Muscle strength in patients hospitalized for COVID-19

Força muscular em pacientes hospitalizados por COVID-19

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Abstract

Introduction: Complications arising from hospitalization due to COVID-19 have great impact on the physical health of individuals. One of the consequences that deserves attention is muscle weakness, which can be influenced by several factors, generating consequences that may need rehabilitation. **Objective:** To relate the degree of peripheral and respiratory muscle strength to sociodemographic, clinical, and hospitalization variables close to discharge after hospitalization due to COVID-19. **Methods:** This cross-sectional study analyzed data for 52 patients hospitalized for COVID-19 who were interviewed close to discharge to determine sociodemographic and clinical profiles and underwent muscle strength testing. Peripheral muscle strength was evaluated using the Medical Research Council scale, and respiratory strength was determined according to maximum inspiratory and expiratory pressure measured with a vacuometer. Hospitalization data were collected from patient medical records. **Results:** Peripheral strength was reduced in 53.9% of the sample, and the related variables ($p < 0.05$) were age, weight, cancer, high blood pressure, physical therapy, and number of physiotherapy sessions. Inspiratory force was reduced by 50% of individuals and expiratory force in 60% individuals, and these reductions were related ($p < 0.05$) to sex, high blood pressure, age, and weight. **Conclusion:** Close to COVID-19 hospital discharge, over 50% of patients exhibited peripheral and respiratory muscle weakness, associated with advanced age, hypertension, and low weight. Those with peripheral weakness received more physiotherapy and had more oncological diseases, while respiratory weakness was more common in men. This underscores the importance of preventive measures and post-hospitalization rehabilitation programs, including physiotherapy, for muscle strength recovery.

Keywords: COVID-19. Hospitalization. Maximum respiratory pressures. Muscle strength. Physical therapy modalities.

Resumo

Introdução: *As complicações decorrentes da hospitalização por COVID-19 têm grande impacto na saúde física dos indivíduos. Uma das consequências que merece atenção é a fraqueza muscular, que pode ser influenciada por diversos fatores, gerando consequências que podem necessitar de reabilitação.* ***Objetivo:*** *Relacionar o grau de força muscular periférica e respiratória com variáveis sociodemográficas, clínicas e de internação próximo à alta após internação por COVID-19.* ***Métodos:*** *Este estudo transversal analisou dados de 52 pacientes hospitalizados por COVID-19 que foram entrevistados próximo à alta para determinar perfis sociodemográficos e clínicos e que foram submetidos a testes de força muscular. A força muscular periférica foi avaliada pela escala do* Medical Research Council*, e a força respiratória foi determinada de acordo com a pressão inspiratória e expiratória máxima medida com vacuômetro. Os dados de internação foram coletados dos prontuários dos pacientes.* ***Resultados:*** *A força periférica esteve reduzida em 53,9% da amostra e as variáveis relacionadas (p < 0,05) foram idade, peso, câncer, hipertensão, fisioterapia e número de sessões de fisioterapia. A força inspiratória foi reduzida em 50% dos indivíduos e a força expiratória em 60% dos indivíduos, e essas reduções foram relacionadas (p < 0,05) ao sexo, pressão arterial elevada, idade e peso.* ***Conclusão:*** *Próximo à alta hospitalar da COVID-19, mais de 50% dos pacientes apresentavam fraqueza muscular periférica e respiratória associada à idade avançada, hipertensão e baixo peso. Aqueles com fraqueza periférica receberam mais fisioterapia e tiveram mais doenças oncológicas, enquanto a fraqueza respiratória foi mais comum em homens. Isto ressalta a importância de medidas preventivas e programas de reabilitação pós-hospitalização, incluindo fisioterapia, para a recuperação da força muscular.*

Palavras-chave: *COVID-19. Hospitalização. Pressões respiratórias máximas. Força muscular. Modalidades de fisioterapia.*

Introduction

Infection by COVID-19 causes various symptoms and morbidities that vary according to individual genetics, ethnicity, age, and geographic location, and mainly affect the respiratory system, although other organ systems are also involved.[1] After two years of the COVID-19 pandemic it is clear that the lungs are most significantly impacted by this coronavirus, and researchers perceived the need to identify damage secondary to the disease. Together with lung impairment, bed rest and immobility are typical of prolonged hospital stays and affect physical condition.[2] Many studies have found that the most common abnormality after hospitalization due to COVID-19 is impaired diffusion capacity, and new research shows that this provokes severe functional consequences in all systems that require post-hospital rehabilitation.[3]

One notable sequela of COVID-19 is the loss of respiratory muscle strength. Reduced inspiratory pressure suggests diaphragm weakness, and when associated with decreased expiratory pressure indicates musculoskeletal weakness, both highly disabling.[4] Although the pathophysiology of COVID-19 explains its relationship with reduced respiratory muscle strength, the literature is still scarce and controversial. Truffaut et al.[5] concluded that half the individuals they followed still had respiratory strength impairment one month after hospital discharge; other authors suggest that recovery from COVID-19 is faster than from other causes of acute respiratory failure.[6] Even so, factors related to hospitalization are known to contribute to the heterogeneous data on this topic. For example, invasive mechanical ventilation itself is a risk factor for diaphragm weakness.[7]

Another factor to be considered at hospital discharge is peripheral muscle strength, which is also associated with impacts on the patient's functionality.[8] The literature still lacks studies on the aftereffects of COVID-19 infection in overall muscle function, but there is believed to be a negative relationship. Long hospitalizations and periods of bed rest, prescribed as a way to minimize metabolic demand and redirect resources toward recovery, accelerate musculoskeletal declines and lead to post-clinical outcomes that require rehabilitation.[8]

This study investigates the relationship between the degree of peripheral and respiratory muscle strength and sociodemographic, clinical, and hospitalization profile among patients close to hospital discharge due to COVID-19.

Methods

This cross-sectional observational study investigated a sample of 52 patients diagnosed with COVID-19 who were admitted to the Santa Casa de Misericórdia Hospital in Vitória, Espírito Santo, Brazil, between November 2020 and July 2021. The study was approved by the institutional review board (CAAE No. 33249120.2.0000.5065).

Patients over 18 years of age who were hospitalized primarily due to COVID-19 (diagnosis confirmed by RT-PCR assay) were included. Patients with difficulties for understanding or responding adequately to questionnaires and performing the proposed tests for any reason or with intercurrences such as subsequent death or hospitalization prolonged for more than 72 hours after the researcher's evaluation were excluded.

The interviews and evaluations were performed at the bedside close up to 72 hours before hospital discharge; the estimated day for discharge was reported in the patients' electronic medical records. The evaluations involved application of a semi-structured questionnaire, scales, and tests to assess social, demographic, and clinical profile and peripheral and respiratory muscle strength. Hospitalization data were collected from the patient's digital medical record after discharge.

The sociodemographic profile was composed of age, sex, marital status, education, and race. The clinical profile consisted of self-reported weight, COVID-19 symptoms, associated diseases, and the presence of dyspnea during daily activities as determined by the modified Medical Research Council Dyspnea Scale (mMRC). Individuals with dyspnea grades 2, 3, and 4 were classified as having dyspnea.[9]

Hospitalization data included days of hospitalization, admission to the intensive care unit (ICU), use and days of oxygen therapy, use of noninvasive and invasive mechanical ventilation (NIV and IMV, respectively), and number of physiotherapy sessions. These data were collected after confirmation of hospital discharge.

Peripheral muscle strength was measured by the Medical Research Council (MRC) instrument validated for the hospital environment by Jonghe et al.[10] This scale ranges from 0 (no contraction) to 5 (normal muscular strength against resistance) for each of the six bilateral muscle groups evaluated (shoulder abductors, elbow flexors, wrist extensors, hip flexors, knee extensors, and dorsiflexors). In accordance with Hermans et al.,[11] muscle weakness was considered when the score was < 48.

Inspiratory and expiratory muscle strength was measured via maximum inspiratory pressure (MIP) and maximal expiratory pressure (MEP), using a calibrated analog manometer (Commercial Médica brand), whose scale has intervals of 10 cmH_2O and a range of -150 to +150 cmH_2O. The measurements were taken with the patient sitting, and each phase of the respiratory cycle was measured three times. The maximum value obtained was used for comparison against the pre-existing standard reference values for the Brazilian population for age and sex described by Costa et al.[12]

The descriptive analysis of the qualitative variables was reported using absolute and relative frequencies, while the quantitative variables were expressed as means and standard deviation or as median and interquartile/minimum and maximum intervals, depending on the normality of the data as determined by the Kolmogorov-Smirnov test. Spearman's correlation test was used to evaluate the correlation between quantitative variables; $r < 0.4$ was considered weak correlation, $r = 0.4 - 0.7$ was considered moderate, and $r > 0.7$ was considered strong.[13] The chi-square test or Fisher's exact test were used to analyze the associations between qualitative variables, and for the qualitative and quantitative variables, the Mann-Whitney test was conducted; 5% ($p \leq 0.05$) significance was adopted for all analyses.

Results

Eight of the 60 patients evaluated were excluded, leaving a total of 52 individuals for the peripheral muscle strength outcome and 50 for respiratory muscle strength (two patients were unable to perform vacuometry). Most of the sample consisted of women with a median age of 59 years and a partner, over nine years of education and self-declared as non-white. In terms of clinical profile, median weight was 79 kg; the most frequent symptoms of COVID-19 were fever, dry cough, and fatigue. Half of the sample had previous high blood pressure and reported dyspnea at discharge (Table 1).

Median hospitalization for the sample was 7.5 days, 19.2% required ICU care, most (67.3%) needed oxygen therapy for a median of 2.5 days, 15.4% required NIV, only one individual required IMV, and 78.8% received physical therapy, for a median of seven sessions (Table 2). Peripheral muscle strength was reduced in 53.9% of the sample. Age, weight, high blood pressure, cancer, and physical therapy were associated with this variable ($p \leq 0.05$) (Figure 1). Assessment of respiratory muscle strength determined that MIP and MEP values were lower than expected in 50% and 60% of the sample, respectively. Inspiratory weakness was significantly associated ($p \leq 0.05$) with sex and high blood pressure, and expiratory weakness was associated with body mass index (BMI) classification (Figure 2).

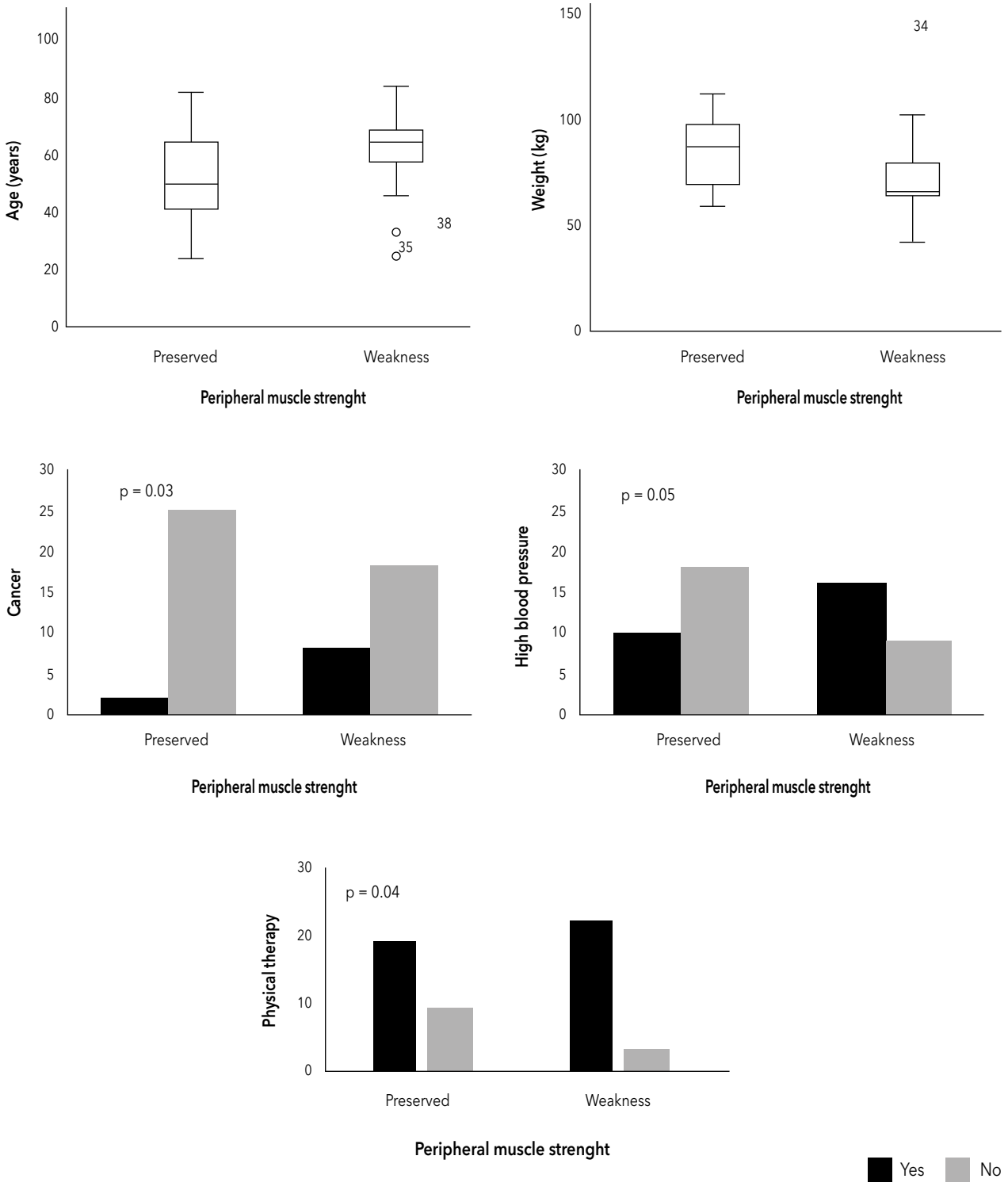

Figure 1 - Sociodemographic and clinical profile of patients (n = 52) hospitalized with COVID-19 between November 2020 and June 2021 at the Santa Casa de Misericórdia Hospital in Vitória, Espírito Santo, Brazil.

Table 1 - Sociodemographic and clinical profile of patients (n = 52) hospitalized with COVID-19 between November 2020 and June 2021 at the Santa Casa de Misericórdia Hospital in Vitória, Espírito Santo, Brazil

Variable	n (%)
Age*	59 (43 – 66)
Sex	
Female	28 (53.9)
Male	24 (46.1)
Marital status	
Partnered	29 (55.8)
Unpartnered	23 (44.2)
Education level	
Up to 9 years	51 (50.1)
> 9 years	35 (67.3)
Race	
White	20 (38.5)
Nonwhite	32 (61.5)
Weight (kg)*	79 (64.5 – 92.5)
Symptoms of COVID-19	
Fever	41 (78.8)
Dry cough	38 (73.0)
Body aches	34 (65.4)
Strong cold	23 (44.2)
Shortness of breath	31 (59.6)
Fatigue	36 (69.2)
Associated illnesses	
High blood pressure	26 (50.0)
Diabetes	13 (25.0)
Cardiopathy	8 (15.4)
Metabolic disease	7 (13.5)
Respiratory disease	8 (15.4)
Cancer	10 (19.2)

Note: *Median (interquartile interval: 25 - 75%).

Table 2 - Hospitalization data and muscle force values for patients (n = 52) hospitalized with COVID-19 between November 2020 and June 2021 at the Santa Casa de Misericórdia Hospital in Vitória, Espírito Santo, Brazil

Variable	n (%)
Days hospitalized*	7.5 (4 – 11)
Required intensive care	10 (19.2)
Required oxygen	35 (67.3)
Days oxygen used*	2.5 (0 – 5)
Non-invasive ventilation	8 (15.4)
Mechanical ventilation	1 (2.0)
Sedation	1 (2.0)
Physical therapy	41 (78.9)
Physical therapy sessions*	7 (1 – 12)
Dyspnea present	26 (50.0)
Peripheral muscle strength	
Medical Research Council Scale total score*	48 (42 – 54)
Muscle weakness	28 (53.9)
Inspiratory muscle strength (n = 50)	
Total maximum inspiratory pressure score*	60 (42.5 – 100)
Inspiratory muscle weakness	25 (50.0)
Expiratory muscle strength (n = 50)	
Total maximum expiratory pressure score*	55 (40.0 – 100)
Expiratory muscle weakness	30 (60.0)

Note: *Median (interquartile interval: 25 - 75%).

An inversely proportional correlation was also observed between age and peripheral muscle strength (r = -0.48), physiotherapy sessions and peripheral muscle strength (r = -0.41), and age and inspiratory muscle strength (r = -0.45). Weight was shown to be directly and moderately correlated with inspiratory and expiratory muscle strength: the higher the weight, the greater the respiratory muscle strength. All statistically significant correlations are shown in Figure 3.

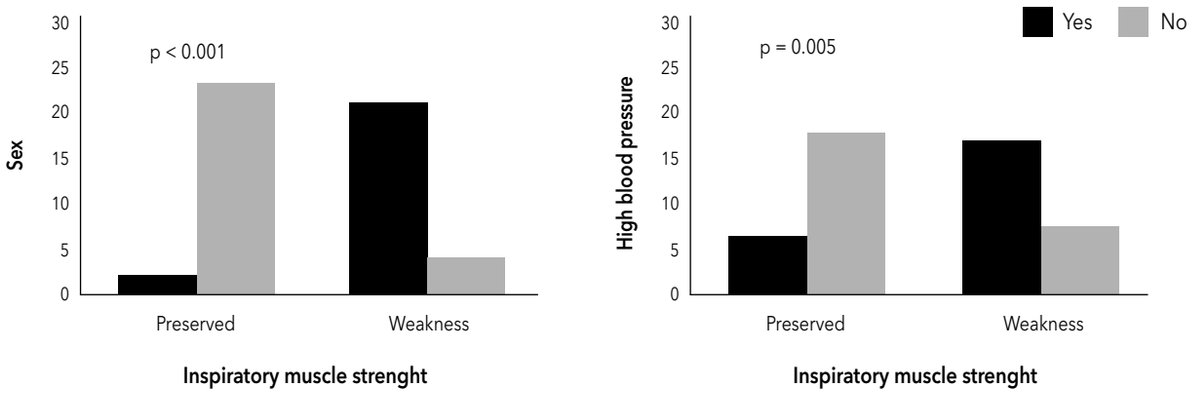

Figure 2 - Association of sociodemographic, clinical, and hospitalization variables according to the presence of respiratory muscle weakness (p < 0.05).

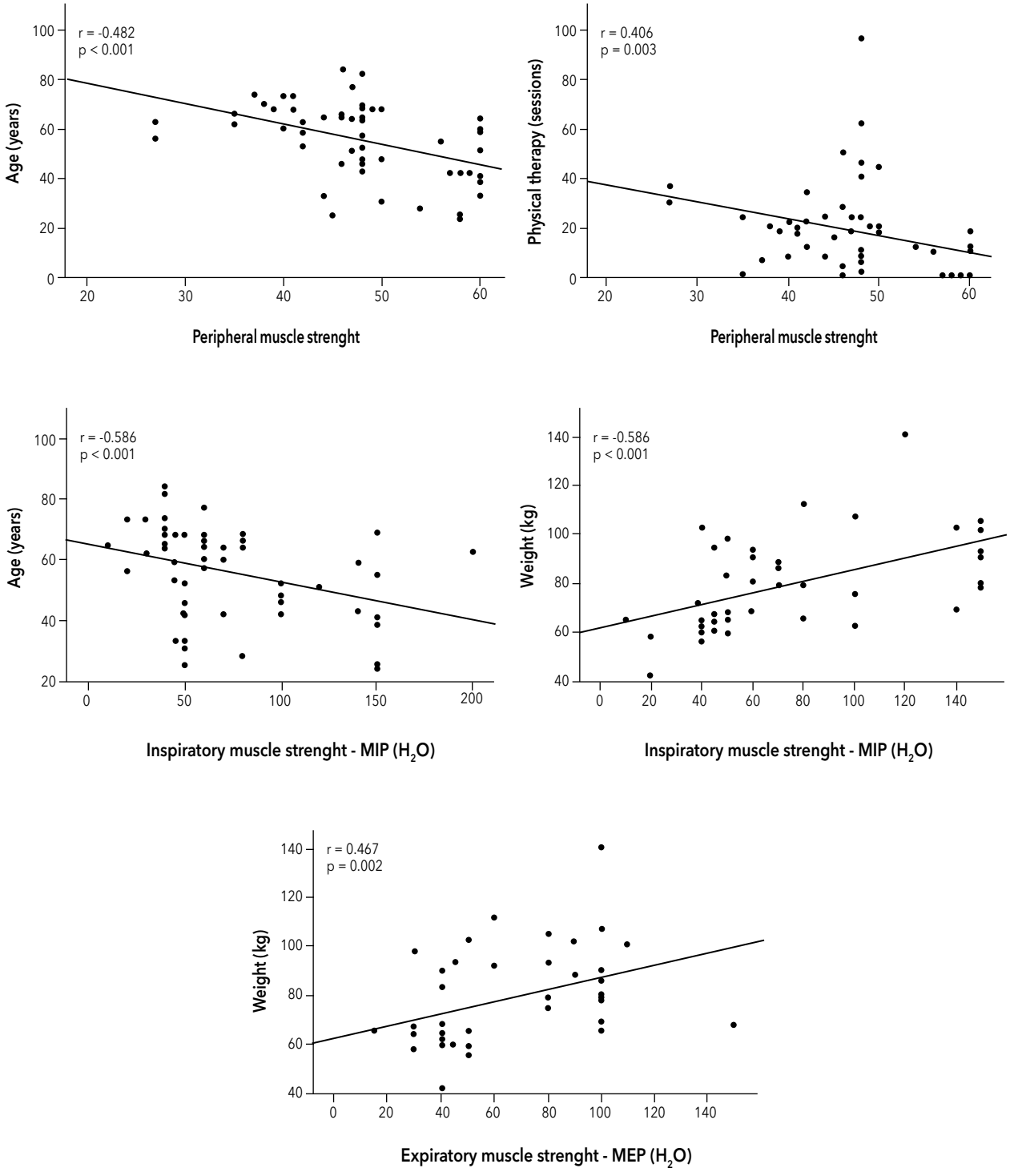

Figure 3 - Correlations between muscle strength and sociodemographic, clinical, and hospitalization variables ($p < 0.05$).

Note: MIP = maximum inspiratory pressure (mmHg); MEP = maximum expiratory pressure (mmHg).

Discussion

Close to discharge, more than half of the sample exhibited peripheral and expiratory muscle weakness and half presented inspiratory muscle weakness, corroborating evidence indicating an association between muscle weakness COVID-19 infection.[4,14,15] Due to low levels of physical activity or associated diseases, muscle strength may diminish prior to infection, and when patients are infected their clinical condition may worsen and lead to hospitalization.[14-16] Immune function is known to improve with regular physical activity, reducing the risk of systemic inflammation, which is the main aggravating factor of COVID-19.[17] Because musculoskeletal weakness is a direct consequence of physical inactivity, these patients will present a low immune response to metabolic stress during infection.[16] Other risk factors described in the literature such as sex, advanced age, and underlying health conditions may also affect muscle strength.[18] In this study, higher levels of inspiratory muscle strength were observed in women than men. Divergent results have indicated that women had lower MIP levels due to reduced muscle mass and fibers.[4] However, hormonal factors and lifestyle habits make women more resistant to infections, helping to preserve muscle during infection by Sars-Cov-2.[19]

Median age was higher in the group with peripheral muscle weakness and inspiratory muscle weakness than in the group without weakness.[14,15] Deterioration of muscle fibers and changes in pulmonary compliance due to aging lead to reduced muscle mass and respiratory deficiency, and levels of physical activity also drop with age.[20,21] For this reason, monitoring muscle strength in the elderly is important for promoting health and managing potential COVID-19-related health risks.[15]

High blood pressure is another risk factor for the severity of COVID-19 due to metabolic and inflammatory changes that cause oxidative damage to the already burdened heart muscle.[22] The observed association between muscle weakness and hypertension is because individuals with lower muscle strength are more likely to develop high blood pressure. This relationship suggests that musculoskeletal weakness is not only an isolated risk factor for severe illnesses but can also influence the manifestation of other risk factors. Additionally, it's worth noting that greater muscle conditioning can release hormones such as oxytocin and peptides, which have the potential to reduce arterial stiffness.[23,24] Therefore, muscle strengthening programs can be considered beneficial for hypertensive patients, assisting in reducing COVID-19-related complications.[23]

Like high blood pressure, cancer is also an isolated risk factor for the disease, with up to 60% greater risk for hospitalization. Immunosuppression resulting from cancer treatment is believed to be largely responsible for this relationship, due to greater degradation and reduced protein synthesis in the muscles.[25-27] Furthermore, characteristics of hospitalization such as immobility and bed rest (which are frequent in cases of cancer and COVID-19) also affect the musculoskeletal system.[2] For this reason, preventing contagion and functional sequelae should be reinforced in this population since they face greater risk of muscle weakness.[2,18]

This study also found that individuals with reduced respiratory strength were lighter than healthy individuals. In hospital settings, patients are often immobile and tend to lose muscle mass and fibers, which can decrease weight and, in turn, muscle strength.[28] Other hypotheses for this finding are the higher median age of the group with muscle weakness, since muscle mass diminishes with increasing age,[28] and the predominance of type II muscle fibers in heavier individuals, since these fibers generate greater muscle strength potential and maintain respiratory pressures within normal ranges.[29] Still, weight is known to not be an independent factor for predicting strength; the pattern of body mass distribution should also be considered, and bioimpedance studies are essential to clarify this association.

In addition to being a risk factor, reduced muscle strength is a consequence of hospitalization due to COVID-19 and of the disease itself.[8,30] The need for respiratory isolation, for example, restricts patients to their beds for long periods.[2] Another point for further investigation is the symptomatology of the disease. Fatigue, body pain, and dyspnea were reported by over half the sample; these symptoms are highly incapacitating, and patients require rest to reduce metabolic demands, leading to immobility.[31]

Another characteristic of hospitalization that contributes to reduced strength is weakness after intensive care; this phenomenon has been addressed in the literature and is directly related to mechanical ventilation.[32] Despite the low prevalence of intensive care and IMV and the absence of significant associations in the study, it is important to understand the role of these and other factors that induce immobility and, in turn, muscle

weakness. Furthermore, oxygen therapy and fears that respiratory profile might deteriorate when physical activity is performed may limit patient movement. Considering that the median hospital stay was over 7 days, it is important to understand the importance of preventing muscle weakness in this population.[7]

Previous studies found significant muscle weakness in a cohort of hospitalized patients compared to individuals that were not hospitalized, and this weakness was seen to persist up to three months after discharge.[8,30] As with other respiratory conditions, more strength is lost in the legs, severely limiting activities such as walking, climbing stairs, and standing for long periods, which can be highly disabling.[8,33]

These findings show that early mobilization and physical exercise are necessary to prevent and recuperate muscle involvement even during the acute phase of COVID-19 infection.[34,35] Physical therapy has gained prominence during the pandemic due to its important role in preventing and rehabilitating functional sequelae of COVID-19 infection within the hospital setting.[34,35]

Even so, this study showed that muscle weakness was significantly associated with patients who received physical therapy and was also inversely related to the number of sessions. As in other studies,[7,36] this finding can be explained by the lack of time and availability of physical therapists within Brazilian hospitals; professionals must prioritize the most severe cases and those with respiratory complications to fairly treat this group of patients.[36] Although this conduct is scientifically based, the patients who are treated already have established sequelae, which reduces their response to treatment and individual functionality, further reinforcing the modern role of the physical therapist as a "rehabilitator." Considering that muscle strength and functionality should be evaluated and treated early in order to halt or impede the progress of muscle weakness and functional disability, preventive physical therapy is important for all individuals infected by COVID-19, especially those who are hospitalized.[36]

This study is limited by its cross-sectional design, which may lead to reverse causality bias between muscle strength and the independent variables, and memory and registration bias due to self-reported variables taken from patient medical records. The sample was also small, due to the difficulty of assessing patients at the time of discharge, and the results reflect a local reality that may compromise external validity.

New prospective multicenter studies with larger samples are suggested to evaluate and monitor muscle strength over the medium and long term. Studies that compare strength between individuals hospitalized due to COVID-19 infection and non-hospitalized individuals are also necessary to better understand cause and effect.

Conclusion

Age, sex, weight, high blood pressure, cancer, physical therapy, and number of physical therapy sessions during hospitalization were related to peripheral and respiratory muscle strength at hospital discharge for COVID-19. These findings reinforce the need for care during hospitalization for this disease via therapeutic interventions directed at this population, especially older people, those with lower weights, and patients with other comorbidities such as high blood pressure and cancer.

Early referral for and management of physical therapy is also important, along with multiprofessional referrals to prevent musculoskeletal and respiratory impacts and to prevent them from persisting after hospital discharge, optimizing functional independence and facilitating patient reintegration into society.

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Authors' contributions

LBL and GTBS contributed equally to the conceptualization, methodology, analysis, data interpretation, and writing the original draft. RRBB protocolled the project, coordinated the study. All authors contributed to the discussion of the results and approved the final version.

References

1. Brasil. Guia de Vigilância Epidemiológica do COVID-19. Brasília: Ministério da Saúde; 2021 [cited 2023 Apr 2]. Available from: https://covid.saude.gov.br

2. Candan S, Elibol N, Abdullahi A. Consideration of prevention and management of long-term consequences of post-acute respiratory. Physiother Theory Pract. 2020;36(6):663-8. DOI

3. Plaza M, Sevilla GGP. Respiratory muscle sequelae in young university students infected by coronavirus disease 2019: an observational study. Rev Assoc Med Bras (1992). 2022;68(2): 245-9. DOI

4. Huang Y, Tan C, Wu J, Chen M, Wang Z, Luo L, et al. Impact of coronavirus disease 2019 on pulmonary function in early convalescence phase. Respir Res. 2020;21(1):163. DOI

5. Truffaut L, Demey L, Bruyneel AV, Roman A, Alard S, De Vos N, et al. Post-discharge critical COVID-19 lung function related to severity of radiologic lung involvement at admission. Respir Res. 2021;22(1):29. DOI

6. Medrinal C, Prieur G, Frenoy E, Quesada AR, Poncet A, Bonnevie T, et al. Respiratory weakness after mechanical ventilation is associated with one-year mortality - A prospective study. Crit Care. 2016 Jul 31;20(1):231. DOI

7. Paneroni M, Simonelli C, Saleri M, Bertacchini L, Venturelli M, Troosters T, et al. Muscle strength and physical performance in patients without previous disabilities recovering from COVID-19 pneumonia. Am J Phys Med Rehabil. 2021;100(2):105-9. DOI

8. Garrigues E, Janvier P, Kherabi Y, Le Bot A, Hamon A, Gouze H, et al. Post-discharge persistent symptoms and health-related quality of life after hospitalization for COVID-19. J Infect. 2020; 81(6):e4-6. DOI

9. Olímpio SC, Marques MG, Moura VMS, Araújo CS, Alcântara E, Vento DA. Modified medical research council (mMRC) e a sua relação com variáveis respiratórias e o tempo de internação em pacientes hospitalizados com doença pulmonar obstrutiva crônica. Rev Bras Cienc Saude. 2019;23(4):485-92. Full text link

10. Jonghe B, Sharshar T, Lefaucheur JP, Authier FJ, Durand-Zaleski I, Boussarsar M, et al. Paresis acquired in the intensive care unit: a prospective multicenter study. JAMA. 2002;288(22): 2859-67. DOI

11. Hermans G, Clerckx B, Vanhullebusch T, Segers J, Vanpee G, Robbeets C, et al. Interobserver agreement of Medical Research Council sum-score and handgrip strength in the intensive care unit. Muscle Nerve. 2012;45(1):18-25. DOI

12. Costa D, Gonçalves HA, Lima LP, Ike D, Cancelliero KM, Montebelo MIL. Novos valores de referência para pressões respiratórias máximas na população brasileira: correções. J Bras Pneumol. 2010;36(3):306-12. DOI

13. Figueiredo Filho DB, Rocha EC, Silva Jr JA, Paranhos R, Neves JAB, Silva MB. Desvendando os mistérios do coeficiente de correlação de Pearson: o retorno. Leviathan. 2014;(8):66-95. DOI

14. Cheval B, Sieber S, Maltagliati S, Millet GP, Formánek T, Chalabaev A, et al. Muscle strength is associated with COVID-19 hospitalization in adults 50 years of age or older. J Cachexia Sarcopenia Muscle. 2021;12(5):1136-43. DOI

15. Af Geijerstam A, Mehlig K, Börjesson M, Robertson J, Nyberg J, Adiels M, et al. Fitness, strength and severity of COVID-19: a prospective register study of 1 559 187 Swedish conscripts. BMJ Open. 2021;11(7):e051316. DOI

16. Sallis R, Young DR, Tartof SY, Sallis JF, Sall J, Li Q, et al. Physical inactivity is associated with a higher risk for severe COVID-19 outcomes: a study in 48 440 adult patients. Br J Sports Med. 2021;55(19):1099-105. DOI

17. Okazaki T, Ebihara S, Mori T, Izumi S, Ebihara T. Association between sarcopenia and pneumonia in older people. Geriatr Gerontol Int. 2020;20(1):7-13. DOI

18. Jordan RE, Adab P, Cheng KK. COVID-19: risk factors for severe disease and death. BMJ. 2020;368:m1198. DOI

19. Organização Pan-Americana da Saúde. Desfechos de saúde e COVID-19 nas Américas: diferenças de sexo. Washington: PAHO; 2021. Full text link

20. Lima TR, Silva DAS, Kovaleski DF, Gonzalez-Chica DA. Associação da força muscular com fatores sociodemográficos e estilo de vida em adultos e idosos jovens no Sul do Brasil. Cienc Saude Colet. 2018;23(11):3811-20. DOI

21. Pascotini FS, Fedosse E, Ramos MC, Ribeiro VV, Trevisan ME. Força muscular respiratória, função pulmonar e expansibilidade toracoabdominal em idosos e sua relação com o estado nutricional. Fisioter Pesqui. 2016;23(4):416-22. DOI

22. Ribeiro AC, Uehara SCSA. Hipertensão arterial sistêmica como fator de risco para a forma grave da COVID-19: revisão de escopo. Rev Saude Publica. 2022;56:20. DOI

23. Mayer KP, Welle MM, Evans CG, Greenhill BG, Montgomery-Yates AA, Dupont-Versteegden EE, et al. Muscle power is related to physical function in patients surviving acute respiratory failure: A prospective observational study. The Am J Med Sci. 2021;361(3):310-8. DOI

24. Celis-Morales CA, Welsh P, Lyall DM, Steell L, Petermann F, Anderson J, et al. Associations of grip strength with cardiovascular, respiratory, and cancer outcomes and all cause mortality: prospective cohort study of half a million UK Biobank participants. BMJ. 2018;361:k1651. DOI

25. Grivas P, Khaki AR, Wise-Draper TM, French B, Hennessy C, Hsu CY, et al. Association of clinical factors and recent anticancer therapy with COVID-19 severity among patients with cancer: a report from the COVID-19 and cancer consortium. Ann Oncol. 2021;32(6):787-800. DOI

26. Lee KA, Ma W, Sikavi DR, Drew DA, Nguyen LH, Bowyer RCE, et al. Cancer and risk of COVID-19 through a general community survey. Oncologist. 2021;26(1):e182-5. DOI

27. Mariano KOP, Alves RS, Mantuani APA, Carvalho SR, Rocha CBJ, Iunes DH, et al. Análise da fadiga relatada e das forças musculares respiratória e periférica em indivíduos com câncer em tratamento. Rev Bras Cancerol. 2020;66(4):e-091051. DOI

28. Almeida LX, Noronha IM, Andrade NVSS, Siqueira F, Onofre T. Correlação da força muscular respiratória com medidas antropométricas e nível de atividade física em adultos da atenção primária. Fisioter Pesqui. 2020;27(4):413-22. DOI

29. Martinez BP, Ramos IR, Oliveira QC, Santos RA, Marques MD, Forgiarini Jr LA, et al. Existe associação entre massa e força muscular esquelética em idosos hospitalizados? Rev Bras Geriatr Gerontol. 2016;19(2):257-64. DOI

30. Tanriverdi A, Savci S, Kahraman BO, Ozpelit E. Extrapulmonary features of post-COVID-19 patients: muscle function, physical activity, mood, and sleep quality. Ir J Med Sci. 2022;191(3):969-75. DOI

31. Cruz IP, Lopes SM, Corrêa KLD, Costa BO, Ribeiro IR, Vasconcelos JH, et al. Mobilização precoce na unidade de terapia intensiva. Braz J Develop. 2021;7(12):121380-9. DOI

32. Goërtz YMJ, Vaes AW, Spruit MA. COPD and pulmonary rehabilitation: new findings from Brazil. J Bras Pneumol. 2021; 46(6):e20200596. DOI

33. Carfì A, Bernabei R, Landi F; Gemelli Against COVID-19 Post-Acute Care Study Group. Persistent symptoms in patients after acute COVID-19. JAMA. 2020;324(6):603-5. DOI

34. Wittmer VL, Paro FM, Duarte H, Capellini VK, Barbalho-Moulim MC. Early mobilization and physical exercise in patients with COVID-19: A narrative literature review. Complement Ther Clin Pract. 2021;43:101364. DOI

35. Thomas P, Baldwin C, Bissett B, Boden I, Gosselink R, Granger CL, et al. Physiotherapy management for COVID-19 in the acute hospital setting: clinical practice recommendations. J Physiother. 2020;66(2):73-82. DOI

36. Fontanela PC, Forgiarini Jr LA, Friedman G. Atitudes clínicas e barreiras percebidas para a mobilização precoce de pacientes graves em unidades de terapia intensiva adulto. Rev Bras Ter Intensiva. 2018;30(2):187-94. DOI