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# Pulmonary rehabilitation improves functional outcomes and quality of life in post-SARS-CoV-2 mild-to-moderate infection patients: a pilot study

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**Abstract**

SARS-CoV-2 infection impairs functional outcomes and quality of life, even in its mild-to-moderate form. It is therefore appropriate to draw attention to the role played by respiratory rehabilitation and physiotherapists in the pulmonary rehabilitation process that post-SARS-CoV-2 patients must undergo**.** We enrolled 80 patients in a prospective case-control study; 40 cases (mild-to-moderate post-SARS-CoV-2 infection patients) and 38 control subjects (i.e., patients affected by other respiratory diseases) completed the same full pulmonary rehabilitation cycle. 6 Minute Walking Distance, Borg CR10 Scale, modified Medical Research Council (mMRC) Dyspnoea scale, EuroQoL EQ-5D-3L questionnaire, Barthel scale, arterial blood gas test and peripheral oxygen saturation (SpO2) were compared for all patients before and after rehabilitation. All patients experienced significant improvements in all parameters analyzed, except for arterial blood gas test. Results were similar for both groups, in particular both groups experienced improvements in mMRC scale, EuroQoL questionnaire, Barthel scale and 6-minute walking distance. Pulmonary rehabilitation appears to improve exercise tolerance, dyspnea and quality of life in patients recovering from mild-to-moderate SARS-CoV-2 infection. Further studies are needed on larger sample size population to validate these results.

**Keywords:** pulmonary rehabilitation, SARS-CoV-2, quality of life, COVID-19, physical activity.

## Introduction

On 11 March 2020, the WHO declared the COronaVIrus Disease 19 (COVID-19) epidemic to be a pandemic. SARS-CoV-2 patients present with respiratory tract infections and flu-like symptoms such as fever, cough, fatigue, sputum production, dyspnoea, sore throat and headache with a clinical picture ranging from mild, with upper respiratory tract involvement, to severe, with life-threatening pneumonia pictures [1]. Given the high level of intensive medical management required by the most severe patients, it is also appropriate to consider the high risk of sequelae to which this cluster of patients are exposed: asthenia, dyspnoea, fatigue and muscle weakness. It is therefore appropriate to draw attention to the role played by respiratory rehabilitation and physiotherapists in the pulmonary rehabilitation process that post-COVID19 patients must undergo [1-6]. In fact, it is necessary to incorporate physical, aerobic and/or resistance training into the rehabilitation sessions, and to assess how these exercises improve the quality of life related to the perception of health and the dyspnoea symptom [1]. Post-COVID-19 functional impairment may compromise an individual's ability to perform activities of daily living, increase the dyspnoea symptom, reduce motor function, alter occupational performance, and hinder social interaction [7]. Facilities must readjust their strategies to address physical, functional and social recovery through pulmonary rehabilitation [8]; in this regard, online exercise rehabilitation videos have been suggested [9], even in COPD patients [10], and robot-assisted rehabilitation has also been proposed [11]. The aim of this prospective cohort study is to demonstrate that physical activity as part of the respiratory rehabilitation of patients with previous SARS-CoV-2 infection is an important strategy to improve the functional respiratory capacity and quality of life of patients, compared with a group of respiratory patients who were not infected with SARS-CoV-2.

## Materials and Methods

The following is an observational prospective case-control study in which two groups of patients were considered: a heterogeneous group of patients with respiratory diseases such as COPD and pulmonary fibrosis (control subjects) and a group of patients with previous mild-to-moderate (i.e., not requiring ICU admission) SARS-CoV-2 infection (cases). Study was conducted at two facilities: Ambulatorio 'La Madonnina' (Reggio Calabria, Italy) and A.S.D. Palestra Planet Sport in Rizziconi (Reggio Calabria, Italy) without any commercial purpose (non-profit) and incorporates data obtained from the accesses made by individual patients in the period between July 2021 and February 2022. The data were obtained from internal

databases and with a digital platform, after obtaining informed consent in accordance with current regulations on privacy and the sharing of sensitive data for scientific purposes. All patients in the abovementioned facility underwent a complete respiratory rehabilitation cycle lasting at least 24 consecutive days (one 120-minute session each day, weekends excluded), led by professional physiotherapists specialized in pulmonary rehabilitation and performed in a dedicated gymnasium; both groups underwent the same rehabilitation program, including respiratory gymnastics, pulmonary rehabilitation devices and exercises enhancing the mobilization of pulmonary secretions. The following parameters were monitored at the beginning and end of the treatment: 6 Minute Walk Distance (6MWD) [12], Borg CR10 Scale (license agreement #18CJP63), modified Medical Research Council (mMRC) Dyspnoea Scale (used with the permission of the Medical Research Council), EuroQol EQ-5D-3L questionnaire (registration No. 53534), Barthel scale (used with permission) [13], arterial blood gas (ABG) analysis and pulse oxymetry (SpO2).

Mild-to-moderate SARS-COV2-infected patients with good functional independence and motivation were recruited and underwent intensive respiratory physiotherapy. Mild-to-moderate disease was defined as individuals with an established SARS-CoV-2 infection showing related signs and symptoms (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) and/or a radiological/clinical evidence of lower respiratory disease, having an oxygen saturation measured by SpO2 ≥94% on room air at sea level [14]. A total of 80 persons (40 with previous SARS-COV2 infection and 40 control subjects with other respiratory disesase, including COPD and interstitial lung diseases, but without ever having contracted the infection) underwent the study, taking into consideration as primary endpoint the meters travelled at the 6-minute walking test (6MWD) and the score obtained on the mMRC dyspnoea scale and how these improved after undergoing a full cycle of respiratory rehabilitation. Secondary endpoints included the comparison at the end of the rehabilitation course of objective improvement the Borg scale, the Barthel dyspnoea index and the EuroQoL; ABG test and SpO2 (both measured at rest) were also evaluated. All parameters were detected at the beginning and at the end of the study (i.e. before the first rehabilitation session and after the last one).

Inclusion criteria for the cases were: a previous established SARS-CoV-2 infection (patients with mild-to-moderate disease undergoing previous short hospitalization and standard drug therapy, Borg Scale >=3, mMRC 3-4. Mild disease is defined as mild symptoms without radiological manifestations of pneumonia [14].

Exclusion criteria for all patients included: potential symptoms of other infection (e.g. fever) within 4 weeks prior to enrollment, long-term oxygen therapy, uncontrolled hypertension and/or heart rate, history of arrhythmias or myocardial infarction within 3 months prior to enrollment. In addition, known respiratory disease was an exclusion criterion for the case group. Statistical analysis was performed on the GraphPad Prism platform (GraphPad Software Incorporated, California, U.S.A.). All data are expressed as mean ± standard deviation for continuous variables and as percentage for categorical variables. A p-value $<0.05$ was considered significant for all tests.

**Results**

A total of 80 patients were enrolled (40 cases and 40 control subjects); unfortunately, 2 control patients were excluded due to not having completed the rehabilitation sessions. The cases were younger at the time of evaluation (68.0±10.7 vs. 73.7±9.3, p=0.015), whereas the male/female ratio showed no significant differences between the two groups (p=0.648). Both cases and the control subjects groups had the same type of perception of the symptom dyspnoea (mMRC score, p=0.785), although the cases had better values at the ABG analysis, resting SpO2 and travelled greater distances at 6MWT (233.8 m ± 95.7 vs. 137.4 m ± 100.3, p=0.001). In addition, the cases had slightly lower Borg scores after exertion (8.1 ± 1.3 vs. 9.0 ± 1.1, p=0.006). No significant differences were observed in the EuroQoL and Barthel dyspnoea questionnaire scores. It is possible to see how there is an improvement in the score of the mMRC scale between cases and controls (-1.6 ± 0.8 $p<0.001$ -1.4 ± 0.7 $p<0.001$), of the Borg CR10 scale (-6.4 ± 1.3 $p<0.001$ -6.7 ± 1.0 $p<0.001$), of the EuroQoL (+42.4 ± 13.8 $p<0.001$ +38.6 ± 14.4 $p<0.001$), of the Barthel dyspnoea index (-27.3 ± 13.0 $p<0.001$ -25.5 ± 12.9 $p<0.001$) and of the 6-minute walk test in terms of distance covered measured in meters walked (+120.5 ± 64.7 $p<0.001$ +86.4 ± 65.3<0.001). It is possible to assess how there is an improvement in statistically significant terms ($p<0.001$) in the data under study (Table 1 and Table 2).

**Discussion**

Post-infection functional impairment by SARS-CoV-2 can affect an individual's ability to perform activities of daily living, increase dyspnoea, reduce motor function, impair occupational performance, and hinder social interaction. Rehabilitation for mild disease can be managed on an outpatient basis, using telemedicine, spas or in a gymnasium [15]. In mild forms of the disease, pulmonary rehabilitation may be considered and include education, airway clearance techniques, exercise, breathing exercises, activity guidance and anxiety management;

in addition, patients should be educated about the clinical course of SARS-CoV-2 infection [16]. Prolonged hospitalization (with or without the use of mechanical ventilation) can have deleterious pulmonary, cardiovascular, muscular, and cognitive effects (such as anxiety and depression); therefore, early mobilization is essential for the recovery of patients with previous SARS-CoV-2 infection; many of these patients show a rapid drop in oxygen saturation at the beginning of the recovery phase, which limits early rehabilitation to some extent. Physical exercises must be adapted to the individual needs and limitations of the patients; symptoms during exercise (such as dyspnoea, desaturation and fatigue) should be considered; high-intensity exercises are not indicated; patients should receive instruction on the physical, psycho-emotional, and nutritional aspects of each phase of rehabilitation [17]. Studies in the literature show that respiratory rehabilitation increases exercise capacity, muscle strength and health-related quality of life in many populations with respiratory disease, in fact, the 2020 Consensus Statement by Barker-Davies et al. states that exercise is necessary in post-COVID19 patients, in particular, the National Institute for Health and Care Excellence (NICE) recommends starting rehabilitation programs when patients are still in the post-acute phase, i.e. within 30 days, in order to achieve maximum functional recovery [18]. It has been reported that post-COVID19 patients may have an impaired functional status when discharged home, even after early mobilization especially in the geriatric population [19], however, a study carried out by the IRCSS Maugeri showed that more distance was covered (in meters) at the six-minute walk test and an improvement in the questionnaires (in particular the Barthel Index) in a group of patients enrolled in the study screened by means of the Short Physical Performance Battery (SPPB), Barthel Index and 6MWD demonstrated that exercise training leads to an objective improvement in the above-mentioned assessment scales [5]. The latter study corroborates the data examined in our prospective cohort study (Barthel dyspnoea Cases group: -27.3 ± 13.0 p-value<0.001, Control subjects' group: -25.5 ± 12.9; p-value<0.001). No statistically significant blood gas values' differences were found for the two groups. The data with reference to SpO2 resulted from the fact that one of the two groups had a younger subpopulation being tested. The improvement in the cases data might also be due to the fact that the test population had a lower average age than the control group.

The study conducted, despite the statistical significance of the data, has several limitations, in fact the sample size is small (total of 78 cases enrolled), the pairing of the two groups was not carried out due to difficulties and problems during the recruitment phase and there is a heterogeneity of the sample in the control group (patients with COPD and pulmonary fibrosis), which present different clinical and pathophysiological characteristics. Furthermore, we did not

collect any spirometry data due to logistical reasons. Finally, recruitment bias (i.e., patients who agree to participate in the study might be different from those who do not) might have affected our results. Nevertheless, the data are encouraging and new prospective randomized controlled trials on similar population groups are desired (especially including spirometry data) to better define the role of respiratory rehabilitation in patients with previous SARS-CoV-2 infection.

## Conclusions

Pulmonary rehabilitation is apparently associated with improvements in exercise tolerance, dyspnea and quality of life in patients who recently suffered from mild-to-moderate SARS-CoV-2 infection. These results, compared to those obtained in a control group, appear to be similar and encouraging. Further studies are needed on larger sample size population (possibly adding spirometry data) to validate these results.

## References


1. Grigoletto I, Cavalheri V, F de Lima F, Cipulo Ramos EM. Recovery after COVID-19: The potential role of pulmonary rehabilitation. Braz J Phys Ther 2020;24:463–4.
2. Polastri M, Nava S, Clini E, et al. COVID-19 and pulmonary rehabilitation: preparing for phase three. Eur Respir J 2020;55:2001822.
3. Curci C, Pisano F, Bonacci E, et al. Early rehabilitation in post-acute COVID -19 patients: data from an Italian COVID -19 Rehabilitation Unit and proposal of a treatment protocol. Eur J Phys Rehabil Med 2020;56:633-41.
4. Glöckl R, Buhr-Schinner H, Koczulla AR, et al. [DGP-Empfehlungen zur pneumologischen Rehabilitation bei COVID-19].[Article in German]. Pneumologie 2020;74:496-504.
5. Zampogna E, Paneroni M, Belli S, et al. Pulmonary rehabilitation in patients recovering from COVID-19. Respiration 2021;100:416-22.
6. Wang TJ, Chau B, Lui M et al. Physical medicine and rehabilitation and pulmonary rehabilitation for COVID-19. Am J Phys Med Rehabil 2020;99:769-74.
7. Orzes N, Pini L, Levi G, et al. A prospective evaluation of lung function at three and six months in patients with previous SARS-COV-2 pneumonia. Respir Med 2021;186:106541.
8. Santana AV, Fontana AD, Pitta F. Pulmonary rehabilitation after COVID-19. J Bras Pneumol 2021;47:e20210034.
9. Ismail AMA. Cancelled elderly exercise sessions during the COVID-19 crisis: can physical therapists help from their homes? Eur J Physiother 2020;22:235.
10. Ismail AMA. Online exercise rehabilitation to stable COPD patients during the second COVID wave: are physiotherapists able to help? Adv Rehabil 2020;34:48-9.

11. Ismail AMA. Robot-assisted rehabilitation: it is the time for utilisation in in-patient health care facilities to maintain the activity of the elderly during the COVID-19 pandemic. Int Marit Health 2021;72:80-1.
12. Pini L, Montori R, Giordani J et al. Assessment of respiratory function and exercise tolerance at 4–6 months after COVID-19 infection in patients with pneumonia of different severity. Intern Med J 2023;202-8.
13. Mahoney FI, Barthel D. Functional evaluation: the Barthel Index. Md State Med J 1965;14:56-61.
14. National Institutes of Health. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. Accessed on: 12 March 2023. Available from: https://www.covid19treatmentguidelines.nih.gov/
15. Antonelli M, Donelli D. Respiratory rehabilitation for post-COVID19 patients in spa centers: first steps from theory to practice. Int J Biometeorol 2020;64:1811-3.
16. Wade DT. Rehabilitation after COVID-19: an evidence-based approach. Clin Med (Lond) 2020;20:359-65.
17. Sun T, Guo L, Tian F, et al. Rehabilitation of patients with COVID-19. Expert Rev Respir Med 2020;14:1249-56.
18. Barker-Davies RM, O'Sullivan O, Senaratne KPP et al. The Stanford Hall consensus statement for post-COVID-19 rehabilitation. Br J Sports Med 2020;54:949-59.
19. Yang YC, Chou CL, Kao CL. Exercise, nutrition, and medication considerations in the light of the COVID pandemic, with specific focus on geriatric population: A literature review. J Chin Med Assoc 2020;83:977-80.

**Table 1:** Demographics. All data are reported as mean ± standard deviation.

| | Cases (post-COVID) n=40 | Control subjects N=38 | p-value |
|---|---|---|---|
| Males | 24 (60%) | 20 (53%) | 0.648 |
| Age (years) | 68.0 ± 10.7 | 73.7 ± 9.3 | 0.015 |
| | | | |
| SpO2 baseline (%) | 94.6 ± 5.8 | 92.9 ± 3.1 | <0.001 |
| SpO2 post rehab (%) | 97.0 ± 2.3 | 97.2 ± 1.4 | 0.739 |
| | | | |
| pH baseline | 7.44 ± 0.04 | 7.41 ± 0.05 | 0.001 |
| pH post rehab | 7.44 ± 0.04 | 7.42 ± 0.05 | 0.011 |
| PaO2 baseline (mmHg) | 69.1 ± 18.6 | 62.6 ± 9.8 | 0.141 |
| PaO2 post rehab (mmHg) | 74.0 ± 12.0 | 70.7 ± 10.6 | 0.080 |
| PaCO2 baseline (mmHg) | 36.6 ± 8.8 | 44.1 ± 7.0 | <0.001 |
| PaCO2 post rehab (mmHg) | 36.6 ± 6.9 | 40.7 ± 7.3 | 0.008 |
| HCO3 baseline (mmol/L) | 25.3 ± 3.3 | 26.3 ± 3.0 | 0.010 |
| HCO3 post rehab (mmol/L) | 25.4 ± 3.1 | 25.6 ± 2.9 | 0.143 |
| | | | |
| mMRC baseline | 3.5 ± 0.8 | 3.5 ± 0.7 | 0.785 |
| mMRC post rehab | 1.9 ± 1.0 | 2.1 ± 0.9 | 0.322 |
| Borg scale baseline | 8.1 ± 1.3 | 9.0 ± 1.1 | 0.006 |
| Borg scale post rehab | 2.1 ± 1.4 | 2.6 ± 1.8 | 0.168 |
| EUROQoL baseline | 34.1 ± 12.7 | 35.4 ± 11.4 | 0.406 |
| EUROQoL post rehab | 76.5 ± 16.8 | 74.6 ± 13.2 | 0.278 |
| Barthel dyspnea baseline | 47.2 ± 18.1 | 48.3 ± 16.1 | 0.844 |
| Barthel dyspnea post rehab | 19.9 ± 18.6 | 22.3 ± 16.3 | 0.231 |
| | | | |
| 6MWT distance baseline (m) | 233.8 ± 95.7 | 137.4 ± 100.3 | 0.001 |
| 6MWT distance post rehab (m) | 316.2 ± 111.5 | 223.1 ± 106.8 | 0.001 |

SpO2**:** peripheral oxygen saturation. Rehab: rehabilitation. mMRC: modified Medical Research Council scale. 6MWT: 6-minute walking test.

**Table 2:** variations of parameters collected between baseline and post rehabilitation. All data are reported as mean ± standard deviation.

| | Cases (post-COVID) N=40 | p-value | Control subjects N=38 | p-value |
|---|---|---|---|---|
| SpO2 (%) | +2.5 ± 5.8 | 0.005 | +4.3 ± 3.3 | <0.001 |
| | | | | |
| pH | 0.00 ± 0.05 | 0.629 | 0.00 ± 0.1 | 0.588 |
| PaO2 (mmHg) | +4.9 ± 18.8 | 0.056 | +8.1 ±12.2 | <0.001 |
| PaCO2 (mmHg) | 0.0 ± 6.4 | 0.978 | -3.3 ± 4.7 | <0.001 |
| HCO3 (mmol/L) | +0.1 ± 2.9 | 0.703 | -0.3 ± 3.4 | 0.399 |
| | | | | |
| mMRC | -1.6 ± 0.8 | <0.001 | -1.4 ± 0.7 | <0.001 |
| Borg scale | -6.4 ± 1.3 | <0.001 | -6.7 ± 1.0 | <0.001 |
| EUROQoL | +42.4 ± 13.8 | <0.001 | +38.6 ± 14.4 | <0.001 |
| Barthel dyspnea | -27.3 ± 13.0 | <0.001 | -25.5 ± 12.9 | <0.001 |
| 6MWT distance (m) | +120.5 ± 64.7 | <0.001 | +86.4 ± 65.3 | <0.001 |

SpO2**:** peripheral oxygen saturation. Rehab: rehabilitation. mMRC: modified Medical Research Council scale. 6MWT: 6-minute walking test.