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ORIGINAL ARTICLE

Influence of body composition during hospitalization on lung function and inspiratory muscle strength in patients with COVID 19: cross-sectional study

Influência da composição corporal durante a hospitalização sobre a função pulmonar e força da musculatura inspiratória em pacientes com COVID-19: estudo transversal

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Abstract

Introduction: Approximately 31% of hospitalized patients with COVID-19 lose more than 5% of their initial weight, leading to muscle weakness. Therefore, body composition has become the focus of investigation, to estimate pulmonary impairment, inspiratory muscle strength, and mortality. *Objectives*: To investigate whether weight loss and body composition of patients hospitalized with COVID-19 have any influence on lung function and inspiratory muscle strength after hospital discharge. *Methods*: Cross-sectional study. Adult patients were assessed after hospitalization due to COVID-19. Outcomes

evaluated were lung function, maximal inspiratory pressure (MIP), body composition, and mortality. Correlations between the variables were estimated by Pearson's Correlation Coefficient. *Results*: Forced Vital Capacity (FVC) was correlated with weight loss, skeletal muscle mass, lean mass, left leg, and fat-free mass; Forced expiratory volume in the first second (FEV1) was correlated only with weight loss; and MIP was correlated with skeletal muscle mass, lean mass, left leg, right leg, and fat-free mass. *Conclusion*: A moderate correlation was observed between FVC and the analyzed body composition variables, except lean mass of left leg; between FEV1 and weight loss; and between MIP and the analyzed body composition variables, except weight loss.
Keywords: COVID-19; body composition; respiratory function test.

Resumo

Introdução: Cerca de 31% dos pacientes hospitalizados com COVID-19 perdem mais de 5% de seu peso inicial, levando a fraqueza muscular. Portanto, a composição corporal tornou-se foco de investigação, para estimar comprometimento pulmonar, força da musculatura inspiratória e mortalidade. *Objetivos*: Investigar se a perda de peso e a composição corporal de pacientes internados com COVID-19 influenciam na função pulmonar e na força muscular inspiratória após alta hospitalar. *Métodos*: Estudo transversal. Pacientes adultos foram avaliados após internação por COVID-19. Os desfechos avaliados foram função pulmonar, pressão inspiratória máxima ($Pi_{máx}$), composição corporal e mortalidade. As correlações entre as variáveis foram estimadas pelo Coeficiente de Correlação de Pearson. *Resultados*: A capacidade Vital Forçada (CVF) foi correlacionada com perda de peso, massa muscular esquelética, massa magra, perna esquerda e massa livre de gordura; o volume expiratório forçado no primeiro segundo (VEF1) correlacionou-se apenas com a perda de peso; e a $Pi_{máx}$ foi correlacionada com massa muscular esquelética, massa magra, perna esquerda, perna direita e massa livre de gordura. *Conclusão*: Observou-se correlação moderada entre CVF e as variáveis de composição corporal analisadas, exceto massa magra da perna esquerda; entre VEF1 e perda de peso; e entre $Pi_{máx}$ e as variáveis de composição corporal analisadas, exceto perda de peso.
Palavras-chave: COVID-19; composição corporal; testes de função respiratória.

Introduction

Coronavirus disease (COVID-19) is related to severe and non-severe symptoms, such as dyspnea, cough, myalgia, asthenia, fever, headache, and muscle weakness, and can negatively affect body weight [1]. Impaired body composition through weight loss impacts the course of the disease and affects muscles and adipose tissues, making patients even more fragile and worsening these symptoms [2,3]. Among hospitalized patients, underweight patients have higher mortality rates [4]. Within 60 days after hospital discharge 9.1% of patients died, especially older adults [5].

Approximately 31% of hospitalized patients with COVID-19 lose more than 5% of their initial weight, increasing the length of the illness and hospital stay, leading to muscle weakness [1,6]. After hospital discharge, this muscle weakness persists in 92% of patients [6]. During the course of the disease, symptoms are often persistent and impactful, and muscle weakness seems to impair lung function and maximal inspiratory pressure (MIP) [7-9].

Considering the weight loss of patients hospitalized with COVID-19, body composition has become the focus of investigation, using bioelectrical impedance analysis (BIA), to estimate pulmonary impairment, inspiratory muscle strength, and mortality [10]. However, there is still uncertainty about the association between the patient's body composition after hospital discharge and these variables. In addition, approximately 80% of patients diagnosed with COVID-19 and hospitalized with clinical worsening, present alterations in lung function at the time of hospital discharge, which can predict the outcome of the COVID-19 disease [11,12]. Among these alterations, it is possible to observe a decrease in FVC and MIP [11,13].

It is probable that adequate body composition can improve clinical outcomes of the disease [14], such as lung function and MIP, and reduce the mortality rate. Some studies have investigated the occurrence of weight loss in patients with COVID-19 at different times; before, during, and after hospital treatment [13,15,16], suggesting the possibility that patients with COVID-19 may be susceptible to weight loss [3]. However, to date, no studies have been published to clarify whether there is an association between body composition and lung function, respiratory muscle strength, and mortality after hospital discharge in patients with COVID-19.

The current cross-sectional study was designed to answer the following question:
- Does the weight loss and body composition (skeletal muscle mass, lean mass, lean leg mass, fat-free mass) of patients hospitalized with COVID-19 have any influence on lung function and inspiratory muscle strength after hospital discharge?

Methods

Design

This study is a cross-sectional study conducted from March to November 2021. The reporting followed the guidelines of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE statement), using the specific extension for cross-sectional studies [17].

Ethical data

This study was conducted following the principles of the Declaration of Helsinki: CAAE 40801920.80000.003.

Eligibility criteria

Adult patients post hospitalization (within 48 hours after discharge) due to COVID-19 infection with undetectable viral load (after hospital discharge), without previous chronic respiratory diseases from 4 reference centers for the treatment of COVID-19 in the city of Macapá (Brazil), and who lost weight during the hospital stay (at least 1 kilogram), were included. Patients with a history of endotracheal intubation during the hospital stay and any patients who wanted to withdraw from participation in the study, were excluded.

Outcomes evaluated

Spirometry, manovacuometry, and BIA were used to assess the outcomes. All tests were performed on the same day, always in the morning. The test execution sequence was randomized for each patient by drawing lots, aiming to minimize the overlapping effects. The random draw was performed using dice, where values “1” and “2” represented spirometry, “3” and “4” represented manovacuometry, and “5” and “6”, the BIA.

1. Lung function was evaluated by spirometry (Spirobank II, MIR, Italy) which was performed following international guidelines [18]. The variables FVC, FEV1, and PEF were analyzed. In addition, the predicted values were recorded based on the Brazilian population [19].
2. MIP (measured in millimeters of mercury (mmHg)) was obtained by means of a Wika manovacuometer (WIKA, Ind, Ipero, SP, Brazil). The tests were carried out according to the guidelines i.e., the maneuvers were performed three to five times, from the residual

volume, with the highest value used for analysis [20,21]. The measurement was considered valid if three acceptable and two reproducible measures were obtained [21].
3. Body composition: Weight loss was calculated based on the weight recorded at the beginning and at the end of the hospital stay, using data from the patient medical record. Skeletal muscle mass, lean mass, lean leg mass, and fat-free mass were evaluated using the BIA InBody 770 device (InBody 770, Cerritos, CA, USA). The InBody 770 uses 30 impedance measurements and six different frequencies. Participants were instructed to be present in the laboratory after fasting for at least three hours and not to perform any exercise on the day of assessment. All tests were conducted in the morning. For the analysis in the InBody 770, the individuals stood barefoot on the platform of the device with the plantar regions on the electrodes and held the unit handles with the thumb and fingers to maintain direct contact with the electrodes. They remained standing for approximately one minute, keeping the elbows fully extended and the shoulder joint abducted at an angle of approximately 30 degrees.
4. Mortality after hospital discharge: the mortality rate was recorded through the number of deaths. Patients were monitored via telephone, over a 3-month period, to observe and record this outcome, in order to establish whether this variable is related to the course of the disease. Phone calls were made once a week.

Statistical analysis

The sample size calculation was based on the Luiz & Magnanini formula [22], assuming an α of 95%, type I error of 5%, and mortality rate 1.3% [23]. A minimum sample size of 20 patients was obtained. Considering possible losses to follow-up for any reason, the sample was increased by 20%, giving a final sample of 25 patients. For dichotomous variables, descriptive statistics were used to describe the baseline. Variables are presented as absolute number and percentage (n (%)) and mean and standard deviation (mean ± standard deviation). The D'Agostino Pearson test was used to test data normality when necessary. The degrees of correlation between the lung function data (FEV1, FVC, and PEF) and body composition, and between the MIP data and body composition were estimated by Pearson's Correlation Coefficient, considering a null correlation when $r = 0$ (zero), weak correlation when $0 < r \leq |0.3|$, moderate correlation when $|0.3| < r \leq |0.6|$, strong correlation when $|0.6| < r \leq |0.9|$, very strong correlation when $|0.9| < r < |1|$, and perfect correlation when $r = 1$ [24]. All statistical analyses were performed using BioEstat 5.3 software (Belém, Pará, Brazil) [25].

Results

During the data collection period, 27 patients were eligible for the study, two of whom were excluded (one patient did not agree to continue in the study and another reported that he had not been hospitalized, but had simply remained in the hospital for a short period only for observation) (figure 1).

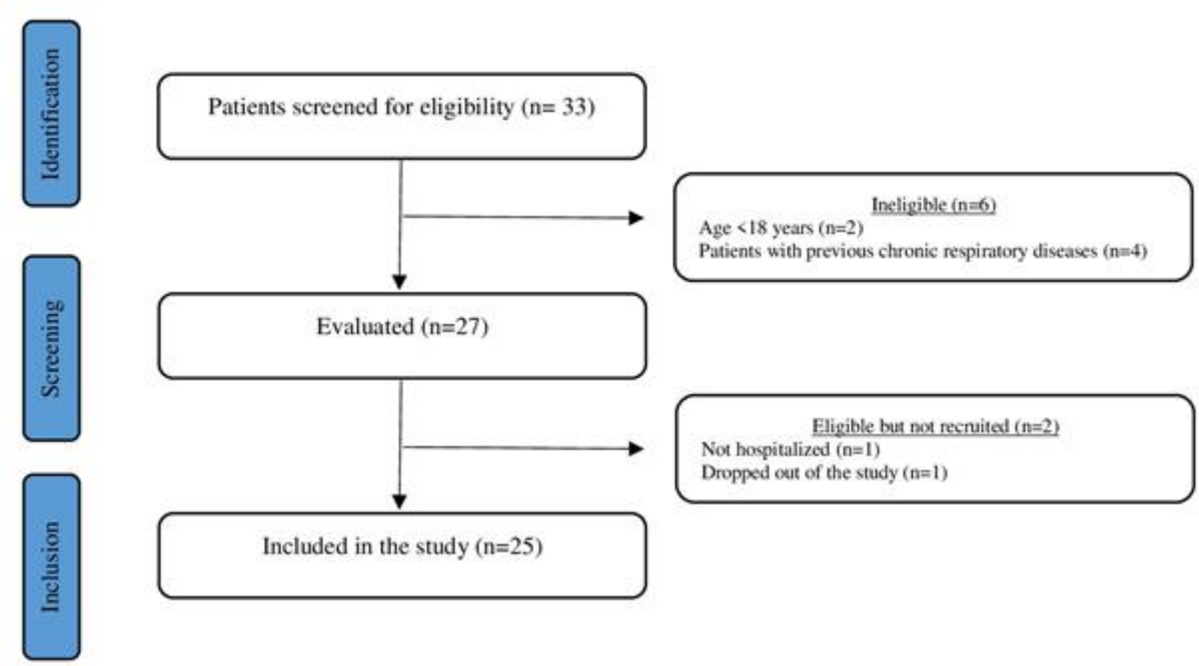

Figure 1 - *Flowchart of the study design*

Twenty-five patients previously infected with the COVID-19 virus and not treated with invasive mechanical ventilation were included in this study. The majority of patients were female, non-smoking, and did not require non-invasive ventilation (NIV) during hospitalization. All patients presented weight loss, ranging from 2 to 23 kg. The length of hospital stay was 15 ± 9.6 days and the most frequently reported symptoms were dyspnea, cough, ageusia, anosmia, and headache (table I). FVC, FEV1, and MIP variables that demonstrated a statistically significant degree of correlation with body composition variables were classified as "moderate correlation" (table II and table III).

Table I - *Patients' characteristics and clinical information*

Variables	n (%)	Mean ± SD
Demographic data		
Sex (female)	13 (52)	
Smoker	1 (4)	
Age (years)		49.1 ± 12.3
Clinical information		
Weight loss (kg)		12.2 ± 6.2
MIP (mmHg)		98.9 ± 32.2
FEV1 in % pred		73.46 ± 23.81
FVC in % pred		103 ± 43.5
PEF in % pred		37.4 ± 17.9
Use of NIV	12 (48)	
Dyspnea	22 (88)	
Dyspnea degree (Score from 0 to 10)		2.8 ± 1.0
Cough	18 (72)	
Ageusia	18 (72)	
Anosmia	18 (72)	
Headache	18 (72)	
Fever	17 (68)	
Sore throat	17 (68)	
Coryza	16 (64)	
Diarrhea	9 (36)	
Nausea	6 (24)	
Hyporexia	8 (32)	
Vomit	2 (8)	

N = absolute number; SD = standard deviation; kg = kilogram; NIV = non-invasive ventilation; MIP = maximal inspiratory pressure; mmHg = millimeters of mercury; FEV1 = forced expiratory volume in one second; FVC = forced vital capacity; PEF = peak of expiratory flow

Table II - *Correlation of weight loss versus pulmonary function and maximal inspiratory pressure*

Correlated variables	R2	r (Pearson)	p value*
Weight loss (kg) versus FVC	0.1464	-0.3826	**0.05**
Weight loss (kg) versus FEV1	0.1607	-0.4009	**0.04**
Weight loss (kg) versus PEF	0.0001	-0.0085	0.96
Weight loss (kg) versus MIP	0.0825	0.2872	0.16

R2 = Determination coefficient; R (Pearson) = measure of degree and direction by the linear correlation coefficient r; p value* = p value of F (regression); kg = kilogram. FVC=forced vital capacity; FEV1=forced expiratory volume in one second; PEF = peak expiratory flow; MIP = maximal inspiratory pressure

Evaluation of the relationship between lung function, MIP, and body composition

Among the variables investigated, five presented a statistically significant negative correlation with FVC: weight loss, skeletal muscle mass, lean mass, lean mass of the left leg, and fat-free mass. Weight loss also presented a statistically significant negative correlation with FEV1 (figure 2). These same variables had a positive correlation with MIP, except weight loss (figure 3). No BIA variable was correlated with PEF (table III).

Table III - *Correlation of BIA versus Lung Function and MIP*

Correlated variables	Mean ± SD	R2	r (Pearson)	p value*
BIA variables correlated with FVC				
Skeletal muscle mass (kg)	26.92±7.24	0.2464	-0.4964	**0.01**
Lean mass (kg)	46.69±11.6	0.2190	-0.4679	**0.01**
Segmental lean mass analysis (left leg) (%)	90.21±7.3	0.1620	-0.4025	**0.04**
Segmental lean mass analysis (right leg) (%)	89.54±7.92	0.1191	-0.3451	0.09
Fat-free mass (kg)	49.14±12.79	0.2026	-0.4501	**0.02**
BIA variables correlated with FEV1				
Skeletal muscle mass (kg)	-	0.0940	-0.3066	0.13
Lean mass (kg)	-	0.0339	-0.1842	0.37
Segmental lean mass analysis (left leg) (%)	-	0.0095	-0.0974	0.64
Segmental lean mass analysis (right leg) (%)	-	0.0086	-0.0928	0.65
Fat-free mass (kg)	-	0.0385	-0.1961	0.34
BIA variables correlated with PEF				
Skeletal muscle mass (kg)	-	0.0320	0.1489	0.39
Lean mass (kg)	-	0.0641	0.2531	0.22
Segmental lean mass analysis (left leg) (%)	-	0.0268	0.1636	0.43
Segmental lean mass analysis (right leg) (%)	-	0.0802	0.2831	0.17
Fat-free mass (kg)	-	0.0623	0.2497	0.22
Correlation of BIA versus MIP				
Skeletal muscle mass (kg)	-	0.1765	0.4201	**0.03**
Lean mass (kg)	-	0.2404	0.4903	**0.01**
Segmental lean mass analysis (left leg) (%)	-	0.1832	0.4280	**0.03**
Segmental lean mass analysis (right leg) (%)	-	0.1535	0.3918	**0.05**
Fat-free mass (kg)	-	0.2375	0.4873	**0.01**

BIA = bioelectrical impedance analysis; MIP = maximal inspiratory pressure; SD = standard deviation; R2 = Determination coefficient; R (Pearson) = measure of degree and direction by the linear correlation coefficient r; p value* = p value of F (regression); FVC = forced vital capacity; FEV1=forced expiratory volume in one second; PEF = peak expiratory flow; kg = kilogram; % = percentage

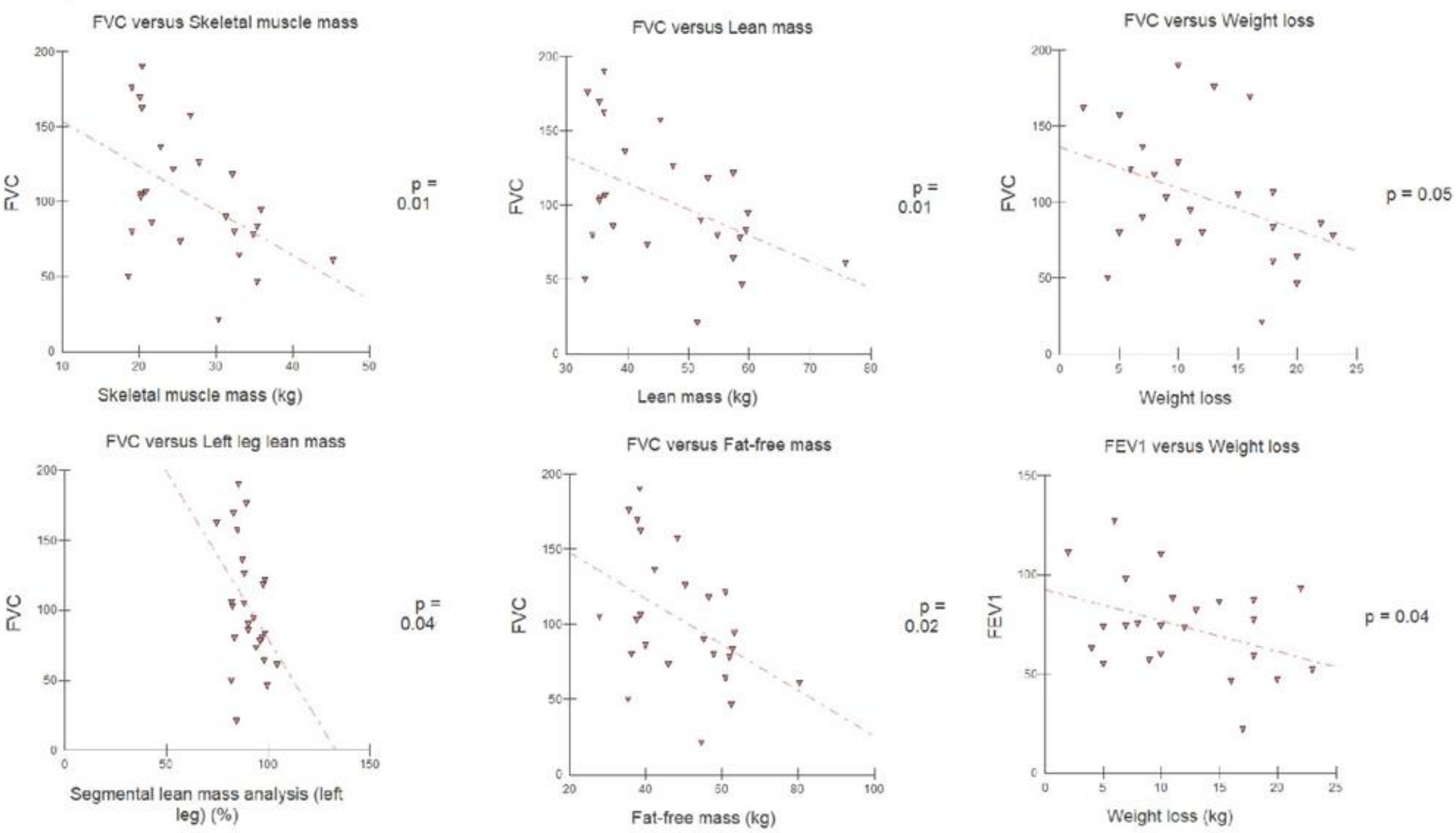

Figure 2 - *Pearson's linear correlation between body composition and FVC and FEV1*

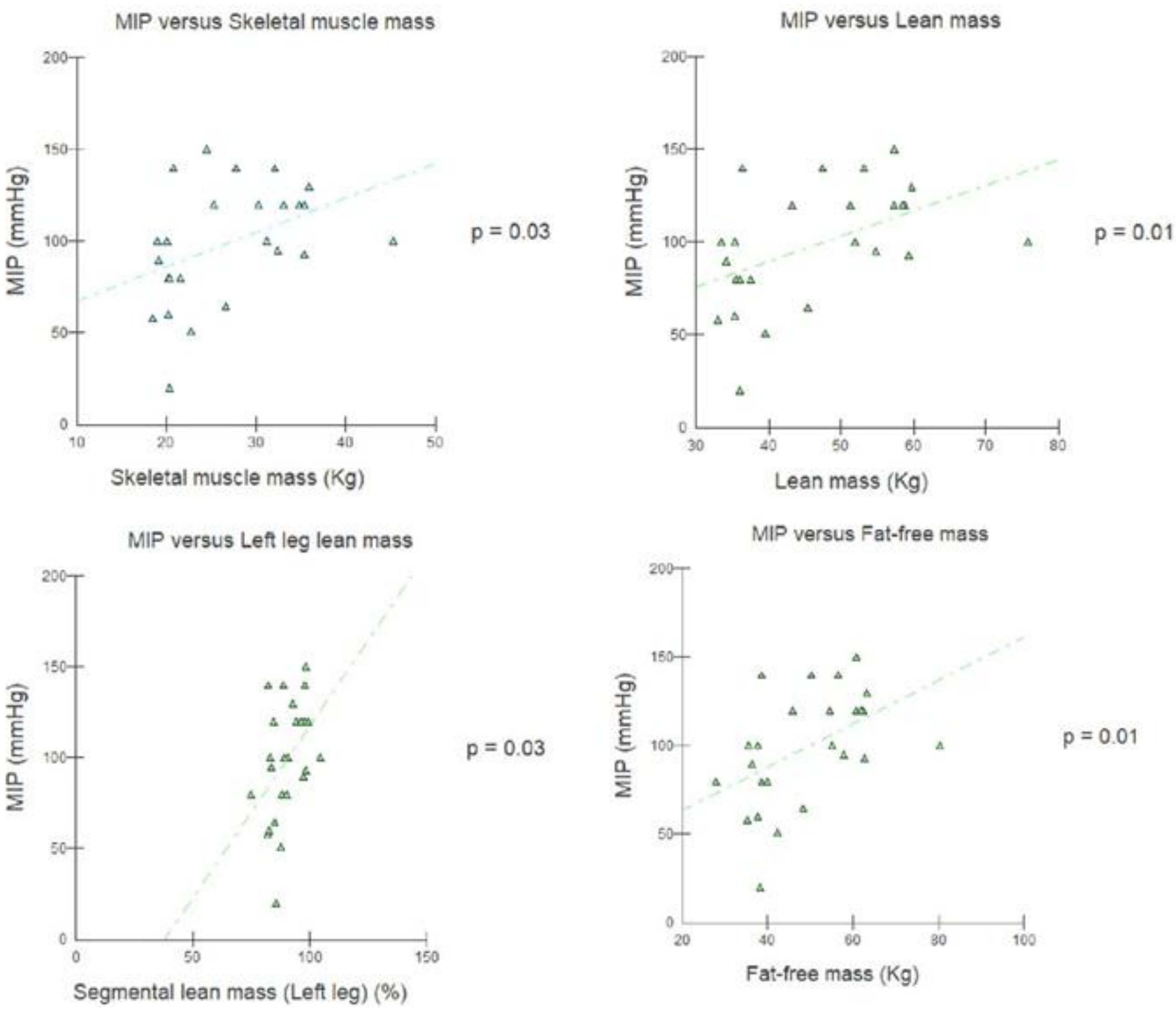

Figure 3 - *Pearson's linear correlation between body composition and MIP*

Mortality rate after hospital discharge

There was no record of death after hospital discharge among the investigated patients.

Discussion

The results of this cross-sectional study, including twenty-five patients after hospital discharge to treat COVID-19 infection, showed that FVC and MIP were associated with body composition (FVC was only not associated with lean mass of the right leg), FEV1 was associated only with weight loss, and PEF was not associated with any variables.

Patients hospitalized due to COVID-19 present impaired lung function, with a reduction in FVC, FEV1, and inspiratory muscle strength [26]. Of the total, 49.1% of patients had an MIP lower than 80% of the predicted, which remained compromised in the period of convalescence from the disease [27]. It is likely that body composition has some influence on these effects, but further investigation is required. In addition, after hospital discharge, approximately 80% of patients presented maintained impairment for a long time, requiring long periods of clinical follow-up and respiratory rehabilitation [11,26].

A study with 34 post-COVID-19 patients observed that patients who lost muscle mass showed a statistically significant correlation between skeletal muscle mass and FVC and FEV1 (0.582 and 0.592, respectively) [28]. Park *et al.* [29] demonstrated that low skeletal muscle mass is associated with a potential risk for pulmonary dysfunction, regardless of age and sex.

This can be explained by the fact that low skeletal muscle mass affects physical performance and functionality, negatively impacting patients' physiology and metabolism [30,31], especially in patients who remain in hospital for more than 20 days, losing lung volume and capacity, which can lead to obstructive and restrictive ventilation disorders [32].

An experimental study investigated significant alterations in body composition in twelve oxygen-dependent patients hospitalized for 13.5 days (ranging from 8.3 to 27.8 days) with symptoms present 4.5 days before admission due to COVID-19 infection. It was observed that active metabolic muscle tissue and intracellular hydration status were altered during the initial active phase of the infection, slowly recovering until hospital discharge.

In addition, the literature points out that body composition is associated with the evolution of COVID-19 [10], leading to more severe symptoms and greater respiratory impairment. Our findings also indicate that the rate of segmental fat in the trunk was not associated with any respiratory functional variable investigated. On the other hand, the lack of an association between the severity of the disease and body composition has been reported, raising the possibility that other factors may interfere in the course of the disease, with greater or lesser severity [33].

Experimental studies with adequate sample sizes are needed to confirm whether body composition influences respiratory outcomes, so that guidance can be given for the inclusion of nutritional support in the treatment of patients with COVID-19 [3]. Thus, early identification of these changes in body composition could help to direct more appropriate actions and minimize the impact of COVID-19 in the patient's life [34].

Study limitations: (i) Lack of nutritional biochemical assessment of patients included in the study, for example, levels of potassium (K), sodium (Na), calcium (Ca), and magnesium (Mg). Currently, in our hospitals, there is no routine assessment of the nutritional biochemistry of patients with COVID 19. This study may point to the need to perform this type of assessment on a daily basis to help answer important clinical questions; (ii) We consider that the sample size of our study was small and a future study should be performed with a larger sample size.

Conclusion

The findings of this study enable us to conclude that there is a negative association between FVC and the analyzed body composition variables, except lean mass of left leg, and between FEV1 and weight loss, a positive association between MIP and the analyzed body composition variables, except weight loss. None of the variables were associated with PEF. These findings are very important so that future experimental studies can investigate the effects of body composition on the recovery of patients with COVID-19. We also suggest studies with a larger sample size to confirm these findings and to more accurately investigate the mortality of patients recovering from sequelae of COVID-19 in the outpatient period.

Conflict of interests
The authors declare no conflict of interest.

Financing source
None

Author's contributions
Conception and design of the study: Luccas JGR, Aguiar CVS, Santos EC;
: Matias LMD, Silva HVC, Aguiar CVS, Pacheco JPR, Rodrigues ET; *Data analysis and interpretation*: Luccas JGR, Matias LMD, Macedo JRFF, Lunardi AC, Santos EC; Statistical analysis: Luccas JGR, Lunardi AC, Santos EC; *Manuscript writing*: Luccas JGR, Lunardi AC, Santos EC; *Critical review of the manuscript for important intellectual content*: Lunardi AC; Santos EC

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