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International Journal of Therapy and Rehabilitation

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--Manuscript Draft--

Manuscript Number:	ijtr.2021.0169R2
Article Type:	Original research
Keywords:	Covid-19; Dyspnoea; Handgrip strength; Maximal inspiratory pressure; Maximal expiratory pressure; Rehabilitation
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Conflicts of interest

The authors have no conflict of interest to declare.

Funding

No funding was received for this work.

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Abstract

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Methods We conducted a retrospective analysis based on prospectively collected data of 192 patients with COVID-19 undergoing a physiotherapeutic regimen during their hospitalisation. Patients were admitted because of COVID-19-related pneumonia from March 25th to June 12th 2020, and from November 2nd 2020 to June 9th 2021. This study investigated dyspnoea intensity using the modified Borg scale, motor function through the 1-minute sit-to-stand test, and daily walked distance. In a subset of 57 patients, we also evaluated handgrip strength and respiratory muscle function. Measurements were taken at baseline and discharge.

Results We classified spontaneously breathing patients according to their PaO_2/FiO_2 severity (mean 225±82 mmHg). At discharge to home or to another hospital facility, patients performed a mean of 12 repetitions (1-minute sit-to-stand test), dyspnoea intensity was 1.4 (modified Borg scale), and they were able to walk a mean distance of 266.7 metres. The mean handgrip strength of the dominant hand was 29.3 Kg, the maximal inspiratory pressure was 43.5 cmH_2O, and the maximal expiratory pressure was 59.1 cmH_2O. Overall, significant differences before and after treatment were detected for all clinical variables. Dyspnoea improved by 0.7 points; walked distance by 200 metres; the number of repetitions at the 1-minute sit-to-stand test by 5.6; the handgrip strength by 1.2 (right hand) and 1.7 Kg (left

hand); the maximal inspiratory pressure by 7.7 cmH_2O, and the maximal expiratory pressure by 9.5 cmH_2O.

Conclusions Patients obtained significant improvements in functional capacity, dyspnoea perception, handgrip strength, and respiratory muscle function. In addition, the treatment was feasible, well tolerated by patients, and no adverse related events were observed in a sub-intensive care setting.

Key words: COVID-19; Dyspnoea; Handgrip strength; Maximal inspiratory pressure; Maximal expiratory pressure; Rehabilitation

INTRODUCTION

As of May 2022, the novel coronavirus disease 2019 (COVID-19) pandemic has caused more than 6 291 947 deaths worldwide (European Centre for Disease Prevention and Control, 2022), including healthcare workers (Nava et al, 2020). At the beginning of the pandemic, little information was available regarding the feasibility of physiotherapy in patients with COVID-19 (Polastri, 2020). One of the primary concerns was: is rehabilitation feasible at an early stage in patients with COVID-19? Which kind of intervention should be implemented in such a population? COVID-19 has overwhelmed national health systems worldwide; therefore, in such a specific context, the term "feasibility" should be intended as the possibility to provide rehabilitative care to patients under unprecedented circumstances. When it comes to COVID-19 it should always be kept in mind the difficulties faced in framing and starting an appropriate rehabilitation intervention.

As figures increased rapidly, international societies and recognised experts on pulmonary rehabilitation released general recommendations to be used as guidance for treating patients (Lazzeri et al, 2020; Polastri et al, 2020; Thomas et al, 2020; Vitacca et al, 2020).

One of the first published clinical experiences was that by Lee et al (2020), who investigated the effects of physiotherapy in nine subjects with COVID-19 via a retrospective study design. Patients in that series were relatively younger (mean age 66 years) and mostly men. Exercise intensity (mobilisation, interval and continuous training) progressed during the hospital stay; secretions clearance was not performed since it did not represent a clinical feature. In another study, Arzani et al (2020) described a case of a woman with COVID-19 who underwent physiotherapy during the recovery phase while hospitalised. In that case, dyspnoea represented a major concern with a modified Borg (mBorg) score=7, which improved after treatment (mBorg score=1). Rehabilitation consisted of motor and respiratory exercises (passive and active movements, positioning, ergometer, incentive spirometer, and vibratory

positive expiratory pressures techniques). Following the intervention, both the St. George Respiratory Questionnaire and the Short Form-36 scores improved after the patient attended 42 physiotherapeutic sessions. Following these two publications, many more articles have been released investigating different aspects of rehabilitative treatments. In this regard, it has been found that physical limitations and impaired performance of daily living activities can persist in a considerable percentage of patients, even after a post-acute rehabilitation programme (Belli et al, 2020).

While some studies did not report the presence of bronchial secretions as a primary concern (Lee et al, 2020), others have provided information supporting the hypothesis that secretions management substantially increased the critical care physiotherapists' workload (Black et al, 2021).

Although an increasing volume of studies contributes to expanding knowledge on rehabilitation for patients with COVID-19 (Ambrose et al, 2022; Arzani et al, 2020; Belli et al, 2020; Black et al, 2021; Eggmann et al, 2021; Lee et al, 2020; Maltser et al, 2021; McLaughlin et al, 2021; Nakamura et al, 2020; Ozyemisci et al, 2021; Polastri et al, 2022; Sakai et al, 2021; Shan et al, 2020; Stutz et al, 2021), information on its effects is still scarce.

For instance, one of the emerging features of rehabilitation practice is the assessment of handgrip strength. In at least two studies, it has been found that there are relationships of rehabilitative interest between clinical conditions and handgrip strength (Ramalingam et al, 2020; Tuzun et al, 2021). In the case study by Ramalingam et al (2020), the patient's handgrip improved in both hands by more than 30% after having attended an inpatient post-acute rehabilitation programme. In another cross-sectional study involving 150 patients, Tuzun et al (2021) found that handgrip strength was lower in women than in men and both scored below the normative values (Massy-Westropp et al, 2011), indicating muscle dysfunction.

Furthermore, it should not also be forgotten that dressing procedures and the availability of personal protective equipment represented an additional effort and a substantial concern for healthcare workers and physiotherapists deployed in COVID-19 settings. If on the one hand, these factors cannot be strictly defined as barriers to treatment, on the other they certainly were a matter of concern, particularly during the first pandemic wave (Ferioli et al, 2020). In addition, the surge of cases, wave after wave, has overwhelmed rehabilitative services highlighting the importance of deploying many more human resources in COVID-19 settings. As already mentioned, an increasing volume of publications is becoming available: nevertheless, the rehabilitative approach in patients with COVID-19 still continues to be a matter of great interest which needs to be explored further.

AIM

The purpose of the current study was to describe the effects of inpatient rehabilitation in acute patients treated in a hospital setting during the COVID-19 outbreak.

METHODS

Design

The present study is a retrospective analysis of prospectively collected data of 192 patients with COVID-19-related pneumonia.

Ethical approval

The local Ethics Committee approved the present study (xxx/xxx/xxx). Participants gave their written informed consent.

Setting

Patients were admitted to the Pneumonology Unit, xx xxxxxx University Hospital (xxxxxxx, xxxxx). This was a 32-bed sub-intensive setting of care with a nurse-to-patient ratio of 1:4. Respiratory supports available ranged from standard oxygen therapy (including high flow oxygen therapy) to noninvasive ventilation. Patients were admitted because of COVID-19-related pneumonia and followed a rehabilitative regimen during their hospitalisation from March 25th to June 12th 2020 (first pandemic wave), and from November 2th to June 9th, 2021.

Participants

Patients (n=192) were admitted to the sub-intensive care unit and subsequently transferred to a step-down level of care intensity once in stable clinical conditions. The severity of patients' respiratory distress was defined by the ratio of the partial pressure of arterial oxygen to the fractional concentration of oxygen in inspired air (PaO_2/FiO_2).

Fifteen patients had been intubated before rehabilitation commenced, and one had a tracheostomy. At baseline (the first rehabilitative session), all subjects were extubated, and only one still had a tracheostomy in place. Individuals who met the following inclusion criteria were included in the study:

- referred to rehabilitation
- not intubated
- having a $PaO_2/FiO_2 \geq 100$ mmHg
- not on noninvasive ventilation during the physiotherapeutic treatment.

Procedures

Data were collected at baseline and discharge starting from March 25th, 2020 until the end of the study, by the medical staff and the resident physiotherapist who provided the treatment.

For the second and third pandemic waves (November 2020 to June 2021), an additional physiotherapist was deployed to the unit to implement the rehabilitative personnel. The two physiotherapists shared all information, the intervention modalities, and the methodology for collecting and reporting data. All cases were discussed during a daily morning briefing.

The use of devices for assisted walking was not recorded in this study. For each patient, PaO_2/FiO_2 values were screened from the arterial blood gas analyses (ABGs).

Measurements

Pain intensity was assessed using the numerical rating scale (NRS) in which 0 represents the absence of pain and 10 is the maximum intensity (Hjermstad et al, 2011). NRS has been found to be a reliable and valid method for assessing pain intensity in several studies (Ferreira-Valente et al, 2011; Hawker et al, 2011). At the beginning of the COVID-19 pandemic, as already highlighted, there were no data available about the course of the disease and patients' characteristics. We decided to observe whether pain was a critical concern in such a population. To the best of our knowledge, there are no other rehabilitation studies reporting pain intensity in a sub-intensive care setting. Our experience could therefore contribute to understanding better patients' characteristics.

To define dyspnoea intensity, we used the modified Borg scale (mBorg) (0–10 score) in which the lower the score, the lower the level of perceived dyspnoea (0=nothing at all; 10=maximal) (Borg, 1982). The mBorg scale is a self-reported measure and a recommended tool to quantify the difficulty of breathing upon exertion (Johnson et al, 2016). The mBorg scale has been used in several studies to investigate shortness of breath in patients with COVID-19 (Simonelli et al, 2021).

Motor function was evaluated by calculating the approximate total daily walked distance (metres) that each patient was able to cover. Patients were asked to record how many metres

they walked according to their room size (Polastri et al, 2013). To calculate the daily walked distance, cooperative patients being able to walk autonomously had simply to note down the number of times they walked inside their room and report these data to the physiotherapist. Conversely, those patients who were not autonomous for walking were assisted by the physiotherapist who, even in this case, recorded daily data.

Patients' exercise capacity was evaluated by performing the 1-minute sit-to-stand test (1m-STS), whose validity and clinimetric properties are discussed in detail elsewhere (Bohannon and Crouch, 2019). The use of 1m-STS has been already described in patients with COVID-19, and different studies have identified variable cut-off values depending on the setting and patients' characteristics (Núñez-Cortés et al, 2021; Simonelli et al, 2021).

Respiratory distress was defined by stratifying the PaO_2/FiO_2 ratio. Firstly, we identified cut-off values of ≤200 and >200 mmHg considering other published research investigating the efficacy of treatments in patients with COVID-19 (Bartoletti et al, 2021; Franco et al, 2020; Wang et al, 2020a), and applying the definition of acute respiratory distress syndrome (ARDS) (Bernard, 2005; Bernard et al, 1994). The severity of patients in our cohort was then determined by thresholds taken from the ARDS Berlin definition (ARDS Definition Task Force et al, 2012) as follows: normal (PaO_2/FiO_2 >300 mmHg); mild (PaO_2/FiO_2 201–300 mmHg); moderate (PaO_2/FiO_2 101–200 mmHg); severe (PaO_2/FiO_2 ≤100 mmHg).

In a subset of 57 patients, we evaluated handgrip strength using a hydraulic dynamometer (Baseline Lite Hydraulic Hand Dynamometer—Fabrication Enterprise Inc, White Plains, NY 10602, USA). The model we have used is a reliable and valid instrument according to Jamar's class (Bellace et al, 2000).

In the same subset of patients, we also evaluated the maximal inspiratory (MIP) and maximal expiratory pressure (MEP) using a respiratory pressure meter (RP Check—MD Diagnostics Ltd., Kent - ME14 5PP, UK). Impairment of respiratory muscles is common in respiratory

diseases, and inspiratory muscle weakness can cause dyspnoea and exercise intolerance (American Thoracic Society, 1999). Evaluation of respiratory muscle performance can be evaluated non-invasively with low-cost portable instruments (Caruso et al, 2015), as realised in the present study.

Intervention

As general criteria to enrol patients in active exercise, we identified the following variables 1) peripheral oxygen saturation (SpO_2) ≥90% (regardless of supplemental oxygen administration), 2) respiratory rate ≤30 breaths per minute, 3) not intubated, and 4) hemodynamically stable (heart rate max ≤120 beats per minute; min diastolic blood pressure ≥80 mmHg, max systolic ≤150 mm Hg).

Patients received one daily treatment session Monday to Friday provided by the same two physiotherapists for all the study duration. Physiotherapists shared and implemented a standard modality regarding frequency, intensity, time, and type of exercise. Each session's minimum expected duration was at least 10-20 minutes and incrementally increased to 30 minutes (depending on the clinical state) (Wang et al, 2020b). Patients were also instructed to execute self-administered active movements during the day. The execution of self-administered exercises was verified daily and personalised in accordance with patients' preferences and physical conditions. Patients were regularly supported with advice on the time, type and intensity of such activities. This part of the treatment was appreciated as patients reported that it improved their motor abilities despite being isolated in their room.

We evaluated SpO_2, dyspnoea intensity and the presence of fever to allocate the person to a given exercise regimen. Patients exercised in different positions in accordance with their symptoms and vital parameters. Exercise intensity was set at defined levels using the mBorg

scale as a measure, and duration varied depending on subjective dyspnoea intensity at rest (Figure 1).

Patients who experienced a dyspnoea intensity higher than 3 (moderate) with SpO_2 ≤93-94% exercised predominantly in a supine position executing bilateral isometric contractions (upper limbs or lower limbs as per patient's conditions or preferences).

For patients reporting a dyspnoea intensity score of 2 (light) and SpO_2 ≥93 – ≤96%, the sitting position at the edge of the bed was encouraged. Other motor tasks included a passage to an upright position (with assistance if needed), marching on the spot, and active limb movements.

Finally, in patients with SpO_2 ≥95% reporting light dyspnoea (mBorg score=2), the following exercises were added: sitting outside the bed, upright position, walking in the room, exercises in standing position such as heel raising, bilateral squat, repeated attempts of sitting to standing.

Patients were also provided with an elastic tubular netting (Surgifix #9, FRA Production Spa, Dustino San Michele, Italy) commonly used in hospital settings and adapted for upper limb active exercise.

In those patients with impaired motor function (unable to exercise, or executing postural passages or maintain a sitting position), in-bed cycling was implemented using an ergometer (MOTOmed letto2, RECK-Technik GmbH & Co. KG, Betzenweiler, Germany) (Polastri et al, 2021). Those patients who could not be able to walk autonomously were provided with a frame or assisted by the physiotherapist or the nurse staff.

Respiratory physiotherapy consisted of deep breathing exercises and breathing control. Since hyper secretive phenotypes were not observed in our cohort secretion clearance techniques were not routinely executed. In more cooperative patients, proprioceptive respiratory training was also provided using manual facilitations on the chest during inspiration and expiration.

Furthermore, these techniques were applied in lateral and prone decubitus when feasible. The number of rehabilitative sessions was not defined a priori, and patients exercised from the baseline until hospital discharge. The collaboration of nurses and healthcare assistants was crucial for promoting daily patients' mobility.

Statistical analysis

For each variable, summary statistics were presented: absolute and percentage frequencies were reported to describe categorical variables, whereas median, minimum and maximum values were used for numerical variables. We stratified the population according to the PaO_2/FiO_2 value at baseline; clinical variables were measured at baseline and discharge. Non-parametric statistical tests were used to check for possible differences between the sample groups and, where applicable, between baseline and discharge. In particular, chi-square tests were used for categorical variables, whereas Wilcoxon tests were used for numerical variables. The comparisons between baseline and discharge were performed through the Wilcoxon test for pairwise samples because of the repeated measurements. Missing data were not included in the analysis. The fixed type I error probability was $\alpha=0.05$, and the statistical analysis was carried out in the R environment (R Core Team, 2020).

RESULTS

This study included 192 patients who attended inpatient rehabilitation 12.9±10.5 days after hospital admission. At baseline, there were 138 males (72%) and 54 females (28%) aged 70.3±2.2 years with a body mass index of 27.3±5.0 (kg/m^2). Fifteen patients (8%) were subjected to mechanical ventilation although when treatment commenced they were extubated and on spontaneous breathing. One hundred seventy-three (90%) were on oxygen therapy (Tables 1 and 2). One hundred twelve patients (58%) were directly discharged home, while

the remaining 80 to an in-hospital non-intensive clinical setting awaiting the negativity of RT-PCR testing or completing their recovery before being cleared. Four patients (2%) died during hospitalisation.

As previously mentioned, measurements were taken on the first day of treatment (Tables 1, 2) and at discharge (Tables 3, 4). The summary of variables is presented both for the whole sample (overall) and for the two subgroups (PaO_2/FiO_2 ≤200, PaO_2/FiO_2 >200 mmHg) (Tables 1–4).

We observed encouraging and significant improvements in all groups at discharge. Dyspnoea intensity passed from 1.4±1.3 to 0.7±0.9 points (mBorg) (*P* <0.001); the distance walked from 6.4±18.1 to 266.7±432.7 metres (*P* <0.001); the number of repetitions at the 1m-STS from 6.4±7.3 to 12.0±9.2 (*P* <0.001); handgrip strength of the right hand from 22.7±9.1 to 23.9±10 Kg (*P* 0.003); handgrip strength of the left hand from 19.6±8.5 to 21.3±9.6 Kg (*P* 0.004); MIP from 35.8±22.2 to 43.5±28.2 cmH_2O (*P* 0.002), and MEP from 49.6±26.7 to 59.1±30.4 cmH_2O (*P* <0.001) (Table 5). However, patients with PaO_2/FiO_2 ≤200 mmHg attended more rehabilitation sessions 11.4±6.2 compared to those with PaO_2/FiO_2 ≥200 mmHg who received 7.6±5.4 treatments (*P* <0.001). In addition, patients with PaO_2/FiO_2 ≤200 mmHg had a longer hospital stay than those with a PaO_2/FiO_2 ≥200 mmHg: 16.6±8.7 vs 10.8±7.5 days (*P* <0.001) (Table 3).

Patients with PaO_2/FiO_2 ≤200 mmHg perceived more intense dyspnoea (1.8±1.3 points mBorg), covered a shorter distance (2.3±7.6 metres), and performed fewer repetitions at the 1m-STS (5.0±6.8) at baseline than those with a PaO_2/FiO_2 ≥200 mmHg (Table 1).

Comparison of 1m-STS and walked distance showed no significant differences between groups, although patients with PaO_2/FiO_2 >200 mmHg walked longer distances (271.1±451.6 metres vs 260.6 ± 405.9 metres; *P* 0.756) and performed more repetitions (12.9±9.1 vs 10.9±9.3; *P* 0.140), as shown in Table 3.

There were no COVID-19 infection cases among professionals providing care. Patients tolerated the treatment well, and there were no events related to it or adverse effects. During the physiotherapeutic sessions patients were monitored (peripheral oxygen saturation, heart rate, arterial pressure) and no deterioration of vital parameters such as hemodynamic instability (heart rate max ≥120 bpm; min diastolic blood pressure ≤80, max systolic ≥150 mmHg) or oxygen desaturation (≤88 %), or severe dyspnoea occurred to interrupt the exercise. Treatment intensity was always personalised depending on patients' clinical status avoiding related risks. In the group PaO_2/FiO_2 >200 mmHg, the number of subjects discharged with oxygen therapy was lower (21 vs 30) than those in the PaO_2/FiO_2 ≤200 mmHg group although there were no significant differences (*P* 0.208) (Table 3).

DISCUSSION

This study describes the rehabilitative course of patients with COVID-19-related pneumonia during hospitalisation in a sub-intensive setting. Although there is an increasing volume of information on the rehabilitative treatment of patients with COVID-19 (Polastri et al, 2022; Polastri and Costi, 2021), we would underline that the interpretation of treatment trajectory was challenging particularly at the beginning of the pandemic. We found that motor function, respiratory muscle performance, and dyspnoea intensity significantly improved. A lack of considerable dyspnoea had previously been reported in COVID-19 even in patients who develop respiratory failure (Bertran Recasens et al, 2020; Guan et al, 2020). This could reflect a neurological involvement (Bertran Recasens et al, 2020) or specific mechanical properties of the lungs –in particular– a high compliance phenotype of the disease (Gattinoni et al, 2020). When the study was initiated, there were no data available for these two variables in patients with COVID-19; therefore, our research provides novel contributions to understanding the effects of inpatient rehabilitation in the sub-intensive setting.

Another peculiar aspect was represented by the analysis of pain intensity; even in this case, since there were no data available, we aimed to comprehend whether pain could have been a potential limiting factor for the development of rehabilitation in patients with COVID-19. Pain intensity was not a primary concern and did not represent per se a limitation to developing an inpatient rehabilitation programme in such a specific population.

We also found that handgrip strength and respiratory muscle function significantly improved at discharge in a subset of patients. On these specific aspects, another study by Li et al (2021) evaluated MIP in a cohort of 13 patients with COVID-19; they showed higher values at admission (mean 66 cmH_2O) and discharge (mean 77 cmH_2O). Differences with Li et al's (2021) study were substantial and regarded the setting of care (acute vs sub-acute) and patients who, in our cohort, had a mean MIP of 35.8 cmH_2O and 43.5 cmH_2O at admission and discharge, respectively. We did not propose a specific inspiratory muscle training programme; MIP increased by 21% in the overall group and in patients with PaO_2/FiO_2 >200 mmHg, and by 22% in patients with PaO_2/FiO_2 ≤200 mmHg.

An appropriate selection of frequency, intensity, type, and time substantially supports an effective rehabilitative practice. To this end, we personalised the treatment considering dyspnoea intensity and peripheral oxygen saturation, as previously detailed in the methods section. Although not sustained by data, we had positive responses from patients who appreciated the intervention, and we cannot exclude a positive effect even in their mood. In this regard, it has been outlined that rehabilitation can play a crucial role in improving different psychological aspects in patients with COVID-19 (Ding et al, 2021).

Eventually, we would like to address the external validity of the current study. Observational designs are frequently criticised because they might not be representative of a wider population (target population). At the same time, a representative sample of a larger population could soon lose its representativeness since the source population changes over

time (Boffetta, 2011). Because external validity largely depends on a target population (Dekkers et al, 2010), that in this specific case is represented by hospitalised patients with a PaO_2/FiO_2 ranging from 152±30 to 280±64 mmHg, we are confident the results of the present study could be extended to a target population of patients with COVID-19-related pneumonia while hospitalised in a sub-intensive setting of care.

Limitations

We recognise that its uncontrolled observational nature represents a primary study limitation. However, we believe that it can contribute to exploring the effects of inpatient rehabilitation in patients with COVID-19 in the sub-intensive setting (Polastri and Costi, 2021).

In addition, the self-reporting evaluation we used to calculate the daily walked distance could be another matter of concern. In this regard, the use of self-reported data without a priori cognitive evaluation –such as Mini-Mental State or Montreal Cognitive Assessment– (Aiello et al, 2022; Carson et al, 2018; Patel et al, 2021) could represent a potential source of bias. However, we are confident this was a suitable approach to assess the motor function in our series, thanks to the possibility of achieving a reliable and straightforward evaluation under such restrictive circumstances. Furthermore, a previous study has confirmed that the daily walked distance is a reliable measure in clinical settings (Polastri et al, 2013).

When analysing our data, different age groups could represent another confounding factor; those in the PaO_2/FiO_2 >200 mmHg were younger than those in the PaO_2/FiO_2 ≤200 mmHg group. Older patients may have a poorer prognosis. Nevertheless, results from a meta-analysis of randomised controlled trials have shown that age (<60 – >60 years) did not influence the mortality rate in patients with COVID-19 and respiratory failure (WHO et al, 2020).

Eventually, we recognise that the pharmacological treatment and the natural course of the disease could have influenced the results.

CONCLUSIONS

The current study showed that inpatient rehabilitation was feasible, and we have not observed adverse events related to it in a sub-intensive care setting in patients with COVID-19. In addition, significant improvements in physical capacity, dyspnoea perception, handgrip strength, and respiratory muscle function were observed.

KEY POINTS

- Inpatient rehabilitation was feasible, and we did not observe adverse events.
- After attending an inpatient rehabilitation programme that lasted 9.3±6.0 daily sessions, patients significantly improved dyspnoea, motor function and respiratory muscle performance.
- Inpatient rehabilitation in patients with COVID-19 enhanced the therapeutic pathway even in those subjects showing a $PaO_2/FiO_2 \leq 200$ mmHg.

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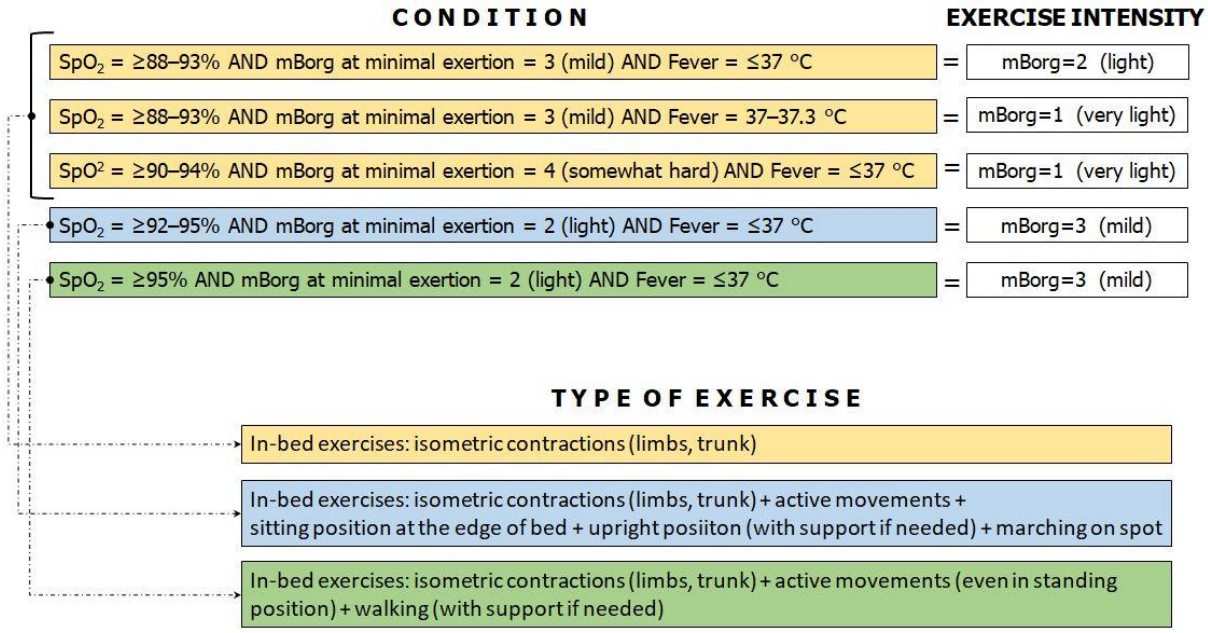
Figure 1. Treatment algorithm



SpO_2: oxygen saturation; mBorg: modified Borg scale.

Table 1. Demographic, anthropometric, and clinical characteristics of patients at baseline				
Variables	**Overall (*n*=192)**	**P/F ≤200 (*n*=82)**	**P/F >200 (*n*=110)**	***P*-value***
Age, *years*	70.3 ± 12.2	72.6 ± 11.0	68.7 ± 12.7	.051
Male, *n (%)*	138 (72)	61 (74)	77 (70)	.173
BMI, *kg/m²*	27.3 ± 5.0	27.0 ± 5.1	27.6 ± 5.0	.310
Previously intubated, *n (%)*	15 (8)	5 (6)	10 (9)	.197
Tracheostomy, *n (%)*	1 (1)	0 (0)	1 (1)	-
Oxygen therapy, *n (%)*	173 (90)	82 (100)	91 (83)	.494
Oxygen therapy HFNC, *n (%)*	61 (32)	46 (56)	15 (14)	**<.001**
Pain intensity, *NRS score*	0.5 ± 1.5	0.3 ± 1.2	0.6 ± 1.6	.057
P/F, *mmHg*	225 ± 82	152 ± 30	280 ± 64	**<.001**
SpO_2, *%*	96 ± 2	95 ± 2	96 ± 2	.491
Dyspnoea intensity, *mBorg score*	1.4 ± 1.3	1.8 ± 1.3	1.2 ± 1.2	**.002**
Walked distance, *metres*	6.4 ± 18.1	2.3 ± 7.6	9.5 ± 22.5	**.004**
1m-STS, *n of repetitions* (*n*=155)	6.4 ± 7.3	5.0 ± 6.8	7.5 ± 7.5	**.049**
LOS before treatment, *days*	12.9 ± 10.5	13.4 ± 9.5	12.6 ± 11.2	.865

P/F: PaO_2/FiO_2; BMI: body mass index; HFNC: high-flow nasal cannula; NRS: numerical rating scale; SpO_2: oxygen saturation; mBorg: modified Borg scale; 1m-STS: 1-minute sit-to-stand test; LOS: length of stay.

Data are expressed as n (%) or mean ± SD. P-values, concerning the comparison between PaO_2/FiO_2 ≤200 and PaO_2/FiO_2 >200 mmHg, are displayed (Wilcoxon test for numerical variables and chi-square test for dichotomous ones). *Statistical significance was set for P <0.05.

Table 2. Demographic, anthropometric, and clinical characteristics of a subset of patients in whom handgrip strength and respiratory muscles strength were assessed at baseline				
Variables	**Overall (n=57)**	**P/F ≤200 (n=22)**	**P/F >200 (n=35)**	***P*-value***
Age, *years*	67.8 ± 11.6	70.0 ± 10.3	66.4 ± 12.1	.290
Male, *n (%)*	37 (65)	13 (59)	24 (69)	.070
BMI, kg/m^2	28.0 ± 5.9	28.1 ± 6.7	27.9 ± 5.5	.743
Previously intubated, *n (%)*	4 (7)	2 (9)	2 (6)	1.000
Oxygen therapy, *n (%)*	53 (93)	22 (100)	31 (89)	.216
Oxygen therapy HFNC, *n (%)*	16 (28)	11 (50)	5 (6)	.134
Pain intensity, *NRS score*	0.6 ± 1.5	0.7 ± 1.8	0.5 ± 1.2	.427
P/F, *mmHg*	225 ± 66	161 ± 31	265 ± 47	**<.001**
SpO_2, *%*	96 ± 2	96 ± 2	96 ± 2	.836
Dyspnoea intensity, *mBorg score*	1.8 ± 1.2	1.9 ± 1.0	1.7 ± 1.2	.517
Walked distance, *metres*	6.2 ± 17.7	3.4 ± 1.4	8.1 ± 20.9	.396
Handgrip strength, *Kg*				
Right hand	22.3 ± 9.7	19.3 ± 7.2	24.1 ± 10.4	.059
Left hand	19.6 ± 8.5	18.1 ± 6.4	20.6 ± 9.5	.313
MIP (*n*=53), *cmH_2O*	35.8 ± 22.2	33.9 ± 14.5	37.1 ± 25.9	.689
MEP, *cmH_2O*	49.6 ± 26.7	48.9 ± 26.3	50.0 ± 26.9	.694

P/F: PaO_2/FiO_2; BMI: body mass index; HFNC: high-flow nasal cannula; NRS: numerical rating scale; SpO_2: oxygen saturation; mBorg: modified Borg scale; MIP: maximal inspiratory pressure; MEP: maximal expiratory pressure.

Data are expressed as *n* (%) or mean ± SD. *P*-values, concerning the comparison between PaO_2/FiO_2 ≤200 and PaO_2/FiO_2 >200 mmHg, are displayed (Wilcoxon test for numerical variables and chi-square test for dichotomous ones). *Statistical significance was set for P <0.05.

Table 3. Clinical characteristics, physical performance and length of stay of patients at discharge				
Variables	**Overall (n= 192)**	**P/F ≤200 (n=82)**	**P/F >200 (n=110)**	***P*-value***
Discharged with O_2, *n (%)*	51 (27)	30 (37)	21 (19)	.208
Treatment sessions, *n*	9.3 ± 6.0	11.4 ± 6.2	7.6 ± 5.4	**<.001**
LOS, *days*	13.3 ± 8.5	16.6 ± 8.7	10.8 ± 7.5	**<.001**
Dyspnoea intensity, *mBorg score*	0.7 ± 0.9	0.9 ± 1.1	0.6 ± 0.8	**<.001**
Walked distance, *metres*	266.7 ± 432.7	260.6 ± 405.9	271.1 ± 451.6	.756
1m-STS (*n*=178), *n of repetitions*	12.0 ± 9.2	10.9 ± 9.3	12.9 ± 9.1	.140

P/F: PaO_2/FiO_2; LOS: length of stay (from baseline to discharge); mBorg: modified Borg scale; 1m-STS: 1-minute sit-to-stand test.

Data are expressed as *n* (%) or mean ± SD. *P*-values, concerning the comparison between PaO_2/FiO_2 ≤200 and PaO_2/FiO_2 >200 mmHg, are displayed (Wilcoxon test for numerical variables and chi-square test for dichotomous ones). *Statistical significance was set for P <0.05.

Table 4. Clinical characteristics, physical performance and length of stay of a subset of patients in whom handgrip and respiratory muscles strength were assessed at discharge				
Variables	**Overall (n=57)**	**P/F ≤200 (n=22)**	**P/F >200 (n=35)**	***P*-value***
Discharged with O_2, *n (%)*	14 (25)	8 (36)	6 (17)	.593
Treatment sessions, *n*	10.0 ± 5.5	11.2 ± 4.2	9.3 ± 6.1	**.038**
LOS, *days*	14.3 ± 8.3	16.5 ± 7.1	12.9 ± 8.6	**.026**
Dyspnoea intensity, *mBorg score*	0.7 ± 0.8	0.9 ± 0.8	0.5 ± 0.7	.116
Walked distance, *metres*	455.1 ± 546.8	514.1 ± 681.5	418.0 ± 449.3	.786
1m-STS (*n*=56), *n of repetitions*	13.5 ± 9.7	13.6 ± 11.1	13.5 ± 8.7	.957
Handgrip strength, *Kg*				
Right hand (*n*=54)	23.9 ± 10.0	22.8 ± 7.3	25.2 ± 10.4	.703
Left hand (*n*=54)	21.3 ± 9.6	20.3 ± 6.5	21.9 ± 11.0	.831
MIP (*n*=51), *cmH_2O*	43.5 ± 28.2	41.1 ± 21.0	44.9 ± 31.7	.912
MEP (*n*=53), *cmH_2O*	59.1 ± 30.4	59.4 ± 25.2	58.9 ± 33.0	.628

P/F: PaO_2/FiO_2; LOS: length of stay (from baseline to discharge); mBorg: modified Borg scale; 1m-STS: 1-minute sit-to-stand test; MIP: maximal inspiratory pressure; MEP: maximal expiratory pressure.

Data are expressed as *n* (%) or mean ± SD. *P*-values, concerning the comparison between PaO_2/FiO_2 ≤200 and PaO_2/FiO_2 >200 mmHg, are displayed (Wilcoxon test for numerical variables and chi-square test for dichotomous ones). *Statistical significance was set for *P* <0.05.

Table 5. Clinical changes from admission to discharge			
Variables	**Baseline**	**Discharge**	***P*-value***
Dyspnoea intensity, *mBorg score*			
Overall	(*n*=192) 1.4 ± 1.3	(*n*=192) 0.7 ± 0.9	**<.001**
P/F ≤200	(*n*=82) 1.8 ± 1.3	(*n*=82) 0.9 ± 1.1	**<.001**
P/F >200	(*n*=110) 1.2 ± 1.2	(*n*=110) 0.6 ± 0.8	**<.001**
Walked distance, *metres*			
Overall	(*n*=192) 6.4 ± 18.1	(*n*=192) 266.7 ± 432.7	**<.001**
P/F ≤200	(*n*=82) 2.3 ± 7.6	(*n*=82) 260.6 ± 405.9	**<.001**
P/F >200	(*n*=110) 9.5 ± 22.5	(*n*=110) 271.1 ± 451.6	**<.001**
1m-STS, *n of repetitions*			
Overall	(*n*=155) 6.4 ± 7.3	(*n*=178) 12.0 ± 9.2	**<.001**
P/F ≤200	(*n*=68) 5.0 ± 6.8	(*n*=78) 10.9 ± 9.3	**<.001**
P/F >200	(*n*=87) 7.5 ± 7.5	(*n*=100) 12.9 ± 9.1	**<.001**
Handgrip strength, *Kg*			
Right hand			
Overall	(*n*=57) 22.7 ± 9.1	(*n*=54) 23.9 ± 10.0	**.003**
P/F ≤200	(*n*=22) 19.3 ± 7.2	(*n*=20) 22.8 ± 7.3	.139
P/F >200	(*n*=35) 24.9 ± 9.5	(*n*=34) 25.2 ± 10.4	.946
Left hand			
Overall	(*n*=57) 19.6 ± 8.5	(*n*=54) 21.3 ± 9.6	**.004**
P/F ≤200	(*n*=22) 18.1 ± 6.4	(*n*=20) 20.3 ± 6.5	.217
P/F >200	(*n*=35) 20.6 ± 9.5	(*n*=34) 21.9 ± 11.0	.830
MIP, *cmH_2O*			
Overall	(*n*=53) 35.8 ± 22.2	(*n*=51) 43.5 ± 28.2	**.002**
P/F ≤200	(*n*=21) 33.9 ± 14.5	(*n*=20) 41.1 ± 21.0	.216
P/F >200	(*n*=32) 37.1 ± 25.9	(*n*=31) 44.9 ± 31.7	.284
MEP, *cmH_2O*			
Overall	(*n*=57) 49.6 ± 26.7	(*n*=53) 59.1 ± 30.4	**<.001**
P/F ≤200	(*n*=22) 48.9 ± 26.3	(*n*=20) 59.4 ± 25.2	.244
P/F >200	(*n*=35) 50.0 ± 26.9	(*n*=33) 58.9 ± 33.0	.300

mBorg: modified Borg scale; P/F: PaO_2/FiO_2; 1m-STS: 1-minute sit-to-stand test; MIP: maximal inspiratory pressure; MEP: maximal expiratory pressure.
Data are expressed as *n* (%) or mean ± SD. *Statistical significance was set for P <0.05.

Figure 1