

Quantification of paravertebral cross-sectional muscle areas and fatty degeneration via magnetic resonance imaging in ankylosing spondylitis: a comprehensive analysis

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Abstract

Aims: Ankylosing spondylitis (AS) is a chronic disease characterized by inflammation of the spine and joints. This study aimed to examine the multifidus (MF) and erector spinae (ES) muscles in AS patients using magnetic resonance imaging (MRI), and to evaluate the clinical implications of muscle findings.

Methods: This study included 43 patients and 40 matched controls. The total (TCSA), functional (FCSA), relative CSAs, and ratios of MF and ES muscles were compared between the groups. The Visual Analog Scale, Bath Ankylosing Spondylitis Metrology Index (BASMI), Bath Ankylosing Spondylitis Functional Index (BASFI), Ankylosing Spondylitis Disease Activity Score with CRP, Ankylosing Spondylitis Disease Activity Score with ESR, Bath Ankylosing Spondylitis Activity Index, and Ankylosing Spondylitis Quality of Life Questionnaire (ASQoL) scores of AS patients were recorded. Comparisons between the two groups were made using the Student's t-test and the Mann-Whitney U test.

Results: The TCSAs of the MF and ES were similar in the two groups. In contrast, MF relative FCSA (p = 0.003), ES relative FCSA (p < 0.001), ES FCSA (p = 0.017), MF FCSA/TCSA (p < 0.001), and ES FCSA/TCSA (p < 0.001) were decreased in AS patients. ES FCSA/TCSA was negatively correlated with BASMI (r = -0.369, p = 0.015), while MF FCSA/TCSA was negatively correlated with BASMI, BASFI, and ASQoL (r = -0.395, p = 0.009; r = -0.321 p = 0.036; r = -0.387, p = 0.010, respectively).

Conclusions: The paravertebral muscle morphology significantly deteriorates in AS patients, exhibiting decreased functional muscle areas and increased fatty degeneration.

Keywords: Ankylosing spondylitis; Chronic pain syndromes; Muscle; Spinal disorders; Spondyloarthropathies

Introduction

Ankylosing spondylitis (AS) is a chronic inflammatory disease affecting the sacroiliac joints, axial skeleton, and paravertebral soft tissues. The inflammatory process results in the progressive fusion of the vertebrae, which ultimately leads to a significant reduction in mobility, stability, and quality of life¹. The alterations to paravertebral musculature may include altered fiber type



distribution, muscular tissue atrophy, and increased collagen fiber accumulation in AS. These changes have been linked to immobilization and persistent inflammation in patients with AS^{2-4} . The mechanisms underlying muscle volume loss and increased fatty infiltration remain unclear. However, studies have associated proinflammatory cytokine expression with muscle degeneration, particularly highlighting elevated levels of TGF-ß1 and TNF- α in patients with $AS^{5,6}$. Genetic factors such as HLA-B27 and alterations in gut microbiota may contribute to abnormal immune responses, potentially resulting in chronic inflammation and muscle atrophy⁷⁻⁹. Another potential underlying pathology is the denervation and neurogenic inflammation of the spinal cord and nerve roots^{10,11}.

The two most widely accepted imaging techniques for evaluating muscle volume are computed tomography (CT) and magnetic resonance imaging (MRI). MRI has emerged as a valuable tool for quantifying muscle changes and has provided a comprehensive understanding of the pathophysiology of AS. While these changes have been studied in the literature, the causal relationship and factors behind them have not been fully addressed^{12,13}. It is important to understand these structural changes and the factors that cause muscle alterations, as this would help to identify the clinical manifestations and prognosis of the disease, develop targeted therapies and new treatment pathways, and prevent structural damage in affected individuals. This research aimed to assess the cross-sectional areas (CSA) and fatty degeneration of paravertebral muscles and examine their correlation with patient characteristics, disease activity, functional limitations, and mobility levels.

Materials and methods

Study Population and Clinical Assessment

Forty-three patients aged between 18-75 years, diagnosed with AS on the basis of the Modified New York criteria, who had a lumbar spine MRI in the last year and were admitted to rheumatology and physical medicine and rehabilitation outpatient clinics of the Karadeniz Technical University Farabi Hospital for routine follow-up, were recruited in this cross-sectional study. The exclusion criteria were the presence of neurological disease, traumatic injury to the spine, history of spine surgery, scoliosis or spondylolisthesis, body mass index \geq 25 kg/m², diseases that may cause sarcopenia (cancer, coronary heart disease, heart failure, thyroid/parathyroid disorders), and discopathies other than bulging. A control group of 40 subjects similar to the patient group in terms of age and sex was enrolled in the study. Exercise status of the participants was questioned (none/1-2 days/week or \geq 3 days/week) while smoking habits were noted as smoker or non-smoker. The duration of symptoms, duration of the disease,



Visual Analog Scale (VAS), Bath Ankylosing Spondylitis Metrology Index (BASMI), Bath Ankylosing Spondylitis Functional Index (BASFI), Ankylosing Spondylitis Disease Activity Score with Creactive protein (ASDAS-CRP), Ankylosing Spondylitis Disease Activity Score with Erythrocyte Sedimentation Rate (ASDAS-ESR), Bath Ankylosing Spondylitis Activity Index (BASDAI), Ankylosing Spondylitis Quality of Life Questionnaire (ASQoL) scores, and the ongoing treatment regimen were recorded for AS patients by a physician blinded to MRI measurements. The institutional review board (IRB number: 2023/90) approval was obtained before the initiation of the study.

Radiological Analysis

Every participant received a lumbar spine MRI, with axial T2-weighted images analyzed at the L4 inferior endplate level using FIJI, an open-source image processing software (National Institutes of Health in Bethesda, Maryland). The analysis focused on both the multifidus (MF) and erector spinae (ES) muscles. The muscles' total cross-sectional areas (TCSA) were determined by outlining their boundaries. Functional CSAs (FCSA), which represent the fat-free area, were calculated by defining a threshold signal intensity to include only lean muscle pixels. This threshold was established by drawing 6 regions of interest (ROIs), 2 for the erector spinae muscle on each side and 1 for the multifidus muscle on each side, on the lean muscle tissue, avoiding visible fat pixels. The highest signal intensity from these ROIs was identified as a threshold to differentiate lean muscle from fat. Pixels above this threshold value were accepted radiologically as fatty tissue (Figure 1). The FCSA to TCSA ratio was then calculated for both MF and ES muscles. To account for individual variations in body shape, weight, and height, relative total and functional CSAs (rTCSA and rFCSA) were computed as the ratio of muscle CSA to L4 inferior endplate CSA. Additionally, MF TCSA/ES TCSA and MF FCSA/ES FCSA ratios were determined.

A radiologist with 14 years of spinal MRI measurement experience conducted all MRI measurements independently twice, with a one-month interval, to minimize potential errors in muscle margin definition. Statistical analysis was performed including the mean of these two measurements. The radiologist who performed these measurements was blinded to the participants' demographic and clinical characteristics.

Statistical Analysis

For descriptive analyses, means and standard deviations were used for normally distributed variables, while medians and interquartile ranges (IQR) were used for non-normally distributed variables. Comparisons between the two groups were made using the Student's t-test for



normally distributed continuous data, and the Mann-Whitney U test was used for non-normally distributed data. Nominal data were presented as frequencies and percentages, with comparisons made using Pearson's chi-square tests. Correlation coefficients and their significance were determined using the Pearson test for normally distributed continuous variables and the Spearman test for non-normally distributed variables. A significance level of 0.05 was used for all statistical tests. Data analysis was conducted using the Statistical Package for the Social Sciences (SPSS), version 23.0 (IBM Corp., Armonk, NY, USA).

Sample Size Calculation

The minimum sample size was calculated to be 80 (40 patients and 40 controls), assuming a power of 80%, a significance level (α) of 0.05, and an effect size of 0.6 for the variable of ES functional CSA. G*power 3.1 version (Heinrich-Heine University of Dusseldorf, Germany) was utilized to estimate the sample size.

Results

This cross-sectional study involved 43 patients (20 females, 23 males) and 40 healthy individuals (19 females, 21 males). The mean age of the AS group and control group was 40.3 ± 10 years and 38.8 ± 6.1 years, respectively. No statistically significant difference was observed between the two groups in terms of gender (p = 0.928), smoking status (p = 0.332), exercise status (p = 0.591), and age (p = 0.417) (Table 1). Thirty-nine patients were under anti-tumor necrosis factor alpha therapy (anti-TNF): infliximab (12 patients, 27.9%), etanercept (9 patients, 20.9%), adalimumab (8 patients, 18.6%), golimumab (6 patients, 14%), certolizumab pegol (3 patients, 7%), and secukinumab (1 patient, 2.3%). Four patients were using only nonsteroidal anti-inflammatory drugs. Mean duration of the disease and symptoms in the patients with AS were 9.32 ± 6.38 and 12.91 ± 7.27 years, respectively. Mean VAS score was 4.14 ± 3.24 . Other clinical features were presented in Table II.

Comparison of the groups in regards of MF and ES muscle areas revealed that MF rFCSA (t = -3.009, p = 0.003), ES rFCSA (u = 464.000, p < 0.001), ES FCSA (t = -2.431, p = 0.017), MF FCSA/TCSA (u = 440.000, p < 0.001), and ES FCSA/TCSA (t = -6.042, p < 0.001) were decreased in patients with AS compatible with an increase of fatty degeneration. MRI measurements of the paravertebral muscles were summarized in Table III.

A moderate, statistically significant negative correlation was determined between MF FCSA/TCSA and BASMI, BASFI, and ASQoL (r = -0.395, p = 0.009; r = -0.321 p = 0.036; r = -0.387,



p = 0.010, respectively). Negative correlation was detected between ES FCSA/TCSA and BASMI (r = -0.369, p = 0.015). ES rTCSA was negatively correlated with disease and symptoms (r = -0.352, p = 0.021; r = -0.323, p = 0.035, respectively) (Table IV).

Discussion

AS patients experience limitations in daily activities, and declined quality of life due to spinal involvement and structural alterations. The paravertebral muscles, which are essential for lumbar vertebral column movement and stabilization, often undergo changes in these patients^{4,14}. In the present study, quantitative MRI analysis revealed that the patients with AS did not show a statistically significant difference in the TCSAs of the MF and ES muscles compared to the control group. However, the rFCSA and FCSA/TCSA were reduced in both the MF and ES muscles of AS patients. These results indicate that fatty degeneration and functional loss occur in the MF and ES muscles of AS patients. Consequently, while the TCSA is largely constant, muscular function may be impacted when muscle tissue is replaced by fat.

To date, conflicting data exist regarding the morphology, strength, mass, and function of paravertebral muscles in AS. Imaging studies are primarily conducted to evaluate the bony changes, syndesmophytes, and ankylosis in AS. A CT-based study revealed that fat accumulation in the paraspinal muscles is associated with skeletal muscle atrophy and fat infiltration in AS¹⁵. However, MRI is a valuable tool to illustrate fatty infiltration and muscle atrophy, offering detailed information on muscle composition with high soft-tissue resolution. Previous researches demonstrated atrophy in the paravertebral muscles of individuals with low back pain, and linked movement limitations were linked to muscle atrophy. Moreover, weakness in paravertebral muscles can lead to lower back pain and postural disorders¹⁶⁻¹⁸.

The evaluation of paravertebral muscle changes depends primarily on two key metrics: muscle CSA and fat deposition. Chon et al. reported that individuals with chronic lumbar radiculopathy experience a decline in MF CSA compared to the normal population¹⁹. Similarly, Barker et al. and Fortin et al. determined that patients with low back pain exhibited significantly lower CSAs of the paravertebral muscle compared to the control group^{20, 21}.

Few studies have examined the alterations in paravertebral muscles using MRI quantification and their relationship to clinical symptoms in AS patients. Huang et al. performed a case-control study to investigate changes in the paravertebral musculature of AS patients using T2 mapping and T2 IDEAL sequences, noting a decrease in MF and ES muscle cross-sectional areas. No statistical association was detected between the MRI measurements, the BASDI, and CRP. Furthermore, ESR, CRP, BASFI, and BASDAI showed no statistically significant relationship with



fat deposition²². In contrast, our results showed that MF FCSA/TCSAs had a moderate negative correlation with BASMI, BASFI, and ASQoL, while ES FCSA/TCSA had a moderate negative correlation with BASMI. Additionally, ES rTCSA was the only MRI parameter negatively associated with the duration of the symptoms and disease. However, no significant relationship was detected between the paravertebral muscle parameters and ASDAS-CRP, ASDAS-ESR, and VAS. Since most of our patients were on anti-TNF treatment, it seems that no significant result could be obtained with the basal effect of these scales.

Resorlu et al. demonstrated that patients with AS had a decreased CSA of paravertebral muscles correlated with disease duration²³. They also reported a significant increase in fat fraction of paravertebral muscles in patients with AS. In contrast to our results, no significant relationship was detected between muscle atrophy and the BASFI or BASDAI. Another study examined 19 patients with AS and 14 with non-radiographic axial spondyloarthropathy. CSAs and graded fatty degeneration of the MF were measured using MRI, and an electrophysiological evaluation was performed. More fatty degeneration was detected in the left multifidus at the L5–S1 level, and denervation of the paraspinal muscles was significantly increased in the AS group²⁴. A similar analysis revealed that patients with AS had increased fat accumulation compared to patients with nonradiographic axial spondyloarthritis²⁵. However, in the three studies mentioned above, fat fraction was assessed using a visual, semi-quantitative method. A retrospective study showed that patients with low back pain exhibited decreased paraspinal muscle mass compared to early-stage AS patients without spinal deformity. In established AS patients, all MRI measurements regarding muscle volume were lower than those in both low back pain patients and patients with early stages of AS. These findings may corroborate a causal link between muscle deterioration and spinal deformity in patients with AS. The potential link between quantitative muscle variables and activity of the disease was not assessed in this study²⁶.

The outcomes of our research did not determine any decrease in TCSAs of the MF and ES, in contrast with similar studies focused on AS. However, a quantitative MRI analysis was conducted using a software program to precisely evaluate fatty degeneration and functional capacities of the ES and MF muscles, which differed from most of the prior studies on this topic. This study was the first to demonstrate the association between the relative and functional areas of the paravertebral muscles and various clinical parameters. Another strength of this study was that the age, sex, exercise, and smoking status of the AS group were statistically similar to those of the control group, which could have influenced the composition of the paravertebral muscles. All previous studies have only included age and sex matched control groups. Additionally, it should be noted that muscle evaluations were conducted exclusively at the inferior end plate level of L4. This study has some limitations. First, the sample size could be larger. A power



analysis based on a moderate effect level was used in sample size calculation. Due to the crosssectional study design, it was not possible to establish causal relationships. However, the results provided significant associations between variables. Longitudinal or experimental studies should be conducted to further investigate causality among the variables in this topic. Understanding the value and knowledge of paravertebral muscle changes in patients with AS may aid clinicians in providing a comprehensive explanation of the long-term structural damage to the paravertebral muscles and targeted treatment strategies.

Conclusion

The systemic and inflammatory course of AS, chronic pain, and abnormalities in the bones/ligaments of the vertebral column may affect the paravertebral muscles. The paravertebral muscle morphology significantly deteriorates in AS patients, exhibiting decreased functional muscle areas and increased fatty degeneration. Future research should further explore the underlying mechanisms responsible for these muscle changes and investigate the impact of targeted interventions on enhancing muscle quality and function in patients with AS.



Tables and Figures

			Patient Group	C	Control Group				
		n	%	n	%				
Gender	Female	20	46.5	19	47.5	0.028+			
	Male	23	53.5	21	52.5	0.928			
Smoking	(+)	18	41.9	21	52.5	0 222†			
	(-)	25	58.1	19	47.5	0.332			
Exercise Status	None	34	79.1	28	70				
	1 - 2 days/week	3	6.9	5	12.5	0.591^{+}			
	≥ 3 days/week	6	14	7	17.5				
Age, mean±SD		40.33±2	10.03	38.85±	6.06	0.417 [‡]			

Table I – Demographic features of the groups

SD, standard deviation; [†]Chi-square test, [‡]Independent samples t test

	mean±SD	Min-max
Symptom Duration	12.91±7.27	2-31
Disease Duration	9.32±6.38	1-27
VAS	4.14±3.24	0-10
BASMI	1.14±1.20	0-4
BASFI	1.52±1.51	0-5.8
ASDAS - CRP	2.71±4.19	0-29
ASDAS - ESR	2.42+3.15	1-22
BASDAI	2.88+1.86	0-6.5
ASQoL	6.12±5.30	0-18

SD, standard deviation; min, minimum; max, maximum; VAS, Visual Analog Scale; BASMI, Bath Ankylosing Spondylitis Metrology Index; BASFI, Bath Ankylosing Spondylitis Functional Index; ASDAS - CRP, Ankylosing Spondylitis Disease Activity Score with C-reactive protein; ASDAS -ESR, Ankylosing Spondylitis Disease Activity Score with Erythrocyte Sedimentation Rate; BASDAI, Bath Ankylosing Spondylitis Activity Index; ASQoL, Ankylosing Spondylitis Quality of Life Questionnaire





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Muscle paramete	ers	Patient Group	Control Group	t	p
MF TCSA (mm²)		2059.02±410.23	2028.18±430.86	0.334	0.739 [†]
MF FCSA(mm²)		1386.74±361.39	1518.68±350.50	-1.686	0.096 ⁺
MF rTCSA		1.49±0.33	1.60±0.37	-1.370	0.174 ⁺
MF rFCSA	mean+SD	1±0.28	1.19±0.28	-3.009	0.003 ⁺
ES TCSA (mm²)	mean±3D	3687.72±894.58	3565.58±876.46	0.628	0.628 ⁺
ES FCSA (mm²)		2351.56±644.84	2732.80±781.64	-2.431	0.017 [†]
ES FCSA/TCSA (%)		63.92±9.04	76.24±9.14	-6.042	< 0.001 ⁺
ES rTCSA		2.65±0.58	2.78±0.54	-1.010	0.315 [†]
	u	p			
MF FCSA/TCSA (%)		69.78 (10.23)	75.08 (9.97)	440.000	< 0.001 [‡]
ES rFCSA	median+IOR	1.57 (0.71)	2.11 (0.71)	464.000	< 0.001 [‡]
MF TCSA/ES TCSA		0.59 (0.15)	0.59 (0.21)	835.000	0.820 [‡]
MF FCSA/ES FCSA		0.62 (0.28)	0.57 (0.14)	721.000	0.205 [‡]

Table III. Comparison of MRI measurements between the groups

TCSA, total cross-sectional area; FCSA, functional CSA; MF, multifidus; ES, erector spinae; r, relative; SD, standard deviation; IQR, interquartile range; [†]Independent samples t test, [‡]Mann-Whitney U test.



Table IV - Correlation analysis of MRI measurements and clinical characteristics

	Symptom		Disease VAS		BASMI BASFI		ASDAS-		ASDAS-		BASDAI		ASQoL					
	Duration		Duration								CRP		ESR					
	r	р	r	Р	r	р	r	р	r	р	r	р	r	р	r	р	r	р
MF TCSA	0.044	0.777	0.014	0.931	0.145	0.353	0.297	0.053	0.089	0.572	0.154	0.326	0.153	0.326	0.030	0.849	-0.006	0.970
(mm²)																		
MF FCSA	0.071	0.651	-0.016	0.918	0.018	0.909	-0.018	0.910	-0.129	0.410	0.110	0.481	0.093	0.553	-0.116	0.459	-0.234	0.131
(mm²)																		
MF FCSA/TCSA	0.051	0.746	-0.077	0.625	-0.158	0.311	-0.395	0.009	-0.321	0.036	-0.012	0.940	-0.038	0.811	-0.214	0.169	-0.387	0.010
(%)																X		
MF rTCSA	0.090	0.566	-0.105	0.502	0.166	0.287	0.117	0.453	0.076	0.627	0.103	0.511	0.114	0.465	0.127	0.419	0.080	0.610
MF rFCSA	-0.022	0.890	-0.126	0.422	0.037	0.812	-0.112	0.473	-0.110	0.481	0.075	0.634	0.068	0.665	-0.037	0.816	-0.147	0.347
ES TCSA	-0.257	0.096	-0.230	0.138	-0.009	0.952	0.074	0.639	-0.027	0.862	0.064	0.685	0.053	0.736	-0.044	0.779	-0.090	0.566
(mm²)												. (-					
ES FCSA	-0.199	0.200	-0.166	0.289	0.007	0.965	-0.177	0.256	-0.109	0.487	-0.062	0.693	-0.075	0.631	0.001	0.993	-0.195	0.210
(mm²)													•					
ES FCSA/TCSA	0.003	0.987	0.007	0.963	-0.028	0.856	-0.369	0.015	-0.147	0.347	-0.213	0.171	-0.225	0.148	0.005	0.975	-0.237	0.126
(%)												Þ						
ES rTCSA	-0.352	0.021	-0.323	0.035	0.082	0.600	-0.056	0.722	-0.001	0.996	0.057	0.716	0.055	0.725	0.103	0.513	0.027	0.865
ES rFCSA	-0.247	0.110	-0.214	0.168	0.051	0.744	-0.248	0.109	-0.076	0.628	0.071	0.652	-0.075	0.633	0.094	0.548	-0.103	0.511
MF TCSA/ES	0.230	0.138	0.193	0.214	0.044	0.778	0.176	0.259	0.051	0.747	0.025	0.875	0.033	0.836	0.007	0.966	0.031	0.841
TCSA																		
MF FCSA/ES	0.267	0.084	0.179	0.251	-0.042	0.788	0.133	0.396	-0.067	0.668	0.151	0.333	0.151	0.334	-0.115	0.462	-0.088	0.575
FCSA																		

TCSA, total cross-sectional area; FCSA, functional CSA; MF, multifidus; ES, erector spinae; r, relative; VAS, Visual Analog Scale; BASMI, Bath Ankylosing Spondylitis Metrology Index; BASFI, Bath Ankylosing Spondylitis Functional Index; ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score with C-reactive protein; ASDAS-ESR, Ankylosing Spondylitis Disease Activity Score with Erythrocyte Sedimentation Rate; BASDAI, Bath Ankylosing Spondylitis Activity Index; ASQoL, Ankylosing Spondylitis Quality of Life Questionnaire



Figure 1. Quantitative paravertebral muscle measurement (A) Selection of six distinct regions of interest to establish upper and lower threshold limits. (B) Sagittal and axial T2-weighted MR images illustrate the measurement of total and functional cross-sectional areas of the multifidus and erector spinae muscles at the L4 inferior end plate.





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