

Feasibility of subacute rehabilitation for mechanically ventilated patients with COVID-19 disease: a retrospective case series

Simone Pancera^{a,b}, Luca N. C. Bianchi^a, Roberto Porta^a, Silvia Galeri^a, Maria Chiara Carrozza^{a,c} and Jorge H. Villafañe^a

In this case series study, we aimed to evaluate the feasibility of a subacute rehabilitation program for mechanically ventilated patients with severe consequences of COVID-19 infection. Data were retrospectively collected from seven males (age 37–61 years) who were referred for inpatient rehabilitation following the stay in the ICU (14–22 days). On admission, six patients were still supported by mechanical ventilation. All patients were first placed in isolation in a special COVID unit for 6–22 days. Patients attended 11–24 treatment sessions for the duration of rehabilitation stay (13–27 days), including 6–20 sessions in the COVID unit. The treatment included pulmonary and physical rehabilitation. The initially nonventilated patient was discharged prematurely due to gallbladder problems, whereas all six mechanically ventilated patients were successfully weaned off before transfer to a COVID-free unit where they stayed for 7–19 days. At discharge, all patients increased limb muscle strength and thigh circumference, reduced activity-related dyspnea, regained

functional independence and reported better quality of life. Rehabilitation plays a vital role in the recovery of seriously ill post-COVID-19 patients. Facilities should develop and implement plans for providing multidisciplinary rehabilitation treatments in various settings to recover functioning and prevent the development of long-term consequences of the COVID-19 disease. *International Journal of Rehabilitation Research* XXX: 000–000 Copyright © 2020 Wolters Kluwer Health, Inc. All rights reserved.

International Journal of Rehabilitation Research 2020, XXX:000–000

Keywords: acute respiratory distress syndrome, COVID-19, intensive care unit, rehabilitation

^aIRCCS Fondazione Don Carlo Gnocchi, Milan and ^bDepartment of Information Engineering, University of Brescia, Brescia, Italy and ^cThe Biorobotics Institute, Scuola Superiore Sant'Anna, Pisa, Italy.

Correspondence to Simone Pancera, PhD, IRCCS Fondazione Don Carlo Gnocchi, Via Capecelatro 66, 20148, Milan, Italy
Tel: +39 0307245282; e-mail: s.pancera002@unibs.it

Received 8 October 2020 Accepted 10 November 2020

Introduction

As initially reported by the WHO, the severe acute respiratory syndrome coronavirus 2 causing coronavirus disease 2019 (COVID-19 disease) can induce acute hypoxemic respiratory failure that in severe cases may lead to acute respiratory distress syndrome (ARDS) [1]. Important concerns emerged regarding the long-term pulmonary, neurological and vascular consequences in the most severely affected patients [2,3]. These conditions often require mechanical ventilation, prolonged ICU stay and subsequent inpatient rehabilitation [4,5]. Moreover, postacute rehabilitation after COVID-19 infection is of great importance considering that the majority of ICU survivors are <65 years old and expected to resume their previous life and occupation [6].

For these reasons, rehabilitation of patients with serious consequences of COVID-19 disease in the tertiary clinical care settings plays a central role during the health emergency as well as in the later phase and should be provided despite organizational difficulties brought about by the pandemic [7,8]. However, planning a well-tolerated rehabilitative intervention is a challenge considering the need to contain the spread of the infection, the

low availability of personal protective equipment and the restricted number of ICU experienced physiotherapists [9]. Moreover, as many countries are currently experiencing a resurgence of the infection, rehabilitation will have to be adapted to a 'new normal' and develop and implement protocols for minimizing disability and preserving the function of post-COVID-19 patients in these challenging conditions.

This series of cases describes an approach to providing rehabilitation during the COVID-19 pandemic in a tertiary subacute rehabilitation center. The novelty is represented by the challenging conditions and the different phases in which the rehabilitation program was reorganized to meet the rehabilitation needs of previously healthy individuals who developed severe consequences of COVID-19 disease.

Methods

Between March and April 2020, seven male patients without smoking history (except patient 7 with 30 pack/year) were referred for pulmonary and physical rehabilitation to our rehabilitation center after ICU admission for severe ARDS caused by COVID-19. Patients' characteristics are

summarized in Table 1. In brief, all patients presented to the emergency room with a history of persistent fever, cough and dyspnea. The COVID-19 infection was confirmed by a positive swab test and chest X-ray. Due to the development of severe ARDS, patients were admitted to ICU where they were intubated and ventilated under continuous sedation. The need for prolonged mechanical ventilation required early tracheostomy, and all patients received nutrition through nasal cannula as well as antibiotics and antiviral drugs during the ICU stay. At discharge from ICU, all patients were in a stable clinical condition. Six still needed mechanical ventilation with positive end-expiratory pressure $<10\text{cmH}_2\text{O}$, whereas one patient was weaned from mechanical ventilation before the ICU discharge. At rehabilitation admission, the patients were still positive for COVID-19 and were isolated into a COVID unit.

All data were collected retrospectively. The internal ethics committee approved the study protocol on 22 April 2020, and all patients provided informed consent to use their information for publication.

Evaluation

A standardized examination was carried out on admission to the COVID rehabilitation unit (T0). The physiotherapists recorded BMI, arterial blood gases and mechanical ventilation parameters before collecting the Barthel Index [10], the Barthel Index based on dyspnea (BID) [11] and the EuroQol questionnaire – 5 dimensions, 3 levels [12]. The same examiner also manually assessed muscle function with the Medical Research Council (MRC) sum score in six muscle groups bilaterally (abduction of the arm, flexion of the forearm, an extension of the wrist, flexion of the hip, extension of the knee and dorsal flexion of the foot) [13], collected the Short Physical Performance Battery (SPPB) [14] and measured quadriceps girth 10 cm above the patella.

The same assessment was repeated after patients were transferred to the COVID-free unit (T1) and at discharge (T2). Additional assessments included maximal inspiratory and expiratory mouth pressure (MicroRPM, Vyair

Medical, USA) at T1 and T2 and with the assessment of lung function using a portable spirometer (Spiropalm, Cosmed, Italy) at T2.

Intervention

Two physiotherapists with experience in caring for critically ill patients were granted access to the COVID unit with the appropriate personal protective equipment (PPE). Unlike the pre-COVID program, the rehabilitation treatment was carried out once a day for 45 min, 5 days a week, and the setting was limited to the patient's room. The treatment included both pulmonary and physical rehabilitation according to the guidelines [15].

Pulmonary rehabilitation of the six patients still ventilated at the admission started with weaning from mechanical ventilation under the supervision of the lung specialist. Physiotherapists began with a spontaneous breathing trial (SBT) of 30 min, during which the patient breathed through a heat and moisture exchanger placed on the tracheostomy and with the necessary oxygen support, calculated by converting the FiO_2 (%) used with the mechanical ventilation. In the event of a successful SBT, the patient switched to the speaking valve during the same day, whereas in the case of SBT failure, the patient was reconnected to the ventilator according to previous criteria [16]. The following day the procedure was repeated for those patients that failed the first attempt of SBT, this time with the addition of a positive expiratory pressure device (Threshold PEP, Philips, USA) applied at the cuffed tracheostomy, with a default resistance of $10\text{cmH}_2\text{O}$ for 20 min. This device was directed toward expiratory muscle training to enhance lung recruitment [17] and its use was limited to 2d after the first SBT. Weaning from mechanical ventilation was considered successful in the absence of ventilatory support for 48 h. After discontinuation of the mechanical ventilation, patients maintained the tracheostomy capped receiving the appropriate amount of oxygen via nasal cannula until the lung specialist considered removal appropriate.

The physical rehabilitation treatment was provided in parallel to the respiratory treatment, with the primary

Table 1 Demographic and clinical characteristics of the patients

Patient	Age (years)	Comorbidities (n)	ICU LOS (d)	Time to tracheostomy in ICU (d)	mechanical ventilation	FiO_2 (%)	$\text{PaO}_2/\text{FiO}_2$ ratio	COVID unit LOS (d)	COVID-free unit LOS (d)	Time to weaning from mechanical ventilation (d)
1	47	1 ^a	19	9	Yes	30	331	8	19	5
2	61	1 ^a	21	7	No	35	244	22	N/A	N/A
3	39	0	14	8	Yes	35	179	15	8	6
4	37	0	16	5	Yes	40	238	15	12	4
5	50	1 ^a	22	5	Yes	28	353	11	12	4
6	47	0	18	3	Yes	24	319	6	7	3
7	57	1 ^a	19	10	Yes	21	276	9	9	3
Mean (SD)	48.3 (8.7)		18.4 (2.8)	8.4 (3.6)		30.4 (6.7)	277.1 (61.5)	12.3 (5.5)	11.2 (4.4)	4.2 (1.2)

FiO_2 , fraction of inspired oxygen; ICU, intensive care unit; LOS, length of stay; N/A, not available; PaO_2 , arterial partial pressure of oxygen; SD, standard deviation.

^aHypertension.

goal of early mobilization [18]. First, physiotherapists promoted the sitting position and neuromuscular electrical stimulation (NMES) of the lower limbs (T-ONE Coach, I-TECH, Italy) via squared electrodes (48×48 mm) applied on the quadriceps for 20–30 min with an amplitude between 15 and 20 mA and a frequency of 50 Hz. As soon as possible, NMES was integrated with leg and arm cranking for 15 min, sit-to-stand training (three sets, 5–10 reps) and finally walking with or without ambulatory assisting devices.

Once patients had two negative consecutive tests for COVID-19 infection, they were moved to a COVID-free unit to continue the rehabilitation program. The COVID-free unit allowed free access for physiotherapists and the treatment setting was extended to include corridors, stairs and the common spaces of the ward, converted into an ad-hoc gym. On the day of the transfer to the COVID-free unit, physiotherapists carried out the intermediate evaluation (T1). Aerobic training with cycle ergometer and strength exercises with elastic bands or free weights were integrated into the physical program following the guidelines [19]. Because setting restrictions did not allow for the field tests necessary to set the workload, patients started the cycle ergometer at the default resistance of 20 watts for 30 min. The load was increased during the following sessions by 10 watts if the Borg score for fatigue and dyspnea was <4, kept unchanged for scores between 4 and 6 or reduced by 10 watts if the score was >6. In the absence of machines, the resistance training was carried out with free weights or elastic bands, starting at 50% of the one-repetition maximum for two sets and 20 repetitions and progressing to 10 reps for three sets at 70% of the one-repetition maximum.

On the last day of the rehabilitation stay, patients underwent the final assessment (T2), as previously described.

Results

During the rehabilitation stay, patients attended 11–24 sessions (Table 2) of which 6–20 sessions took place in the COVID unit. One patient was discharged early because of an acute gallbladder problem unrelated to the rehabilitation treatment with no adverse effects in the remaining six patients.

The Barthel Index score indicated functional dependence (defined as Barthel Index score ≤70) in six patients at T0, whereas case 7 was functionally independent on baseline [20]. At T1, all patients regained functional independence except case 1, who recovered full functionality at T2. Similarly, patients were unable to sustain the SPPB test at T0, whereas at T1 they progressed towards the complete recovery of motor function, again except for case 1 that recovered motor function at T2.

ICU acquired weakness (MRC sum score <48) was noted at baseline in two patients, whereas at T1 all patients had the MRC sum score >48 and almost normal muscle strength at T2. The quadriceps girth increased from 2.5 to 6.5 cm for both legs in six subjects that completed the program.

The BID score indicated a major improvement in activity-related dyspnea between T0 and T1, except for case 1 that showed higher dyspnea at T1 and case 2 that started from a lower value at baseline.

MIP values increased from T1 to T2 in three patients, remain unchanged in case 1, or decreased in two patients. MEP values increased in five patients except case 6. The spirometry values obtained at T2 showed reduced lung volumes in all patients but case 1, as reported in Table 3.

Discussion

This study describes the inpatient rehabilitation of patients with severe consequences of COVID-19 disease

Table 2 Clinical outcomes

Case	Evaluation	Sessions (T0-T1, T1-T2)	BMI, kg/m ²	BI (0–100)	BID (0–100)	EQ-5D-3L (1–3)	SPPB (0–12)	MRC Score (0–60)	Q girth (L/R, cm)
1	T0	–	26.4	25	83	33 323	0	47	38.0/39.5
	T1	7	27.9	52	71	33 321	0	50	40.5/41.5
	T2	17	28.4	100	0	11 111	12	57	44.5/45.5
2	T0	–	27.1	8	85	33 332	0	44	41/41.5
	T1	20	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	T2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
3	T0	–	20.8	23	86	33 323	0	49	37/39.5
	T1	13	22.7	86	18	22 222	10	53	41.5/41.5
	T2	6	23.2	100	2	11 111	12	56	43.5/44
4	T0	–	18.5	28	83	33 323	0	51	31.5/32
	T1	13	20.1	90	10	11 212	12	55	33/32.5
	T2	10	20.3	100	2	11 112	12	60	34/34.5
5	T0	–	26.9	19	80	33 333	0	52	40.5/40.5
	T1	10	27.4	86	18	21 212	10	55	43/43
	T2	10	28.1	100	5	11 112	12	58	44/44.5
6	T0	–	24.6	30	78	33 322	0	51	41/41.5
	T1	6	25.1	90	10	11 211	12	56	43/43.5
	T2	5	25.8	100	0	11 111	12	60	43.5/44
7	T0	–	28.7	77	40	22 211	8	54	42/43
	T1	8	29.3	90	33	11 111	12	58	43.5/44.5
	T2	8	30	100	5	11 111	12	60	45/45.5

BI, Barthel Index; BID, Barthel Index based on dyspnea; EQ-5D-3L, EuroQol questionnaire – 5 dimensions, 3 levels; MRC sum score, Medical Research Council sum score; N/A, not available; Q girth, quadriceps size taken 10 cm above patella; SPPB, Short Physical Performance Battery.

Table 3 Pulmonary function results

Case	Evaluation	MIP/MEP, cmH ₂ O (% predicted)	FEV1/FVC (%)	FEV1, L (% predicted)	FVC, L (% predicted)	VC, L (% predicted)
1	T1	85/96 (73/44)	N/A	N/A	N/A	N/A
	T2	115/115 (99/53)	88.8	4.21 (112)	4.74 (100)	4.43 (94)
2	T1	N/A	N/A	N/A	N/A	N/A
	T2	N/A	N/A	N/A	N/A	N/A
3	T1	99/136 (81/60)	N/A	N/A	N/A	N/A
	T2	107/138 (88/61)	80.4	3.04 (73)	3.78 (74)	3.77 (73)
4	T1	75/113 (61/49)	N/A	N/A	N/A	N/A
	T2	67/121 (55/53)	87.9	3.18 (83)	3.62 (77)	3.28 (70)
5	T1	41/58 (35/27)	N/A	N/A	N/A	N/A
	T2	40/61 (35/28)	89.3	2.78 (76)	3.11 (67)	3 (65)
6	T1	64/100 (55/46)	N/A	N/A	N/A	N/A
	T2	71/102 (61/46)	81.5	3.04 (78)	3.73 (76)	2.34 (48)
7	T1	88/82 (79/39)	N/A	N/A	N/A	N/A
	T2	80/120 (72/57)	90.8	2.48 (67)	2.73 (58)	2.64 (56)

FEV1: forced expiratory volume in the 1 sec; FVC: forced vital capacity; MEP: maximal expiratory pressure; MIP: maximal inspiratory pressure; N/A: not available; VC: vital capacity.

and the organizational difficulties to provide adequate treatment even in a specialized rehabilitation center. The impact of COVID-19 has indeed affected both the acute and subacute phases of rehabilitation causing significant limitations in terms of the settings, access to rehabilitation equipment and availability of professionals. In this regard, the study provides novel information about the organization and provision of a subacute rehabilitation treatment during the COVID-19 pandemic that led to the complete functional recovery of seven retrospectively studied patients.

The long-lasting consequences of ARDS and prolonged ICU stay may affect exercise capacity, respiratory function and neurological impairments leading to a postintensive care syndrome with consequences on the quality of life [13]. Furthermore, the development of muscle weakness is a common finding in patients discharged from ICU and occurs in almost half of the subjects receiving prolonged mechanical ventilation [21]. Previous data on ARDS survivors show that less than 50% return to work within 1 year following the discharge and those resuming work activities complain about reduced functionality and quality of life [22]. However, unlike the known literature on critical patients, the COVID-19 disease has filled the ICUs with previously healthy and active individuals, and the long-term impact on their quality of life remains unclear.

Under these premises, a standard rehabilitation program for ARDS should include an early intervention starting during the ICU stay and continuing to the subacute phase to reduce the complications of immobilization and the effects of prolonged mechanical ventilation. However, during the COVID-19 pandemic, the majority of patients could not receive rehabilitation treatment in ICU and this task was left to specialized rehabilitation centers, which had already undergone unexpected and urgent organizational changes [23]. For example, due to the risk of spreading the infection to other patients and health professionals, we divided inpatient rehabilitation

into two phases. The first phase taking place in the COVID unit was the most challenging and imposed important limitations: first, the length and number of daily sessions had to be reduced to save PPE for health-care workers on the frontline. Also, physiotherapists had to provide basic care, such as dressing and feeding, to limit the risk of infection and relieve other already busy professionals, which further limited the available treatment time. Second, patients' respiratory progress could also be delayed due to the limitations in the COVID unit. For example, the use of different instruments for airways clearance and respiratory exercises was limited to disposable tools, and the recovery of the motor function and muscle strength was likewise limited by the time, setting and devices available to physiotherapists. Nonetheless, almost all patients achieved most of the functional gains in the COVID unit, supporting the decision to start rehabilitation early despite all challenges.

The transition to a COVID-free unit allowed for expanding the interventions and evaluation before discharge. However, the treatment carried out on the standard ward was not without limitations compared to the pre-COVID state, because even in this phase physiotherapists had to provide the treatment without access to the usual spaces and resources. For example, it was not possible to utilize common field tests, such as the 6-min walk test to assess initial workload and progress, nor the group sessions to foster a greater patient involvement.

This study is limited by its retrospective and descriptive nature; thus, no conclusions can be drawn on the effectiveness of the provided treatment or in comparison to other types of intervention. Another limitation is that outcomes assessed at baseline were simple tests, whereas the two later evaluations were more extensive, limiting their direct comparison. Finally, low Barthel Index scores at T0 likely reflected a floor effect because patients just left the ICU. Although such low baseline values are expected to increase over time, the overall improvement in the Barthel Index was impressive.

Conclusion

This study showed that it is feasible to provide subacute rehabilitation to patients with severe COVID-19 disease as soon as after discharge from an ICU. The teamwork and professional skills of the involved physiotherapists made it possible to overcome the organizational difficulties caused by the pandemic and deliver rehabilitation in different settings, thus allowing the continuity of care that resulted in full functional recovery of the studied patients. The details described herein offer practical insights in the face of the second wave of the COVID-19 pandemic. Prospective studies are needed to investigate the long-term consequences of the COVID-19 disease and the effects of rehabilitation treatments.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

References

- 1 WHO. Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected: Interim guidance V 1.2. [Internet]. Available at: [https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-\(n-cov\)-infection-is-suspected](https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(n-cov)-infection-is-suspected). [Accessed 10 April 2020]
- 2 Leisman DE, Deutschman CS, Legrand M. Facing COVID-19 in the ICU: vascular dysfunction, thrombosis, and dysregulated inflammation. *Intensive Care Med* 2020; **46**:1105–1108.
- 3 Wang L, Shen Y, Li M, Chuang H, Ye Y, Zhao H, et al. Clinical manifestations and evidence of neurological involvement in 2019 novel coronavirus SARS-CoV-2: a systematic review and meta-analysis. *J Neurol* 2020; **267**:2777–2789.
- 4 Ambrosino N, Makhbah DN. Comprehensive physiotherapy management in ARDS. *Minerva Anestesiol* 2013; **79**:554–563.
- 5 Connolly B, Salisbury L, O'Neill B, Geneen LJ, Douiri A, Grocott MP, et al. Exercise rehabilitation following intensive care unit discharge for recovery from critical illness. *Cochrane Database Syst Rev* 2015; **6**:CD008632.
- 6 Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A, et al. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy Region, Italy. *JAMA* 2020; **323**:1574–1581.
- 7 Pedersini P, Corbellini C, Villafañe JH. Italian physical therapists' response to the novel COVID-19 emergency. *Phys Ther* 2020; **100**:1049–1051.
- 8 Wang TJ, Chau B, Lui M, Lam GT, Lin N, Humbert S. Physical medicine and rehabilitation and pulmonary rehabilitation for COVID-19. *Am J Phys Med Rehabil* 2020; **99**:769–774.
- 9 Thomas P, Baldwin C, Bissett B, Boden I, Gosselink R, Granger CL, et al. Physiotherapy management for COVID-19 in the acute hospital setting: clinical practice recommendations. *J Physiother* 2020; **66**:73–82.
- 10 Shah S, Vanclay F, Cooper B. Improving the sensitivity of the Barthel Index for stroke rehabilitation. *J Clin Epidemiol* 1989; **42**:703–709.
- 11 Vitacca M, Paneroni M, Baiardi P, De Carolis V, Zampogna E, Belli S, et al. Development of a Barthel Index based on dyspnea for patients with respiratory diseases. *Int J Chron Obstruct Pulmon Dis* 2016; **11**:1199–1206.
- 12 Rabin R, de Charro F. EQ-5D: a measure of health status from the EuroQol Group. *Ann Med* 2001; **33**:337–343.
- 13 De Jonghe B, Sharshar T, Lefaucheur JP, Authier FJ, Durand-Zaleski I, Boussarsar M, et al.; Groupe de Réflexion et d'Etude des Neuromyopathies en Réanimation. Paresis acquired in the intensive care unit: a prospective multicenter study. *JAMA* 2002; **288**:2859–2867.
- 14 Bakhru RN, Davidson JF, Bookstaver RE, Kenes MT, Welborn KG, Morris PE, Clark Files D. Physical function impairment in survivors of critical illness in an ICU Recovery Clinic. *J Crit Care* 2018; **45**:163–169.
- 15 Jang MH, Shin MJ, Shin YB. Pulmonary and physical rehabilitation in critically ill patients. *Acute Crit Care* 2019; **34**:1–13.
- 16 Boles JM, Bion J, Connors A, Herridge M, Marsh B, Melot C, et al. Weaning from mechanical ventilation. *Eur Respir J* 2007; **29**:1033–1056.
- 17 D'Arosca F, Garabelli B, Savio G, Barison A, Appendini L, Oliveira LVF, et al. Comparing airways clearance techniques in chronic obstructive pulmonary disease and bronchiectasis: positive expiratory pressure or temporary positive expiratory pressure? A retrospective study. *Braz J Phys Ther* 2017; **21**:15–23.
- 18 Doiron KA, Hoffmann TC, Beller EM. Early intervention (mobilization or active exercise) for critically ill adults in the intensive care unit. *Cochrane Database Syst Rev* 2018; **3**:CD010754.
- 19 Spruit MA, Singh SJ, Garvey C, ZuWallack R, Nici L, Rochester C, et al.; ATS/ERS Task Force on Pulmonary Rehabilitation. An official American Thoracic Society/European Respiratory Society statement: key concepts and advances in pulmonary rehabilitation. *Am J Respir Crit Care Med* 2013; **188**:e13–e64.
- 20 Schweickert WD, Pohlman MC, Pohlman AS, Nigos C, Pawlik AJ, Esbrook CL, et al. Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. *Lancet* 2009; **373**:1874–1882.
- 21 Kress JP, Hall JB. ICU-acquired weakness and recovery from critical illness. *N Engl J Med* 2014; **370**:1626–1635.
- 22 Herridge MS. Recovery and long-term outcome in acute respiratory distress syndrome. *Crit Care Clin* 2011; **27**:685–704.
- 23 Pancera S, Galeri S, Porta R, Pietta I, Bianchi LNC, Carrozza MC, Villafañe JH. Feasibility and efficacy of the pulmonary rehabilitation program in a rehabilitation center: case report of a young patient developing severe covid-19 acute respiratory distress syndrome. *J Cardiopulm Rehabil Prev* 2020; **40**:205–208.