*Med. J. Cairo Univ., Vol. 93, No. 3, Accepted 21/7/2025*
*DOI: 10.22608/MJCU. 1297-1306, September 2025*
*www.medicaljournalofcairouniversity.net*

# The Role of Myostatin in Rheumatoid Arthritis-Associated Sarcopenia

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## Abstract

*Background:* Fifty percent of patients with Rheumatoid Arthritis (RA) can develop muscle loss. Primary sarcopenia appears in older individuals. However, secondary sarcopenia can appear in younger individuals with chronic inflammation. RA patients may have a higher risk for developing secondary sarcopenia due to chronic inflammation. Myostatin is a part of the transforming growth factor-β superfamily and negatively regulates skeletal muscle growth.

*Aim of Study:* To assess serum level of myostatin in RA patients and to study its relation to sarcopenia and disease activity.

*Results:* The serum myostatin level was significantly high in RA patients versus controls. RA group showed significant decrease in skeletal muscle mass index (SMI), grip strength, 6-minutes walking distance test and gait speed when compared to controls.

Serum myostatin level showed significant negative correlation with SMI, Grip strength, 6-m walking distance test and Gait speed. A significant high levels of serum myostatin was found in pre-sarcopenia and sarcopenia stages in RA patients compared to those with normal muscle status. Serum myostatin level was related to grades of disease activity, also there was a significant association between different sarcopenia stages with different grades of DAS28-CRP. A higher incidence of sarcopenia and pre-sarcopenia stages was found in RA patients at risk of malnutrition.

*Conclusion:* This study concluded that higher serum myostatin levels were present in RA patients compared to healthy controls.

Myostatin is an important risk factor which may contribute to development of RA associated sarcopenia in addition to malnutrition and persistent disease activity.

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***Key Words:*** *Rheumatoid arthritis – Myostatin – Sarcopenia – Disease activity.*

## Introduction

**RHEUMATOID** Arthritis (RA) is a common inflammatory autoimmune disease characterized by synovial inflammation, irreversible erosive joint destruction and impaired quality of life **[1].**

Fifty percent of patients with RA can develop muscle loss that will lead to rheumatoid cachexia in around 25% (ranges from 7% to 33%) which is associated with poor quality of life **[2,3].**

Sarcopenia is characterized by loss of muscle strength and muscle mass. It leads to adverse health outcomes, such as an increased risk of falls, fractures, impaired mobility, lower activities of daily living (ADL) and poor quality of life (QOL) **[4-7].**

Sarcopenia is a multifactorial syndrome and multiple factors are involved in the etiology of sarcopenia as malnutrition (low protein, energy, and vitamin D intake), hormonal changes, increases in inflammatory cytokine levels (IL-6, TNF-α, and IL-1β) and oxidative stress. These factors act synergistically, leading to muscle degradation, atrophy and loss of muscle mass, and decreased muscle regeneration **[8,9].**

Primary sarcopenia is mostly age-dependent and appears in older individuals; however, secondary sarcopenia can appear in younger individuals with chronic inflammation **[10].**

Patients with rheumatoid arthritis (RA) may have a higher risk for developing secondary sarcopenia due to chronic inflammation, decreased physical activity caused by pain and deformity of the joints, and concomitant treatments such as the use

of glucocorticoids (GCs) [11-13]. Myostatin is a part of the transforming growth factor-β superfamily. It is a cytokine produced and released by myocytes, that negatively regulates skeletal muscle growth. Its inactivation can induce skeletal muscle hypertrophy, while its overexpression causes muscle atrophy. Moreover, Myostatin enhances proteolysis and inhibits protein synthesis in skeletal muscle [14].

It was suggested that myostatin could be also involved in synovitis and joint damage in animal models of RA [15]. Therefore, it was interesting to explore the association of myostatin with joint inflammation and sarcopenia in RA patients.

The aim of this work was to assess serum level of myostatin in RA patients and to study its relation to sarcopenia and disease activity.

## *Patients and Methods*

A case control study was conducted on 45 RA patients, diagnosed according to ACR/EULAR 2010 classification criteria for RA. Patients were recruited from outpatient clinic of Rheumatology and Rehabilitation Department in Mansoura University Hospital during the period from August 2022 to April 2023. Patients with psoriatic arthritis, SLE, Pregnant, lactating, DM, thyroid dysfunctions, chronic viral hepatitis, malignancy and other factors associated with musculoskeletal abnormalities as sedentarism were excluded. 45 apparent healthy individuals with matched age and sex with the RA patients were included in the control group. Before participation, the aims and procedures of the study were explained in detail to all participants and a written consent was obtained from each participant. This study was approved by the research board of Faculty of Medicine, Mansoura University: code: MS.21.11.1745.

All patients subjected to complete history taking including medications for the current disease as disease modifying anti-rheumatic drugs (DMARDS), non-steroidal anti-inflammatory drugs (NSAIDS), steroids, biological therapy or medications for any other diseases as diabetes mellitus or hypertension. Full general, neurological and musculoskeletal examination done for all included subjects.

*Assessment of muscle status (Sarcopenia):*

Grip strength was measured using a hand-held CAMRY dynamometer (CAMRY EH101, Sensun Weighing Apparatus Group Ltd, Guangdong, China). Each participant was seated, his elbow by his side and flexed to right angle, and a neutral wrist position, Then the participant squeezed the dynamometer with all of his strength, typically three times with each hand. An average score was then calculated [16]. Probable sarcopenia is suggested if handgrip is <27kg (59.52lbs) and <16kg (35.27 lbs), for males and females, respectively.

Skeletal muscle mass index (SMI) was obtained with a dual-energy X-ray absorptiometry (DXA). All participants undergone a whole-body scan using DXA machine (GE medical systems-Lunar Madison, WI USA 41170). SMI was calculated using the following formula: sum of skeletal muscle mass of extremities (SMME) ([arms + legs]/divided by height squared) [17]. Cut-off points of Skeletal muscle mass index (SMI) for Men: 7.26kg/$m^2$ and for Women: 5.5kg/$m^2$ [10].

*6-m walking test:* Each participant was asked to walk as far as possible along a 30 meter distance corridor for a period of 6 minutes and the 6-min walk distance (6MWD) is measured in meters. The distance of ≤400 meter during 6 minutes is an indicator of severe sarcopenia [18].

*Gait speed test:* Gait speed test is called the 4-minutes usual walking speed test, with speed measured using a stopwatch. The speed of ≤0.8 meter/second is an indicator of severe sarcopenia [19].

*Interpretation of Sarcopenia:*

The European Working Group on Sarcopenia in Older People (EWGSOP) classified sarcopenia into 3 stages:

- The presarcopenia stage is identified by low muscle mass without impact on muscle strength or physical performance.
- The sarcopenia stage is identified by low muscle mass, plus low muscle strength.
- or low physical performance.
- Severe sarcopenia stage is identified when all three criteria of the definition are met (low muscle mass, low muscle strength and low physical performance) [10].

DAS28 CRP was used to assess the DA [20]. The HAQ-DI questionnaire was used to evaluate patient's functional capacity to perform daily activities [21].

*Serum myostatin determination:*

Serum concentration of myostatin was measured by enzyme-linked immunosorbent assay (ELISA) using a commercial kit (Wuhan Fine Biotech co., Ltd China. Catalogue No.: EH1870).

Nutritional status was assessed using MNA-SF (Mini Nutritional Assessment Short Form) [22].

*Statistical analysis:*

All statistical analyses were performed using SPSS software, version 20.0. Continuous variables were assessed for normality prior to further analysis. All continuous variables showed normal distribution were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. Group comparisons of normally distributed continuous variables were carried out using the independent samples Student's *t*-test. For comparisons involving more than two groups, one-way ANOVA was applied to normally distributed continuous data. Categorical variables were analyzed using the Chi-square test. Correlations between two normally distributed continuous variables were assessed using Pearson's correlation coefficient. Multiple linear regression analysis was conducted with serum myostatin as the dependent variable and various clinical and physical function measures as independent variables, to identify factors that best predicted serum myostatin levels. Receiver Operating Characteristic (ROC) curve analysis was used to evaluate the ability of serum myostatin to distinguish between individuals with and without sarcopenia. A *p*-value of <0.05 was considered statistically significant.

## Results

The study included 34 females (75.6%) and 11 males (24.4%) and their age range from 18 to 50 years old and 45 healthy controls; 30 (66.7%) females and 15 (33.3%) males. Table (1) showed that the range of disease duration was between 3 and 20 years, the median duration of morning stiffness ranged from 15 and 90 minutes, the range of tender joints count was between 6 and 23 joints and the range of the number of swollen joints was 4 and 20 joints. DAS and Functional status of RA patients as well as the medications used during the study are shown in Table (1).

The serum myostatin level in RA patients ranged from 220.4 to 1963.0pg/ml with a mean ± SD of 1214.6±530.5pg/ml while in controls ranged from 155.2 to 1157.0pg/ml with a mean ±SD of 621.9±308.1pg/ml and this difference was significant ($p$<0.001). RA group showed significant decrease in relative skeletal muscle mass index, grip strength, 6-minutes walking distance test and gait speed when compared to control subjects ($p$<0.001). Pre-sarcopenia and sarcopenia stages were found in RA patients [18 (40.0%) & 5 (11.1%) respectively] while nothing of these stages were found in controls, twenty two of RA patients (48.9%) & all control subjects 45 (100.0%) showed absence of sarcopenia. These differences were statistically significant ($p$<0.001), see Table (2).

Table (1): Descriptive analysis of the clinical characteristics and medications intake among the RA patients.

| | Range | Mean ± SD |
|---|---|---|
| *RA characteristics:* | | |
| - Disease duration (years) | 3 – 20 | 10.7±5.2 |
| - Duration of morning stiffness (minutes) | 15 – 90 | 47.7±22.8 |
| - TJC | 6 – 23 | 15.4±4.9 |
| - SJC | 4 – 20 | 11.8±4.8 |
| *DAS and Functional status:* | | |
| - DAS28-CRP (<2.3 - >4.1) | 1.71 – 5.09 | 3.5±0.98 |
| - HAQ (0 - 3) | 0.50 – 3.28 | 1.5±0.53 |
| *Medications (n, %):* | | |
| - Methotrexate | 24, 55.6% | |
| - Steroids (2.5 – 10) mg | 15, 33.3% | |
| - HCQ | 35, 77.8% | |
| - LFN | 21, 46.7% | |
| - Biologics | 9, 20.0% | |

TJC: Tender joint count. MTX: Methotrexate.
SJC: Swollen joint count. HCQ: Hydroxychloroquine.
DAS: Disease activity score. LFN: Leflunomide.
HAQ: Health assessment questionnaire.

Table (2): Comparison of serum myostatin level, muscle status and sarcopenia stages between the RA group and control group.

| | RA Group (n=45) | Control Group (n=45) |
|---|---|---|
| - Serum myostatin level (pg/ml) (Mean ± SD) | 1214.6±530.5 | 621.9±308.1 |
| - Relative skeletal mass index by DXA (Mean ± SD) | 6.3±1.2 | 7.1±0.9 |
| - Grip strength (Pound) (Mean ± SD) | 45.6±19.1 | 82.7±40.9 |
| - 6-m walking distance test (meter/6 min) (Mean ± SD) | 383.0±115.8 | 565.1±100.9 |
| - Gait speed (meter/sec) (Mean ± SD) | 0.9±0.3 | 1.6±0.3 |
| *Stages of sarcopenia (N, %):* | | |
| - No sarcopenia | 22 (48.9%) | 45 (100.0%) |
| - Pre-sarcopenia | 18 (40.0%) | 0 (0.0%) |
| - Sarcopenia | 5 (11.1%) | 0 (0.0%) |

$p \leq 0.05$ is significant
$X^2$: Chi square test.
RA: Rheumatoid arthritis.
DXA: Dual energy X-ray absorptiometry.

Serum Myostatin level did not show significant difference between RA patients taking MTX, HCQ, leflunomide, biologics or glucocorticoids compared to patients not taking the drugs ($p$>0.05).

Table (3) showed that serum myostatin levels were related to grades of disease activity (F=3.658, $p$=0.020).

Table (3): Relation of serum myostatin level and RA disease activity.

| | Serum myostatin level (pg/ml) Mean ± SD | One-way ANOVE | |
|---|---|---|---|
| | | F | *p* |
| *DAS28-CRP (N):* | | | |
| Remission (9) | 809.0±400.1 | | |
| Low disease activity (10) | 1069.6±510.9 | | |
| Moderate activity (15) | 1158.1±483.5 | | |
| High activity (11) | 1567.0±482.4 | 3.658 | 0.020* |

$p\leq0.05$ is significant.
DAS: Disease activity score.

Fig. (1) showed that significant higher levels of serum myostatin were found in pre-sarcopenia and sarcopenia stages in RA patients compared to those with normal muscle status ($p$=0.040).

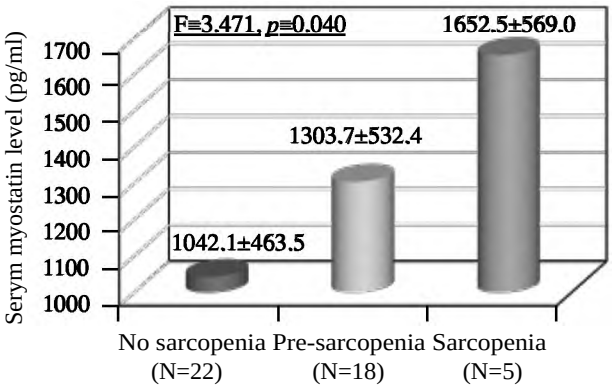


Fig. (1): Comparison of the Serum myostatin level among different sarcopenia stages in RA patients.

Table (4) showed that significant association was found between different sarcopenia stages with different grades of DAS28-CRP ($X^2$=13.575, $p$=0.035 and F=11.762, $p$<0.001). Moreover, higher incidence of sarcopenia and pre-sarcopenia stages was found in RA patients at risk of malnutrition than those with normal nutritional status ($p$=0.017). However, there is no significant association between different sarcopenia stages and different medications taken by RA patients ($p$>0.05).

In RA patients; serum myostatin level showed significant correlation with ESR ($p$=0.003), CRP ($p$=0.014), duration of morning stiffness ($p$=0.019), TJC ($p$=0.005), SJC ($p$=0.020), DAS28-CRP ($p$<0.001) and HAQ but there was no significant correlation with Hb concentration, WBCs count, Platelets count, RF titer, Anti-CCP titer, ALT, Creatinine, age and BMI ($p$>0.05), see Table (5).

Serum myostatin level showed significant negative correlation with relative skeletal muscle mass index ($p$=0.030), Grip strength ($p$<0.001), 6-m walking distance test ($p$=0.004) and Gait speed ($p$=0.006). In contrast, no significant correlation was found between serum myostatin level and MNA-SF ($p$>0.05) (Table 5).

The multiple linear regression analysis explored the association between serum myostatin levels and various clinical and physical function measures. Among the predictors included in the model, higher SJC (B=47.56, $p$=0.030) and greater disability as measured by the HAQ (B=560.53, $p$=0.028) were both significantly associated with increased serum myostatin levels.

Other variables, such as duration of morning stiffness ($p$=0.077) and nutritional status measured by the MNA-SF ($p$=0.075), showed trends toward significance, indicating possible associations with serum myostatin that did not reach statistical significance in this sample. Notably, inflammatory markers such as ESR and CRP, disease duration, grip strength, gait speed, and other physical performance measures, did not demonstrate significant relationships with myostatin levels (Table 6).

Roc curve analysis revealed moderate ability of serum myostatin for differentiation cases with sarcopenia than those without sarcopenia with an AUC=0.698 (Fig. 2).

Table (4): Comparison of the DAS28-CRP category and MNA-SF category among different sarcopenia stages in RA patients.

| | Sarcopenia stages | | | | | | $X^2$/F | *p* |
|---|---|---|---|---|---|---|---|---|
| | No Sarcopenia (N=22) | | Pre-Sarcopenia | | Sarcopenia (N=5) | | | |
| | N | % | N | % | N | % | | |
| Activity grade based on *DAS28-CRP:* | | | | | | | | |
| Remission (<2.6) | 6 | 27.3 | 3 | 17.6 | 0 | 0.0 | | |
| Low (2.6-3.2) | 7 | 30.4 | 3 | 17.6 | 0 | 0.0 | | |
| Moderate (3.2-5.1) | 5 | 21.7 | 9 | 52.9 | 1 | 20.0 | | |
| High (>5.1) | 4 | 17.4 | 3 | 17.6 | 4 | 80.0 | 13.575 | 0.035* |
| DAS28-CRP (mean ± SD) | 2.9±0.78 | | 3.6±0.89 | | 4.8±0.21 | | 11.762# | <0.001* |
| *MNA-SF category:* | | | | | | | | |
| At risk of malnutrition MNA Score (8-11) | 8 | 36.4 | 12 | 66.7 | 5 | 100.0 | | |
| Normal MNA Score (12-14) | 14 | 63.6 | 6 | 33.3 | 0 | 0.0 | 8.182 | 0.017* |
| MNA-SF score (mean ± SD) | 12.1±1.8 | | 10.9±1.5 | | 9.6±0.9 | | 6.275# | 0.004* |

# F-value. *p*≤0.05 is significant. DAS: Disease activity score.
One-way ANOVA test. $X^2$ : Chi square test. CRP: C-reactive protein.

Table (5): Correlation between Serum Myostatin level with demographic, clinical, muscle status and laboratory findings in RA patients.

| | Serum myostatin level (pg/ml) | |
|---|---|---|
| | *r* | *p* |
| *Demographic data:* | | |
| Age | -0.052 | 0.736 |
| BMI | 0.241 | 0.111 |
| *RA characteristics:* | | |
| Disease duration (years) | 0.332 | 0.026* |
| Duration of morning stiffness (minutes) | 0.348 | 0.019* |
| TJC | 0.410 | 0.005* |
| SJC | 0.346 | 0.020* |
| *DAS and functional status:* | | |
| DAS28-CRP | 0.535 | <0.001* |
| HAQ | 0.490 | <0.001* |
| Relative skeletal muscle mass index | -0.323 | 0.030* |
| Grip strength (pounds) | -0.476 | <0.001* |
| 6-m walking distance test (meters) | -0.424 | 0.004* |
| Gait speed (meter/second) | -0.406 | 0.006* |
| MNA-SF | -0.111 | 0.470 |
| *Blood Picture:* | | |
| Hb concentration (mg/dl) | -0.023 | 0.880 |
| WBCs count (x1000/$mm^3$) | -0.047 | 0.758 |
| Platelets count (x1000/$mm^3$) | 0.076 | 0.618 |
| *Acute Phase Reactants:* | | |
| ESR (mm 1st hour) | 0.426 | 0.003* |
| CRP (mg/dl) | 0.364 | 0.014* |
| *Autoantibodies:* | | |
| RF titer (IU/ml) | -0.007 | 0.966 |
| Anti-CCP titer (U/ml) | -0.202 | 0.183 |
| *Liver and Kidney function tests:* | | |
| ALT (mg/dl) | 0.142 | 0.352 |
| Creatinine (mg/dl) | -0.042 | 0.786 |

*p*≤0.05 is significant. CRP : C-reactive protein.
Hb: Hemoglobin. RF : Rheumatoid factor.
WBCs: White blood cells. ACCP : Anti citrullinated protein antibody.
ESR: Erythrocyte sedimentation rate. ALT: Alanine aminotransferase.

Table (6): Multiple linear regression analysis with Serum myostatin as the dependent variable and various clinical and physical function measures as independent variables.

| | Unstandardized Coefficients | | Standardized Coefficients | *t* | Sig. |
|---|---|---|---|---|---|
| | B | Std. Error | Beta | | |
| (Constant) | -2725.803 | 1396.528 | | -1.952 | 0.060 |
| ESR | 2.316 | 4.284 | 0.091 | 0.541 | 0.593 |
| CRP | 1.114 | 4.054 | 0.044 | 0.275 | 0.785 |
| Disease duration | -15.135 | 17.260 | -0.148 | -0.877 | 0.387 |
| Duration of morning stiffness | -8.071 | 4.405 | -0.347 | -1.832 | 0.077 |
| TJC | 4.032 | 16.800 | 0.038 | 0.240 | 0.812 |
| SJC | 47.557 | 20.955 | 0.435 | 2.269 | 0.030 |
| DAS28-CRP | 109.029 | 136.566 | 0.201 | 0.798 | 0.431 |
| HAQ | 560.529 | 243.783 | 0.565 | 2.299 | 0.028 |
| Grip strength | 2.991 | 5.339 | 0.108 | 0.560 | 0.579 |
| Relative skeletal muscle index | 115.257 | 92.331 | 0.267 | 1.248 | 0.221 |
| 6-minute walk distance | 0.094 | 1.131 | 0.021 | 0.084 | 0.934 |
| Gait speed | 111.824 | 351.606 | 0.074 | 0.318 | 0.753 |
| MNA.SF | 130.751 | 71.058 | 0.443 | 1.840 | 0.075 |

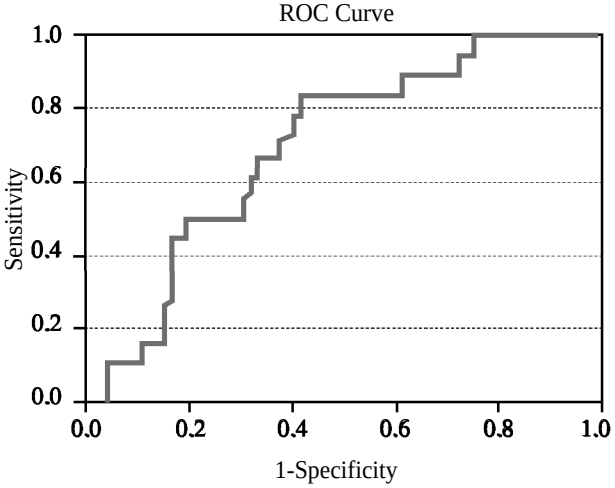


Fig. (2): Roc curve analysis for the ability of serum myostatin for differentiation cases with sarcopenia than those without sarcopenia (AUC=0.698).

## Discussion

In the current study, the serum myostatin level in RA patients was significantly higher compared to controls ($p$<0.001).

These results confirmed the earlier studies by [23-25] who also reported higher myostatin levels in RA patients compared to their controls.

On the other hand [26], demonstrated higher myostatin levels in healthy controls than RA patients. This difference may be due to the different method that he used to detect serum myostatin (colorimetric competitive immunoassay) and the RA patients in his study were in remission.

In the current study, there was no correlation between serum myostatin level with age and BMI ($p$<0.05). This come in accordance with another report who reported that serum myostatin level not related to age and BMI [23].

In the current study, there was a significant correlation between serum myostatin level and disease duration ($p$=0.026).

This finding agreed with Murillo-Saich et al., 2021 who also found that myostatin level correlated with disease duration ($p$=0.02) [23].

Moreover, there was a significant correlation between serum myostatin level and duration of morning stiffness ($p$=0.019), TJC ($p$=0.005) and SJC ($p$=0.020).

The current study showed a significant decrease in muscle mass, grip strength, 6-min walking distance test and gait speed in RA patients compared to controls ($p$<0.001).

These results are comparable to previous study done by Santo et al., 2018 who reported the decrease in muscle mass, grip strength, 6-min walking distance test and gait speed in RA patients [2].

Accordingly, we concluded that pre-sarcopenia and sarcopenia stages are significantly higher in RA patients than controls ($p$<0.001) which is in agreement with earlier studies done by Santo et al., 2018 [2], Lin et al., 2019 [27], Dao et al., 2021 [28] and Gonzalez-Ponce et al., 2022 [25] who documented the higher prevalence of sarcopenia among RA patients.

However, Metsios et al., 2009 [29] and Bokhorst et al., 2012 [30] found a very low prevalence of RS (8.5% and 1% respectivly) of RA patients.

This variation may be due to the lack of consensus on the clinical criteria for diagnosis, different methods of body composition assessment and the heterogeneity of the RA populations studied. Differences in ethnicity/race and epidemiological risk factors also can influence the variability in the prevalence rates reported across studies [2].

In the current study, serum myostatin level showed significant –ve correlation with relative skeletal mass index ($p$=0.030), Grip strength ($p$<0.001), 6-m walking distance test ($p$=0.004) and Gait speed ($p$=0.006).

These findings agreed with Kerschan-Schindl et al., 2019 [26] and Gonzalez-Ponce et al., 2022 [25] who also observed that the increase in myostatin serum level was associated with low skeletal muscle mass and weak grip strength ($p$<0.05).

These results indicate that the higher the myostatin level, the worse the physical functionality of patients with RA [25].

Moreover, this study showed that there was a significant correlation between serum myostatin level and different sarcopenia stages in RA patients (p=0.040). The cases with pre-sarcopenia and sarcopenia stages had higher myostatin level than those without sarcopenia.

These findings confirmed the earlier studies done by Murillo-Saich et al., 2021 [23] and Gonzalez-Ponce et al., 2022 [25] who found an inverse correlation between myostatin level and skeletal muscle mass index. Both studies agree with the hypothesis that myostatin is a –ve regulator of muscle growth.

Nevertheless, Lin et al., 2022 demonestrated a +ve correlation between serum myostatin level and muscle mass ($p$<0.001) [24]. This difference could be due to the different methods used to assess muscle mass and different clinical criteria used for diagnosis of sarcopenia.

The assessment of RA disease activity for our patients using DAS28-CRP revealed that 11.1% (n=5) patients were in remission, 15.6% (n=7) had low disease activity, 46.7% (n=21) had moderate activity while 26.7% (n=12) patients had high disease activity.

In the current study, there was a significant +ve correlation between serum myostatin level and DAS28-CRP in RA patients ($p$=0.001). Moreover higher serum myostatin levels were found in low to moderate disease activity compared to inactive patients, while the highest serum myostatin levels were found in patients with high disease activity ($p$=0.020).

This finding agreed with Murillo-Saich et al., 2021 [23] and Lin et al., 2022 [24] who also showed that RA patients with high myostatin level had the highest level of DAS28-CRP.

In the current study, In RA patients; there was a significant +ve correlation between serum myostatin level and the Health Assessment Questionnaire (HAQ) ($p$<0.001) which agreed with Kerschan-Schindl et al., 2019 [26], Murillo-Saich et al., 2021 [23] and Gonzalez-Ponce et al., 2022 [25] who also found a +ve correlation between myostatin and HAQ ($p$<0.001).

Also, this study showed that serum myostatin level had a significant correlation with ESR ($p$<0.003) and CRP ($p$<0.014) which support the earlier study of Murillo-Saich et al., 2021 [23] who demonstrated similar results.

On the other hand, there was no significant correlation of serum myostatin with Hb concentration, WBCs count, Platelets count, RF titer, Anti-CCP titer, ALT or Creatinine ($p$>0.05). Also, serum myostatin level did not show significant difference between RA patients on different medications.

In the current study, a significant correlation was found between different sarcopenia stages and different grades of DAS28-CRP ($p$=0.035).

This was in accordance with Ngeuleu et al., 2017 [31], Lin et al., 2019 [27] and Gonzalez-Ponce et al., 2022 [25] who showed that the risk of rheumatoid sarcopenia increased with moderate/severe disease activity and high levels of myostatin.

In the current study, significant correlation was found between different sarcopenia stages and nutritional status with higher incidence of pre-sarcopenia and sarcopenia stages in RA patients at risk of malnutrition than patients with normal nutritional status ($p$=0.017), this come in accordance with Lin et al., 2019 who found that Mini Nutritional Assessment Short Form (MNA-SF) scores were significantly lower in sarcopenic patients than non-sarcopenic patients [27]. These results clarify the effect of healthy nutrition on preventing sarcopenia.

In contrast, no significant correlation was found between Serum Myostatin level and MNA-SF ($p$>0.05).

In the current study we showed that there was no significant association between different sarcopenia stages and different medications taken by RA patients.

However, Torii M et al., 2019 **[3]** reported that sarcopenic patients were more frequently treated with glucocorticoids and were less frequently treated with biological DMARDs compared to non sarcopenic patients.

The previous results could reflect the potential role of myostatin on inflammation and could be an indicator for disease activity and support the results observed by Murillo- Saich et al., 2021 **[23]**.

Despite the obtained results, the current study has some limitations. Mainly in the form of the small included sample size and being a single center study. Also, the cross sectional nature of the study and better results could be obtained with prospective studies to assess the effect of treatment regimen on the myostatin level.

In conclusion, higher serum myostatin levels were present in RA patients compared to healthy controls. Moreover, these levels were significantly associated with disease activity which may reflect the potential role of myostatin in triggering the inflammatory process of the disease.

Myostatin is an important risk factor which may contribute to development of RA associated sarcopenia in addition to malnutrition and persistent disease activity. Therefore, it may have an essential role in early detection of pre- clinical sarcopenia and it could be a therapeutic target to minimize the burden of sarcopenia on patient quality of life.

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# دور مادة الميوستاتين فى وهن العضلات المصاحب لمرض الرثيان المفصلى

نظـرة عامـة: يُعـد التهـاب المفاصـل الروماتويـدى (RA) مرتبطـاً بفقـدان الكتلـة العضليـة، حيـث يُصـاب نحـو ٥٠٪ مـن المرضـى بالسـاركوبينيا، ويتطـور الأمـر إلـى الكاشيكسـيا الروماتويديـة لـدى حوالـى ٢٥٪ منهـم. وعلـى عكـس السـاركوبينيا الأوليـة المرتبطـة بتقـدم العمـر، يمكـن أن تصيـب السـاركوبينيا الثانويـة الأفـراد الأصغـر سـناً نتيجـة الالتهـاب المزمـن، قلـة النشـاط البدنـى، وتأثيـرات الأدويـة مثـل الكورتيكوسـتيرويدات.

يُعد الميوستاتين من منظمات النمو السلبية للعضلات الهيكلية، وقد يكون له دور رئيسى فى هذه العملية.

الهـدف مـن الرسـالة: تقييـم مسـتوى الميوسـتاتين فـى مصـل الـدم لـدى مرضـى التهـاب المفاصـل الروماتويـدى، ودراسـة علاقتـه بالسـاركوبينيا ونشـاط المـرض.

المـواد والطـرق: أجريـت دراسـة علـى ٤٥ مريضـاً بالتهـاب المفاصـل الروماتويـدى (وفقـاً لمعاييـر ACR/EULAR 2010)، بالإضافـة إلـى ٤٥ فـرداً سـليماً مماثـلاً فـى العمـر والجنـس كمجموعـة ضابطـة. تم جمـع العينـات مـن مستشـفيات جامعـة المنصـورة والمنصـورة العـام الجديـد بـين أغسـطس ٢٠٢٢ وأبريـل ٢٠٢٣.

شـملت تقييمـات السـاركوبينيا قيـاس قـوة القبضـة (بجهـاز CAMRY)، مؤشـر كتلـة العضـلات الهيكليـة (عـن طريـق DXA)، واختبـارى المشـى لمـدة ٦ دقائـق وسـرعة المشـى. تم تقييـم الحالـة التغذويـة باسـتخدام مقيـاس MNA-SF، وقيـاس مسـتوى الميوسـتاتين فـى المصـل باسـتخدام اختبـار ELISA.