

Exercise reconditioning in the post-acute phase of COVID-19 rehabilitation in patients with chronic respiratory insufficiency: a retrospective observational study

Mariapina RASI¹; Francesca RUBINO¹; Gianluca BATTAGLIA¹; Carmela BONOMO¹; Concetta SORCE¹; Giuseppe ENEA^{2*}

1. Fondazione Istituto San Raffaele G. Giglio di Cefalù, Unità funzionale di riabilitazione cardiorespiratoria - UOC di Riabilitazione
2. IRCCS – ISMETT (Istituto Mediterraneo per i Trapianti e Terapie ad alta specializzazione), Rehab Service

* Corresponding author.

E-mail address: genea@ismett.edu; pippoenea@gmail.com

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COVID-19, post-COVID pathology syndrome, exercise reconditioning, respiratory insufficiency, rehabilitation.

ABSTRACT

Introduction:

The COVID-19 pandemic had a profound impact on a global scale, affecting various aspects of society, health, and well-being. It has strained healthcare systems and led to social and welfare repercussions. In the context of post-acute COVID-19 rehabilitation, there is a need to explore effective interventions for individuals, particularly those with chronic respiratory insufficiency. This study aims to evaluate the effectiveness of exercise reconditioning as a rehabilitation strategy in this specific population.

Methods:

A retrospective observational study was conducted at the “G. Giglio Institute Foundation’s Rehabilitation Operative Unit” in Cefalù (Palermo) between March 2020 and May 2022. The study included individuals who had been diagnosed with COVID-19 pneumonia, required hospitalization in the COVID-19 unit or intensive care unit (ICU) due to severe respiratory failure and with “post-COVID pathology syndrome” (PCS) picture. Various assessments (6MWT; FiO₂; FIMM; Borg dyspnea and fatigue score; mMRC; PaO₂ and PaCO₂) were conducted to determine exercise capacity. A personalized reconditioning program based on international guidelines was designed for each patient, focusing on aerobic training. Measurements of vital signs were taken during training sessions.

Results:

A total of 24 individuals, with a mean age of 65.41 years, were included in the study. The average duration of hospitalization in the rehabilitation department was 53.17 days. Most participants had pre-existing respiratory and non-respiratory pathologies. All individuals developed COVID-19 interstitial pneumonia, and some required intensive interventions such as intubation or ECMO support. Pulmonary fibrosis and Critical Illness Myopathy (CIM) were observed in a significant portion of the participants. Significant improvements were observed in the 6MWT distance traveled, Functional Independence Measure (FIM) scale score, fraction of inhaled oxygen (FiO₂), and dyspnea scores. Perceived exertion measures also showed positive changes.

Discussion and conclusion:

The findings of this study indicate that personalized reconditioning plan is effective in improving the functional capacity and overall condition and quality of life of individuals with post-COVID pathology syndrome. These findings highlight the importance of an interdisciplinary approach and tailored rehabilitation programs in this population. Further research is needed to explore the long-term effects of exercise reconditioning in this population.

INTRODUCTION

The COVID-19 pandemic had a significant global impact, leading to profound social and welfare repercussions and placing immense strain on healthcare systems worldwide (WHO - World Health Organization, n.d.). The epidemiological data from the World Health Organization (Health Emergency Dashboard, 29 July 2022) reaffirm the magnitude of the pandemic, with 600,555,262 confirmed cases and 6,472,914 deaths reported globally as of

September 2022 (Ministero della salute, n.d.). In Italy, the Ministry of Health and the “Istituto Superiore di Sanità” monitored the situation through the establishment of a “Control and Monitoring Cabin” during Phase 2 (Decr. Min. Health of 30 April 2020), providing weekly reports on variables such as the RT index (time-varying reproductive number), ICU (Intensive care unit) bed occupancy rates, vaccinations, and the number of infected individuals (Ministero della salute, n.d.). The pathogenesis of COVID-19 typically involves distinct phases,



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starting with initial contact and progressing to the development of clinical manifestations, including pneumonia and, in some cases, severe pulmonary conditions (Ministero della Salute - Istituto Superiore di Sanità, 2021; Tomà, 2021). The final stage can manifest as Adult Respiratory Distress Syndrome (ARDS) or, in some cases, disseminated intravascular coagulation. Additionally, the SARS-CoV-2 virus can lead to a persistent condition known as Post-COVID Pulmonary Fibrosis (PCPF), even (WHO - World Health Organization, n.d.) after recovering from the initial infection. PCPF, observed in approximately one-third of ARDS cases associated with COVID-19, is characterized by “Diffuse Alveolar Damage” (DAD) and is influenced by the duration of infection (George et al., 2020; Rai et al., 2021). It is highlighted how the COVID-19 pandemic period has led to the development of new protocols and knowledge in imaging diagnostics (Nicolò et al., 2023; Spanò et al., 2020).

COVID-19 is a systemic and multiorgan disease with diverse symptoms that can result in a chronic condition known as “post-COVID pathology syndrome” (PCS) or “Long COVID.” At the moment, with the studies available, it seems that the distinction between post COVID and long COVID is very blurred, due to a temporal evaluation only (between 12 and 24 weeks for the first condition and over 24 weeks for the second). (Mumoli et al., 2021) proposed that the terminology should be maintained simple (e.g., acute and persistent Covid-19 vs. long Covid) based on a strict temporal cut-off (i.e., less or more than the 12 weeks). These clinical manifestations extend beyond respiratory symptoms and can involve multiple organs, presenting with both general and specific symptoms. Common symptoms include persistent fatigue, asthenia, fever, widespread pain (muscles and joints), and decreased (Bagnato et al., 2021; Vitacca et al., 2022). An interdisciplinary approach is essential in defining a personalized rehabilitation program in the post-acute phase of COVID-19 rehabilitation (American College of Sports Medicine et al., 2018; Paneroni et al., 2022).

The initial phase of the recovery pathway for patients with severe illness is often established in the ICU, where recovery goals are established. In the ICU, the focus is on optimizing mechanical ventilation and oxygen therapy (including ventilatory settings, C-pap, high-flow nasal cannula, or facemask/nasal cannula). The initial steps aim to improve respiratory function and ventilation-perfusion ratios through mobilization techniques (e.g., prone or supine-seated positions) and, if possible, weaning from respiratory support. From a functional perspective, early mobilization and muscle strengthening are crucial to overcome muscle weakness and enable standing and walking. Subsequently, during the post-acute phase, symptoms related to chronic respiratory insufficiency or exercise deconditioning may persist. These patients are typically referred to the Rehabilitation department for ongoing physical therapy. The objective of this study is to evaluate the effectiveness of exercise reconditioning in PCS rehabilitation with respect to predefined outcomes.

METHODS

The retrospective observational study was conducted at the “G. Giglio Institute Foundation’s Rehabilitation Operative Unit” in Cefalù (Palermo) between March 2020 and May 2022. The analysis was based on recorded data from medical records. The inclusion criteria were as follows:

- Negative molecular swab for SARS-CoV-2.
- Diagnosis of COVID-19 pneumonia with bilateral interstitial pneumonia confirmed by chest CT scan (Bagnato et al., 2021; Rai et al., 2021).
- Hospitalization in a COVID-19 ordinary inpatient unit or COVID-19 intensive care unit (ICU) due to severe respiratory failure treated with O₂-therapy, mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).
- Presence of chronic respiratory insufficiency, regardless of the need for O₂-therapy at low flows, high flows, and/or mechanical ventilation (invasive and non-invasive).
- PCS

The exclusion criteria were defined as follows:

- Severe neurological damage resulting in only partially recoverable residual disability following COVID-19 infection.
- Pre-existing orthopedic limitations (e.g., joint blocks).
- Pre-existing neuromuscular pathology prior to COVID-19 infection.

Some of the patients included in the study developed Critical Illness Myopathy (CIM) or Critical Illness Polyneuropathy (CIP), which led to reduced functional autonomy in activities of daily living. These patients received personalized treatments aimed at muscle recruitment and strengthening, verticalization, and walking training to regain their autonomy. In some cases, they also benefited from robotic therapy using devices such as Erigo (Garlet et al., 2022) or Hunova (Saglia et al., 2019). Subsequently, the patients underwent re-adaptation to effort and aerobic training. The recovery pathway for aerobic training began with an initial multidisciplinary evaluation by a team of pulmonologists, geriatricians, cardiologists, neurologists, physiotherapists, nurses, and neuropsychologists. The physiotherapy assessment included the use of the following rating scales to determine exercise capacity:

- 6 Minutes Walking Test (6MWT) to measure the distance traveled in meters and as a percentage of the theoretical value (according to ATS guidelines for chronic respiratory disease) (“ATS Statement,” 2002).
- Modified Borg CR10 scale to assess fatigue and dyspnea during exertion (Peroy-Badal et al., 2024).
- mMRC scale to evaluate dyspnea (Peroy-Badal et al., 2024).

A personalized program was designed for each patient based on the FITT principles (frequency, intensity, time, and type) outlined in international guidelines for respiratory and cardiovascular rehabilitation (ATS/ERS (American Thoracic Society European Respiratory Society), 2020; Carlucci et



al., 2022; Paneroni et al., 2022; Rai et al., 2021). All sessions were supervised and continuously monitored. Aerobic training consisted of six days of physiotherapy per week, with a total duration of 150 minutes per day, divided between morning and afternoon sessions. The reconditioning methods used were based on the guidelines for chronic respiratory pathology and included interval training and/or endurance training, tailored to each patient's individual needs, initial assessment, and degree of respiratory and motor impairment. Patients with respiratory insufficiency at the time of admission received oxygen therapy based on medical indications and physiotherapy evaluation. The stratification for training was as follows:

- Less deconditioned subjects (without O₂ therapy on admission) or those with O₂ therapy at low flows and a slight to intermediate reduction in the distance traveled during the 6MWT compared to the theoretical value underwent endurance training (progressive training at a constant time and variable load).

- Subjects with severe ventilatory limitations and dyspnea that worsened during exercise (receiving high-flow oxygen therapy with a venturi-mask or high-flow nasal cannula) or those with a severe reduction in the 6MWT compared to the theoretical value followed an interval training program. This involved alternating periods of load with short periods of rest, while monitoring saturation and dyspnea during exercise to achieve an optimal training stimulus. The goal was to transition these patients to the endurance training reconditioning method once their respiratory symptoms allowed it.

The daily reconditioning program consisted of two sessions:

- Morning session: 30 minutes of aerobic training on a cycle ergometer, 30 minutes on a treadmill (including 5 minutes of warm-up and cool-down), and 30 minutes of "Motomed" upper limb exercises for endurance and muscle strength training.

- Afternoon session: 60 minutes of calisthenics exercises. The intensity of the reconditioning was determined based on the threshold of moderate to intense dyspnea (corresponding to a rating of 4-6 on the Borg CR10 scale) and moderate to intense muscular fatigue (4-6 on the Borg CR10 scale).

Measurements of heart rate, respiratory rate, blood pressure, and oxygen saturation were taken at the beginning and end of each training session. The minimum oxygen saturation (SPO₂) and maximum heart rate achieved during training were also recorded. Once the respiratory symptoms improved and the patient's general clinical condition, as assessed by the medical doctor through diagnostic tests such as blood gases, CT scans, and blood chemistry tests, indicated improvement, and weaning from oxygen therapy, mechanical ventilation, and tracheostomy, the patient was discharged to their home address. Upon discharge, the physiotherapy evaluation was repeated to assess the outcome indicators. The pri-

mary outcome measure was:

- Change in 6MWT compared to the baseline evaluation.

The secondary outcome measures included:

- Changes in the Functional Independence Measure (FIM) scale score (ranging from 18 to 126).

- Changes in the fraction of inhaled oxygen (FiO₂).

- Changes in PaO₂ and PaCO₂ values evaluated by blood gas analysis.

- Numerical changes in tracheostomized patients compared to admission.

- Total number of days spent in the rehabilitation ward.

- Variation in the modified Borg CR10 scale scores for fatigue (Borg F) and dyspnea (Borg D) during exercise.

- Change in the mMRC scale score for dyspnea.

All patient information was treated with complete privacy, and written consent for the use of data for scientific research purposes was obtained upon admission. Approval to perform this analysis was given by local ethics committee Palermo 1 (29 Jun. 2022)

STATISTICAL ANALYSIS

The statistical analysis was performed using IBM SPSS Statistics version 28 software. The sample size for the study was 24 individuals. Descriptive statistics were used to summarize the demographic and clinical characteristics of the study population. For the variable "days of hospitalization", the main statistical indices were calculated, although the specific values are provided in the text.

To assess whether there was a significant change in the parameters (FIM, 6MWT, mMRC, FiO₂, Borg F, Borg D, PaCO₂, and PaO₂) between admission and discharge, the non-parametric Wilcoxon test was applied. This choice was made because the sample size did not meet the minimum requirement for parametric tests (i.e., a sample size of at least 30). The Wilcoxon test is appropriate for analyzing paired data when the distributional assumptions for the t-test are not met. Furthermore, a delta variable was created for each parameter by calculating the difference between the value at discharge and the value at admission. This allows for the evaluation of the change in each parameter over time. To compare the distribution of the parameters between different subgroups (smokers vs. non-smokers, intensive care vs. non-intensive care, intubation vs. non-intubation, pulmonary fibrosis vs. non-pulmonary fibrosis, CIM vs. non-CIM), the non-parametric Mann-Whitney test was used. The Mann-Whitney test is appropriate for comparing independent groups when the assumptions for parametric tests are not met. A significance level of 0.05 was used for all analyses, indicating that a p-value less than 0.05 would be considered statistically significant.



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RESULTS

A total of 24 individuals (18 men, 6 women) aged 33 to 85 years with severe COVID-19 interstitial pneumonia were included in the study (Table 1). Respiratory risk factors, such as smoking and pre-existing pathologies, were observed in the participants. Notably, severe disease was primarily found in unvaccinated individuals, except for one

vaccinated. All subjects were admitted to the COVID-19 hospitalization unit from various hospitals in Palermo province.

The mean hospitalization duration in the rehabilitation department was 53.17 days, with a median of 41.50 days (SD 47.27). The participants had a range of pre-existing respiratory and non-respiratory pathologies, including COPD, pulmonary hypertension, emphysema, asthma, tuberculosis, and more (Table 2).

Table 1. Characteristics of the population under study

General characteristics	%
Gender (M%)	75%
Age (mean; SD)	65.41; 13.41pm
History of smoking (yes%)	41.6%
COVID-19 vaccination (yes%)	4.10%
Hospitalization in ICU (yes%)	54.10%
Intubation (yes%)	37.50%
ECMO (yes%)	12.5%
NIV (yes%)	66.6%
Pulmonary fibrosis (yes%)	70.3%
CIM (yes%)	66.6%
SPE lesion (yes%)	12.5%

Table 2- existing comorbidities in the population under study

Respiratory comorbidities not present at admission	%
Arterial hypertension	45.8
COPD	20.8
Diabetes	16.7
Arrhythmia	12.5
Hypertrophic prostatic	8.3
Dyslipidemia	8.3
Asthma	8.3
Obesity	8.3
IMA; / Heart disease ischemic chronic	8.3
Parkinson	4.2
OSAS	4.2
S. Guillain-Barre	4.2
Lung adenocarcinoma	4.2
Pneumomediastinum	4.2
Emphysema Bully	4.2



All individuals in the study developed COVID-19 interstitial pneumonia and required treatment for severe respiratory failure. ICU admission was necessary for 13 individuals, with nine requiring intubation and three receiving ECMO support (Table

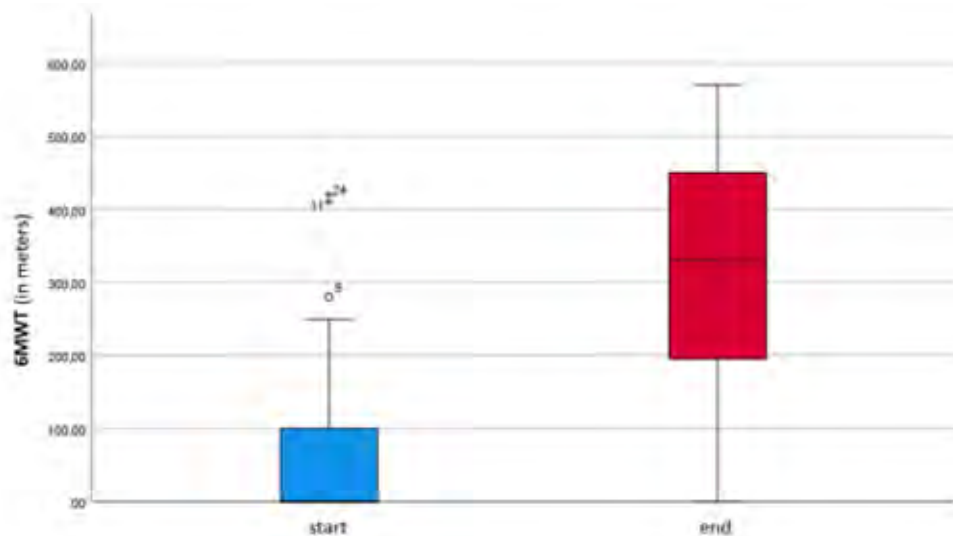
3). Pulmonary fibrosis was observed in 70.3% of the individuals based on CT examination, and 66.6% of the participants developed Critical Illness Myopathy (CIM) (Table 3).

Table 3 - summary table of outcomes

Outcomes	MEDIAN ENTRANCE (1st Q-3rd Q; SD)	MEDIAN RESIGNATION (1st Q-3rd Q; SD)	variation	P-VALUE
6MWT (in meters)	0 (0-110; 134.28)	330 (187.50-450; 166.77)	+330	<0.001
6MWT (% theoretical)	0 (0-25; 25.45)	61 (43-84.50; 29.72)	+61%	<0.001
FIMM (18 - 126)	87 (51.75-103.50; 31.49)	120 (106-126; 14.98)	+33	<0.001
mMRC (0 - 4)	4 (3-4; 089)	2 (0.25-2; 1.02)	-2	<0.001
FiO ₂ (21% - 100%)	25 (21-34.50; 12.57)	21 (21-21; 2.55)	-4	<0.001
Borg F (0 - 10)	10 (6.25-10; 2.82)	3 (2-5; 1.94)	-7	<0.001
Borg D (0 - 10)	10 (5.25-10; 2.72)	3 (1.25-5; 2.26)	-7	<0.001
PaCo2	37.4 (34.43-42.85; 6.45)	37.85 (34.75-41.93; 5.04)	+0.45	0.310
PaO2	74.5 (63.20-88; 15.52)	77.55 (73.15-85; 10.50)	+3.05	0.171

Significant improvements were observed in various outcome measures at discharge (Table 3). The 6MWT showed notable improvement in distance traveled and percentage of theoretical value adjusted for age. Functional evaluation indicated

substantial recovery and reduced need for supplemental oxygen therapy. Fatigue and dyspnea scores significantly decreased. Blood gas parameters, including PaO2 and PaCO2, remained stable.



Associations between outcome measures and population characteristics were explored (Table 4). Significant differences were found in the 6MWT parameter between smokers and non-smokers, as

well as in populations with and without pulmonary fibrosis. Regarding ICU hospitalization, a significant change was observed only in the Borg dyspnea parameter (Table 4).



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Table 4 - Outcome values in relation to study population variables

outcome / median	smoking	not smoking	P Value	ICU admission	NOT ICU admission	P Value	Intubated	NOT Intubated	P Value	fibrosis	NOT fibrosis	P Value	CIM	NOT CIM	P Value
6MWT (in meters)	150	315	0.019	290	180	0.569	170	190	0.815	290	120	0.047	235	170	0.653
6MWT (% theoretical)	24.5	58.50	0.011	54	41	1	25	46	0.379	54	25	0.075	47.5	37.5	0.976
MRC extension	-2	-2	0.172	-2	-2	0.392	-2	-2	0.726	-2	-2	0.418	-2	-1.5	0.383
Fio2	-2	-2	0.437	-8	0	0.252	-8	0	0.318	-4	-4	0.710	-6	0	0.132
Borg F	-5.5	-5.5	0.931	-6	-4	0.494	-7	-5	0.770	-6	-3	0.166	-5.5	-3	0.569
Borg D	-5.5	-5.5	0.403	-7	-3	0.047	-6	-4	0.558	-5	-2	0.234	-6	-2	0.045
PaCo2	0.6	-0.05	0.172	0.6	0.4	0.733	-0.4	0.6	0.084	0.6	0.3	0.288	-0.05	0.5	0.417
PaO2	1.25	0.9	0.879	2.95	0.4	0.151	4	0.9	0.325	0.65	5	0.413	1.6	0.65	0.519

DISCUSSION

The present study aimed to investigate the clinical characteristics and outcomes of individuals hospitalized with severe COVID-19 interstitial pneumonia in the post-acute phase of COVID-19 rehabilitation. Our findings shed light on various aspects related to the demographics, risk factors, comorbidities, treatment interventions, and functional recovery of these individuals. Regarding the demographic characteristics of our study population, there was a predominance of male participants, consistent with previous reports indicating a higher susceptibility of males to severe forms of COVID-19 (Wu et al., 2020). The age range of our participants was wide, reflecting the susceptibility of individuals across different age groups to COVID-19 infection. It is worth noting that all individuals included in our study had pre-existing pathologies, both respiratory and non-respiratory, which might have contributed to the severity of their illness and prolonged hospitalization. These findings highlight the importance of considering comorbidities in the assessment and management of PCS patients.

The clinical course of the disease in our study population was characterized by the development of severe respiratory failure, leading to hospitalization in the rehabilitation department. The majority of individuals required intensive care, with a significant proportion undergoing oro-tracheal intubation and ECMO support. This highlights the critical nature of their respiratory compromise and the need for advanced interventions to support their respiratory function. The occurrence of pulmonary fibrosis in a substantial proportion of individuals is noteworthy and aligns with previous studies reporting long-term pulmonary sequelae following severe COVID-19 pneumonia (George et al., 2020). The presence of CIM, observed in two-thirds of our population, further highlights the multisystem involvement and muscle weakness associated with critical illness in COVID-19 patients (Rodriguez et

al., 2022).

The functional outcomes assessed in our study demonstrated significant improvements in various measures between admission and discharge. Notably, the 6-minute walk test (6MWT), a widely used measure of functional capacity, showed a substantial increase both in terms of distance traveled and as a percentage of the theoretical value adjusted for age. This improvement reflects the positive impact of rehabilitation interventions on individuals' physical abilities and suggests a potential for functional recovery even in severe cases of COVID-19 pneumonia (Basak et al., 2022). The reduction in perceived dyspnea and fatigue, as indicated by the modified Medical Research Council (mMRC) and modified CR10 Borg scales, further supports the positive impact of rehabilitation in improving individuals' overall respiratory function and quality of life (Demoule et al., 2022).

Interestingly, we found no clinically significant variations in blood gas parameters, such as PaO₂ and PaCO₂, between admission and discharge. This can be attributed to the effective use of oxygen therapy and ventilation devices during the hospitalization period, which helped maintain adequate oxygenation and ventilation levels. It is noteworthy that the majority of individuals were able to be discharged without the need for respiratory aids, highlighting the positive outcomes achieved through comprehensive rehabilitation interventions.

Our study also explored the associations between outcomes and certain population characteristics. Significant differences were observed in the variation of the 6MWT parameter between smokers and non-smokers, indicating a potential impact of smoking on functional recovery (Alharthy et al., 2020). Additionally, the presence of pulmonary fibrosis was associated with a similar variation in the 6MWT, suggesting that the presence of fibrotic changes in the lungs may influence individuals' functional outcomes (Kızıllırmak et al., 2023). However, it is important to note that the small sample size limited the statistical power to

detect significant associations, and further studies with larger cohorts are warranted to validate these findings.

There are certain limitations to our study that should be acknowledged. Firstly, the small sample size restricts the generalizability of our findings to a larger population. Secondly, the lack of a control group limits our ability to compare the outcomes of COVID-19 pneumonia patients. Additionally, the retrospective nature of the study introduces potential biases and limitations in data collection. Future prospective studies with larger sample sizes and control groups are needed to further elucidate these findings. Despite accumulating a growing body of data on this patient population, providing safety and feasibility parameters for respiratory physiotherapy, it is important to share data with the scientific community, even as the current phase of reduced impact on the general population sees a continuous decline.

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CONCLUSIONS

The results obtained in this study are valuable; however, the limited sample size necessitates integrating the findings with data from other studies conducted in diverse geographical areas to validate the conclusions. The aggregation of data could also allow for stratification by age groups or other variables.

Based on the available data, we can already draw some conclusions regarding the efficacy of exercise reconditioning in the post-acute phase of COVID-19 rehabilitation. This approach has shown positive outcomes in terms of improving secondary respiratory conditions such as pneumonia and pulmonary fibrosis, as well as addressing motor disorders resulting from prolonged bed rest in medical or critical care settings. These findings suggest that exercise reconditioning can be effective in improving functional outcomes and reducing symptoms in individuals with post-acute COVID-19 syndrome and chronic respiratory insufficiency. The study highlights the importance of a multidisciplinary approach in the rehabilitation of these patients, involving various healthcare professionals.



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