Association between the risk of sarcopenia and clinical complications of covid-19 in hospitalized older adults: a multicenter cohort study

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Abstract

Objective: To investigate whether the risk of sarcopenia in older adults diagnosed with covid-19 is associated with the need for intensive care, mechanical ventilation, and mortality. *Method*: A multicenter cohort study was conducted, including older adults (≥65 years) with laboratory-confirmed covid-19 diagnosis. Data related to sociodemographic, clinical, and nutritional characteristics were collected. The risk of sarcopenia was assessed using the Sarcopenia Risk Screening questionnaire. Outcome variables included the need for intensive care, mechanical ventilation, and mortality. Logistic regressions were performed to assess the association between clinical outcomes and the risk of sarcopenia, adjusting for the following variables: age, gender, family income, physical activity, hypertension, diabetes, cardiovascular disease, chronic obstructive pulmonary disease, and body mass index. *Results*: The study included 264 older adults with covid-19, with an average age of 71.7 (±8.2) years. One hundred and forty-eight older adults (56.1%) were at risk of sarcopenia. Hypertension, diabetes, and cardiovascular disease were the most common comorbidities identified in older adults, at 75.4%, 45.5%, and 28.4%, respectively. The presence of sarcopenia risk in hospitalized older adults with covid-19 increased the odds of ICU admission by more than 2-fold (OR: 2.71 [1.57; 4.68], p<0.001), nearly 5-fold for mechanical ventilation (OR: 5.19 [2.75; 9.78], p<0.001), and over 3-fold for mortality (OR: 4.05 [2.05; 7.98], p<0.001). *Conclusion*: In hospitalized older adults with covid-19, pre-existing risk of sarcopenia was a predictor of unfavorable clinical outcomes.

Keywords: SARS-CoV-2. Aging. Respiration, Artificial. Muscle Strength. Mortality.

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INTRODUCTION

Age is one of the most significant risk factors for severe infection caused by SARS-CoV-2 and its adverse health outcomes[1]. The reduction in immune response due to aging can predispose older adults to complications arising from viral infection. Immunosenescence manifests as the loss of naive T cells and the functionality of effector cells, decreased lymphocyte proliferation, and dysregulated cytokine production[1-3]. The presence of comorbidities such as hypertension, diabetes, cancer, and cardiovascular diseases, as well as functional status, are also factors that may contribute to the severity of the disease and mortality in the older population[1,3].

The deterioration of muscle mass and function that occurs in older adults contributes to the impairment of respiratory function in patients affected by covid-19[4]. Sarcopenia, characterized by low muscle strength combined with reduced muscle quality/quantity, is associated with a higher risk of adverse outcomes in individuals aged 60 and above, such as falls, fractures, physical disability, and mortality[5].

The diagnosis of sarcopenia requires instruments and methods that are often costly and not readily available in many Brazilian hospitals. However, for screening the risk of sarcopenia and selecting individuals for diagnosis, it is recommended to use the Sarcopenia Risk Screening (SARC-F) method[5,8]. This is a quick and easy-to-administer tool that can be self-completed by the older individual, exhibiting high specificity and has already been associated with negative outcomes such as an increased risk of hospitalization and death[8]. Some conducted studies have shown that the risk of sarcopenia, as defined by SARC-F, is linked to the outcome of mortality and longer hospitalization in older adults hospitalized with covid-19[9,10]. However, these studies were conducted at a single center and evaluated only the mortality outcome.

With this study, it is hoped that the risk of sarcopenia can be early identified in older adults hospitalized, through a simple and cost-effective tool, enabling healthcare professionals to directly intervene in the care of these patients, thus reducing potential clinical complications and strengthening the healthcare for the older adutls. Therefore, this study aims to determine whether the risk of sarcopenia in hospitalized older adults with covid-19 is associated with clinical outcomes such as the need for intensive care, mechanical ventilation, and mortality.

METHOD

A multicenter cohort study, part of a larger study titled "Clinical, Nutritional, and Sociodemographic Aspects Associated with Mortality in Patients with covid-19: A Multicenter Study in Northeastern Brazil," conducted between July 2020 and March 2021. The study was carried out in Brazil, specifically in the Northeastern region, encompassing the states of Alagoas, Bahia, Ceará, Maranhão, Paraíba, Pernambuco, Piauí, Rio Grande do Norte, and Sergipe. The preparation of this article followed the recommendations of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE)[11] checklist.

The research project was approved by the Research Ethics Committee of the various collaborating centers, with the approval number 4314132. Ethical and bioethical principles were adhered to throughout all stages of the study, in accordance with Resolution N°. 466/2012 and Resolution N°. 510/2016. All research participants signed the Informed Consent Form (ICF).

The final sample of this study followed a non-probabilistic convenience sampling plan, consisting of 264 older adults who were part of the main study and had all the necessary variables for sarcopenia screening correctly filled in the SARC-F. The study was conducted in 14 hospitals located in the Northeastern region of Brazil, comprising three temporary healthcare facilities (field hospitals), nine public healthcare institutions, and two philanthropic units.

The inclusion criteria for this study consisted of older adults aged >65 years, of both sexes, who were hospitalized in the healthcare facilities participating in this research, and who had a confirmed diagnosis of covid-19 through laboratory tests such as Reverse Transcription Polymerase Chain Reaction (RT-PCR),

Point of Care Testing (POCT), Reverse Transcription Loop-Mediated Isothermal Amplification (RT-LAMP), or SARS-CoV-2 Antigen Test. Older adults who did not respond or complete the screening tool for sarcopenia risk or did not have recorded weight and height data were excluded.

Data were collected directly from the participating individuals, either retrospectively or prospectively, depending on the time of laboratory-confirmed covid-19 diagnosis. Participants had their data collected by healthcare professionals from research partner services and were followed until the outcome (death or hospital discharge). Patients whose participation in this study was interrupted for any reason (e.g., transfer to hospitals where research follow-up was not possible, or a request to discontinue their participation in the study) were considered as lost to follow-up and excluded from the study.

After the inclusion of participants in the research, demographic and clinical data were collected directly from them through a structured form. Variables related to identification, sociodemographic, and economic characteristics, such as age, gender, ethnicity, marital status, education, employment status, and family income, were used in the study. Age was categorized into two classes, with individuals aged >80 years being considered as "longevous," and those aged <80 years as "non-longevous."

Lifestyle information and clinical data, such as the presence of comorbidities, alcohol consumption, smoking, engagement in physical activity, and sarcopenia risk, were also collected variables. Eligible patients for the research responded whether they had a diagnosis of comorbidities like diabetes, hypertension, cardiovascular disease, cancer, chronic obstructive pulmonary disease, and conservative or hemodialysis-based kidney disease treatment. Similarly, they were asked about alcohol consumption and smoking. Those who reported alcohol use, even rarely (e.g., once a month), were considered "drinkers," and those who reported smoking, regardless of frequency, were categorized as "smokers."

Regarding physical activity, older adults who self-reported engaging in moderate-intensity aerobic activity for at least 30 minutes a day, five days a week, or intense activities for at least 20 minutes a day, three times a week, were considered physically active, following criteria from the American College of Sports Medicine and the American Heart Association[12]. Sarcopenia risk was identified based on the application of the SARC-F directly with the older individual, considering the information relating to the period prior to hospital admission. This sarcopenia screening tool consists of 5 items related to strength, assistance with walking, rising from a chair, climbing stairs, and the occurrence of falls. For each component of the assessment, responses range from 0 to 2 points, and sarcopenia risk is considered when the SARC-F score is >4 points[13].

Weight and height data were self-reported by patients at the time of their admission to the study, and the Body Mass Index (BMI) was calculated based on them, obtained by the ratio of weight to the square of height[14]. The BMI was interpreted according to the classification proposed by Lipschitz[15], which categorizes older adults as follows: underweight (BMI <22 kg/m^2), normal weight (BMI from 22 to 27 kg/m^2), and overweight (BMI >27 kg/m^2).

The outcome variables considered in this study were intensive care unit (ICU) admission, mechanical ventilation, and/or death, identified in the patients' medical records during the follow-up in this research.

Measures of central tendency and dispersion were calculated for continuous variables, and frequencies were examined for categorical variables. The behavior of the variables was assessed using the Shapiro-Wilk normality test.

In order to guide the selection of variables included in the multivariate model, a Directed Acyclic Graph (DAG) was designed. It illustrates the causal pathways between the risk of sarcopenia and outcomes such as the need for intensive therapy, mechanical ventilation, and death (Figure 1). The DAG was developed with the assistance of DAGitty software. Thus, the minimum set of variables to estimate this effect was proposed by two models. Model 1 was adjusted for the following variables: age, gender, smoking, physical activity, cardiovascular disease, diabetes, hypertension, chronic obstructive pulmonary disease, and BMI. Model 2 included variables such as age, gender,

family income, smoking, cardiovascular disease, diabetes, hypertension, chronic obstructive pulmonary disease, and BMI. Logistic regressions were performed to calculate the odds ratios, with the chosen dependent variables being ICU admission, death, and mechanical ventilation, while the sarcopenia risk identified with SARC-F was the independent variable. The adjustment variables used were those highlighted in Model 1 and Model 2 above. For all analyses, a significance level of 5% was adopted.

DATA AVAILABILITY

The entire dataset supporting the results of this study is available upon request to the corresponding author.

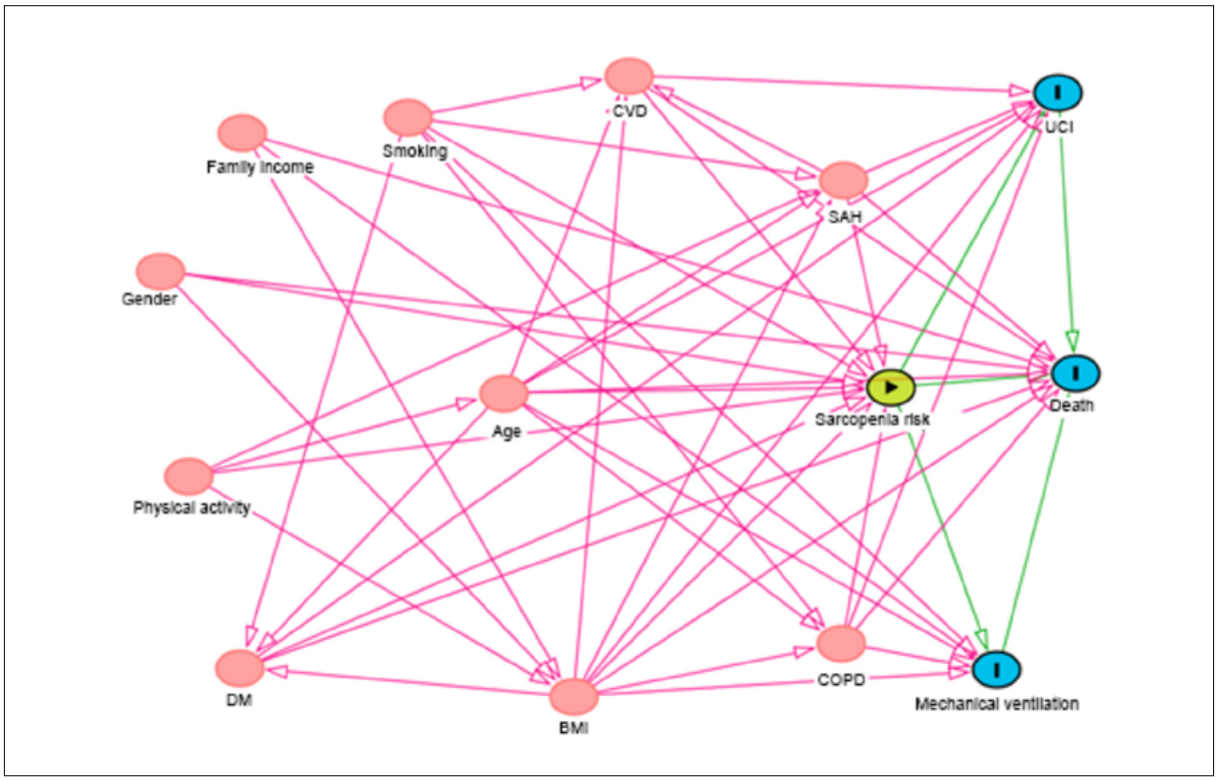

Figure 1. Directed acyclic graph showing the pathways between the risk of sarcopenia and outcome variables. Circles represent the variables included in the study, and arrows indicate the causal relationships between them. Northeast Region, Brazil, 2020-2021.

CVD: Cardiovascular Disease; DM: Diabetes Mellitus COPD: Chronic Obstructive Pulmonary Disease, SAH: Systemic Arterial Hypertension BMI: Body Mass Index; ICU: Intensive Care Unit.

RESULTS

Initially, with a selection from the main database, there were 289 potentially eligible older adults (>65 years). However, 25 were excluded due to loss to follow-up, resulting in a final sample of 264 older adults.

The mean age was 71.7 (±8.28) years, with the majority being male (n=142; 53.8%), and approximately a quarter being long-lived (n=52; 19.7%). The majority had a family income of less than or equal to 2 Brazilian minimum wages (n=178; 67.4%), as shown in Table 1.

Hypertension, diabetes, and cardiovascular disease were the main comorbidities identified and were present in 75.4% (n=199), 45.5% (n=120), and 28.4% (n=75) of these patients, respectively. Regarding BMI classification, 42.0% of older adults (n=111) were classified as overweight, and 15.5% (n=41) had low weight. Sarcopenia risk was present in the majority of this sample (n=148; 56.1%) (Table 2).

In the univariate analysis, it was observed that the risk of sarcopenia in older adults with covid-19 was related to all the studied outcomes, ICU admission, mechanical ventilation, and death (Table 3).

In the multivariate analysis, the risk of sarcopenia in older adults hospitalized with covid-19 increased by more than 2.5 times the chances of ICU admission ($p<0.001$), by approximately 5 times the chances of mechanical ventilation ($p<0.001$), and by more than 3.5 times the chances of death ($p<0.001$), in both models analyzed (Table 4).

Table 1. Sociodemographic and lifestyle characteristics of older adults with covid-19 (N=264). Northeast Region, Brazil, 2020-2021.

Variable	n (%)
Age	
Non-longevous	212 (80.3)
Longevous	52 (19.7)
Gender	
Female	122 (46.2)
Male	142 (53.8)
Years of education	
<5	89 (33.7)
≥5	175 (66.3)
Occupation	
Employed/informal worker	18 (6.9)
Unemployed	24 (9.2)
Retired	219 (83.9)
Family income	
≤2 Brazilian minimum wages	178 (67.4)
>2 Brazilian minimum wages	86 (32.6)
Alcoholism	
No	233 (84.5)
Yes	41 (15.5)
Smoking	
No	241 (91.3)
Yes	23 (8.7)
Physical activity	
No	210 (79.5)
Yes	54 (20.5)

Source: Self-prepared, based on statistical analyses.

Table 2. Clinical and nutritional characteristics of older adults with covid-19 (N=264). Northeast Region, Brazil, 2020-2021.

Variable	n (%)
Hypertension	
No	65 (24.6)
Yes	199 (75.4)
Diabetes	
No	144 (54.5)
Yes	120 (45.5)
Cancer	
No	241 (91.3)
Yes	23 (8.7)
Cardiovascular disease	
No	189 (71.6)
Yes	75 (28.4)
Chronic Obstructive Pulmonary Disease (COPD)	
No	242 (91.7)
Yes	22 (8.3)
Chronic Kidney Disease (Conservative Treatment)	
No	247 (93.9)
Yes	16 (6.1)
Chronic Kidney Disease (Hemodialysis)	
No	247 (93.9)
Yes	16 (6.1)
Body Mass Index	
Low Weight	41 (15.5)
Eutrophy	112 (42.4)
Overweight	111(42.1)
Sarcopenia	
No risk	116 (43.9)
Risk presente	148 (56.1)
Intensive Care Unit (ICU)	
No	133 (50.4)
Yes	131 (49.6)
Mechanical ventilation	
No	171 (64.8)
Yes	93 (35.2)
Death	
No	192 (72.7)
Yes	72 (27.3)

Source: Self-prepared, based on statistical analyses.

Table 3. Univariate analysis between the risk of sarcopenia and clinical outcomes in older adults with covid-19 (N=264). Northeast Region, Brazil, 2020-2021.

	Intensive Care Unit			Mechanical Ventilation			Death		
	No (%)	Yes (%)	*p*	No (%)	Yes (%)	*p*	No (%)	Yes (%)	*p*
Sarcopenia Risk									
Yes	59 (39.9)	89 (60.1)	<0.001	77 (52.0)	71 (48.0)	<0.001	91 (61.5)	57 (38.5)	<0.001
No	74 (63.8)	42 (36.2)		94 (81.0)	22 (19.0)		101 (87.1)	15 (12.9)	

Source: Self-prepared, based on statistical analyses conducted through univariate logistic regression.

Table 4. Multivariate analysis between the risk of sarcopenia and clinical outcomes in older adults with covid-19 according to models proposed by the DAG. Northeast Region, Brazil, 2020-2021.

	Intensive Care Unit					Mechanical Ventilation					Death				
	OR	CI95%	x^2	R^2	*p*	OR	CI95%	x^2	R^2	*p*	OR	IC95%	x^2	R^2	*p*
Model 1															
Sarcopenia Risk	2.71	1.57;4.68	23.8	0.06	<0.001	5.19	2.75;9.78	41.2	0.12	<0.001	4.05	2.05;7.98	30.7	0.09	<0.001
Model 2															
Sarcopenia Risk	2.61	1.50;4.52	23.6	0.06	<0.001	4.95	2.62;9.35	40.9	0.11	<0.001	3.52	1.78;6.94	37.7	0.12	<0.001

OR: odds ratio; 95% CI: 95% confidence interval. Model 1, adjusted for the following variables: age, gender, physical activity, smoking, diabetes, hypertension, cardiovascular disease, chronic obstructive pulmonary disease, and BMI. Model 2, adjusted for: age, gender, income, smoking, diabetes, hypertension, cardiovascular disease, chronic obstructive pulmonary disease, and BMI. Source: Self-prepared, based on statistical analyses conducted through multivariate logistic regression.

DISCUSSION

In this study, it was evident that the risk of sarcopenia increased the chances of unfavorable clinical outcomes, such as ICU admission, the need for mechanical ventilation, and death, in older adults hospitalized with covid-19.

Sarcopenia is considered a complex geriatric syndrome with a multifactorial pathogenesis and a limitation to the functional capacity of the older individual. This syndrome is closely related to immunosenescence and the consequent impairment of the proliferation of peripheral mononuclear cells, an increase in the neutrophil-to-lymphocyte ratio, and damaged homeostasis of natural killer lymphocytes, implying deficient immune system function, increasing the risks of clinical complications in older individuals hospitalized due to SARS-CoV-2 infection[16].

Furthermore, sarcopenia is characterized by an inflammatory state primarily in muscle tissue. The progression of age is related to determinants of risk factors for the development of the sarcopenic phenotype, such as changes in body composition with increased fat infiltration into muscles, hormonal changes, and increased oxidative stress with higher production of reactive oxygen species, which are associated with increased proteolysis and reduced protein synthesis[17]. Similarly, the occurrence of non-communicable chronic diseases such as hypertension, diabetes, and cardiovascular diseases can predispose to muscle alterations due to an increase in the levels of inflammatory mediators and disturbances in mitochondrial function[17,18].

Aguiar et al.[19], in a study conducted in a northeastern state with adults and older individuals hospitalized with covid-19, demonstrated a higher probability of sarcopenia in older individuals who were non-exercisers, had hypertension, diabetes, and were admitted to an intensive care unit.

Corroborating with the present study, Ma et al.[20] found a similar result by showing that the risk of severe illness in older individuals with a risk of sarcopenia was nearly three times higher than in

those without risk. Physiological changes resulting from sarcopenia, such as an increase in inflammatory markers - tumor necrosis factor-alpha (TNF-α), interleukin (IL)-6, IL-1, and C-reactive protein (CRP) - combined with the cytokine storm induced by SARS-CoV-2, contribute to the progression and severity of covid-19 and consequently to the occurrence of clinical complications and higher mortality from this cause[16,21].

Furthermore, the study conducted by Ufuk et al.[22] showed that a low pectoral muscle index, a measure associated with sarcopenia, evaluated by computed tomography, was a predictor of mechanical ventilation and death in adult patients hospitalized for covid-19. The loss of muscle mass caused by sarcopenia directly contributes to respiratory failure resulting from covid-19, due to the reduction in the thickness of the diaphragmatic muscle, pectoral muscles, and intercostal muscles, resulting in the need for intensive care and prolonged mechanical ventilation[7,23].

In a study conducted at a university hospital in Brazil involving adult and older patients, it was observed that the risk of sarcopenia, assessed using the SARC-F, was higher in patients who died compared to those who were discharged, corroborating the results shown in this research[24]. An inefficient immune response to infection and the presence of a higher number of comorbidities may be related to the increased risk of death in these patients[25]. Immunosenescence, a typical phenomenon of aging, combined with the loss of muscle cells due to sarcopenia, results in alterations in the immune system, consequently making it more challenging to combat pathogens such as SARS-CoV-2[26,27].

With the completion of this research, it becomes evident that the risk of sarcopenia in older adults is an additional factor for severe illness caused by the coronavirus. Therefore, it is essential to identify older adults at risk of sarcopenia who also have covid-19 to intensify their care. Furthermore, it is essential to emphasize the preventive care of sarcopenia in this population, before infection with SARS-CoV-2 or any other infectious disease, through appropriate nutritional interventions, regular physical activity, and the adoption of healthy lifestyle habits with the goal of promoting active aging and functional independence, thereby reducing the risks associated with the loss of muscle mass and strength.

Some limitations may be presented for this study, such as nutritional assessment through self-reporting and medical records, and the absence of a sarcopenia diagnosis. The non-evaluation of anthropometric measures for classifying nutritional status was adopted in accordance with the recommendations of national and international protocols to avoid the risk of covid-19 exposure for healthcare professionals. Additionally, in many cases, it would not be possible to measure anthropometric data due to individual limitations, such as mobility difficulties, especially in patients in the ICU and on mechanical ventilation. Nevertheless, the use of self-reported measures has demonstrated good agreement with measured data in older adults[28], making these measurements valid in the current context. The diagnosis of sarcopenia requires expensive equipment to measure muscle mass and trained professionals for assessing strength and physical function, criteria that are often not available in most healthcare centers in Brazil. However, the SARC-F questionnaire is easy to administer and quick, making it suitable for assessing muscle loss in older adults. Studies and meta-analyses have shown the high specificity of this screening tool, linking it to a decline in physical performance, hospitalization, quality of life, and mortality[8,29,30]. On the other hand, the sample size and the multicenter nature of this study conducted in different states in the Northeast region of Brazil are strengths that reinforce the discussion about the effects of sarcopenia on the clinical outcomes of older adults with covid-19.

CONCLUSION

In older adults with covid-19, the preexistence of sarcopenia risk was a predictor of unfavorable clinical outcomes, including the need for intensive care, mechanical ventilation, and death. Despite the limitations discussed, this study underscores that screening and early identification of sarcopenia using screening tools like SARC-F in hospitalized older adults, or even in primary care settings, can help improve patient care and prevent negative outcomes.

AUTHORSHIP

- Thamires Otaviano Marques de Souza – Responsible for all aspects of the study, vouching for any issues related to the accuracy or integrity of any part of the study.
- Bárbada Lima Queiroz – Conception and design or analysis and interpretation of the data approval of the version for publication.
- Muller Ribeiro-Andrade – Writing or critical review of article approval of version for publication.
- Mateus de Lima Macena – Responsible for all aspects of the study, vouching for any issues related to the accuracy or integrity of any part of the study.
- André Eduardo da Silva Júnior – Responsible for all aspects of the study, vouching for any issues related to the accuracy or integrity of any part of the study.
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