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Original Article

Sarcopenia and overweight in women with systemic lupus erythematosus

Sarcopenia e excesso de peso em mulheres portadoras de lúpus eritematoso sistêmico

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ABSTRACT

Objective: To investigate the prevalence of sarcopenia according to the categories of body mass index (BMI) in women with systemic lupus erythematosus (SLE) assisted by a teaching hospital in Maceió, Alagoas, Brazil. Methods: Cross-sectional analysis with patients selected by convenience, which included socioeconomic, demographic, clinical, anthropometric and sarcopenia data. The anthropometric evaluation included BMI, body circumferences, skin folds, bioimpedance analysis and fat percentage. Sarcopenia was assessed according to the diagnostic criteria proposed by the European Working Group on Sarcopenia in the Elderly-EWGSOP (2019), which includes a SARC-F screening protocol, muscle strength, muscle mass and physical performance. Pearson's chi-square test was distributed, adopting a significance level of p < 0.05 and a 95% confidence interval. Results: 62.8% of the women presented overweight, followed by 32.5% with normal weight and 4.6% with malnutrition. Sarcopenia was not detected in our sample. However, the SARC-F screening identified 17.5% possible cases of sarcopenia, while 21.4% of the patients had probable sarcopenia according to the criteria of low handgrip strength (HGS). Still, a portion of the sample showed reduction in physical performance, with no statistical differences according to the BMI categories. Also, 66.6% of women with probable sarcopenia and all those screened by SARC-F for sarcopenia, presented overweight. Conclusion: The reduced muscle strength, performance and the high weight are an alert do decrease in muscle functionality, making clear the need for early care of this population as well as adaptations of the sarcopenia assessment instrument for SLE.

Keywords: autoimmune disease; overweight; obesity; skeletal muscle; adipose tissue.

RESUMO

Objetivo: Investigar a prevalência de sarcopenia de acordo com as categorias de índice de massa corporal (IMC) em mulheres com lúpus eritematoso sistêmico assistidas por um hospital de ensino de Maceió, Alagoas. Métodos: Análise transversal com pacientes selecionadas por conveniência, que incluiu dados socioeconômicos, demográficos, clínicos, antropométricos e de sarcopenia. A avaliação antropométrica incluiu IMC, circunferências corpóreas, pregas cutâneas, análise de bioimpedância e percentual de gordura. A sarcopenia foi avaliada segundo os critérios diagnósticos propostos pelo European Working Group on Sarcopenia in Older People-EWGSOP (2019), que inclui um protocolo de triagem SARC-F, a força muscular, a quantidade muscular e o desempenho físico. Foi aplicado o teste de qui-quadrado de Pearson, adotando nível de significância de p < 0,05 e intervalo de confiança de 95%. Resultados: 62,8% das mulheres apresentaram excesso de peso, seguidas de 32,5% com eutrofia e 4,6% com desnutrição. Não foi detectada sarcopenia em nossa amostra. Contudo, a triagem SARC-F apontou 17,5% possíveis casos de sarcopenia, enquanto 21,4% das pacientes tiveram provável sarcopenia de acordo com o critério de baixa força de preensão manual (FPM). Ainda, uma parcela da amostra apresentou redução de desempenho físico, sem diferenças estatísticas de acordo com as categorias de IMC. Ainda, 66,6% das mulheres com provável sarcopenia e todas aquelas triadas pelo SARC-F para sarcopenia, apresentaram excesso de peso. Conclusão: O desempenho, a força muscular diminuída e o elevado excesso de peso são alertas para a diminuição de funcionalidade muscular, ficando claro a necessidade do cuidado precoce desta população, bem como adaptações do instrumento avaliativo de sarcopenia para o LES.

Palavras-chave: doença autoimune; sobrepeso; obesidade; músculo esquelético; tecido adiposo.

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Introduction

Systemic lupus erythematosus (SLE) is a chronic and autoimmune inflammatory disease, characterized by the deposition of immune complexes in several organs, leading to tissue damage [1]. Although genetic, environmental, hormonal, and pharmacological factors may play an important role in the development and clinical course of the disease, its etiopathogenesis is still unclear [1,2].

During periods of exacerbation, in view of the multisystemic nature of SLE, the disease may present itself in different ways. Skin and joint changes, pleuritis, pericarditis, nephritis, neuropsychiatric and hematological changes are commonly identified and may vary according to the predisposition of each patient affected by the disease [1,3].

In addition to these, skeletal muscle changes can affect the clinical course of SLE and the quality of life of these patients [4]. Among these changes, sarcopenia has been highlighted, defined as a progressive and generalized disorder of skeletal musculature characterized by low muscle quantity and / or quality, accompanied by low muscle strength and low physical performance, the latter being used as a measure of the severity of this syndrome [5]. Moreover, this disorder is common with advancing age, but it can also be a result of chronic non-communicable diseases (CNCDs) contributing to the development of complications and adverse outcomes [5-7]. In addition to sarcopenia, other changes in body composition can be detected and include abnormalities in nutritional status. An increase in the prevalence of overweight / obesity and a proportion, albeit lower, of malnutrition have been identified [8].

In view of the compromised quality of life resulting from SLE, patients who manifest musculoskeletal and body composition changes are dependent on the performance of routine activities and greater physical inactivity, greater perception of pain in muscles and joints, greater neurocognitive impairment, increased risk of fracture, increased risk of cardiovascular complications, metabolic syndrome and ovarian failure, further compromising quality of life [9-15].

Data available in the literature on the factors that corroborate the development and worsening of disorders in body composition and conservation of muscle mass point out that among such factors are the use of glucocorticoids, the metabolic changes inherent to the disease and the food profile [16-18].

In clinical practice, changes in body composition can occur independently of changes in body mass index (BMI), which suggests a difficulty in diagnosing sarcopenia influenced by adequate nutritional status or being overweight [12,16]. Knowing this, the present study aimed to describe the prevalence of sarcopenia according to the categories of BMI in women with SLE assisted by a teaching hospital in Maceió, Alagoas.

Methods

This is a cross-sectional study that is part of a larger project entitled "Sarcopenia in Systemic Lupus Erythematosus", approved by the Ethics and Research Committee of the Federal University of Alagoas (Opinion No. 3.138.940 / CAAE 89436418.1.0000.5013). The collections took place between August 2018 and September 2019 at the Integrated Center for Nephrology at the Professor Alberto Antunes University Hospital, according all ethical criteria. The sample consisted of 43 female patients selected for convenience, including those over the age of 18, with a previously established medical diagnosis of SLE according to the recommendations of the American College of Rheumatology [3]. Elderly, pregnant patients, with cancer and HIV positive serology, hepatitis B and C were excluded from the sample.

Socioeconomic and demographic variables included age, place of birth and origin, marital status (with or without a stable union), race (black and non-black), functional illiteracy over time of schooling (\leq 4 years) [19], employment relationship, family income (\leq 1 minimum wage / month and> 1 minimum wage / month), per capita income (\leq 1/2 minimum wage / month and> 1/2 minimum wage / month) and access to piped water. In addition, the socioeconomic characterization protocol of the Brazilian Association of Research Companies (ABEP) [20] was applied, through which the stratification of the population studied was made into classes.

Regarding the clinical variables, the presence of systemic arterial hypertension (SAH), diabetes mellitus (DM), other autoimmune diseases, lifestyle (smoking, alcoholism and physical activity), use of medications (immunosuppressants, antimalarials and corticosteroids), family background of LES, urinary anamnesis (foam in the urine and hematuria), presence of edema were investigated.

The anthropometric evaluation included the calculation of BMI, waist circumference (WC) and percentage of fat. BMI, calculated from weight divided by height squared (Kg/m²), was classified as malnutrition (<18.5kg/m²), eutrophy (\geq 18.5 to < 25kg/m²), overweight (\geq 25 to < 30 kg/m²) and obesity (\geq 30kg/m²) [21]. WC was adopted as a measure of cardiovascular risk (CVR) [22]. The fat percentage was calculated from the sum of 4 skin folds and classified, according to sex and age group, having been dichotomized as above average or on average or below average [23,24]. Overweight and obesity were grouped into a single category of overweight, when the BMI classification was made.

In the present study, the assessment of sarcopenia followed the algorithm proposed by the European Working Group on Sarcopenia in Older People (EWGSOP2, 2019) [5]. The consensus, recently revised, includes a screening protocol and three criteria for the definition and diagnosis of sarcopenia, namely: low muscle strength, low muscle strength and low physical performance.

Screening for sarcopenia was done with SARC-F. This is a screening protocol composed of 5 components (strength, assistance in walking, getting up from a chair, climbing stairs and falls) that has a very high specificity that mainly predicts severe

cases of sarcopenia. Patients who scored \leq 4 were at risk for sarcopenia.

The probable sarcopenia was detected from low muscle strength (< 16 kg/ force), assessed by handgrip strength (HGS). This, in turn, was measured with a manual hydraulic dynamometer with a scale from 0 to 90 kg and a resolution of 2 kg, for which the highest value of three measurements, in Kg/force, of the dominant hand was adopted. The measurements were performed with the arm positioned following the shoulder line, forming a 90° angle between the arm and forearm. During the procedure, the participants were verbally encouraged to squeeze as hard as possible.

To confirm the diagnosis of sarcopenia, the low muscle quantity (< 5.5 kg/m²) was measured with a portable tetrapolar bioelectrical impedance device (BIA) operating in 50 kHz mono-frequency. To perform the test, the patients were placed in the supine position and should meet according to the conditions required by the device. The arithmetic means of three measurements were adopted, and the resistance values then obtained were applied to estimate the appendicular skeletal muscle mass (ASMM) using the Janssen formula [25]. The MMEA value obtained was adjusted for the size of the body, dividing it by height, in meters squared.

Physical performance was assessed by 3 different methods. In the Timed-UP and GO (TUG) the evaluated patients got up from a chair and walked to a marked point 3 meters away and returned to the chair as the time spent between getting up and sitting in the chair at the end of the test was timed. As for the gait speed method, expressed in meters per second, the patients traveled at the usual speed at 4 meters as time was measured. In the Short Battery of Physical Performance (SPPB), which includes walking speed, patients were asked to perform a balance test (in which they had to remain balanced for a minimum of 10 seconds) and a chair position test (in which the act of sitting and getting up from the chair was requested in 5 repetitions, with a score being assigned according to the time required by each patient to complete this test or even its interruption through some limitation). To diagnosing severe sarcopenia, a low gait speed (\leq 0.8 m/s) was used.

The collected data were tabulated and analyzed using the SPSS version 20.0 statistical package, adopting a 95% confidence interval. Pearson's chi-square test was performed, for which a significance level of p < 0.05 was adopted, and analysis of variance (ANOVA). Still, the results were expressed by means of descriptive statistics (frequencies, means and standard deviation (SD).

Results

The socioeconomic, lifestyle, anthropometric, clinical characterization are shown in more detail in Table I. 43 patients with SLE with a mean age of $34.67 \pm$ 8.67 years were included. The highest proportion of patients who declared themselves black (88.4%), the highest proportion of participants who fell in class C (51.2%), followed by those in class D (39.5%) is noteworthy. When asked about their lifestyle, the proportion of patients who denied their current practice or history of smoking, alcoholism and regular physical activity was higher. Out of the clinical conditions investigated, lupus nephritis was the most prevalent (53.6%). On physical examination,

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Variable	Patients, n (%)		
Age, mean (± SD)	34.67±8.67		
Place of birth (interior)	25 (58.1)		
Origin (interior)	22 (51.2)		
Stable union	22 (51.2)		
Self-declared black women	38 (88.4)		
Functional illiteracy (≤ 4 years)	10 (23.3)		
Employment bond	19 (44.2)		
Monthly Income (≤ 1 MW)	23 (53.5)		
Per capita income (≤ 1⁄2 MW)	30 (69.8)		
Water supply	40 (93)		
ABEP socioeconomic classification			
А	0		
B1-B2	4 (9.3)		
C1-C2	22 (51.2)		
D-E	17 (39.5)		
Alcoholism	3 (7)		
Ex-alcoholism	13 (30.2)		
Smoking	1 (2.3)		
Ex-smoking	5 (11.6)		
Regular physical activity	11 (25.6)		
SAH	18 (41.8)		
DM	2 (4.6)		
NL	22 (53.6)		
Another autoimmune disease	11 (25.6)		
Autoimmune medication	43 (100)		
Corticosteroids	30 (69.8)		
Family background of SLE	5 (11.6)		
Foam in the urine	7 (17.9)		
Hematuria	3 (7.7)		
Edema	15 (35.7)		
CVR	33 (76.7)		
% Fat (above average)	33 (86.8)		
Nutritional status			
Malnutrition	2 (4.6)		
Eutrophy	14 (32.5)		
Overweight	27 (62.8)		

Table I - Socioeconomic, clinical, lifestyle and anthropometric characterization of women with systemic lupus erythematosus assisted by a teaching hospital in Maceió/AL, 2018-2019

N = absolute value; SD = standard deviation; SM = minimum wage; ABEP = Brazilian Association of Companies and Research; SAH = systemic arterial hypertension; DM = diabetes mellitus; NL = lupus nephritis; SLE = systemic lupus erythematosus; CVR = cardiovascular risk the occurrence of edema (35.7%) was identified, something already expected in our patients due to drug therapy (100% of patients using autoimmune medication and almost 70% using corticosteroids). As for anthropometric data, a higher prevalence of CVR was identified (76.7%), a higher proportion of high fat percentage (86.6%) and a higher prevalence of overweight in terms of nutritional status (62.8%).

As for the assessment of sarcopenia, the SARC-F screening data revealed 17.5% of possible cases of sarcopenia. When applied the criteria of low muscular strength, detected from the low HGS, the probable sarcopenia was pointed out in 21.4% of the patients. Sarcopenia, which was formally confirmed by the association of the previous parameter with low ASMM, was not detected in any of the patients. An important observation was that all possible cases of sarcopenia identified by the SARC-F instrument were from the overweight / obesity group. In addition, 66.6% of patients with probable sarcopenia also belonged to this group (Table II). Statistical difference, between groups by BMI, was only observed for MMEA (p < 0.012) (Table III), with the obese group presenting a higher ASMM than the eutrophic group (p < 0.046, Tukey), data not shown.

In addition to low muscle strength, impaired physical performance was also detected, with a higher proportion in the overweight / obesity group as observed in the low TUG score (66.6%), low SPPB score (77.7%) and low speed gait (66.6%) (Table III).

Variable	Total n (%)	Malnutrition n (%)	Eutrophy n (%)	Overweight n (%)	р
Low SARC-F score	7 (17.5)	0	0	7 (100)	0.078
Probable sarcopenia	9 (21.4)	1 (11.1)	2 (22.2)	6 (66.6)	0.488
Sarcopenia	0	0	0	0	-
Severe sarcopenia	0	0	0	0	-

 Table II - Diagnosis of sarcopenia by BMI category, according to the EWGSOP (2019), in patients with systemic lupus erythematosus assisted by a teaching hospital in Maceió/AL, 2018-2019

Pearson's chi-square test (Statistical significance = p < 0.05); (-): statistics not computed due to the constant occurrence of the variables; n = absolute value; SARC-F = simple five-component question-naire

Table III - Parameters for assessing Sarcopenia according to the EWGSOP (2019), by BMI category, in patients with systemic lupus erythematosus assisted by a teaching hospital in Maceió/AL, 2018-2019

Variable	Total	Malnutrition n (%)	Eutrophy n (%)	Overweight n (%)	р
HGS, mean (± SD)	22.1 (7.81)	19.5 (4.5)	22.59 (7.75)	22.04 (7.99)	0.881*
ASMM, mean (± SD)	8.56 (1.6)	6.69 (0.35)	7.78 (1.12)	9.10 (1.6)	0.012*
TUG, low score, n (%)	3 (7.3)	0	1 (33.3)	2 (66.6)	0.918
SPPB, low score, n (%)	9 (22.5)	0	2 (22.2)	7 (77.7)	0.499
Low walking speed, n (%)	6 (15)	0	2 (33.3)	4 (66.6)	0.829

Pearson's chi-square test (Statistical significance = p < 0.05); n = absolute value; SD = Standard deviation; *Anova (Statistical significance = p < 0.05); HGS = handgrip strength (expressed in kilograms / force); ASMM = appendicular skeletal muscle mass (expressed in kg/height2; TUG = Timed-Up and Go; SPPB = Short Physical Performance Battery

Discussion

The inflammatory nature of SLE and corticosteroid therapy can affect body composition, compromising the conservation of skeletal muscle mass, in addition to favoring weight gain in the form of body fat. In the context of SLE, these changes in body composition can occur independently of BMI, making it difficult to diagnose possible sarcopenia [16]. Despite the literature discussing the changes in body composition caused by SLE and its treatment, in our study the occurrence of this syndrome was not observed. Unlike the work carried out in Baghdad, which found a 35% prevalence of sarcopenia in women with SLE, although it did not differ from the controls, it was statistically associated with the percentage of fat mass [26].

Among the reasons that can help in the interpretation of the finding of our study is the fact that, in the vast majority, the patients included in the analyzes were of childbearing age, in addition to the fact that no elderly patient was included. The reduction of sex hormones (testosterone, estrogen and dehydroepiandrosterone-DHEA), common with advancing age, especially in the post-menopausal period, may have implications for the conservation of skeletal muscle mass [27]. However, despite the conservation of skeletal muscle mass, we identified impaired muscle functionality, pointing to a possible limitation of the evaluation method for sarcopenia in our patients.

The inconsistencies that exist between consensus, which establish not only different assessment methods, but also different cutoff points for the diagnosis and classification of sarcopenia [28], hinder our assessment. It is worth mentioning that there are no methods for diagnosing sarcopenia adapted by pathologies. According to the EWGSOP update, in 2019, it is suggested that, in our sample, muscle strength may be a more important parameter than the amount of skeletal muscle capable of pointing out muscle damage. Physical strength is a more reliable parameter in the assessment of function and reduces more rapidly when compared to the simultaneous loss of muscle mass, covering the impact of sarcopenia in this young and female population.

The level of disease activity can also influence body composition. The metabolic changes inherent in SLE involve the elevation of pro-inflammatory cytokines (tumor necrosis factor- α (TNF- α), leukins-6 and -1) that are responsible for the reduction of muscle protein synthesis and anabolic factors such as growth hormone (GH) and insulin-like growth factor 1 (IGF-1), in addition to causing anorectic effects. Although it was not a variable investigated in the present study, none of the patients reported exacerbation of SLE symptoms, which may also explain the non-occurrence of sarcopenia in the sample [10,18]. Another important point is that the evaluated group has continuous treatment by a specialized group within the hospital, which may also have interfered with the results. Despite all the limitations of the Unified Health System (SUS), the hospital is a reference center in the state of Alagoas. According to EWGSOP2 (2019), 21.4% had low muscle strength, that is, probable sarcopenia, which already refers patients to cause assessment and interventions, in addition to decreased physical performance. These data suggest the occurrence of other possible syndromes that may affect muscle function, such as dinapenia, frailty syndrome, among others, which, although identified as geriatric syndromes, deserve to be studied and understood in the context of SLE [5,29]. Still, the reduction in strength and physical performance was more common in overweight patients. Excess adiposity can have an impact on muscle quality and, thus, on physical function (strength and performance). The deposition of fat between muscle fibers leads to mitochondrial dysfunction in order to increase lipid peroxidation and, therefore, metabolic intermediates and reactive oxygen species (ROS), causing insulin resistance (IR), increased oxidative stress and lipotoxicity in the myocyte leading to dysfunction or apoptosis of these cells [30-32].

In our sample, excess weight was more frequent (62.8%). Obesity has been observed in patients with lupus and there are numerous causes attributed to this outcome, among which the reduction of the basal metabolic rate, the reduction in the levels of physical activity, the inflammatory nature of the disease, the therapy with corticosteroids can be pointed out [4,12,16,18]. Similar to this work, a study developed in Minas Gerais that evaluated the nutritional status and the level of physical activity in patients with SLE, found a higher prevalence of overweight (35.9%) and obesity (28.3%) [18]. Another study that characterized SLE patients residing in Malta, identified a prevalence of 31.5% of overweight and 29.3% of obesity [8].

In the United States, a study carried out with black women evaluated obesity as a risk factor for SLE and found a prevalence of 31.6% and 30.2% of overweight and obesity, respectively [33]. Still in this study, overweight in adolescence was associated with the development of SLE in adulthood, however the authors draw attention to the biological mechanisms and exposure windows between obesity and SLE in black women. It is interesting to mention that studies have shown a higher prevalence of SLE and risk of mortality in black women when compared to white women, and that in addition to obesity, psychological stress during childhood may also be associated with the development of the disease [34,35].

Obesity may be associated with SLE severity and activity and an increased risk of developing the disease, although little is known about the pathophysiological mechanisms involved. The excess of adiposity could increase the levels of serum inflammatory markers and in this context the adipokines could play an important role. A leptin has been associated with a T helper 1 (Th1) lymphocyte response culminating without an increase in pro-inflammatory cytokines as a TNF- α , increased survival of autoreactive T lymphocytes through Bcl expression - 2, reduction of regulatory T cells and higher SLE disease activity index scores (SLEDAI). Resistin, also elevated in autoimmune diseases, especially in rheumatoid arthritis, is related to greater inflammation, higher BMI, in addition to being correlated with renal dysfunction markers in SLE [10,12,33,36].

In view of what has been discussed so far, the impact of SLE on quality of life is evident, not to mention the costs, individual and collective, for health that include access to medicines, exams and consultations that can compromise the necessary uninterrupted support [9,37]. In this context, individualized dietary management and nutritional guidelines promote improvements in eating habits that can help control the disease [38]. Modulations in the diet may include caloric deficit, adequate protein supply, reduction of total fats contemplating the supply of omega-3 polyunsaturated fatty acids (PUFA ω -3), supplementation of vitamin A, vitamin D, complex B vitamins, especially folate, B6 and B12, vitamin C, adequacy in the supply of vitamin E, a diet rich in selenium, adequate in calcium and supplementation when necessary, adjusted in sodium and limited in iron. The benefits of such strategies include the control of disease activity, improvement of immune function and control of the inflammatory condition of SLE marked by the reduction of circulating autoantibodies and their deposition in tissues, in addition to the reduction of pro-inflammatory cytokines, suppression of macrophage activity, reduction of oxidative stress markers [17,39]. Individuals with SLE, especially those with cardiovascular risk factors such as obesity, SAH, DM and metabolic syndrome, can benefit from such dietary modulations [40].

Aware of the limitations of the present study, we can point out those related to the sample itself, which, due to the use of antihypertensives, water retention resulting from corticotherapy, can influence the results obtained in BIA, a method of greater financial accessibility when compared to DXA. The presence of other chronic conditions hindered our understanding of the impact of SLE, as well as being overweight on the conservation of lean mass, or more specifically in this case, the muscle function that was compromised in the sample, since sarcopenia and other chronic conditions share of many mechanisms involving a chronic inflammatory condition. Finally, the authors point out the dependence on a larger research group, which limited data collection with a larger number of participants.

Conclusion

In this study, sarcopenia was not identified, however, low muscle strength and reduced physical performance were observed. A higher prevalence of overweight was also found. Such data draw attention to the need for further studies on the relationship of body composition and the deterioration of muscle functionality. For this, it is suggested that the nutritional assessment and diagnostic tools for sarcopenia are adapted considering the particularities of patients with SLE, such as water retention and periods of remission and exacerbation of the disease, which will allow the identification of excess adiposity, as well as the deterioration of muscle mass and/ or function, in order to assist in early and individualized therapeutic interventions

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Conflict of interests

The authors declare no conflict of interest.

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Author's contributions

Conception and design of the research: Monteiro JRS, Cardoso MCCM, Santos JCF; Data collection: Monteiro JRS, Cardoso MCCM, Santos JCF; Analysis and interpretation of data: Monteiro JRS, Cardoso MCCM, Santos JCF; Statistical analysis: Oliveira ACM; Writing of the manuscript: Monteiro JRS; Critical revision of the manuscript for important intellectual content: Cardoso MCCM, Santos JCF, Oliveira ACM.

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