# Sarcopenia and risk of malnutrition as risk factors for complications from COVID-19

## Sarcopenia e risco de desnutrição como fatores de risco para complicações da COVID-19

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## ABSTRACT

**Purpose:** This study aimed to associate nutritional and sarcopenia risk with clinical outcomes in elderly patients with COVID-19. **Methods:** This is a longitudinal retrospective cohort study. Hospitalized elderly individuals diagnosed with COVID-19 were included in the study. Nutritional risk was assessed using the Malnutrition Universal Screening Tool (MUST), and Sarcopenia risk was assessed using the SARC-F. Associations were assessed through multivariable logistic models. **Results:** In total, 127 patients (mean age: 71.25 ±8.06 years) were followed up until the clinical outcome. Sarcopenia risk was diagnosed in 63.8% of the sample, whereas nutritional risk was observed in 72%. Hospitalization in the intensive care unit (ICU) was required in 48.8% of the sample, 38.6% required mechanical ventilation, and 32.3% died. Elderly individuals with sarcopenia risk were more likely to be hospitalized in ICUs (OR: 5.62; 95%CI: 2.2-14.3), require mechanical ventilation (OR: 4.0; 95% CI: 1.5-10.2), and die (OR: 5.06; 95% CI: 1.7-14.2). The risk of malnutrition assessed through MUST was an important risk factor for death (OR = 30.15; 95% CI: 3.6-245.8; p<0.01). **Conclusion:** Sarcopenia risk was a risk factor for death, hospitalization in ICU, and mechanical ventilation, while nutritional risk was a risk factor for death.

**Keywords:** Aging, COVID-19, Hospitalization, Intensive care units, Malnutrition.

## RESUMO

**Objetivo:** Este estudo teve como objetivo associar o risco nutricional e de sarcopenia com desfechos clínicos em pacientes idosos com COVID-19. **Métodos:** Trata-se de um estudo de coorte retrospectivo longitudinal. Idosos hospitalizados com diagnóstico de COVID-19 foram incluídos no estudo. O risco nutricional foi avaliado usando o *Malnutrition Universal Screening Tool (MUST)* e o risco de sarcopenia foi avaliado usando o SARC-F. As associações foram avaliadas por modelos logísticos multivariados. **Resultados:** No total, 127 pacientes (média de idade: 71,25 ±8,06 anos) foram acompanhados até o desfecho clínico. Risco de sarcopenia foi diagnosticado em 63,8% da amostra, enquanto risco nutricional foi observado em 72% deles. Além disso, 48,8% da amostra necessitou de internação em unidade de terapia intensiva (UTI), 38,6% necessitaram ventilação mecânica e 32,3% foram a óbito. Idosos com risco de sarcopenia tiveram maior chance de internação em UTI (OR: 5,62; IC 95%: 2,2-14,3), necessidade de ventilação mecânica (OR: 4,0; IC 95%: 1,5-10,2) e óbito (OR: 5,06; IC 95%: 1,7-14,2). O risco de desnutrição avaliado pelo MUST foi um importante fator de risco para óbito (OR = 30,15; IC 95%: 3,6-245,8; p<0,01). **Conclusão:** O risco de sarcopenia foi fator de risco para óbito, internação em UTI e ventilação mecânica, enquanto o risco nutricional foi fator de risco para óbito.

**Palavras-chave:** Envelhecimento, COVID-19, Hospitalização, Unidade de Terapia Intensiva, Desnutrição.

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## INTRODUCTION

Coronavirus disease (COVID-19) is an infection caused by the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) virus, which affects individuals' respiratory system and may lead to mild, moderate, or severe infections[1]. According to data from the Epidemiological Bulletin of the Ministry of Health, published in December 2021, Brazil ranks third among the countries with the largest number of COVID-19 cases; 22,234,626 individuals have been infected since the beginning of the pandemic. The country comes right after the United States and India, ranking second in absolute number of deaths[2].

According to the international literature, preexisting comorbidities act as complicating factors in the clinical evolution of hospitalized patients[3,4]. Among them, one finds cardiovascular diseases, respiratory system diseases, diabetes mellitus, and hypertension[5]; obesity has also emerged as a risk factor for death in these patients[6]. The elderly population with comorbidities has been shown to be more susceptible to the severe form of COVID-19; consequently, it is more prone to require hospitalization[7,8]. This group is even more vulnerable because it is often affected by malnutrition and sarcopenia, which are associated conditions that lead to impaired functional capacity and frailty, as well as unfavorable clinical outcomes in patients with COVID-19[9].

Most importantly, sarcopenia is a multifactorial disease that shows a chronic inflammatory process secondary to oxidative stress and leads to reduced muscle mass and strength[10]. Increased level of inflammatory mediators such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and C-reactive protein (CRP), appears to be linked to several age-associated diseases and increased disability and frailty levels[11,12]. These factors appear to compromise elderly individuals' prognosis and survival rates and worsen clinical outcomes associated with COVID-19 in this population[13,14].

Consequences of malnutrition for hospitalized patients, such as impaired immune function, reduced skeletal and respiratory muscle strength, longer hospitalization time, and higher mortality rate, have already been consolidated in the literature[15]. According to Stefano et al. (2021)[16], the risk of malnutrition for patients with COVID-19 is a negative prognostic factor in terms of mortality rate, hospitalization time, and clinical status at hospital discharge. However, it is necessary to conduct further research on this topic. Thus, it is extremely important to conduct studies that investigate aspects related to COVID-19 infection, weight loss, and lean mass, as perceived in sarcopenia, in elderly individuals.

Thus, this study aims to associate nutritional and sarcopenia risk with clinical outcomes in elderly patients diagnosed with COVID-19 who were hospitalized.

## MATERIAL AND METHODS

### Study type, sampling, and collaborating centers

A retrospective cohort was carried out with secondary data deriving from a multicenter cohort. It was conducted in Northeastern Brazil and titled "Clinical, nutritional and sociodemographic aspects associated with mortality rates in patients with COVID-19: multicenter study in Northeastern Brazil".

The sampling procedure followed a non-probabilistic convenience model, which comprised all elderly individuals who participated in the main research and patients hospitalized in any of the research partner services in Alagoas State. COVID-19 treatment-reference services in Alagoas State were herein selected: four of them were in the State's capital – including a federal university hospital – and three hospitals were located in inland cities.

### Inclusion and exclusion criteria

Patients' identification was performed by dieticians from partner hospitals. Male and female individuals in the age group 60 years or older, with laboratory-confirmed COVID-19 diagnosis, who lived in Alagoas State, and were hospitalized to treat this disease in one of the health services linked to the current research were included in the present study. Patients whose semiological evaluation indicated signs and symptoms typical of COVID-19 but whose laboratory diagnosis was negative were excluded from the study.

## Research protocol

Data in the original study were collected retrospectively through patients' medical records, and/or in a prospective manner when patients were followed up by dieticians from the aforementioned services, who were duly trained for this research. The food intake form was applied through a guided interview conducted by phone or through an electronic form completed by patients or their family members in the Google Forms platform; contents of the last interview modality were stored in the project's restricted Google account. All data analyzed in the current study were collected from the main research database.

The aforementioned form collected sociodemographic data, such as patients' sex, age, schooling, and skin color, for sample featuring purposes.

Lifestyle evaluation focused on identifying alcoholic beverage intake, smoking habits, and physical activity reports. All individuals who reported drinking alcoholic beverages were considered drinkers, even if they rarely did it (< 1 time/month), whereas those who reported never drinking alcoholic beverages or who reported having abstained from doing it for at least 30 days before the suspected COVID-19 condition were considered non-drinkers. Individuals who reported smoking at interview time, regardless of frequency, were classified as smokers; whereas those who never smoked tobacco or who reported having abstained from doing it for at least 30 days before the suspected COVID-19 condition were classified as non-smokers. Individuals who reported practicing moderate-intensity aerobic activity for at least 30 min/day for 5 days a week or intense activity for at least 20 min/day, three times a week, were considered physically active, based on criteria set by the American College of Sports Medicine and by the American Heart Association[17].

## Clinical data

Data associated with hypertension, diabetes mellitus, cancer, cardiovascular diseases (CVD), chronic obstructive pulmonary disease (COPD), and asthma, among other chronic diseases, were collected to fill in patients' pathological history.

The "Malnutrition Universal Screening Tool" (MUST) was used to screen participants' nutritional risk based on three clinical parameters, namely: body mass index (BMI), unintentional weight loss in the last 3 to 6 months, and severe illness associated with drastic nutritional intake reduction or with fasting longer than 5 days; each item scores from zero to two[18]. All patients in the current study who required intensive care and/or mechanical ventilation during hospitalization scored in item "disease severity". After all the aforementioned items were considered, the final score was added to establish patients' overall risk of malnutrition. Score 0 classifies patients in the group of low risk of malnutrition; score equal to 1 in the medium-risk group; and score higher than 2, in the high-risk group. The total sample was divided into nutritional risk (medium and high risk based on MUST) and no nutritional risk (low risk based on MUST) for results' presentation purposes.

Patients' current weight, habitual weight, and self-reported height were collected for anthropometric evaluation. BMI was calculated based on collected data about patients' weight and height, and classified based on recommendations by Lipschitz (1994)[19]. BMI < 22 kg/m² was classified as thinness; 22-27 kg/m² as eutrophy; and > 27 kg/m² as overweight. Unintentional weight loss in the last 6 months was also calculated based on the difference between patients' usual and current weight reported at the time they joined this study; the loss of more than 4.5 kg or 5% of patients' initial weight was one of the items used to assess frailty in elderly individuals, as suggested by Fried et al. (2001)[20].

The SARC-F questionnaire was used to assess sarcopenia risk based on five components, namely muscle strength, assistance to walk, ability to stand up from a chair, climbing stairs, and frequency of falls. Each component receives a score ranging from 0 to 2 points; the sum of all items can reach 10 points. Individuals whose score is higher than or equal to 4 points are classified as sarcopenia risk[21]. The data used for the SARC-F questionnaire implied conditions prior to COVID-19 infection.

Hospitalization in ICU, mechanical ventilation, and death were the clinical endpoints analyzed in the current study.

## Follow-up

All patients were followed up by the dietician of the investigated service until clinical outcome (discharge or death), regardless of the day it happened. Information about their clinical evolution, complications, mechanical ventilation, and comorbidities was recorded.

## Statistical analysis

Data referring to continuous variables were presented as mean and standard deviation, whereas those referring to categorical variables were presented as frequency. The chi-square test was used to check whether there was an association between qualitative variables. In addition, logistic regressions were performed: outcomes comprised clinical complications (hospitalization in ICU, mechanical ventilation, or death); predictor variables comprised risk of sarcopenia or nutritional risk; and adjustment variables comprised age, sex, CVD, hypertension, and diabetes mellitus. A significance level of 5% was adopted. Statistical analyses were performed in Jamovi statistical software version 2.2.3.

## Ethical aspects

This research was submitted and approved by the Ethics and Research Committee of the Universidade Federal de Alagoas (process number, CAAE: 31113120.0.1001.5013). After the inclusion and exclusion criteria analysis, individuals were invited participate in the study voluntarily; those who accepted it signed the informed consent form.

## RESULTS

In total, 130 elderly patients hospitalized in Alagoas State were eligible to participate in the current study, although three were excluded due to follow-up loss. The final sample comprised 127 patients who were followed up until the clinical outcome. The mean age of the sample analyzed was 71.25 ±8.06 years; 52% (n = 66) of patients were men. Hypertension (78.2%; n = 97) was the most prevalent comorbidity among the investigated ones, followed by diabetes mellitus (45.6%; n = 57) and CVD (27.3%; n = 33), as shown in Table 1.

**Table 1**

Clinical featuring of patients subjected to COVID-19 treatment.

| Variables | N | % |
|---|---|---|
| Age (years) (n=127) | | |
| <80 | 103 | 81.1 |
| ≥ 80 years | 24 | 18.9 |
| Sex (n=127) | | |
| Male | 66 | 52.0 |
| Female | 61 | 48.0 |
| Race/color (n=85) | | |
| White/Asian descendant | 29 | 34.1 |
| Brown | 47 | 55.3 |
| Black | 6 | 7.1 |
| Indigenous | 3 | 3.5 |
| Lifestyle (n=127) | | |
| Drinking habit | 21 | 16.2 |
| Smoking habit | 14 | 11.0 |
| Exercising | 27 | 21.3 |
| Comorbidities | | |
| Hypertension (n=124) | 97 | 78.2 |
| DM (n=125) | 57 | 45.6 |
| CVD (n=121) | 33 | 27.3 |
| COPD (n=120 | 14 | 11.7 |
| BMI classification (n=114) | | |
| Low weight | 17 | 14.9 |
| Ideal weight | 38 | 33.3 |
| Overweight | 59 | 51.8 |
| Unintentional Weight Loss (n=87) | 29 | 33.7 |
| Sarcopenia risk (n=127) | 81 | 63.8 |
| Nutritional risk (n=114) | | |
| Low Risk (0 point) | 31 | 27.2 |
| Medium Risk (1 point) | 9 | 7.9 |
| High Risk (≥ 2 points) | 74 | 64.9 |
| Hospitalization in ICU (n=127) | 62 | 48.8 |
| Mechanical ventilation (n= 127) | 49 | 38.6 |
| Death (n=127) | 41 | 32.3 |

BMI – body mass index; COPD – chronic obstructive pulmonary disease; CVD – cardiovascular disease; DM – diabetes mellitus; ICU – intensive care unit.

Sarcopenia risk was diagnosed in 81 (63.8%) of the 127 elderly individuals who completed the SARC-F, whereas approximately 72.8% of the 114 evaluated elderly individuals presented a risk of malnutrition: 7.9% of them were classified as medium risk (MUST =1 point) and 64.9% as high risk (MUST ≥2 points). Regarding clinical complications, 48.8% of the sample required hospitalization in ICU, 38.6% required mechanical ventilation, and 32.3% died. Other data featuring the analyzed sample are described in Table 1.

Table 2 shows the association among predictor variables, clinical complications, and observed outcomes. Age ≥ 80 years was associated with the need of mechanical ventilation (p=0.04), whereas incidence of CVD has shown association with death outcome (p=0.03). Patients' sex, hypertension, diabetes mellitus, COPD, BMI, and weight loss did not show association with clinical complications or death outcomes.

Possible associations between nutritional risk and the need for hospitalization in ICU and mechanical ventilation were not assessed because, based on MUST criteria, all patients who required hospitalization in ICU or mechanical ventilation were assigned a score of two; consequently, they were placed in the nutritional risk group.

The current results pointed out that elderly individuals at risk of sarcopenia were 5.62 times (95% CI: 2.2-14.3; p<0.01) more likely to require hospitalization in ICU, 4 times (95% CI: 1.5-10.2; p<0.01) more likely to need mechanical ventilation as respiratory support, and 5.06 times (95% CI: 1.7-14.2; p<0.01) more likely to die after the model was adjusted by sex, age, CVD, COPD, hypertension, and diabetes, as shown in Table 3. The risk of malnutrition assessed through MUST was an important risk factor for death (OR = 30.15; 95% CI: 3.6-245.8; p<0.01).

**Table 2**

Univariate analysis between predictor variables and observed clinical events.

| | Clinical events | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | ICU | | | Mechanical Ventilation | | | Death | | |
| | No (%) | Yes (%) | p-value* | No (%) | Yes (%) | p-value* | No (%) | Yes (%) | p-value* |
| Age ≥ 80 years | 50 | 50 | 0.89 | 79.2 | 20.8 | 0.04 | 62.5 | 37.5 | 0.54 |
| Sex | | | | | | | | | |
| Male | 54.5 | 45.5 | | 63.6 | 36.4 | | 69.7 | 30.3 | |
| Female | 47.5 | 52.5 | 0.43 | 59.0 | 41.0 | 0.59 | 65.6 | 34.4 | 0.62 |
| Comorbidities | | | | | | | | | |
| Hypertension | 52.6 | 47.4 | 0.45 | 62.9 | 37.1 | 0.30 | 67.0 | 33.0 | 0.97 |
| DM | 47.4 | 52.6 | 0.43 | 59.6 | 40.4 | 0.80 | 61.4 | 38.6 | 0.20 |
| CVD | 36.4 | 63.6 | 0.07 | 57.6 | 42.4 | 0.79 | 51.5 | 48.5 | 0.03 |
| COPD | 50 | 50 | 0.94 | 71.4 | 28.6 | 0.32 | 64.3 | 35.7 | 0.89 |
| BMI classification | | | | | | | | | |
| Low weight | 52.9 | 47.1 | | 64.7 | 35.3 | | 82.4 | 17.6 | |
| Ideal weight | 47.4 | 52.6 | | 63.2 | 36.8 | | 57.9 | 42.1 | |
| Overweight | 44.1 | 55.9 | 0.80 | 52.5 | 47.5 | 0.48 | 64.4 | 35.6 | 0.21 |
| Unintentional Weight Loss | 55.2 | 44.8 | 0.40 | 69.0 | 31.0 | 0.39 | 75.9 | 24.1 | 0.18 |
| Sarcopenia risk | 40.7 | 59.3 | <0.01 | 51.9 | 48.1 | <0.01 | 56.8 | 43.2 | <0.01 |
| Nutritional risk | | | | | | | | | |
| No risk | | | | | | | 96.8 | 3.2 | |
| Risk | 26.5 | 73.5 | | 42.2 | 57.8 | | 53.0 | 47.0 | <0.01 |

BMI – body mass index; COPD – chronic obstructive pulmonary disease; CVD – cardiovascular disease; DM – diabetes mellitus; ICU – intensive care unit.
*p-value at chi-square test

**Table 3**

Multivariate analysis between sarcopenia risk and nutritional risk with clinical events.

| | Clinical events* | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | ICU | | | Mechanical Ventilation | | | Death | | |
| | OR | IC 95% | p-value | OR | IC 95% | p-value | OR | IC 95% | p-value |
| Sarcopenia risk | 5.6 | 2.2;14.3 | <0.01 | 4.0 | 1.5;10.2 | <0.01 | 5.0 | 1.7;14.2 | <0.01 |
| Nutritional risk | | | | | | | 30.1 | 3.6:245.8 | <0.001 |

ICU – intensive care unit.

* Binary logistic regression analysis was adjusted for the variables age, sex, cardiovascular disease, chronic obstructive pulmonary disease, hypertension, and diabetes mellitus.

## DISCUSSION

There was a high prevalence of sarcopenia and nutritional risks in elderly patients hospitalized in COVID-19 reference institutions in Alagoas State – 63.8% and 72.8%, respectively. Sarcopenia and nutritional risks were risk factors for death after the model was adjusted for variables such as age, sex, CVD, COPD, hypertension, and diabetes mellitus. Sarcopenia risk was also associated with hospitalization in ICU and the need for mechanical ventilation.

The literature has already established that malnutrition leads to several changes in the immune system, and makes the human body more susceptible to infections[22]. This factor may explain the high prevalence of sarcopenia and malnutrition risks observed in the sample herein and in previous studies[23,24]. A study conducted with elderly individuals hospitalized in Wuhan City at the beginning of the COVID-19 pandemic showed that 80.2% of elderly patients with COVID-19 were at risk of malnutrition or already malnourished[23]. These prevalence rates are higher than those reported for elderly patients hospitalized due to other comorbidities[25]. Furthermore, Stefano et al. (2021)[16] used MUST to estimate the risk of malnutrition in 515 patients hospitalized with COVID-19 and found a risk prevalence of 18.1%. However, it is worth emphasizing that their sample was younger than the one assessed in the present study (65.1 ± 14.3 years).

The multivariate analysis showed a risk of malnutrition as a risk factor for death. Stefano et al. (2021)[16] also found an association between the risk of malnutrition calculated based on MUST and death (HR 1.25; 95% CI 1.04-1.51; p=0.019), even after the model was adjusted for age, treated hypertension, hospitalization in ICU, and oxygen therapy; their results corroborated the current findings. High expression of pro-inflammatory factors triggered by patients' altered nutritional status and the pathophysiology of SARS COV-2 infection is likely an explanation for this association.

Increased expression of factors such as angiotensinogen, angiotensin-converting enzyme 2 (ACE2), IL-6, and TNF- α was observed in malnutrition and obesity cases[26]. This finding is worrisome, mainly after the study by Hoffmann et al. (2020)[27], who collected evidence that SARS-CoV-2 uses ECA2 receptors to enter the host cell. Thus, these authors evidenced an association between the renin-angiotensin system and the severity of SARS-CoV-2 infection[27].

Moreover, malnutrition decreases lipid tissue, changes adipokine production, and leads to restrictions in innate and adaptive immunity[28]. COVID-19 severity has been associated with the hyperinflammatory state, which is featured by cytokine storm due to the dysregulated release of IL-2, IL-7, IL-10, TNFα, among others[29,30]. Therefore, this finding suggests that malnourished patients are more susceptible to developing the most severe forms of COVID-19; consequently, they are more likely to die.

Like the present study, Wierdsma et al. (2021)[31] found a high prevalence of sarcopenia risk in 73% of patients hospitalized due to COVID-19. During the COVID-19 pandemic, individuals, mainly the elderly population, were advised to stay home as long as possible to prevent

contagion. Consequently, it led to decreased exercise and changes in food intake. These behaviors can accelerate sarcopenia, lead to muscle mass and function deterioration, increase body fat level.

The current results have suggested that patients at risk of sarcopenia are more likely to be hospitalized in ICU, require mechanical ventilation and die. According to a recent meta-analysis, critically ill patients with sarcopenia presented an increased risk of death compared to those without sarcopenia[32]; these results corroborate the current findings. Loss of muscle mass in critically ill patients is a common complication; estimated muscle mass loss in the most critically ill patients ranges from 2% to 3% a day[33]. Prolonged resting and immobilization can accelerate this process and potentially lead to loss of respiratory muscle functionality and unfavorable clinical outcomes.

The present study has some limitations. First, weight and height information were self-reported due to contact restrictions imposed by the COVID-19 pandemic. However, high correlations between self-reported and measured measures were reported in the literature[34]. Among the strengths of the current study is the use of validated and standardized instruments, such as MUST, which is recommended for use in patients with COVID-19. This tool has shown high sensitivity and specificity in a systematic review of studies conducted with screening tools applied to elderly individuals with COVID-19[35].

## CONCLUSION

Nutritional risk, sarcopenia risk, and history of unintentional weight loss are associated with the COVID-19-related death of elderly individuals living in Alagoas State. Furthermore, sarcopenia risk in this sample was associated with the need for hospitalization in ICU and mechanical ventilation.

Thus, screening focused on identifying the risk of malnutrition and sarcopenia in elderly patients with COVID-19 is of paramount importance since the early identification of these risks enables implementing a more targeted nutritional intervention to prevent the establishment or worsening of malnutrition and improve patients' prognosis.

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