controls at the time of diagnosis, despite no significant difference in sarcopenia prevalence. Since the overall differences in TPM, TSM, and PMI between groups may be partially attributed to the observed age discrepancy, we performed decade-based subgroup analyses to minimize this potential source of bias (12). Stratifying the study population by age allowed for more balanced comparisons across similar age intervals. However, this approach inevitably reduced the number of participants per subgroup, which may have limited the statistical power to detect differences in certain strata. In addition, the average height between the two groups was significantly different. While this may have directly influenced raw muscle area measurements (TSM and TPM), indices normalized to height (SMI and PMI) remained unaffected by this discrepancy. In the age-stratified analysis, the most consistent and statistically significant differences in muscle indices (TSM, TPM, SMI, and PMI) were observed in the 50–60 age group. This aligns partially with prior studies that reported reduced muscle mass and increased sarcopenia prevalence in older sarcoidosis patients or those with more advanced disease (13, 15, 16). However, unlike those studies, which often included treated populations or relied on indirect methods such as bioelectrical impedance or ultrasound, our study focused exclusively on treatment-naïve female patients and used CT-based volumetric analysis, providing a more objective and precise evaluation of muscle status. The fact that measurable muscle loss was already evident in this midlife subgroup may suggest early or subclinical muscle alterations potentially driven by cumulative inflammatory, metabolic, or mitochondrial effects. Although variances were equal, the unequal sample sizes between groups in this age bracket (n = 26 in sarcoidosis vs. n = 13 in controls) reduce the statistical robustness of this finding and require cautious interpretation. Nevertheless, this does not undermine the possibility that subtle, multifactorial processes related to sarcoidosis may lead to detectable muscle loss even in the absence of overt symptoms or treatment. These findings underscore the need for longitudinal studies incorporating larger, age-stratified cohorts to further explore early muscle involvement in sarcoidosis. In light of these age-specific findings, it is also important to consider why the overall prevalence of sarcopenia did not significantly differ between groups, despite the observed reductions in muscle indices. This discrepancy may reflect threshold-related limitations in classification systems or the influence of confounding factors not captured in our study design. In light of these age-specific findings, it is also important to consider why the overall prevalence of sarcopenia did not significantly differ between groups, despite the observed reductions in muscle indices. Several previous studies have reported increased sarcopenia prevalence among sarcoidosis patients, particularly those with chronic disease or significant pulmonary involvement (13, 16). However, most of these studies included patients who had already initiated corticosteroid therapy or assessed muscle mass using indirect methods such as BIA or ultrasound, which may not fully reflect early or subtle muscle loss. In contrast, our cohort was composed of treatment-naïve female patients evaluated at the time of diagnosis. It is possible that in early-stage sarcoidosis, systemic inflammation has not yet exerted sufficient cumulative effect to produce measurable sarcopenia. Moreover, although we applied validated diagnostic thresholds adjusted for age, sex, and BMI (11, 12), such classifications may lack sensitivity to detect marginal deficits in muscle quantity. The fact that muscle indices such as TSM and TPM were significantly lower in the sarcoidosis group—even in the absence of categorical sarcopenia—suggests that early subclinical muscle loss may precede overt sarcopenia, especially in middle-aged patients. This underlines the value of volumetric assessments in identifying early-stage muscular changes that may not yet fulfill formal diagnostic criteria. Moreover, the absence of significant correlations between inflammatory markers and muscle mass

indices in our cohort suggests that systemic inflammation might not yet have exerted a measurable effect on muscle tissue at the time of diagnosis. Previous literature indicates that in sarcoidosis, systemic inflammatory activity may evolve over time and may not be fully reflected in early laboratory markers (14). Furthermore, commonly used markers such as CRP and ESR are non-specific and may not capture localized or subclinical inflammatory processes contributing to sarcopenia (19). It is also possible that mechanisms beyond inflammation, including oxidative stress, mitochondrial dysfunction, and altered muscle metabolism, play a role in sarcoidosis-related muscle changes, as supported by prior studies (15). These findings support the need for prospective, longitudinal studies that include a broader panel of inflammatory and metabolic parameters. In a study comparing the blood parameters of sarcoidosis patients with the control group, they found that the Hgb, MCV and lymphocyte values of sarcoidosis patients were significantly lower than the control (20). Consistent with this, in our study, we found that MCV and lymphocyte values of sarcoidosis patients were significantly lower than the control group. However, we did not detect any significant difference in Hgb values for both groups. This is probably due to the heterogeneity of the patient population in the control group. The primary limitation of our study is its retrospective, cross-sectional design, which inherently limits the ability to establish causal relationships between sarcoidosis and muscle mass reduction. Although we used validated, age- and BMI-adjusted thresholds for defining sarcopenia, the sarcoidosis group was older and shorter on average than the control group, which may have influenced muscle measurements despite these adjustments. In addition, our control group was selected from emergency department patients without known chronic diseases; however, the presence of acute clinical conditions may have subtly affected baseline muscle physiology, potentially introducing selection bias. Furthermore, unmeasured confounding variables such as nutritional status, physical activity levels, and socioeconomic background could not be assessed, which may have independently impacted muscle mass. These factors are known contributors to sarcopenia and should be accounted for in future prospective studies with well-characterized and population-based control cohorts (11). Another important limitation of our study is the potential for selection bias related to the composition of the control group. Although we applied strict exclusion criteria to remove individuals with chronic illnesses or medications known to affect muscle mass, our control group was derived from emergency department patients. While these individuals did not have any known systemic disease, their acute clinical presentations may have influenced muscle physiology to some extent. Therefore, residual confounding cannot be entirely ruled out, and the control group may not fully reflect a healthy baseline population. Additionally, muscle assessment relied solely on CT-derived area measurements, without direct evaluation of muscle strength or performance. As stated in EWSGOP2, three parameters are evaluated under the titles of muscle strength, muscle quantity/quality and physical performance when evaluating muscle atrophy. However, it is worth mentioning that in the literature, data such as SMI, PMI and TPM have been consistently shown to predict muscle atrophy. Based on this, although we did not evaluate muscle atrophy clinically in our study, it is possible to predict it meaningfully through indicators in order to inspire future clinical studies. Additionally, the absence of male patients with sarcoidosis is another limitation, as it limits the possibility of a gender-specific comparison between the sexes. However, it is worth noting that the literature already indicates clear distinctions between muscle indexes in men and women, which mitigates this limitation in our muscle measurement evaluation (11). However, future research should consider conducting homogeneous studies exclusively focused on male patients to address sex-specific differences and provide a more comprehensive understanding of muscle mass alterations in sarcoidosis. In conclusion, this study evaluated muscle mass in female sarcoidosis patients at the time of diagnosis using CT-based measurements. Although overall sarcopenia prevalence was not increased, muscle indices were lower in sarcoidosis patients, with significant differences observed in the 50–60 age group. These findings suggest that muscle loss may become more apparent with age in sarcoidosis, even before treatment. Further longitudinal studies are needed to explore this association.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g., consultancies, stock ownership, equity interests, patent/licensing, arrangement etc-) that might pose a conflict of interest in connection with the submitted article.

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References

1. Judson MA. The clinical features of sarcoidosis: a comprehensive review. Clin Rev Allergy Immunol. 2015;49:63–78. doi:10.1007/s12016-014-8450-y
2. Iannuzzi MC, Fontana JR. Sarcoidosis: clinical presentation, immunopathogenesis, and therapeutics. JAMA. 2011; 305:391–9. doi:10.1001/jama.2011.10
3. Boots AW, Drent M, Swennen EL, et al. Antioxidant status associated with inflammation in sarcoidosis: a potential role for antioxidants. Respir Med. 2009;103:364–72. doi:10.1016/j.rmed.2008.10.007
4. Hunninghake GW, Costabel U, Ando M, et al. ATS/ERS /WASOG statement on sarcoidosis. Sarcoidosis Vasc Diffuse Lung Dis. 1999;16(2):149–73.
5. Wessendorf TE, Bonella F, Costabel U. Diagnosis of sarcoidosis. Clin Rev Allergy Immunol. 2015;49:54–62. doi:10 .1007/s12016-015-8475-x
6. Sharma OP. Fatigue and sarcoidosis. Eur Respir J. 1999;13:713–4. doi:10.1034/j.1399-3003.1999.13d01.x
7. Drent M, Lower EE, De Vries J. Sarcoidosis-associated fatigue. Eur Respir J. 2012;40:255–63. doi:10.1183 /09031936.00002512
8. Raasing L, Veltkamp M, Datema M, Korenromp I, Grutters JC, Vogels OJ. Sarcoidosis-related small fiber neuropathy: focus on fatigue, pain, restless legs syndrome, and cognitive function. Sarcoidosis Vasc Diffuse Lung Dis. 2025;42(1):16214. doi:10.11138/sarcoidosis.2025.16214
9. Pozzan R, Salton F, Confalonieri P, et al. Autoantibodies in sarcoidosis: innocent bystander or promising biomarker for organ involvement? Sarcoidosis Vasc Diffuse Lung Dis. 2024;41(4):e2024056. doi:10.4081/sarcoidosis.2024 .e2024056
10. Fanzani A, Conraads VM, Penna F, et al. Molecular and cellular mechanisms of skeletal muscle atrophy: an update. J Cachexia Sarcopenia Muscle. 2012;3:163–79. doi:10.1007 /s13539-012-0074-6
11. Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. 2019;48:16–31. doi:10.1093/ageing/afy169
12. van der Werf A, Langius JAE, et al. Percentiles for skeletal muscle index, area and radiation attenuation based on computed tomography imaging in a healthy Caucasian population. Eur J Clin Nutr. 2018 Feb;72(2):288-296. doi: 10.1038/s41430-017-0034-5
13. Cremers JP, Drent M, Elfferich MD, et al. Body composition profiling in a Dutch sarcoidosis population. Sarcoidosis Vasc Diffuse Lung Dis. 2013 Dec 17;30(4):289-99. PMID: 24351620.
14. Starshinova AA, Malkova AM, Basantsova NY, et al. Sarcoidosis as an autoimmune disease. Front Immunol. 2020;10:2933. doi:10.3389/fimmu.2019.02933
15. Spruit MA, Thomeer MJ, Gosselink R, et al. Skeletal muscle weakness in patients with sarcoidosis and its relationship with exercise intolerance and reduced health status. Thorax. 2005;60:32–8. doi:10.1136/thx.2004.022244
16. Esme M, Karcioglu O, Oncel A, et al. Ultrasound assessment of sarcopenia in patients with sarcoidosis. J Ultrasound Med. 2022;41:951–9. doi:10.1002/jum.15780
17. Chaigne B, Rodeia S, Benmostefa N, et al. Corticosteroid-sparing benefit of intravenous immunoglobulin in systemic sclerosis-associated myopathy: a comparative study in 52 patients. Autoimmun Rev. 2020;19:102431. doi:10.1016/j .autrev.2019.102431
18. Minetto MA, D'Angelo V, Arvat E, et al. Diagnostic work-up in steroid myopathy. Endocrine. 2018;60:219–23. doi:10.1007/s12020-017-1472-5
19. Cederholm T, Bauer JM, Boirie Y, Schneider SM, Sieber CC, Rolland Y. Toward a definition of sarcopenia. Clin Geriatr Med. 2011;27(3):341–53. doi:10.1016/j.cger.2011.04.001
20. Korkmaz C, Demircioglu S. The association of neutrophil /lymphocyte and platelet/lymphocyte ratios and hematological parameters with diagnosis, stages, extrapulmonary involvement, pulmonary hypertension, response to treatment, and prognosis in patients with sarcoidosis. Can Respir J. 2020;2020:1696450. doi:10.1155/2020/1696450