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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. Therefore, it is 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 category-ratio 10 scale, modified Medical Research Council (mMRC) dyspnea scale, European quality of life 5-dimensions-3-level (EuroQoL EQ-5D-3L) questionnaire, Barthel scale, arterial blood gas test, and peripheral oxygen saturation were compared for all patients before and after rehabilitation. All patients experienced significant improvements in all parameters analyzed, except for the arterial blood gas test. Results were similar for both groups; in particular, both groups experienced improvements in the mMRC scale, EuroQoL EQ-5D-3L questionnaire, Barthel scale, and 6-minute walking distance. Pulmonary rehabilitation appears to improve exercise tolerance, dyspnea, and quality of life in patients recovering from a mild-to-moderate SARS-CoV-2 infection. Further studies are needed on a larger sample size population to validate these results.

Introduction

On March 11, 2020, the World Health Organization 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, dyspnea, 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 is exposed: asthenia, dyspnea, fatigue, and muscle weakness. It is therefore appropriate to draw attention to the role played by respiratory rehabili-

tation and physiotherapists in the pulmonary rehabilitation process that post-COVID-19 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 dyspnea symptom [1]. Post-COVID-19 functional impairment may compromise an individual's ability to perform activities of daily living, increase the dyspnea 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 chronic obstructive pulmonary disease (COPD) patients [10], and robot-assisted rehabilitation has also been proposed [11]. This prospective cohort study aims 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 a previous mild-to-moderate (*i.e.*, not requiring intensive care unit admission) SARS-CoV-2 infection (cases). The study was conducted at two facilities: *Ambulatorio "La Madonnina"* in Reggio Calabria (Italy) and *A.S.D. Palestra Planet Sport* in Rizziconi (Reggio Calabria, Italy) without any commercial purpose (non-profit) and incorporated 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 following current regulations on privacy and the sharing of sensitive data for scientific purposes. All patients in the abovementioned facilities 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 category-ratio 10 scale (license agreement #18CJP63), modified Medical Research Council (mMRC) dyspnea scale (used with the permission of the Medical Research Council), European quality of life (EuroQol) 5-dimensions-3-level questionnaire (registration No. 53534), Barthel scale (used with permission) [13], arterial blood gas (ABG) analysis and pulse oxymetry [peripheral oxygen saturation (SpO2)].

Mild-to-moderate SARS-CoV-2-infected patients with good functional independence and motivation were recruited and underwent intensive respiratory physiotherapy. The 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-CoV-2 infection and 40 control subjects with other respiratory diseases, including COPD and interstitial lung diseases, but without ever having contracted the infection) underwent the study, taking into consideration as the primary endpoint the meters traveled at the 6MWD test, and the score obtained on the mMRC dyspnea 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 of the Borg scale, the Barthel dyspnea index, and the EuroQoL; the 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 previously 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 another infection (*e.g.*, fever) within four weeks before enrollment; long-term oxygen therapy; uncontrolled hypertension and/or heart rate; history of arrhythmias or myocardial infarction within three months before 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, USA). All data are expressed as mean ± standard deviation for continuous variables and as percentages for categorical variables. A $p<0.05$ 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 *versus* 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 subject groups had the same type of perception of the symptom dyspnea (mMRC score, p=0.785), although the cases had better values at the ABG analysis, resting SpO2, and traveled greater distances at the 6-minute walking test (6MWT) (233.8±95.7 m *versus* 137.4±100.3 m, p=0.001). In addition, the cases had slightly lower Borg scores after exertion (8.1±1.3 *versus* 9.0±1.1, p=0.006). No significant differences were observed in the EuroQoL and Barthel dyspnea 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 category-ratio 10 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 dyspnea index (-27.3±13.0, $p<0.001$; -25.5±12.9, $p<0.001$) and the 6MWT in terms of distance covered measured in meters walked (120.5±64.7, $p<0.001$; 86.4±65.3, $p<0.001$). It is possible to assess how there is an improvement in statistically significant terms ($p<0.001$) in the data under study (Tables 1 and 2).

Discussion

Post-infection functional impairment by SARS-CoV-2 can affect an individual's ability to perform activities of daily living,

increase dyspnea, 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 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 the 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 a 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.

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

	Cases (post-COVID-19) 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; PaO2, partial arterial pressure of oxygen; PaCO2, partial arterial pressure of carbon dioxide; HCO3, bicarbonate; rehab, rehabilitation; mMRC, modified Medical Research Council scale; EUROQoL, European quality of life questionnaire; 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-19) 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; PaO2, partial arterial pressure of oxygen; PaCO2, partial arterial pressure of carbon dioxide; HCO3, bicarbonate; rehab, rehabilitation; mMRC, modified Medical Research Council scale; EUROQoL, European quality of life questionnaire; 6MWT, 6-minute walking test.

Physical exercises must be adapted to the individual needs and limitations of the patients; symptoms during exercise (such as dyspnea, desaturation, and fatigue) should be considered; high-intensity exercises are not indicated, and 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 for post-COVID-19 patients; in particular, the National Institute for Health and Care Excellence recommends starting rehabilitation programs when patients are still in the post-acute phase, *i.e.*, within 30 days, to achieve maximum functional recovery [18].

It has been reported that post-COVID-19 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 m) at the 6MWT 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, 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 dyspnea cases group: -27.3±13.0, $p<0.001$; control subjects' group: -25.5±12.9, $p<0.001$). No statistically significant blood gas value differences were found for the two groups. The data concerning SpO2 resulted from the fact that one of the two groups had a younger subpopulation being tested. The improvement in the case 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 (a total of 78 patients 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 presents 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 a 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 a 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. Pneumologie 2020;74:496-504. [Article in German].
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;14:61-5.
14. National Institutes of Health. Coronavirus disease 2019 (COVID-19) treatment guidelines. Available from: https://www.covid19treatmentguidelines.nih.gov/. Accessed on: 12/03/2023.
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.