ОРИГИНАЛНИ СТАТИИ
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PREVALENCE OF SARCOPENIA IN ADULT PATIENTS WITH ANKYLOSING SPONDYLITIS

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Abstract. *Ankylosing spondylitis is a chronic, progressive inflammatory rheumatic disease that involves primarily the sacroiliac joints and the axial skeleton. Sarcopenia is characterized by progressive and generalized loss of skeletal muscle mass and strength with a risk of adverse outcomes such as physical disability and poor quality of life. The study aimed to assess the prevalence of sarcopenia in patients with ankylosing spondylitis. A cross-sectional study was conducted at Rheumatology Unit from January 2019 to July 2019. The study population consisted of 50 Iraqi patients diagnosed with AS. Demographic data, physical activity using General Practice Physical Activity Questionnaire (GPPAQ), disease activity scores using Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) were recorded. Sarcopenia assessment was done by using a dual-energy x-ray absorptiometry scan for body composition analysis and measuring skeletal mass index (SMI). The maximal voluntary grip strength of the hand was measured with an electronic dynamometer. Physical function was assessed by a 4-meter usual gait speed test. The prevalence of presarcopenia was 6%, while sarcopenia was documented in 10% of patients. The mean value of body mass index (BMI) is significantly lower in patients with sarcopenia ($p = 0.001$). The vast majority of the sarcopenic group (80%) were physically inactive which was statistically significant compared with the non-sarcopenic group ($p = 0.033$). No significant association of treatment with anti-TNF or its duration was found between sarcopenia and non-sarcopenia groups ($p = 0.377$; $p = 0.187$). Both lean mass (LM) and handgrip showed fair validity to differentiate between AS patients. Patients with AS are at higher risk of developing early sarcopenia. Lower BMI and longer disease duration increase the risk of sarcopenia, while differences in gender, smoking and the use of anti-TNF do not influence the risk. Physical activity may improve muscle strength and perhaps decrease the risk.*

Key words: *ankylosing spondylitis, sarcopenia, presarcopenia, anti-TNF*

INTRODUCTION

Ankylosing Spondylitis (AS) is a chronic, progressive inflammatory rheumatic disease that involves primarily the sacroiliac joints and the axial skeleton. It is the major subtype and the main outcome of an inter-related group of rheumatic diseases named spondyloarthritides [1, 2]. Age of disease onset usually peaks in the second and third decades of life. Approximately 80% of patients with AS experience symptoms at ≤ 30 years of age, while only 5% will present with symptoms at ≥ 45 years of age [3]. The estimated prevalence of AS in Iraq was 0.9 % [4]. Low back pain and stiffness is the most common

symptom and the first manifestation in approximately 75% of patients [5].

Sarcopenia is a progressive and generalized skeletal muscle disorder that is associated with an increased likelihood of adverse outcomes including falls, fractures, physical disability, and mortality [6]. The term sarcopenia is derived from the Greek words sarx (flesh) and penia (poverty), describes a condition characterized by loss of muscle mass and muscle strength [7].

Baumgartner et al. used a Skeletal muscle index cutoff of -2SDs below the mean of a young reference group, and the prevalence of sarcopenia ranged from 13% to 24% in persons aged 65 to 70 years and

was over 50% for those older than 80 years [8]. Another study reported that sarcopenia was prevalent in 10% of men and 8% of women and that reduced skeletal muscle was independently associated with functional impairment and disability, particularly in older women [9].

The European Working Group on Sarcopenia in Older People (EWGSOP) updates the clinical algorithm for diagnosis in 2018; sarcopenia is probable when low muscle strength is detected. A sarcopenia diagnosis is confirmed by the presence of low muscle quantity or quality. When low muscle strength, low muscle quantity/quality, and low physical performance are all detected, sarcopenia is considered severe [6]. It is divided into three stages for helpful in light of setting appropriate recovery goals as well as selecting treatments and intervention: pre-sarcopenia stage, sarcopenia stage, and severe sarcopenia [10]. According to EWGSOP, sarcopenia is subcategorized into primary and secondary Sarcopenia [6].

AS patients are at risk of accelerated muscle loss. By leading to reduced muscle power, resistance, and physical activity, the loss of muscle mass contributes to the restriction in functional independence and daily living activities [11]. Up to our knowledge, no previously reported study has examined the prevalence of sarcopenia in the Iraqi population, however, some studies estimated the prevalence of sarcopenia in certain diseases like systemic lupus erythematosus [12].

This study assessed the prevalence of sarcopenia in Iraqi patients with AS and evaluated the impact of sociodemographic and clinical characteristics of AS on sarcopenia.

METHODS

Study design and setting

A cross-sectional study was conducted among AS patients who presented consecutively to the Rheumatology Unit of Baghdad Teaching Hospital/ Medical City from the period of January 2019 to July 2019. A total of 50 Iraqi patients with AS after fulfilling modified NEWYORK diagnostic criteria) [13] were enrolled in the study.

Selection criteria

1. Inclusion criteria were defined as any cooperative individual aged between 18 to 60 years with primary AS regardless of the disease onset.

2. Exclusion criteria were defined as any individual younger than 18 years old, or any individual not keen to participate in the study, any overlapping

with another rheumatological disease, pregnancy; possible other causes of secondary sarcopenia (malnutrition, diabetes, chronic kidney disease, chronic obstructive pulmonary disease, heart failure); recent steroid therapy (over the last three months) and presence of metacarpophalangeal joint derangement.

Data collection

All medical procedures were done after obtaining oral informed consent from the participants. A private subject interview was done including full medical and drug history. Data were collected using a pre-constructed data collection sheet, protocol for each participant (Appendix 1, 2, 3), (Appendix 4), and (Appendix 5) [6, 14]. The physical activity of each participant was assessed by the General Practice Physical Activity Questionnaire (GPPAQ) (Appendix 6) [15].

Measuring sarcopenia parameters

Body composition measurements: a dual-energy x-ray absorptiometry scan (DXA) scan (393 rue Charles Lindbergh, 34130 Mauguio France) was used for the body composition analysis. Fat mass, lean mass, and bone mineral density (BMD) were measured by DXA. Total and regional body composition was evaluated by using a whole-body DXA scan. The muscle mass of the four limbs from the DXA scan summed as appendicular skeletal muscle mass (ASMM) and defined SMI was calculated as ASMM/height² (kg/m²). Cut off point is < 6.0 kg/m² for women and 7.0 kg/m² for men [6].

Muscle strength: handgrip strength was measured using an electronic hand dynamometer (EH101 CAMRY, China) [16], the width of the dynamometers grip was individually adjusted to the hand size of the participant. Tests were performed in an upright standing position, arms down by the side, and full elbow extension [17]. Two test trials were performed, both for the dominant and non-dominant hand, the best trial was included in the analysis [18]. The cutoff value for handgrip strength < 27 kg for men and < 16 kg for women [6].

Physical performance was assessed by the 4-meter usual walking speed test, with speed measured manually with a stopwatch, a single cut-off speed ≤ of 0.8 m/s for both genders was considered as impaired physical performance [6]. Gait speed is considered a quick, safe, and highly reliable test for sarcopenia, and it is widely used in practice [19].

Pre-sarcopenia was defined according to Baumgartner's definition by SMI < 7 kg/m² for men and < 6 for women. Sarcopenia was defined by

the combined presence of the two following criteria according to the EWGSOP: a low muscle mass by whole-body DXA and a low muscle strength assessed by the handgrip. Severe sarcopenia was defined by the combination of the three criteria: low muscle mass by whole-body DXA, low muscle strength, and impaired physical performance by Gait speed test.

Ethical consideration

Ethical approval was obtained from the Ethical Committee of the University of Baghdad, College of Medicine, Rheumatology and Medical Rehabilitation Unit, and following the Declaration of Helsinki. Signed informed consent was taken from each participant in the study.

Statistical analysis

Statistical presentation and analysis of the present study were conducted using the mean, standard deviation, and Chi-square for linear correlation coefficient, t-test, and ANOVA by SPSS V20. ROC-curve: – Receiver Operating Characteristic curve analysis. Sensitivity, Specificity, PPV, NPV, and accuracy were calculated (Carter J V, 2016). $P < 0.05$ was considered significant.

RESULTS

The mean age of AS patients were (36.64 ± 7.684) years. The studied group consisted of 47 (94%) men and 3 (6%) women. Smoking was frequently higher in the AS patients. The physical activity was statistically non-significant. The mean BMI in AS patients was (28.447 ± 6.287), (Table 1). From a total of 50 patients with AS, 31 (62%) were having active disease and 19 (38%) were inactive (Figure 1).

About 12 (24%) patients were not received anti-TNF treatment, while 38 (76%) patients were kept on anti-TNF. Anti-TNF agents included Etanercept, Infliximab, or Adalimumab (Figure 2).

The data showed that mean of disease duration in AS patients were (6.92 ± 4.985) years, the mean of BASDAI was (4.16 ± 1.714), and the mean duration of anti-TNF was (25.816 ± 24.655) months (Table 2).

The prevalence of presarcopenia among AS group was 6%, while the prevalence of sarcopenia was 10%, with no significant ($p = 0.152$) (Table 3).

The results showed that the mean age of AS patients without sarcopenia was (37.089 ± 7.192) years, whereas those with sarcopenia was (32.6 ± 11.48) years, with no significant differences ($p = 0.219$). The mean value of BMI is significantly low-

er in patients with sarcopenia than in those without sarcopenia ($p = 0.001$). Sarcopenic patients were normal-weight (80%) and the remaining (20%) were underweight ($p < 0.001$), when compared with the non-sarcopenic group, which showed significantly higher BMI (Table 4).

The vast majority of the sarcopenic group (80%) were physically inactive, which was statistically significant compared with the non-sarcopenic group ($p = 0.033$), (Table 5). Handgrip was significantly higher in physically active groups, whereas LM, SMI, and gait speed were of no significant over subgroups (Table 6).

There was no significant association of treatment with anti-TNF or its duration between sarcopenia and non-sarcopenia groups ($p = 0.377$ and $p = 0.187$), respectively (Table 7).

Longer disease duration is significantly associated with sarcopenia ($p = 0.008$), while disease activity is insignificantly associated with sarcopenia ($p = 0.382$) (Table 8).

Both LM, and handgrip showed fair validity in AS patients by applying Receiver operating characteristic (ROC), sensitivity (68%), specificity (68%) when the area under the curve (AUC) was 0.71. Both SMI, and usual gait speed failed in the AS patients (AUC) for SMI 0.537, and the usual gait speed test was 0.546 (Table 9) (Figures 3, 4, 5).

Table 1. Demographic and clinical characteristics of AS patients

Variable		Patients		**P-value
		No.	%	
Age (years)	Mean $\pm$ SD	36.64 ± 7.684		
Gender	Male	47	94	0.05
	Female	3	6	
BMI (kg/m ²)	Underweight	1	2	0.733
	Normal	12	24	
	Overweight	20	40	
	Obese	17	34	
Smoking	Active smoking	17	34	0.04
	Non-smoking	22	44	
	Ex-smoking	11	22	
Physical activity	Inactive	13	26	0.94
	Moderate Inactive	18	36	
	Moderate active	12	24	
	Active	7	14	

BMI, body mass index; SD, standard deviation; ** Chi-square of linear correlation coefficient

Fig. 1. Disease activity in AS group

Fig. 2. Anti-TNF treatment in AS group

Table 2. Mean values of disease duration, BASDAI, and duration of anti-TNF

Disease characteristic	Mean ± SD
Disease duration (years)	6.92 ± 4.985
BASDAI	4.16 ± 1.714
Duration of anti-TNF (months)	25.816 ± 24.655

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; Anti TNF, anti-tumor necrosis factor

Table 3. The prevalence of presarcopenia, sarcopenia in the studied group

Results	n	%	**P-value
No sarcopenia	42	84	0.071
Pre-sarcopenia	3	6	
Sarcopenia	5	10	
Total	50	100	

** Chi-square of linear correlation coefficient

Table 4. Mean age and BMI association between sarcopenic and non-sarcopenic

	No sarcopenia	Sarcopenia	**P-value
	Mean ± SD		
Age (years)	37.089 ± 7.192	32.6 ± 11.48	0.219
BMI (kg/m ²)	29.372 ± 5.908	20.12 ± 1.974	0.001

BMI, Body Mass Index; **Chi-square of t-test

Table 5. Demographics association between sarcopenia and non-sarcopenia

No.		No sarcopenia		Sarcopenia		*P-value
		%	No.	%	No.	
Gender	Male	42	93.33	5	100	0.552
	Female	3	6.67	0	0	
BMI	Underweight	0	0	1	20	< 0.001
	Normal	8	17.78	4	80	
	Overweight	20	44.44	0	0	
	Obese	17	37.78	0	0	
Smoking	Active smoking	14	31.11	3	60	0.309
	Non-smoking	20	44.44	2	40	
	Ex-smoking	11	24.44	0	0	
Physical Activity	Inactive	9	20	4	80	0.033
	Moderate Inactive	17	37.78	1	20	
	Moderate active	12	26.67	0	0	
	Active	7	15.56	0	0	

BMI, body mass index; *ANOVA

Table 6. Physical activity effect on sarcopenia parameters

Parameter	Physical activity				*P-value
	Inactive	Moderate Inactive	Moderate active	Active	
	Mean ± SD				
LM (kg)	41.866 ± 6.51	44.49 ± 5.221	46.862 ± 6.384	46.203 ± 7.392	0.214
SMI	7.791 ± 1.024	7.804 ± 0.875	8.372 ± 0.972	8.267 ± 1.082	0.315
Handgrip	32.615 ± 7.217	28.611 ± 7.822	35.592 ± 6.961	39.557 ± 8.492	0.01
Usual Gait Speed	0.892 ± 0.196	0.973 ± 0.114	0.888 ± 0.198	0.991 ± 0.07	0.279

LM, lean mass; SMI, skeletal muscle mass; SD; standard deviation; *ANOVA

Table 7. Anti-TNF treatment association between groups

No.		No sarcopenia		Sarcopenia		*P-value
		%	No.	%		
Anti-TNF	No	10	22.22	2	40	0.377
	Yes	35	77.78	3	60	
Duration (Mean $\pm$ SD)		24.257 $\pm$ 24.354		44 $\pm$ 24.98		0.187

Anti TNF-anti tumor necrosis factors

Table 8. Disease characteristics association between sarcopenia and non-sarcopenia group

		Result		*P-value
		No sarcopenia	Sarcopenia	
		Mean $\pm$ SD / No. (%)		
Duration from diagnosis (years)		6.311 $\pm$ 4.719	12.4 $\pm$ 4.219	0.008
BASDAI		4.104 $\pm$ 1.77	4.66 $\pm$ 1.088	0.497
Disease Activity	Inactive	18 (40)	1 (20)	0.382
	Active	27 (60)	4 (80)	

BASDAI, Bath Ankylosing Spondylitis Activity Index; SD, standard deviation; *t-test

Table 9. ROC analysis and validity of LM, SMI, handgrip, usual gait speed test to differentiate between patients

	AUC	Cutoff	Sensitivity	Specificity	PPV	NPV	Accuracy
LM (kg)	0.710	≤ 46.984	68	68	68	68	71%
SMI	0.537	> 7.7	68	50	57.6	61	53.7%
Handgrip	0.719	≤ 34	56	80	73.7	64.5	71.9%
Usual Gait Speed	0.546	> 0.92	60	60	60	60	54.6%

LM, lean mass; SMI, skeletal muscle index; AUC, area under the curve

Fig. 3. ROC curve of LM of AS patients with sarcopenia

Fig. 4. ROC curve of SMI of AS patients with sarcopenia

Fig. 5. ROC curve of handgrip of AS patients with sarcopenia

DISCUSSION

To the best of our knowledge, this is the first study that assessed the prevalence of sarcopenia in a sample of Iraqi patients with Ankylosing Spondylitis.

Sarcopenia had been found in patients with younger age, lower BMI, longer disease duration, and lower physical activity. The prevalence of sarcopenia is not influenced by gender and smoking. The use of anti-TNF Lean mass and handgrip were fairly valid tests to differentiate between patients and controls.

This study showed the predominance of male with AS to female with a ratio of 15:1 which is comparable to another study conducted at Baghdad Teaching Hospital by Al-Osami et al. [20] and another one by Abdul-Wahid et al. [21], which showed the male to female ratio was 13:1 and 11:1, respectively.

In the current study, 10 of patients were found to have sarcopenia. These results are slightly lower than the results reported in a similar study at the

American College of Rheumatology/the Association of Rheumatology Health Professionals Annual Scientific Meeting in San Diego in 2017 [22], when the prevalence was 15% and 26% by applying Asian working group for sarcopenia (AWGS) criteria and Korea criteria respectively.

Barros et al. [23] and Barone et al. [24] showed the prevalence of sarcopenia equals 16.6% and 22.7%, respectively.

The prevalence of presarcopenia in the current study was 6% in both groups which disagree with another two studies, EL Maghraoui et al. [25] and Barone et al. [24], where the prevalence of presarcopenia was much greater 49.3%, 36.3%, respectively. These differences in the prevalence might be attributed to the following factors: sarcopenia is an age-related condition and the patients who enrolled in the former study were older compared to the mean age of patients in ours (40.9 ± 11 years vs 36.64 ± 7.684 years). Another explanation is the differences in methodology and the cutoff values that had been used in the diagnosis of sarcopenia and pre-sarcopenia.

The results showed that the AS patients with sarcopenia had a lower mean value of BMI compared to patients without sarcopenia, but when the patients stratified according to their categories of BMI, the results demonstrated that sarcopenia was more common in normal and underweight patients (80%, and 20%), respectively. These results are in agreement with the studies of Song et al. [22] and El Maghraoui et al. [25], where they revealed that AS patients with sarcopenia tend to have lower BMI than the patients without it.

Physical activity is the major stimulus for muscle anabolism and therefore may be of high importance in the prevention of muscle loss. Chronic diseases such as AS interfere with patients' physical functioning and quality of life. As a consequence, patients are at risk for physical inactivity and eventually loss of muscle mass [26, 27].

Data from our study revealed a statistically significant difference between the two groups (sarcopenia and non-sarcopenia groups) in that all of the patients with sarcopenia had reduced physical activity. These results are comparable to a study done in 2012 by Plasqui G. et al. [26], which assessed the relation of physical activity and body composition in AS patients and revealed that body composition is positively related to physical activity.

The data showed that the prevalence of sarcopenia was not associated with disease activity, while in other studies like Barone et al. [24] and

El Maghraoui et al. [25], there was a correlation of BASDAI measurement with sarcopenia. BASDAI is exclusively based on subjective patient evaluation, which may be responsible for this conflict.

Further analysis showed that patients with sarcopenia had a statistically significant longer disease duration ($p = 0.008$), this in line with the other two studies Song et al. [22] and El Maghraoui et al. [25]. However, the results of the current study and these two studies were inconsistent with another two studies, Barone et al. [24] and Kim et al. [28], which revealed the disease duration does not influence the prevalence of sarcopenia.

Treatment with anti-TNF can induce a significant and sustained reduction in disease activity and systemic inflammation. This study estimates the effect of Anti-TNF on sarcopenia status as anti-TNF treatment is expected to prevent cachexia [25]. The data did not reveal significant differences between patients who were receiving treatment with anti-TNF and those who were not on treatment. The duration of treatment did not show a significant difference in the development of sarcopenia in AS patients. These results are consistent with two other studies Barone et al. [24] and El Maghraoui et al. [25]. The results and the other two mentioned studies are inconsistent with two other studies, Barros et al. [23], and Barriot et al. [29], which showed the reversal of sarcopenia status in patients who were treated with anti-TNF. These differences may be attributed to the availability of these medications and the class of Anti-TNF used in different studies.

However, it is the only study in Iraq that estimate the prevalence of sarcopenia in AS patients, which evaluate the preventable risk factors of sarcopenia in those group of population, for the purposes of the improvement of the quality of life.

CONCLUSIONS

Patients with AS are at higher risk of developing early sarcopenia. Lower BMI, longer disease duration increases the risk of sarcopenia, while gender differences, smoking, and the use of anti-TNF do not influence the risk of sarcopenia. Physical activity improves muscle strength and decreases the risk of sarcopenia.

STUDY LIMITATIONS

A small sample size of adult population was analyzed and the scope of the observation period is short – 1/2 year. It is a single-center study, and the evaluation of disease activity was based on disease

scoring, but not on biochemical indexes or pro-inflammatory cytokine measurements.

Conflict of interests: None

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