

Prevalence of sarcopenia in kidney transplants and their association with determinant factors of muscle homeostasis

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SUMMARY

INTRODUCTION: Sarcopenia is characterized by the involuntary loss of lean body mass associated with a progressive reduction of muscle strength.

OBJECTIVE: To determine the prevalence of sarcopenia in kidney transplant recipients and its association with the determining factors that control muscle homeostasis.

METHODS: We evaluated renal transplant recipients undergoing follow-up at the University Hospital of the Federal University of Maranhão from June 2017 to July 2018 and who met the inclusion criteria. Sarcopenia was defined according to the European criteria. The skeletal muscle mass index was measured by dual-energy radiological absorptiometry; the values $<7,26 \text{ kg/m}^2$ for men and $<5,5 \text{ kg/m}^2$ for women were adopted for muscle depletion. For handgrip strength, values of $<30 \text{ kg}$ for men and $<20 \text{ kg}$ for women were considered as reduced muscle strength. In both sexes, the cutoff point for walking speed was $<0,8 \text{ m/s}$.

RESULTS: We evaluated 83 renal transplant recipients with a mean age of $48.8 \pm 12,1$ years and predominantly males (57,8%). The prevalence of sarcopenia was 19,3%. Among individuals without sarcopenia, 17,9% had a decrease in handgrip strength and 40,3% had altered gait speed.

DISCUSSION: Individuals submitted to renal transplant may develop sarcopenia while still young and already present altered muscle function and strength even before the depletion of lean body mass.

CONCLUSION: Early diagnosis may allow the prevention of sarcopenia and provide a better quality of life for patients.

KEYWORDS: Kidney transplantation. Sarcopenia. Muscle strength.

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INTRODUCTION

Sarcopenia is a syndrome characterized by the involuntary loss of lean body mass (LBM) associated with a reduction of its strength and function and is a frequent change that accompanies the physiological process of aging. Although sarcopenia is usually associated with advanced age, it can accompany various chronic diseases in younger patients¹.

In chronic kidney disease (CKD), sarcopenia is associated with the results of a change in the balance between catabolism and anabolism that controls the homeostasis of muscles¹. In individuals with CKD, sarcopenia promotes the loss of muscle strength already at the moment of conservative treatment and progresses with the loss of renal function¹. In CKD, sarcopenia increases morbidity¹ and is strongly correlated with higher mortality, physical disability², and increased cardiovascular events³.

When there is kidney failure, among the possible renal replacement therapies (RRT), transplant emerges as the best option⁴. Sarcopenia in renal-transplant patients (RxT) has been studied in recent years; however, the literature is still scarce.

Considering the association of sarcopenia with adverse events and that it can occur very early in individuals with CKD, impacting their prognosis and survival, the objective of this study was to determine the prevalence of sarcopenia in renal-transplant patients (RxT) and its association with the determining factors that control muscle homeostasis.

METHODS

This is a cross-sectional study conducted on RxT at the Center for Kidney Disease Prevention of the University Hospital of the Federal University of Maranhão (HUUFMA), from June 2017 to July 2018. This study was part of a larger study, entitled "Nutritional Status of Renal Transplant Patients in The State of Maranhão", which was approved by the Human Research Ethics Committee of HUUFMA (Opinion no 1.872.021).

Variables were used to calculate the sample size, with its upper and lower limits defined by tolerance and characterized by a measure defined by a number, based on unpaired data, considering there was no control group. The study was completed in 213 individuals. The following were adopted as inclusion criteria: individuals aged above 20 years, of both sexes, RxT, undergoing outpatient follow-up on

HUUFMA. We did not include pregnant women and people with amputated limbs, suffering from neurological diseases or sequelae from cerebrovascular accidents who were predisposed to a reduction of handgrip strength (HGS) or cognitive impairment, in addition to those with contagious or chronic consumptive diseases. Thus, the final sample comprised 83 individuals who met the criteria. All those who agreed to participate in the study signed an informed consent form.

We adopted two classifications for Body Mass Index (BMI): the one proposed for adults by the World Health Organization⁵ and Lipschitz⁶ for the elderly. The distribution of abdominal fat was assessed by waist circumference (WC)⁷.

Sarcopenia was defined per the criteria of the European Working Group on Sarcopenia in Older People (EWGSOP)⁸. For the assessment of body composition, patients were submitted to densitometry tomography by dual-energy x-ray absorptiometry (DEXA). To determine the LBM, the relative skeletal muscle index (RSMI) was measured according to the criteria established by Baumgartner and defended by the European Working Group on Sarcopenia in Older People.⁸ The State of LBM decrease was assigned to cases in which the RSMI values were lower than 7.26 kg/m² for men and 5.5 kg/m² for women.

The handgrip strength (HGS) was used to assess muscle strength. The cut-off point was <30 kg for men and <20 kg for women.⁸

Muscle performance was assessed by calculating the gait speed test. A speed of less than 0.8 m/s was considered a risk for sarcopenia.⁸

Data Analysis

The categorical variables were presented through frequencies and percentages, and quantitative variables, based on mean and standard deviation values (mean ± SD). The normality of the variables was tested by the Shapiro-Wilk test. The analysis of numerical variables by the presence of sarcopenia was carried out by student t-test for variables with normal distribution and Mann Whitney test for the others. The analysis of categorical variables by the presence of sarcopenia was carried out using the chi-square test. We adopted a 95% confidence interval (1.96 standard deviation and standard error of 5%). Analyses were made using the Stata software, version 14.0®.

RESULTS

We assessed 83 RxT (mean age 48.8 ± 12.1 years). The prevalence of sarcopenia was 19.3%. Adult patients with and without sarcopenia had a mean BMI in the range of eutrophy, but with a statistically significant difference (24.7 ± 4.9 kg/m² vs 19.1 ± 2.4 kg/m², respectively; p-value = 0.018). Whereas elderly individuals without sarcopenia presented mean BMI values in the range of excess body weight (28.3 ± 4.3 kg/m²), while those with sarcopenia were in the range of eutrophy (24.3 ± 8.4 kg/m²); however no statistical difference was observed (p-value=0.070).

The mean values of the WC of the men and women showed a high risk for cardiovascular diseases for those without sarcopenia (94.6 ± 11.9 cm and 87.5 ± 13.6 cm, respectively) and low risk for those with sarcopenia (82.5 ± 13.7 cm and 77.9 ± 20.6 cm, respectively), but with a statistically significant difference only among men (p-value=0.007) (Table 2).

Men and women without sarcopenia also showed preserved (08.1 ± 0.8 kg/m² and 6.6 ± 0.7 kg/m², respectively) and significantly higher (p-value < 0.001) mean values of LBM when compared to the group with sarcopenia (6.7 ± 0.4 kg/m² and 5.2 ± 0.3 kg/m², respectively), which were altered (Table 2).

The gait test showed an alteration for both groups assessed, but with a greater reduction of muscle performance in individuals with sarcopenia (0.74 ± 0.17 m/s vs 0.68 ± 0.40 m/s; p-value=0.009). HGS

TABLE 2. CLINICAL, ANTHROPOMETRIC, AND BIOCHEMICAL CHARACTERISTICS AND COMPARISON BETWEEN WITH SARCOPENIA AND WITHOUT SARCOPENIA IN THE POPULATION STUDIED, SÃO LUÍS - MA, 2019.

Variable	Without sarcopenia Mean \pm SD	With sarcopenia Mean \pm SD	p-value
Age (years)	49.4 \pm 1.4	46.1 \pm 3.6	0.463
BMI (kg/m ²)			
Adults	24.7 \pm 4.9	19.1 \pm 2.4	0.018
Elderly	28.3 \pm 4.3	24.3 \pm 8.4	0.070
WC (cm)			
Men	94.6 \pm 11.9	82.5 \pm 13.7	0.007
Women	87.5 \pm 13.6	77.9 \pm 20.6	0.161
Lean Body Mass (kg/m ²)			
Men	8.1 \pm 0.8	6.7 \pm 0.4	<0.001
Women	6.6 \pm 0.7	5.2 \pm 0.3	<0.001
Gait Test (m/s)	0.74 \pm 0.17	0.68 \pm 0.40	0.009
Hand Grip Strength (kg)			
Men	30.6 \pm 8.7	25.0 \pm 4.9	0.021
Women	19.7 \pm 3.2	18.7 \pm 3.7	0.476
Transplant Time (months)	65.4 \pm 54.3	60.3 \pm 61.7	0.503
Albumin (g/dL)	4.3 \pm 0.4	4.3 \pm 0.4	0.910
Hemoglobin (mg/dL)	12.78 \pm 1.59	12.36 \pm 1.64	0.356
Total cholesterol (mg/dL)	165.9 \pm 38.1	175.3 \pm 37.3	0.393
HDL-c (mg/dL)	50.3 \pm 17.9	47.7 \pm 16.8	0.662
LDL-c (mg/dL)	84.7 \pm 33.2	88.7 \pm 19.3	0.715
Triglycerides (mg/dL)	173.7 \pm 110.1	157.3 \pm 74.7	0.586
Blood Glucose (mg/dL)	106.3 \pm 41.5	93.1 \pm 27.2	0.231
Serum Creatinine (mg/dL)	1.50 \pm 0.97	1.56 \pm 0.60	0.832
Cclearance Creatinine (ml/min/1.73 ²)	58.9 \pm 19.7	55.9 \pm 23.5	0.601

WC: Waist circumference

FIGURE 1. ALTERED CRITERIA FOR CHARACTERIZING SARCOPENIA IN THE POPULATION STUDIED, SÃO LUÍS - MA, 2019.

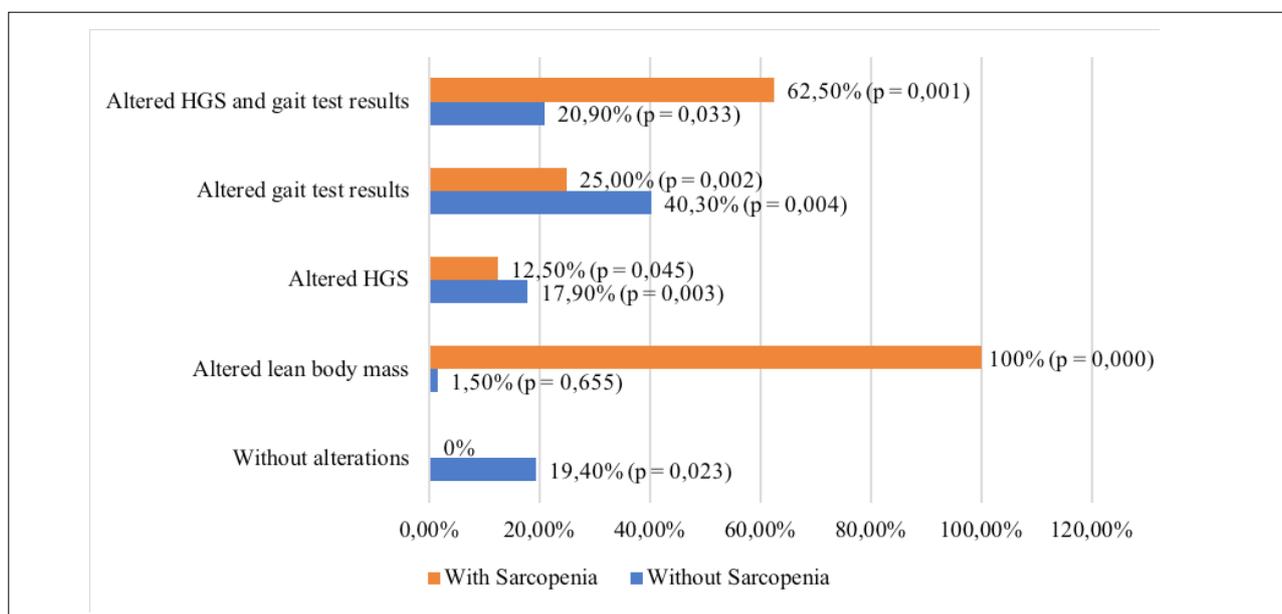


TABLE 1. SOCIODEMOGRAPHIC, CLINICAL AND NUTRITIONAL CHARACTERISTICS OF THE POPULATION STUDIED, SÃO LUÍS - MA, 2019.

Variables	N	%
Sex		
Female	35	42.2
Male	48	57.8
Age range		
≥ 20 <40 years	19	22.9
≥ 40 <60 years	49	59.0
≥ 60 years	15	18.1
Color		
White	8	9.6
Black	17	20.5
Brown	55	66.3
Others	3	3.6
Income		
>1 MW	3	3.6
1 to 2 MW	44	53.1
2 to 4 MW	23	27.7
≥4 MW	13	15.6
Formal education		
≤9 years	30	36.1
>9 years	53	63.9
Alcohol Consumption		
No former consumption	76	91.6
Yes	7	8.4
Smoking		
Not a former smoker	83	100.0
Type of donor		
Living	38	45.8
Deceased	45	54.2
RxT Time		
<6 months and < 1 year	14	16.9
≥ 1 year and <3 years	24	28.9
≥ 3 years and <5 years	11	13.2
≥ 5 years	34	41.0
Diabetes		
Present	13	16.2
Hypertension		
Present	70	87.5
Sarcopenia		
Present	16	19.3
BMI		
Low weight	6	7.2
Eutrophy	29	34.9
Overweight	32	38.5
Obesity	16	19.4

MW: minimum wage. BMI: body mass index.

was reduced only in men with sarcopenia (25.0 ± 4.9 kg), with a statistically significant difference (p -value=0.021) when compared to those without sarcopenia. On the other hand, for women, HGS was

reduced in both groups (19.7 ± 3.2 kg and 18.7 ± 3.7 kg; p -value=0.476) (Table 2).

Based on the analysis of the criteria for characterizing sarcopenia, it is possible to observe that among RxT patients with sarcopenia, 12.5% presented decreased HGS (p -value = 0.045), 25.0% altered gait test results (p -value = 0.002), and 62.5% altered HGS and gait test results (p -value = 0.001). It is worth noting that, although only 1.5% of the cases without sarcopenia presented decreased lean body mass (p -value = 0.655), 17.9% had decreased HGS (p -value = 0.003), 40.3% altered gait test results (p -value=0.004), and 20.9% had both criteria altered (p -value=0.033) (Figure 1).

DISCUSSION

Studies on RxT indicate that sarcopenia occurs in younger age in comparison to the general population.^{5,8-10} The only study conducted on RxT in Brasil found that the prevalence of this syndrome was more than double (49.6%)¹¹, the highest percentage up until now reported in the literature. It is likely that sarcopenia in CKD starts during the period of conservative treatment, progressing with the loss of renal function and increasing morbidity.¹

The prevalence of sarcopenia can also vary as a result of the methodology employed in its characterization since there is no universal operational definition and/or diagnostic criteria. In addition, the characteristics of the studied population can also interfere in the prevalence of sarcopenia since many factors lead to its development and progression, including advanced age, sedentary lifestyle, prolonged hospitalization, insulin resistance in the general population, among others.⁸

The BMI, in more than half of the sample (57.9%), remained in the range of overweight and obesity. It is worth noting that the index is not reliable regarding the differentiation of body fat (BF) and LBM, since throughout our lives can we maintain a stable weight and slowly lose LBM, gaining BF in equal volume, thus maintaining the same BMI for years; something that actually occurs in many people. In addition, sarcopenia can be difficult to identify, making it crucial to use other measurements that identify LBM.¹² We suppose that the weight gain in RxT is a result of several factors, such as recovery from anemia, a better quality of life, and increased appetite caused by the administration of steroids and immunosuppressants.¹³

Considering the above, it is necessary to raise questions about the quality of the diet of RxT, since this population is considered high risk for the development of obesity and changes in lipid and blood glucose metabolism due to the use of immunosuppressant drugs and the increased dietary freedom since dietary restrictions decrease dramatically post-transplant. The diet of a RxT individual is similar to that of a healthy one, without marked restrictions for sodium, phosphorus, and potassium, which causes this population to eat, in the postoperative stage, without pondering current and future complications, after all, they have gone through periods of dietary restriction.¹⁴

However, despite this share of RxT with excess weight and the preserved LBM, even in those without sarcopenia impaired HGS and gait were observed. According to findings of other studies, HGS was reduced in 40% of RxT.⁴ There is already evidence of a dissociation between muscle mass and strength; the decline in HGS seems to be faster than the concomitant loss of LBM.¹⁵

This study presented as a limitation its cross-sectional design and the lack of assessment of adherence to the diet in the population studied. On the other hand, it presented as a strong point the assessment of sarcopenia in a population more susceptible to nutritional changes. In addition, we used the DEXA, considered the gold standard for assessing muscle mass with greater precision. Additionally, the research was carried out in a reference hospital for RxT in the state of Maranhão, the only center for renal transplant patient follow-up in the state.

RESUMO

INTRODUÇÃO: A sarcopenia é caracterizada pela perda involuntária da massa magra associada à redução da força e função muscular, de modo progressivo.

OBJETIVO: Determinar a prevalência de sarcopenia em transplantados renais e sua associação com os fatores determinantes que controlam a homeostase do músculo.

MÉTODOS: Foram avaliados indivíduos transplantados renais em acompanhamento no Hospital Universitário da Universidade Federal do Maranhão no período de junho de 2017 a julho de 2018 e que preencheram os critérios. A sarcopenia foi definida de acordo com o critério europeu. O índice de massa muscular esquelética foi medido por meio da densitometria computadorizada por absorciometria radiológica de dupla energia; valores $<7,26 \text{ kg/m}^2$ para homens e $<5,5 \text{ kg/m}^2$ para mulheres foram adotados para depleção muscular. Para força de prensão manual, valores de $<30 \text{ kg}$ para homens e $<20 \text{ kg}$ para mulheres foram considerados como redução da força muscular. Em ambos os sexos, o ponto de corte para velocidade de marcha reduzida foi $<0,8 \text{ m/s}$.

RESULTADOS: Foram avaliados 83 transplantados renais, com média de idade de $48,8 \pm 12,1$ anos e predominância de indivíduos do sexo masculino (57,8%). A prevalência de sarcopenia foi de 19,3%. Entre os indivíduos sem sarcopenia, 17,9% já tinham diminuição da força de prensão manual e 40,3%, alteração do teste de marcha.

DISCUSSÃO: Indivíduos submetidos ao transplante renal podem desenvolver sarcopenia jovens e apresentar alteração da função e da força muscular mesmo antes da depleção da massa magra.

CONCLUSÃO: O diagnóstico precoce pode permitir a prevenção da sarcopenia e propiciar melhor qualidade de vida aos pacientes.

PALAVRAS-CHAVE: Transplante de rim. Sarcopenia. Força muscular.

CONCLUSIONS

Sarcopenia can develop in younger ages in RxT, and muscle strength and gait test results can be reduced even before a decrease in LBM. Another fact evidenced in this study was the prevalence of excess weight in this population, reinforcing the concern with the quality of the diet after RxT, since dietary restrictions decrease and these individuals have greater freedom in their food choices. This reinforces the importance of a thorough assessment of nutritional status in these patients, considering the differentiation of body composition and evaluating the individual holistically. Therefore, early diagnosis of the syndrome may allow for more rapid and effective intervention in RxT, preventing mobility disorders, falls, functional disability, and worsening of quality of life.

Author's Contribution

Cleodice Alves Martins and Ana Karina Teixeira da Cunha França contributed significantly in all stages of the project. The other authors contributed in data collection or analysis and interpretation and in the approval of the final version of the text.

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