ORIGINAL ARTICLE

https://doi.org/10.1590/1806-9282.20220974

Associations between muscle strength, dyspnea and quality of life in post-COVID-19 patients

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SUMMARY

OBJECTIVE: Patients with severe coronavirus disease 2019 (COVID-19) develop high muscle weakness. The objective of this study was to analyze the physical fitness of post-COVID-19 patients and its relationship with dyspnea and health-related quality of life (HrQoL).

METHODS: This observational, retrospective, cross-sectional study was conducted between October and November 2021 in the Universidad Europea de Madrid (Spain), with 32 post-COVID-19 patients aged 63.2 (14.1) years. Muscle strength, aerobic capacity, maximal respiratory mouth pressures, dyspnea, and HrQoL were analyzed 6–12 months after discharge for COVID-19. To analyze the relationship between continuous variables, Spearman's correlation test and Pearson's correlation test were performed.

RESULTS: The participants had a mean handgrip strength of 22.1 (9.0) kg and very poor HrQoL. Negative moderate correlations were found between handgrip strength and length of hospital and intensive care unit stay (r=−0.37; p=0.002). In addition, muscle strength was negatively correlated with dyspnea (r=−0.37; p=0.008) and HrQoL, and moderate-large negative correlations were found between dyspnea and HrQoL.

CONCLUSION: Higher handgrip strength was associated with lower COVID-19 severity and less sequelae. Therefore, either the patients with severe COVID-19 suffered greater muscle breakdown, or higher muscle strength acted as a mitigating factor for the disease. It is suggested that post-COVID-19 rehabilitation programs should focus on increasing muscle strength. Also, adequate physical fitness could mitigate the physical and mental post-COVID-19 sequelae.

KEYWORDS: COVID-19. SARS-CoV-2. Muscle strength. Hand strength. Quality of life.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a viral infection that causes severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and, in severe cases, induces severe systemic inflammation, causing lung damage and respiratory distress, requiring hospitalization, and sometimes even admission to intensive care units (ICUs)[1].

The chronic fatigue syndrome is one of the more frequent post-COVID sequelae, possibly due to the significant muscle mass reductions that have been observed in COVID-19 patients after 20 days admitted to the ICU[2]. These findings have also been reported in hospitalized patients during the first SARS-CoV epidemic, almost two decades ago, with significant decreases in handgrip strength and the distance covered during the 6-min walk test (6MWT), several months after hospital discharge[3]. Significant muscle mass and muscle strength loss have also been reported in other patients admitted to the ICU, possibly due to a decrease in protein synthesis and an increase in muscle breakdown, resulting in a drastic increase in protein catabolism[4].

At present, COVID-19 infection is thought to cause muscle breakdown due to systemic inflammation, the so-called cytokine storm. Indeed, C-reactive protein, IL-6, IL-1b, or alpha-TNF can directly induce muscle proteolysis and decrease protein synthesis, especially when the inflammation is associated with the lung[5]. COVID-19 patients admitted to the ICU present higher C-reactive protein levels compared to other patients admitted to the ICU and also a direct correlation between inflammation and muscle breakdown[6].

Patients affected by a more severe COVID-19 are those who develop higher muscle weakness[7] and also those with higher levels of inflammatory markers[8]. Another fact to highlight is that elderly patients, who are the majority of patients with severe COVID-19, already have a situation of muscle breakdown and systemic inflammation, even reaching sarcopenia[9]. On the contrary, physical exercise exerts an anti-inflammatory effect[10], so possibly more active people or people with better physical fitness suffer a milder COVID-19 and less severe sequelae, such as dyspnea or a decrease in the health-related quality of life (HrQoL)[11].

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Conflicts of interest: the authors declare there is no conflict of interest. Funding: none.
Received on August 23, 2022. Accepted on September 08, 2022.

The objective of this study was to analyze the physical fitness of post-COVID-19 patients and its relationship with dyspnea and HrQoL.

METHODS

Study design

This observational, retrospective, cross-sectional study was conducted between October and November 2021.

Settings and participants

A total sample of 32 post-COVID-19 patients were recruited via email between October and November 2021 in the Universidad Europea de Madrid (Spain). A code was assigned to participants prior to statistical analysis, thus guaranteeing the confidentiality of their data. The inclusion criteria were having being discharged from COVID-19 infection (diagnosed with a PCR test) 6–12 months ago and not having fever or symptoms of re-infection at the present moment.

Ethical considerations

This study respected the Helsinki guidelines at all times and followed the ethical standards of Spain. All the participants read and signed an informed consent statement before becoming part of this investigation.

Measurements

Anthropometric variables: Height and weight were measured using a stadiometer and a scale. Then, the body mass index (BMI, in kg/m^2) was calculated.

Muscle strength was assessed through the Medical Research Council (MRC) scale, which grades the patient's strength from 0 (no muscle activation) to 5 (muscle activation against examiner's full resistance, full range of motion) on 12 different muscle groups[12]. Also, *handgrip strength* was measured using the Takei 5001 Hand Grip analog dynamometer. Handgrip strength has a large correlation with general strength, functionality, and all-cause mortality. A score <27 kg is considered a risk factor for all-cause mortality[13].

Aerobic capacity was assessed through the 6MWT, which is a sub-maximal exercise test, 126 where the distance covered walking over a time of 6 min is used as the outcome (in m)[14].

To assess respiratory muscles function, *maximal inspiratory pressure* (MIP) and *expiratory mouth pressure* (MEP) were measured using the Micro Respiratory Pressure Meter (FS985, Micro Medical, Los Angeles, CA, USA). The participants performed the maneuvers in a sitting position with a stuffy nose through a clamp that prevented air leaks and a straight back, following the protocol of the "Sociedad Española de Pneumología y Cirugía Torácica." The highest values of MIP and MEP were recorded and expressed in cm of H_2O[15].

Dyspnea was assessed through the modified MRC scale, which is a self-rating tool to measure the degree of disability that breathlessness poses on day-to-day activities on a scale from 0 (no breathlessness, except on strenuous exercise) to 4 (too breathless to leave the house, or breathless when dressing or undressing)[16].

Health-related quality of life: To assess HrQoL, the participants filled out the Short Form-36 Health Survey Questionnaire v2 (SF-36). It consists of 36 items, which gives a score from 0 (worst self-perception of HrQoL) to 100 (best self-perception of HrQoL) in 8 sections, which are regrouped into two main components: Physical Component Summary and Mental Component Summary[17].

A 30-day mortality probability during the COVID-19 infection was measured using the SEIMC COVID-19 score, which consists of five items that give a total score from 0 (lowest risk) to 30 (highest risk), where age of the participants >40 years is the more relevant item[18].

Respiratory severity score during the COVID-19 infection was measured with the Brescia respiratory severity scale, which simplifies the clinical summary of a patient's status, providing a score from 0 (lowest severity) to 8 (highest severity)[19].

The *length of hospital stay and the length of stay in the ICU* were recorded, expressed in days. These variables, along with the 30-day mortality probability and the respiratory severity score, were given by the hospital discharge report, which was provided by the participants.

Statistical analysis

Shapiro-Wilk test was employed to assess the normality. Then, a descriptive analysis was developed for all the subjects using mean (standard deviation) (SD) for the parametric variables and median (interquartile) for nonparametric variables. In addition, to analyze the relationship between continuous variables, Spearman's correlation test and Pearson's correlation test were performed for the nonparametric and parametric variables, respectively. The magnitudes of correlation between continuous variables were qualitatively interpreted using the following criteria: trivial (r≤0.1), small (r=0.1–0.3), moderate (r=0.3–0.5), large (r=0.5–0.7), and very large (r=0.7–0.9). After Bonferroni correction was applied, the statistical significance was set at an alpha level of <0.01. All analyses were conducted using IBM SPSS for Windows (version 27, IBM Corp., Armonk, NY, USA).

RESULTS

Sociodemographic data of the sample

First, 43 patients were recruited via email, and 11 (26%) were excluded because the COVID-19 infection had occurred more than 12 months ago. Finally, a total of 32 participants aged 63.2 (14.1) years (59% female) were analyzed. Their mean BMI was 26.6 (3.7) kg/m^2. Most of the participants (78%) required hospital stay, with a mean length of 37.0 (48.0) days, while 12.5% of the participants required ICU stay for 45.8 (18.4) days (Table 1).

Muscle strength and aerobic capacity

The participants had a mean handgrip strength of 22.1 (9.0) kg. Regarding aerobic capacity, the mean distance covered in the 6MWT was 373.5 (114.0) m (Table 2).

Table 1. Characteristics of the study population (n=32) and COVID-19 severity.

Variables	Mean (SD) or median (IQR)
Age	63.2 (14.1)*
Gender	n=13 male
	n=19 female
Body mass index (kg/m^2)	26.6 (3.7)†
Respiratory severity score (Brescia scale)	2.1 (2.5)*
30-Day mortality probability (SEIMC score)	7.8 (5.7)*
Duration of hospital stay (days) (n=25 patients)	37.0 (48.0)*
Duration of intensive care unit stay (days) (n=4 patients)	45.8 (18.4)*

IQR: interquartile range. *Values are represented as mean (standard deviation) (SD). †Values are represented as median (IQR).

Table 2. Muscle strength, aerobic capacity, dyspnea, and quality of life in 32 post-COVID-19 patients.

Variables	Mean (SD) or median (IQR)
Dyspnea score	1.0 (0.0)*
Maximal inspiratory pressure (cm H_2O)	53.0 (27.3)†
Maximal expiratory pressure (cm H_2O)	61.5 (26.0)†
Handgrip strength (kg)	22.1 (9.0)†
Muscle strength (MRC scale)	60.0 (0.0)*
6-Min walk test (m)	373.5 (114.0)†
SF-36 Physical Component Summary	36.8 (9.2)†
SF-36 Mental Component Summary	36.6 (13.3)†

IQR: interquartile range. *Values are represented as mean (standard deviation) (SD). †Values are represented as median (IQR).

Respiratory muscles function

The participants had an MIP of 53.0 (27.3) cm H_2O and an MEP of 61.5 (26.0) cm H_2O (Table 2).

Health-related quality of life

Regarding HrQoL, the mean values of the summary scores were as follows: Physical Component Summary 36.8 (9.2) and Mental Component Summary 36.6 (13.3) (Table 2).

30-Day mortality and respiratory severity score

The mean SEIMC COVID-19 score was 7.8 (5.7), and the Brescia respiratory severity score was 2.1 (2.5) (Table 1).

Correlations between the continuous variables

Moderate-large negative correlations were found between dyspnea and muscle strength MRC (r=−0.37; p=0.008) and between dyspnea and the Mental Component Summary (HrQoL) (r=−0.41; p=0.006) (Table 3).

Handgrip strength showed negative moderate correlations with 30-day mortality (r=−0.36; p=0.001), length of hospital stay (r=−0.37; p=0.002), and length of ICU stay (r=−0.37; p=0.002). Also, there was a negative moderate correlation between the duration of ICU stay and muscle strength MRC (r=−0.42; p=0.007) (Table 3).

Age showed positive large correlations with length of hospital stay (r=0.56; p=0.001) and 30-day mortality (r=0.84; p=0.000) (Table 3).

Finally, the 6MWT score showed a positive moderate correlation with the Physical Component Summary (HrQoL) (r=0.36; p<0.001) (Table 3).

DISCUSSION

Some participants of this study had a mild COVID-19 and recovered at home, while most of the participants had a severe COVID-19 and required hospital stay or ICU stay for a month, probably because they were older adults. The participants were evaluated 6–12 months after discharge for COVID-19.

Also, the participants had low handgrip strength, below the cutoff point of 27 kg, which is considered a risk factor for all-cause mortality[13]. Also, they had a poor performance in the 6MWT. In addition, according to the predictive equation of the MIP and MEP values of the participants should be 67.6 and 76.2 cm H_2O, respectively. So, the participants presented 22% lower values of MIP and 19% lower values of MEP, compared to the predictive values of the equation of Souto-Miranda et al.[20] These findings have also been reported in other observational studies with post-COVID-19 patients[21].

Table 3. Correlations between the continuous variables.

		Brescia	SEIMC-score	Length of hospital stay	Length of ICU stay	Dyspnea	Age	Hand grip	6MWT	SF-36 physical	SF-36 mental
Brescia	Pearson r		0.27	0.76*	0.85*		0.27	-0.24	-0.37	-0.22	0.34
	p-value		0.122	0.000	0.000		0.128	0.185	0.048	0.193	0.285
SEIMC-score	Pearson r			0.33	0.11		**0.84***	**-0.36***	-0.42	0.17	0.15
	p-value			0.063	0.547		**0.000**	**0.001**	0.025	0.587	0.247
Length of hospital stay	Pearson r				0.82*		0,342	**-0.37***	-0.52	-0.62	-0.43
	p-value				0.000		0,051	**0.009**	0.041	0.023	0.034
Length of ICU stay	Pearson r						**0.56***	**-0.37***	-0.35	-0.68	-0.46
	p-value						**0.001**	**0.002**	0.063	0.051	0.061
Dyspnea	Spearman r	-0.21	-0,31	-0.41	-0.05		-0.24	0.14	-0.11	-0.46	**-0.41***
	p-value	0.131	0.092	0.020	0.800		0.188	0.461	0.566	0.043	**0.006**
Age	Pearson r							-0.23	-0.51	-0.11	-0.13
	p-value							0.204	0.041	0.275	0.185
Hand grip	Pearson r								0.39	0.36	0.41
	p-value								0.038	0.028	0.078
MRC scale	Spearman r	-0.11	-0.04	-0.56	**-0.42***	**-0.37***	0.08	0.22	0.41	0.26	0.34
	p-value	0.509	0.853	0.151	**0.007**	**0.008**	0.646	0.219	0.027	0.098	0.28
6MWT	Pearson r									**-0.36***	0.39
	p-value									**0.000**	0.13

ICU: intensive care unit; 6MWT: 6-min walking test. Bold indicates statistically significant values. *Statistical significance was set at an alpha level of <0.01.

Handgrip strength showed inverse moderate correlations with the 30-day mortality, length of hospital stay, and length of ICU stay. In addition, there was a negative moderate correlation between the duration of ICU stay and muscle strength MRC. Interestingly, muscle weakness was seen mainly in patients with a more severe COVID-19 disease, as reported in other studies[7]. In contrast, physical exercise and handgrip strength are associated with lower inflammation[10], so perhaps patients with better physical fitness had some protection against COVID-19 since the most severe forms of this disease develop in patients with higher levels of inflammation[5].

Most severely affected COVID-19 patients are elderly who have frequently high levels of systemic inflammation and muscle breakdown, even reaching sarcopenia[8]. Interestingly, in this study, the age of the participants showed a positive large correlation with the length of hospital stay and a negative moderate correlation with the handgrip strength, so the older patients presented a more severe COVID-19 and had lower levels of muscular strength.

According to the dyspnea scale, the participants had "shortness of breath when hurrying on the level or walking up a slight hill," which showed an inverse negative correlation with muscle strength MRC and could had a great negative impact on HrQoL, as negative moderate-large correlations were found between dyspnea and HrQoL. In turn, 6MWT showed a positive moderate correlation with HrQoL. The participants of this study were in the 10th percentile of Physical and Mental Component Summaries, compared to the references values of their age[22], so they had very poor HrQoL.

Therefore, the physical and mental sequelae that the post-COVID-19 patients present may depend largely on muscular strength and aerobic capacity. Physical exercise could, therefore, be a mitigating factor for this disease. In turn, post-COVID-19 rehabilitation programs should focus on muscle strength to reduce dyspnea and increase the HrQoL.

Despite the relevant findings found in this study, the main limitation is that it is an observational cross-sectional study, and causalities cannot be established. In addition, some variables were measured with self-reported tools, which can lead to potential bias or subjectivity. However, muscle strength should be addressed in the rehabilitation of the post-COVID-19 sequelae and in the prevention of severe affections of the disease.

CONCLUSION

Higher handgrip strength was associated with lower COVID-19 severity and lower mortality. Therefore, either the patients with severe COVID-19 suffered greater muscle breakdown, or higher muscle strength acted as a mitigating factor for the disease. Also, lower muscle strength was associated with higher dyspnea, and higher dyspnea was associated with lower HrQoL. Adequate physical fitness could mitigate the physical and mental post-COVID-19 sequelae. In turn, post-COVID-19 rehabilitation programs should focus on increasing muscle strength.

AUTHORS' CONTRIBUTIONS

GGPS: Conceptualization, data curation, formal analysis, investigation, methodology, project administration, resources, software, supervision, validation, supervision, validation, visualization, writing – original draft, writing – review & editing. **BSP:** Conceptualization, data curation, investigation, methodology, project administration, resources, supervision, validation, supervision, validation, visualization, writing – original draft, writing – review & editing.

REFERENCES

1. Ali AM, Kunugi H. Approaches to nutritional screening in patients with coronavirus disease 2019 (COVID-19). Int J Environ Res Public Health. 2021;18(5):2772. https://doi.org/10.3390/ijerph18052772
2. 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. https://doi.org/10.1097/PHM.0000000000001641
3. Disser NP, De Micheli AJ, Schonk MM, Konnaris MA, Piacentini AN, Edon DL, et al. Musculoskeletal consequences of COVID-19. J Bone Joint Surg Am. 2020;102(14):1197-204. https://doi.org/10.2106/JBJS.20.00847
4. Hodgson CL, Tipping CJ. Physiotherapy management of intensive care unit-acquired weakness. J Physiother. 2017;63(1):4-10. https://doi.org/10.1016/j.jphys.2016.10.011
5. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med. 2020;46(5):846-8. https://doi.org/10.1007/s00134-020-05991-x
6. Puthucheary ZA, Rawal J, McPhail M, Connolly B, Ratnayake G, Chan P, et al. Acute skeletal muscle wasting in critical illness. JAMA. 2013;310(15):1591-600. https://doi.org/10.1001/jama.2013.278481
7. De Lorenzo R, Conte C, Lanzani C, Benedetti F, Roveri L, Mazza MG, et al. Residual clinical damage after COVID-19: a retrospective and prospective observational cohort study. PLoS One. 2020;15(10):e0239570. https://doi.org/10.1371/journal.pone.0239570
8. Zhao X, Li Y, Ge Y, Shi Y, Lv P, Zhang J, et al. Evaluation of nutrition risk and its association with mortality risk in severely and critically Ill COVID-19 patients. JPEN J Parenter Enteral Nutr. 2021;45(1):32-42. https://doi.org/10.1002/jpen.1953
9. Orsucci D, Trezzi M, Anichini R, Blanc P, Barontini L, Biagini C, et al. Increased creatine kinase may predict a worse COVID-19 outcome. J Clin Med. 2021;10(8):1734. https://doi.org/10.3390/jcm10081734
10. Ferreira MJ, Irigoyen MC, Consolim-Colombo F, Saraiva JFK, De Angelis K. Physically active lifestyle as an approach to confronting COVID-19. Arq Bras Cardiol. 2020;114(4):601-2. https://doi.org/10.36660/abc.20200235
11. 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-e6. https://doi.org/10.1016/j.jinf.2020.08.029
12. Fontela PC, Glaeser SS, Martins LF, Condessa RL, Prediger DT, Forgiarini SG, et al. Medical research council scale predicts spontaneous breathing trial failure and difficult or prolonged weaning of critically Ill individuals. Respir Care. 2021;66(5):733-41. https://doi.org/10.4187/respcare.07739
13. Lera L, Albala C, Leyton B, Márquez C, Angel B, Saguez R, et al. Reference values of hand-grip dynamometry and the relationship between low strength and mortality in older Chileans. Clin Interv Aging. 2018;13:317-24. https://doi.org/10.2147/CIA.S152946
14. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med. 2002;166(1):111-7. https://doi.org/10.1164/ajrccm.166.1.at1102
15. Evans JA, Whitelaw WA. The assessment of maximal respiratory mouth pressures in adults. Respir Care. 2009;54(10):1348-59. PMID: 19796415
16. Rajala K, Lehto JT, Sutinen E, Kautiainen H, Myllärniemi M, Saarto T. mMRC dyspnoea scale indicates impaired quality of life and increased pain in patients with idiopathic pulmonary fibrosis. ERJ Open Res. 2017;3(4):00084-2017. https://doi.org/10.1183/23120541.00084-2017
17. Alonso J, Prieto L, Antó JM. The Spanish version of the SF-36 Health Survey (the SF-36 health questionnaire): an instrument for measuring clinical results. Med Clin (Barc). 1995;104(20):771-6. PMID: 7783470
18. Berenguer J, Borobia AM, Ryan P, Rodríguez-Baño J, Bellón JM, Jarrín I, et al. Development and validation of a prediction model for 30-day mortality in hospitalised patients with COVID-19: the COVID-19 SEIMC score. Thorax. 2021;76(9):920-9. https://doi.org/10.1136/thoraxjnl-2020-216001
19. Duca A, Piva S, Focà E, Latronico N, Rizzi M. Calculated decisions: Brescia-COVID Respiratory Severity Scale (BCRSS)/algorithm. Emerg Med Pract. 2020;22(5 Suppl):CD1-CD2. PMID: 32297727

20. Souto-Miranda S, Jácome C, Alves A, Machado A, Paixão C, Oliveira A, et al. Predictive equations of maximum respiratory mouth pressures: a systematic review. Pulmonology. 2021;27(3):219-39. https://doi.org/10.1016/j.pulmoe.2020.03.003

21. Torres-Castro R, Vasconcello-Castillo L, Alsina-Restoy X, Solis-Navarro L, Burgos F, Puppo H, et al. Respiratory function in patients post-infection by COVID-19: a systematic review and meta-analysis. Pulmonology. 2021;27(4):328-37. https://doi.org/10.1016/j.pulmoe.2020.10.013

22. Vilagut G, Valderas JM, Ferrer M, Garin O, López-García E, Alonso J. Interpretación de los cuestionarios de salud SF-36 y SF-12 en España: componentes físico y mental. Medicina Clínica. 2008;130(19):726-35. https://doi.org/10.1157/13121076