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Muscle strength and physical performance in patients without previous disabilities recovering from COVID-19 pneumonia

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ABSTRACT

In this cross-sectional study, we evaluated skeletal muscle strength and physical performance (1min- STS and SPPB tests), dyspnea, fatigue and Single Breath Counting at discharge from a post-acute Covid Department, in patients recovering from COVID-19 pneumonia who had no locomotor disability prior to the infection.

Quadriceps and biceps were weak in 86% and 73% of patients, respectively. Maximal Voluntary Contraction for quadriceps was 18.9 (6.8) Kg and for biceps 15.0 (5.5) Kg, i.e. 57 and 69% of the predicted normal value (%pred). The number of chair rises in the 1min-STS was 22.1 (7.3) (63% pred), while the SPPB score was 7.9 (3.3) (68% pred). At the end of the 1min-STS test, 24% of patients showed exercise-induced desaturation. The SBC count was 35.4 (12.3), i.e. 71.8% that of healthy controls. Mild-to-moderate dyspnea and fatigue were found after ADL [Borg score 0.5 (0-2) and 1 (0-2)] and after the 1min-STS [Borg score 3 (2-5) and 1 (0-3)]. Significant correlations were observed between muscle strength and physical performance indices (R from 0.31 to 0.69).

The high prevalence of impairment in skeletal muscle strength and physical performance in hospitalized patients recovering from COVID-19 pneumonia without prior locomotor disabilities suggests the need for rehabilitation programs after discharge.

Keywords: Respiratory failure, pulmonary rehabilitation, intermediate care, outcome, fatigue

INTRODUCTION

COVID-19 disease is an infectious condition characterized by rapid human-to-human transmission. Studies describe a wide variety of clinical presentations ranging from absence of symptoms to light flu, pneumonia with acute respiratory failure, and severe Acute Respiratory Distress Syndrome (ARDS) requiring admission to the Intensive Care Unit (ICU) and possible death.[1]

Muscle soreness, fatigue and weakness are reported symptoms in COVID-19, regardless of the severity of clinical presentation.[2] Limited data are available on the prevalence and severity of *de novo* COVID-19-related skeletal muscle impairment and disability at hospital discharge. Critical illness myopathy associated to COVID-19 as a spectrum of myophatic changes induced by the virus has been reported in COVID-19 survivors[3] as well as in post-mortem examinations which documented immune-mediated focal myofiber necrosis or atrophy in patients with Severe Acute Respiratory Syndrome (SARS).[4] Morever, delayed neurologic sequelae such as peripheral neuropathy, Bickerstaff brainstem encephalitis (BBE), and Guillain-Barre syndrome (GBS) have been described following both MERS-CoV [5] and SARS-CoV-1 infection.[6] In addition, in patients requiring an ICU stay, the muscle impairment could be related to systemic inflammation, mechanical ventilation, sedation and prolonged bed rest.[7]

The aim of this cross-sectional study was to describe skeletal muscle strength, exercise intolerance and symptoms in a cohort of patients recovering from COVID-19 pneumonia without pre-existing locomotor disabilites. The secondary aim was to investigate associations between these functional outcome measures.

METHODS

At the Istituti Clinici Scientifici Maugeri IRCCS, Lumezzane (Italy), we conducted a cross-sectional analysis in consecutive patients recovering from COVID-19 pneumonia at the time of discharge from the post-acute Departement. We included patients admitted from 1st April to 30th April 2020. Inclusion criteria were: normoxaemia [pulse oximetry (SpO_2) >94%] at rest, spontaneous breathing, respiratory rate < 22 bpm zand absence of fever for at least of 3 days. Exclusion criteria were: refusal to participate, the presence of cognitive or locomotor impairment prior to the infection and any pre-existing condition such as orthopedic or neurological comorbidities limiting the ability to cope with activities of daily life, as defined by a Barthel index[8] score equal to 100.

Ethics Committee approval was obtained (EC2414, 23 April 2020) and written informed consent was obtained from all patients. This study conforms to all STROBE guidelines and reports the required information accordingly (see Supplemental Checklist, Supplemental Digital Content 1, http://links.lww.com/PHM/B167).

During the hospital admission, patients received best practice respiratory care according to the evolving information and current research.[9] One or more of the following drugs were added as specific therapy for COVID-19: cloroquine, antiviral medication, cortico-steroids, anticoagulants, patients also received the therapy prescribed for their underlying comorbidities. Patients received 20-min of daily individual physiotherapy sessionspromoting early mobilisation, lung expansion and airways clearance.[10]

The following measurements were performed at the time of discharge:

a) Muscle strength by means of Maximal Voluntary Contraction (MVC) (isometric contraction) of dominant biceps brachii and quadriceps. Reference values for healthy normal individuals were calculated using the equation of Andrews et al.[11] (data from a Caucasian population aged 50-79 years). The following reference equations were used: for brachial biceps (N): =229.421-84.837 * gender (0=male, 1=female) + 0.165 * Weight - 1.503 * Age; for quadriceps (N): =358. 5-87.6 * gender + 0.30 * Weight - 3.14 * Age). Subjects were labeled with “muscle weakness” for a muscle group if the muscle strength was inferior to 80% of the predicted normal value.

b) Exercise tolerance and exercise induced oxygen desaturation was evaluated with the 1-Minute Sit-To-Stand (1min-STS) test[12] using the reference values for healthy normals of Strassmann et al.[13] The predicted normal values used referred to European, sex- and age-stratified subjects up to the age of 79 years. Desaturation was defined as a reduction in SpO_2 with more than 4% compared to rest;

c) Physical performance was assessed using the Short Physical Performance Battery (SPPB) with as the predicted normal values those suggested by Bergland et al.[14]; these refer to a Norwegian population aged ≥40 years and are stratified for age and sex;

d) Exercise induced muscle contractile fatigue was evaluated as the difference in MVC of the quadriceps before and after the 1min-STS;[15]

e) Perceived symptoms of dyspnoea and fatigue assessed by the modified BORG scale[16] were collected at rest and immediately after the 1min-STS as well as during patient’s activities of daily living (ADL) such as walking in the hospital room, going to the toilet and eating;

f) The Single-Breath Counting (SBC) test[17] which measures how far an individual can count with a normal speaking voice after a maximal inhalation (from total lung capacity). The counting follows the rhythm to a metronome set at 2Hz. A correlation with standard pulmonary function measures has been shown in adults.[17]

Data were analyzed using statistical software (STATA 13.1) and expressed as mean and standard deviation for continuous measures and percentage for categorical or binary data. T-test was used to investigate differences between subgroups of patients and to investigate whether values deviated from predicted normal values. A Pearson's correlation test was used to detect associations between quadriceps strength, 1min-STS and respiratory muscle performance and other clinical and functional variables. A value of $p<0.05$ was considered for statistical significance.

RESULTS

Of 114 patients admitted to the hospital, 41 met the inclusion criteria and were included in the study (**Table 1**). Seventy-three patients were excluded because of one or more of the following conditions: resting SpO_2 < 94% (n=35), pre-existing neurological (n=26), orthopedic comorbidities (n=22), cognitive impairment (n=21), reported previous motor disability (n=20), fever (n=10), continued use of non-invasive ventilation (NIV) (n=8), tachypnoea (n= 5).

Quadriceps and biceps weakness was observed in 86% and 73% of patients, respectively. Mean MVC of quadriceps was 18.9 (6.8) Kg, while that of biceps was 15.0 (5.5) Kg, respectively 54 (17) % and 69 (18) % of the predicted normal value. Number of rises during the 1min-STS was 22.1 (7.3) [63 (21) % of normal value] and SPPB score was 7.9 (3.3) [71 (31)% of the predicted value].

Figure 1 shows the percentage of predicted values of muscle strength and physical performance measures in the overall group and in patients according to the presence or not of comorbidities. At the end of the 1min-STS test, 24% of patients showed exercise-induced desaturations and the quadriceps strength decreased by 1.4 (1.6) Kg [7.4 (8.1) % of baseline value]. **Table 2** shows dyspnoea and leg fatigue perceived by the patients, as assessed by the Borg scale. The majority (53%) of patients still had a 'good' physical autonomy as assessed by the SPPB (scores 9-12), whereas 25% showed high levels of disability (scores <5) and 22% had low-moderate disability (scores from 5 to 8).

Weak but statistically significant correlations were observed between muscle strength and indices of physical performances (R from 0.31 to 0.69). Significant inverse relationships were observed between quadriceps strength and length of stay in the acute hospital (R= -0.35, p=0.03), between biceps strength and age (R=-0.33, p=0.0324) and between 1min-STS and symptoms [dyspnoea (R=-0.40, p=0.01) and fatigue (R=-0.35 p=0.03) at rest and dyspnoea (R=-0.49 , p= 0.001) and fatigue (R=-0.35, p= 0.03) during ADL].

The SBC test was 35.4 (12.3) counts, which equals 72 % of data recorded in 40 healthy controls (personal data due to lack of predictive normal values), suggesting a reduction in Vital Capacity and/or Expiratory Flow.

After discharge 28 patients returned home, 4 patients were transferred to a dedicated pulmonary rehabilitation ward, 7 patients were presecribed 1 month of tele-rehabilitation at home and one patient was transferred to another acute hospital.

DISCUSSION

This is the first report showing impairement in comprehensively assessed physical performance in individuals in the early recovery from COVID-19 infection at discharge from hospital. Our results indicate that patients who have recovered from respiratory distress requiring assisted ventilation or oxygen therapy, and who were without any prior disability, have reduced physical performance. Despite the relatively small sample size and the possible lack of external validity of these results, our findings may be useful to guide clinicians taking care of patients surviving COVID-19 infection.

Although there was a weak significant inverse relationship between quadriceps strength and length of stay in the acute hospital, the reduction in physical performance observed in our patients cannot be ascribed to a prolonged ICU stay and/or prolonged mechanical ventilation, as the vast majority of our patients had not suffered from such conditions. Only 2 out of 41 patients had been intubated in the acute hospital for 5 and 9 days and their length of stay was 13.5 (0.7) days.

Almost one out of four of our patients, normoxaemic at rest, showed significant exercise induced oxygen desaturations during the 1min-STS and patients reported low levels of perceived dyspnoea or fatigue as assessed by the Borg scale. Indeed, the low intensity and short duration of this test might have underestimated the severity of exercise induced desaturations as compared to standard exercise tests such as the 6-min walking test or cardiopulmonary exercise tests.The latter tests, however, would have been impossible to conduct in our clinical conditions. Similarly, the evaluation of symptoms during hospital activities is clearly influenced by the level of effort chosen by patients. We assessed perceived leg fatigue using the Borg scale. More specific tools like the Chronic Respiratory Questionnaire, the Fatigue Impact Scale, or the Fatigue Severity Scale may be more appropriate, allthough no scale is specifically validated for COVID-19.[18] Nevertheless, the reduction in post 1min-STS quadriceps strength indicates that leg fatigue was present in our patients.

Our patients received pharmacotherapy. No adverse effects were reported but, at the time of the writing of this manuscript, no pharmacotherapy has proven to be safe and effective for treating patients with COVID-19 disease.[19] Furthermore, we cannot exclude potential effects of any of these drugs on peripheral muscle strength or physical performance.

Limitations of the study

First, for safety reasons, it was impossible to perform standard lung or respiratory muscle function tests including the assessment of lung diffusion capacity. Therefore, we used the SBC test as a surrogate and found a reduction in SBC values.This suggests, but not proves, an impairment in lung function.[20] Hence, we are unable to define to what extent the decline in physical performance can be ascribed to impairment in lung or respiratory muscle function. With 25% of patients showing significant desaturations even during a short 1min STS test, it is highly likely that lung function (diffusion) impairment may remain clinically relevant in many patients, even after discharge.

Second, a parallel COVID-free control group could not be studied due to the local lockdown. Between March and July 2020 our unit was dedicated full-time to COVID-19 patients, while patients with others chronic diseases were strictly maintained at home. However, muscles of the upper and lower limbs of our COVID-19 patients appear weaker compared to patients with chronic cardio-respiratory conditions of similar age (data published previously by the present authors).[21]

Third, our study may lack external validity due to our restrictive inclusion criteria and the restriction to limited the study to patients without functional limitations prior to their COVID-19 infection. This, however, allowed to focus on the direct effect of the virus on muscle and functional ability, reducing confounding effects.

Last, the lack of baseline measures at the time of admission to the post-acute hospital is unfortunate. This would have allowed to describe muscle strength and function closer to nadir as well as to assess the impact of the post-acute care. Similarly, follow-up data after the period of inpatient rehabilitation might have contributed to an even more comprehensive description of the recovery of these patients.

Conclusion

We observed a high prevalence of muscle weakness and physical performance impairment in patients recovering from a moderate to severe COVID-19 pneumonia and hospitalised without any prior motor limitation. With the limitations imposed by the present clinical circumstances, these findings strongly suggest the need for follow-up evaluation of physical function and rehabilitation programs in a large fraction of these patients.

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LEGEND TO FIGURE

Figure 1. Comparison of muscle strength (panels A and B) and physical performance (panels C and D) expressed as percentage of the predicted values in the overall group and according to the presence or not of comorbidities.

Legend: 1min-STS= 1 minute Sit-To-Stand, SPPB=Short Physical Performance Battery.

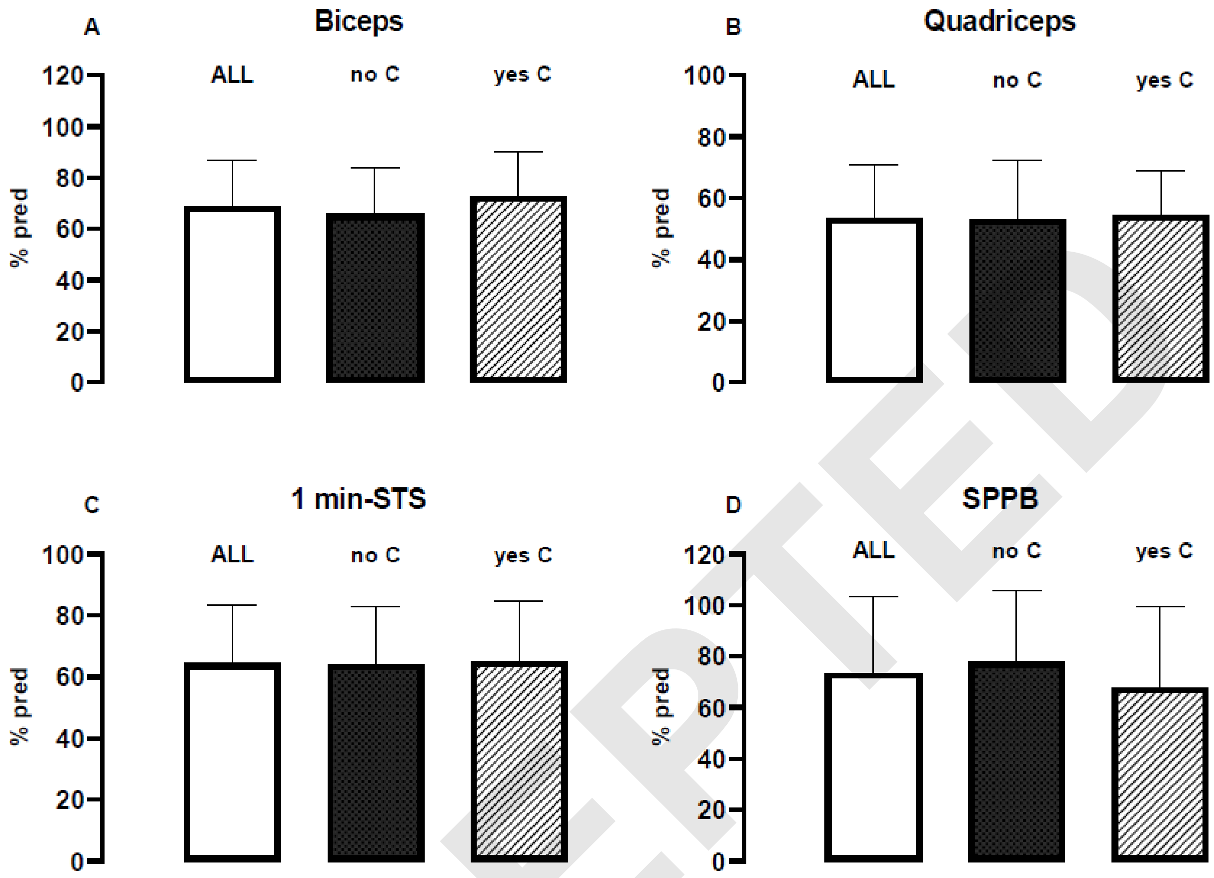
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Figure 1

Table 1. Patients characteristics

Patients, n	41
Age, years	67.1 (11.6)
Range (min-max)	40-88
Males, n (%)	25 (61.0)
BMI, Kg/m^2	26.7 (4.9)
Patients with comorbidities, n (%)	17 (41.5)
cardiac comorbidities, n (%)	15 (36.6)
pulmonary comorbidities, n (%)	6 (14.6)
SpO_2/FiO_2 at discharge	454.9 (8.7)
Time from symptom onset, days	28.6 (8.2)
Acute care hospital LOS, days,	9.7 (5.5)
Post acute hospital LOS, days	10.6 (7.2)
Total hospital LOS, days	20.7 (7.5)
Patients treated with CPAP or NIV	
In acute care hospital, n (%)	9 (21.4)
In post acute hospital, n (%)	1 (2.3)
Patients treated with Invasive Mechanical Ventilation, (n) %	2 (4.8)
Patients treated with Oxygen therapy only	
In acute care hospital, n (%)	28 (68.3)
In post acute hospital, n (%)	36 (85.7)

Maximal FiO_2 used during hospitalization	0.49 (0.25)
Drugs: patients, n (%)	
Antiviral	20 (80.5)
Steroids	7 (17.1)
Antirheumatics	32 (78.0)
Antibiotics	30 (73.2)
Antithrombotics	18 (43.9)

Legend: Data are reported as mean (Standard deviation) or numbers (%). BMI= Body-Mass Index, SpO_2= Pulse Oxymetry, FiO_2= Oxygen Inspiratory Fraction, LOS=Lenght of stay, CPAP= Continuous Positive Airways Pressure, NIV= Non Invasive Ventilation.

Table 2. Perceived dyspnoea and leg fatigue.

	DYSPNOEA	LEG FATIGUE
At rest, Borg score	0 (0-1)	0 (0-1)
During ADL, Borg score	0.5 (0-2)	1 (0-2)
During ADL, % of patients with Borg Score ≥ 3	17	20
At the end of 1min-STS, Borg scale	3 (2-5)	1 (0-3)
At the end of 1min-STS, % of patients with Borg Score ≥3	70	29

Legend: Data are described as median and interquartile range. ADL= Activities of Daily Living, 1min-STS= 1 minute Sit to Stand**.**