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 ICU2. 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 discharge3. 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 catabolism4.

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 lung5. 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 breakdown6.

Patients affected by a more severe COVID-19 are those who develop higher muscle weakness7 and also those with higher levels of inflammatory markers8. 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 sarcopenia9. On the contrary, physical exercise exerts an anti-inflammatory effect10, 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.
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/m²) 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. 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.

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).

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 H₂O.

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).

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.

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.

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).

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/m². 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/m²)                        | 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 H₂O)           | 53.0 (27.3)†              |
| Maximal expiratory pressure (cm H₂O)            | 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 H₂O and an MEP of 61.5 (26.0) cm H₂O (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).

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 mortality13. 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 H₂O, 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 patients21.
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. In contrast, physical exercise and handgrip strength are associated with lower inflammation, 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.

Most severely affected COVID-19 patients are elderly who have frequently high levels of systemic inflammation and muscle breakdown, even reaching sarcopenia. Interestingly, 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 have 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, 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.

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