American Journal of Physical Medicine & Rehabilitation Articles Ahead of Print
DOI: 10.1097/PHM.0000000000001549

Feasibility and Efficacy of Cardiopulmonary Rehabilitation following COVID-19

Matthias Hermann, MD[1]; Anna-Maria Pekacka-Egli[2]; Fabienne Witassek, PhD[3]; Reiner Baumgaertner, MD[4]; Sabine Schoendorf[2]; Marc Spielmanns, MD[2,5]

[1] University Heart Center Zurich, Department of Cardiology, University Hospital Zürich, Zürich, Switzerland

[2] Pulmonary Medicine and Sleep Medicine Center, Zürcher RehaZentren Klinik Wald, Switzerland

[3] AMIS Plus Data Center, Epidemiology, Biostatistics and Prevention Institute, University of Zurich, Zurich, Switzerland

[4] Cardiology, Zürcher RehaZentren Klinik Wald, Switzerland

[5] Department for Pulmonary Medicine, Faculty of Health, University Witten-Herdecke, Germany

Corresponding author:

Marc Spielmanns MD, PhD

Zürcher RehaZentren Klinik Wald, 8636 Wald, Switzerland

spielmanns@me.com; Tel: 0041 55 256 6822

Author Disclosures:

The authors refer no competing or financial benefits. No financial support for the research, authorship, and/or publication of this article was received. This paper is not under consideration elsewhere and none of the contents have been published.

Brief Report

Abstract

The COVID-19 pandemic affects a large number of patients with a rapid progression of respiratory failure often requiring hospitalization or intensive care unit treatment in some patients. Survivors of severe COVID-19 suffer from persistent weakness and cardiorespiratory failure. Feasibility and potential benefit of cardiopulmonary rehabilitation (CR) after COVID-19 remains unclear. Therefore, we retrospectively analyzed a cohort of COVID-19 patients in a single center inpatient rehabilitation clinic and describe performance and outcome during CR.

Patients were referred from acute care hospitals for rehabilitation after severe COVID-19. The cohort (n=28) was divided in ventilated or not ventilated patients for further analysis. 50% were female, mean age was 66 years and patients stayed in the acute hospital for 19.3±10.7 days before referral for CR. 17 patients (61%) needed previous ICU treatment in the acute care hospital. Risk factors, assessments and questionnaires on admission were comparable in both groups. Significant enhancements were observed in 6-minute walking test and Feeling Thermometer which were independent of previous ventilation status.

In conclusion, comprehensive CR following COVID-19 is safe, feasible and effective. Improvements in physical performance and subjective health status were independent of previous ventilation.

Key Words: COVID-19, Rehabilitation, Outcome, 6-MWT, Feeling-Thermometer

Introduction

Infection with the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV2), hereafter referred as COVID-19, often affects patients with chronic health conditions and takes a more severe course in patients with comorbidities such as cardiovascular disease, diabetes mellitus, and obesity.[1] A feature of severe COVID-19 is the rapid progression of respiratory failure often requiring hospitalization or even intensive care unit (ICU) treatment.[2] Severe outcome of COVID-19 is particular driven by a so called systemic endotheliitis, a severe cytokine storm and activated coagulation and mortality of severe COVID-19 is high.[3,4] Survivors suffer from reduced lung function, critical illness polyneuropathy and myopathy and cardiorespiratory deconditioning that could be described as a form of Post Intensive Care Unit Syndrome (PICS).[5,6]

Survivors of severe COVID-19 are significantly impaired in all activities of daily living and are in need of multimodal rehabilitation with particular knowledge in cardiovascular and pulmonary medicine. After acute respiratory distress syndrome associated with COVID-19 and subsequent ICU treatment, most patients suffer from reduced lung function, critical illness polyneuropathy and critical illness myopathy and cardiorespiratory deconditioning.[7] In addition, high prevalence of anxiety and depression has been reported after ICU treatments and hospital admission for COVID-19 might be associated with fear of survival of patient and families.[8-10]

However, as the whole COVID-19 condition is so new, there are scarce data available about feasibility, safety and success of in-patient CR in COVID-19 patients. We hypothesized that CR

Copyright © 2020 Wolters Kluwer Health, Inc. All rights reserved.

for COVID-19 is safe and feasible and therefore aimed to characterize patients referred to in-patient rehabilitation and describe performance and outcome during rehabilitation.

Methods

Participants and Procedures

The cohort presents patients referred for CR to the Zürcher RehaZentren Wald, Switzerland after hospitalization in acute care hospitals for COVID-19 between March and May 2020. Patients were retrospectively analyzed to describe potential differences, performance and outcome during rehabilitation. Patients were eligible for rehabilitation as soon as they were hemodynamically and respiratory stable (no catecholamine or invasive ventilation) and without the need for permanent monitoring. In the initial phase of the Corona crisis in Switzerland, patients were admitted after being asymptomatic for 2 days and 10 days after onset of infection. Initially patients were admitted after 2 days of no symptoms and 10 days after onset of infection, and later patients were required to have at least one negative swab before transfer.. For these patients isolation was not necessary according to the current guidelines in Switzerland and were cared for on a normal ward. All patients gave written informed consent and local ethics committee approved the study protocol (BASEC-No 2020-01061).

The cohort was divided into mechanically ventilated patients (n=12) or not ventilated patients (n=16) in the acute hospital setting in order to analyze the impact of very severe COVID-19. Within two days after admission for rehabilitation all patients were assessed with questionnaires, such as Chronic Respiratory Questionnaire (CRQ), Hospital Anxiety and Depression Scale (HADS), and Cumulative Illness Rating scale (CIRS) and Functional Independence Measure

(FIM). To measure changes during rehabilitation, functional assessments with 6-minute walk test (6-MWT) and Feeling Thermometer (FT) were performed on admission and before discharge. All patients were deemed cognitively able to provide valid responses to the questionnaires by treating physicians. Comorbidities, Lung function, and laboratory values including blood gas analysis were assessed.

CR Intervention

The patients participated in a multimodal 2-4 weeks inpatient CR, which was carried out according to a protocol adapted to the severity of the disease. This program normally included a total of 25-30 therapy sessions, which took place on 5-6 days per week. It consisted of an individualized exercise training including aerobic exercise and strength training.

Training intensity for aerobic exercise was mainly derived from an initial 6-MWT, only in some patients exercise cycle ergometer tests were performed. The aerobic program consisted primarily of supervised in- and outdoor walking, or stationary cycling. Patient were monitored using pulse oxymetry during their exercise. criteria for stopping or reducing exercise intensity was SpO_2 < 88%, symptom limited (Borg $\geq$6) or/and reaching their submaximal heart rate.

Strength training was performed 3 x 20 repetitions with the maximum tolerated load. The intensity of the monitored endurance training sessions was adjusted continuously, with the aim of achieving the maximum tolerated exercise load during each training session. When a drop in oxygen saturation was observed, oxygen was added with a maximum of 4 L via nasal cannula to keep the oxygen saturation at >90%. Respiratory physiotherapy consisted of teaching breath

control (pursed lip breathing, secretion mobilization and diaphragmatic breathing), energy saving techniques and controlled coughing exercises. Twice a week (1 h each), all patients participated in educational sessions, which in addition to self-management, included coping skills and nutrition interventions, self-medication, management of infections and exacerbations, dyspnoea, use of oxygen, as well as activities of daily living. To the underweight and overweight patients a nutritional advice and diabetes advice was offered.

If needed the patients took part in a structured smoking cessation program, and received psychosocial support.

Non-invasive ventilation (NIV) using breathing support administered through a face mask in order to reduce the work load of breathing and improve gas exchange was initially used in 3 patients during night time only and not during exercise training.

Hygiene Concept during rehabilitation

For the treatment and management of COVID-19 patients, the recommendations of the Swiss Noso (Swiss National Institute of Infection-Prevention) and the Health Department of the Kanton Zurich were applied. An assessment of the hygienic risk was made for the individual patient. If isolation was indicated the patients were transferred to the isolation ward where they were supervised in a single room. The staff in close contact with these patients (especially nursing staff and physiotherapists) had to wear FFP-2 masks, long-sleeved disposable fluid repellent gowns or disposable fluid repellent coveralls, eye protection, and gloves. Temporary isolation was stopped following negative COVID-19 swab. In some cases, the viral RNA was still

detected in the PCR although being asymptomatic leading to the continued isolation until at least one test was negative. In isolated patients, individual therapies were carried out 1-2 times a day for 15-45 minutes depending on the level of performance, according to the severity of the illness and were adjusted in the course of time. Therapies took place in the patients room and instructions for self-training were given as well as smaller therapy devices, such as elastic resistance bands and/or breathing training devices such as RC-Cornet® or VRP1-flutter®. Some training devices were stored in a central location in the isolation ward and were disinfected after each therapy, such as motorized training devices, stepper, ergometer, etc. Respiratory therapies, psychological support, massages, nutrition and diabetes counselling, social services, etc. were provided. The frequency of these treatments were adapted to the individual and diagnosed limitations and needs of the patients.

Exercise capacity

Exercise capacity was measured at hospital admission and discharge using the 6-min walk test (6-MWT), performed once at the beginning and once at the end of the CR program after 20 days, according to the guidelines of the American Thoracic Society (ATS) and carried out by experienced, well-instructed examiners.[11]

Quality of life

As standardized health-related quality of life (HRQoL) measurement tool, the German version of the Chronic Respiratory Questionnaire (CRQ) was used. The questionnaire measures eight dimensions of HRQoL and allows calculation of two summary scales of physical and mental health.[12]

Copyright © 2020 Wolters Kluwer Health, Inc. All rights reserved.

Functional Independence Measure (FIM)

The FIM is an 18-item measurement tool that explores an individual's physical, psychological and social function.[13] We used this tool to assess a patient's level of disability as well as change in patient status in response to rehabilitation.

Cumulative Illness Rating scale (CIRS)

CIRS was used as an indicator of health status and predicted 18-month mortality and rehospitalization especially in hospitalized elderly patients.[14]

Hospital Anxiety and Depression Scale (HADS)

The HADS was originally designed as a short, easy-to-use, 14-item screening tool for depression and anxiety symptoms in the hospital outpatient setting.[15] It is composed of two 7-item subscales (both ranging from 0 to 21 with higher scores indicating more severe distress.

Feeling Thermometer (FT)

We used the FT to determine and compare patients' feelings about their actual wellbeing by applying a numeric rating of their feelings toward an imaginary scale in terms of degrees, with their attitudes corresponding to temperatures.

Lung function, blood gas analysis and oxygen therapy

Spirometry and body plethysmography (Master Screen Body; Jaeger GmbH, Hoechberg, Germany) were performed on CR discharge according to recent guidelines.[16] Blood gases were

taken at rest under room air condition (Radiometer ABL800, Willich, Germany) at the admission to CR.

Statistics

Binary variables were presented as frequencies and the Fisher`s exact test was used for group-comparison. Normally distributed continuous variables were presented as mean with standard deviation (SD) and the T-Test was used for comparison between groups. Not normally distributed continuous variables were presented as median with inter-quartile range (IQR) and the Mann-Whitney-U-Test was used for group-comparison. P-value <0.05 was considered as statistically significant.

Results

50% were female, mean age was 66 years and duration of stay was 19.3±10.7 days before referral for CR.(Table 1) 17 patients (61%) needed ICU treatment and 12 patients needed ventilation in the acute hospital setting with a mean duration of 10.8±6.3 days. Ventilated patients had a longer ICU stay in days (17.0 (5.9) vs 6.4 (3.8); p<0.002) and total duration of the hospitalization in days (27.6 (9.1) vs 12.7 (1.7); p<0.001). All patients performed a CR with a mean duration of 20 days. Partially CR was provided with limited intensity due to hygiene concept and necessary isolation. 21 patients (75%) still needed nasal oxygen therapy and 3 (11%) received non-invasive ventilation (NIV) during the night on admission to CR. None died or had to be retransferred to the acute hospital setting. 85% of the patients were still isolated on admission while 15% of them had least one negative SARS-CoV-2 swab taken in the acute clinic before transfer to the rehabilitation clinic.

Risk factors were comparable in both groups according to the comorbidities. At admission to CR CIRS, HADS and FIM scores were similar for the ventilation group in comparison to the non-ventilated group. This was also true for the Questionnaires (HADS, CRQ), 6-MWT and FT (Table 1).

Significant enhancements were observed in 6-MWT (+130m) and FT (+40 points) for total cohort with no significant differences in the intergroup comparison between ventilated and non-ventilated patients. (Figure) Chest x-ray was performed in 27 patients before discharge showing persistent bilateral infiltrations in 20 patients (74%). Lung function testing before discharge showed persistent obstructed ventilation in just a few cases but predominantly restricted ventilation and reduced diffusion capacity were observed in most of the patients, without significant differences between both groups (mean FEV1 56% pred (± 12), mean FEV1%FVC 81% (± 9), mean TLC 62% pred (± 8), mean transfer factor of the lung for carbon monoxide 56% pred (± 12). 7 patients (25%) still required supplemental oxygen at discharge from CR. However, all patients were able to return back home without professional nursing support.

The findings in the laboratory results indicated that patients with previous ventilation had significant higher inflammation markers (CRP, leucocytes) on admission to CR while there were no significant differences between both groups in the level of Creatinin, Hemoglobin, D-Dimere, BGA, and respiratory parameters (Table 1 and Table 2).

Discussion

We demonstrated that CR could be performed safely and with beneficial effect in a rehabilitation cohort of COVID-19 patients. All patients with severe COIVD-19 being referred for CR were stable enough to participate in a comprehensive program irrespective of restrictions due to hygiene safety requirements. Functional capacity and subjective health status improved significantly, as assessed by 6-MWT and FT. Interestingly, patients with previous mechanical ventilation showed identical improvements in 6-MWT and FT as patients without ventilation and no major differences in patient's baseline characteristics including risk factors, respiratory parameters and functional measures. However, the intergroup comparison of the 6-MWT showed an increase of 26.9 meters for the ventilated group compared to non-ventilated patients. Although statistically not relevant, this result was above the minimal important difference of 25m in pulmonary patients. [17] An explanation might be their longer stay in the acute hospital with more time to recover, which possibly also explains the missing difference in the 6-MWT on admission to CR. We would have expected, in contrast to the observation that patients with the lowest initial distance walked in 6-MWT have a higher probability of reaching the minimal important difference.[18] The almost identical improvements in both groups suggest a classic deconditioning rather than the muscle dysfunction that is often discussed in context with COVID-19. At discharge we found in most patients a restricted ventilation according to their lung function which is in line with data from 2005 of 97 SARS survivors, showing in 24% persistent reduction of lung diffusion and exercise capacity at 1-year follow-up.[19]

The need for rehabilitation during the COVID-19 pandemic has been published recently.[20] We demonstrate that inpatient CR is apparently feasible and safe in COVID-19 patients, as long as

proper safety precautions, close medical management, and supplemental oxygen are available and used if needed.

Limitations

Like all retrospective analyses, the validity of the data is already limited by the study design itself. Referring the severe and very severe COVID-19 patients to this CR program leads to a one-sided view of COVID-19, which is why the results cannot be transferred to the total cohort of COVID-19 patients, probably leading to a selection bias. Another limitation is the short observation period of an average of 20 days. It is not sure that all patients received exactly the same CR content, as the program had to be varied or limited in some patients due to isolation. In addition, the single-center approach and the lack of a control group limit the validity of the data.

Conclusion

Comprehensive CR following COVID-19 is safe, feasible and effective. Improvements were significant according to physical performance and subjective health status regardless of previous ventilation. Safety issues regarding a strict hygiene concept addressing contact isolation and personal protection equipment was important but could also be implemented within CR.

References

1. Lew HL, Oh-Park M, Cifu DX. The War on COVID-19 Pandemic: Role of Rehabilitation Professionals and Hospitals. *Am J Phys Med Rehabil.* May 4 2020.

2. Murthy S, Gomersall CD, Fowler RA. Care for CRitically Ill Patients With COVID-19. *JAMA.* Mar 11 2020.

3. Varga Z, Flammer AJ, Steiger P, et al. Endothelial cell infection and endotheliitis in COVID-19. *Lancet.* May 2 2020;395(10234):1417-1418.

4. Guzik TJ, Mohiddin SA, Dimarco A, et al. COVID-19 and the cardiovascular system: implications for risk assessment, diagnosis, and treatment options. *Cardiovasc Res.* Apr 30 2020.

5. Cao B, Wang Y, Wen D, et al. A Trial of Lopinavir-Ritonavir in Adults Hospitalized with Severe Covid-19. *N Engl J Med.* May 7 2020;382(19):1787-1799.

6. Rawal G, Yadav S, Kumar R. Post-intensive Care Syndrome: an Overview. *J Transl Int Med.* Jun 2017;5(2):90-92.

7. Zhao HM, Xie YX, Wang C. Recommendations for respiratory rehabilitation in adults with COVID-19. *Chin Med J (Engl).* Apr 9 2020.

8. Simpson R, Robinson L. Rehabilitation After CRitical Illness in People With COVID-19 Infection. *Am J Phys Med Rehabil.* Jun 2020;99(6):470-474.

9. Nikayin S, Rabiee A, Hashem MD, et al. Anxiety symptoms in survivors of CRitical illness: a systematic review and meta-analysis. *Gen Hosp Psychiatry.* Nov - Dec 2016;43:23-29.

10. Rabiee A, Nikayin S, Hashem MD, et al. Depressive Symptoms After CRitical Illness: A Systematic Review and Meta-Analysis. *CRit Care Med.* Sep 2016;44(9):1744-1753.

11. Laboratories ATSCoPSfCPF. ATS statement: guidelines for the six-minute walk test. *Am J Respir CRit Care Med.* Jul 1 2002;166(1):111-117.

12. Guyatt GH, Berman LB, Townsend M, Pugsley SO, Chambers LW. A measure of quality of life for clinical trials in chronic lung disease. *Thorax.* Oct 1987;42(10):773-778.

13. LinaCRe JM, Heinemann AW, Wright BD, Granger CV, Hamilton BB. The structure and stability of the Functional Independence Measure. *Arch Phys Med Rehabil.* Feb 1994;75(2):127-132.

14. Salvi F, Miller MD, Grilli A, et al. A manual of guidelines to score the modified cumulative illness rating scale and its validation in acute hospitalized elderly patients. *J Am Geriatr Soc.* Oct 2008;56(10):1926-1931.

15. Snaith RP, Zigmond AS. The hospital anxiety and depression scale. *Br Med J (Clin Res Ed).* Feb 1 1986;292(6516):344.

16. Miller MR, Hankinson J, Brusasco V, et al. Standardisation of spirometry. *Eur Respir J.* Aug 2005;26(2):319-338.

17. Holland AE, Hill CJ, Rasekaba T, Lee A, Naughton MT, McDonald CF. Updating the minimal important difference for six-minute walk distance in patients with chronic obstructive pulmonary disease. *Arch Phys Med Rehabil.* Feb 2010;91(2):221-225.

18. Spielmanns M, Gloeckl R, Schmoor C, et al. Effects on pulmonary rehabilitation in patients with COPD or ILD: A retrospective analysis of clinical and functional predictors with particular emphasis on gender. *Respir Med.* Apr 2016;113:8-14.

19. Hui DS, Wong KT, Ko FW, et al. The 1-year impact of severe acute respiratory syndrome on pulmonary function, exercise capacity, and quality of life in a cohort of survivors. *Chest.* Oct 2005;128(4):2247-2261.

20. Stein J, Visco CJ, Barbuto S. Rehabilitation Medicine Response to the COVID-19 Pandemic. *Am J Phys Med Rehabil.* May 18 2020.

Figure legend

Figure (A, B): change during rehabilitation. Improvement in 6-MWT (A) and Feeling Thermometer (B)

Figure (A, B): change during rehabilitation. Improvement in 6-MWT (A) and Feeling Thermometer (B)

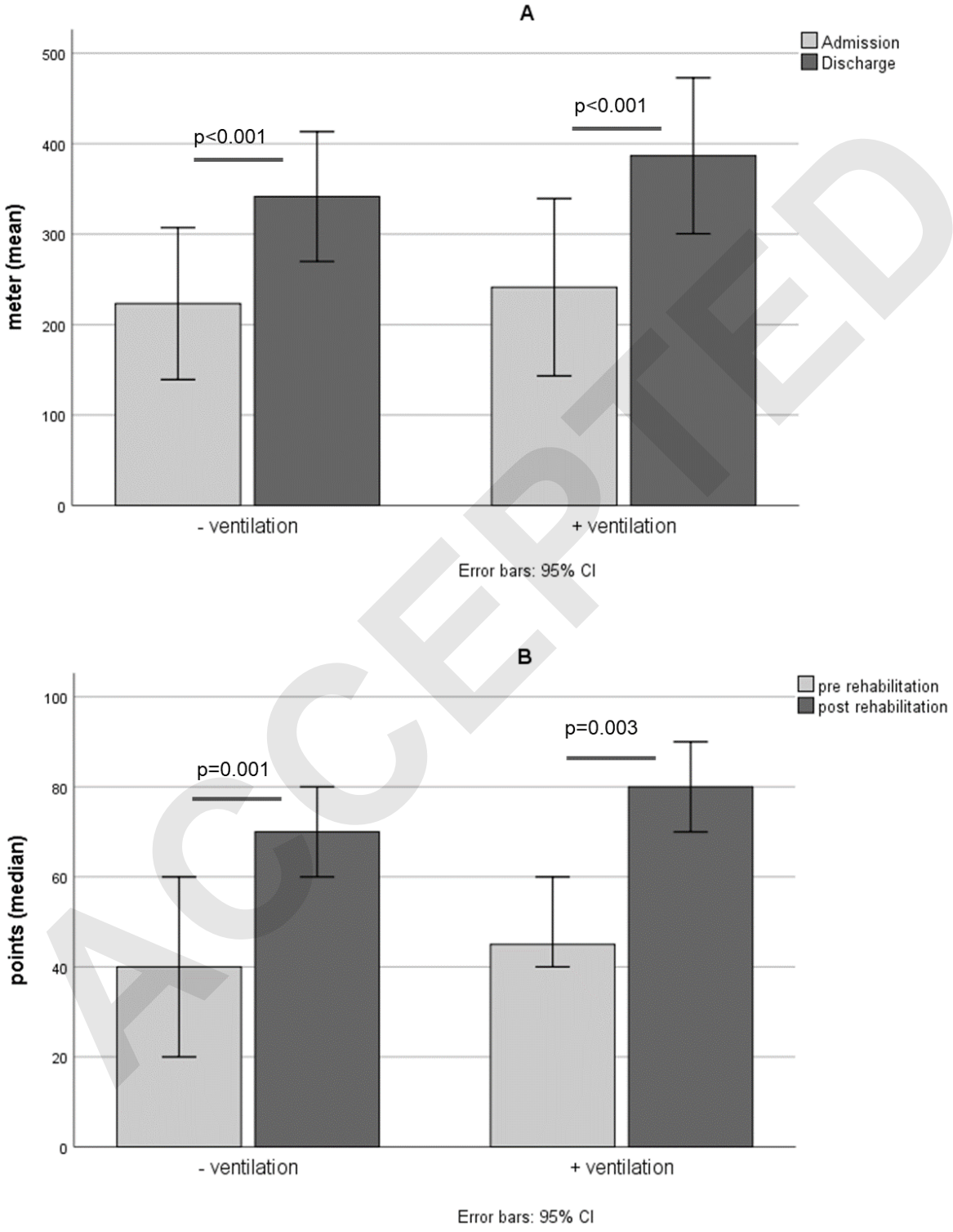

Table 1: Baseline characteristics and results of cardiopulmonary rehabilitation in severe COVID-19 patients

	Total group N=28	**+ ventilation N=12**	**- Ventilation N=16**	**p value**
Age [mean (SD)]	66.04 (9.3)	64.3 (8.9)	67.4 (9.7)	0.390
Sex, male, n [%]	14/28 (50.0)	9/12 (75.0)	5/16 (31.3)	0.054
BMI [mean (SD)]	27.6 (4.9)	26.9 (3.5)	28.1 (5.7)	0.553
ICU stay, n [%]	17/28 (60.7)	12/12 (100.0)	5/16 (31.3)	<0.001
Hospitalisation days (acute) [mean (SD)]	19.3 (10.7)	27.6 (9.1)	12.7 (6.5)	<0.001
ICU days, n [mean (SD)]	13.9 (7.3)	17.0 (5.9)	6.4 (3.8)	0.002
Comorbidities prior COVID-19, n [%]				
Coronary artery disease	4/28 (14.3)	1/12 (8.3)	3/16 (18.8)	0.613
Stroke	1/28 (3.6)	0/12 (0.0)	1/16 (6.3)	1.000
Hypertension	14/28 (50.0)	5/12 (41.7)	9/16 (56.3)	0.704
Type 2 diabetes	7/28 (25.0)	4/12 (33.3)	3/16 (18.8)	0.418
Dyslipidemia	6/28 (21.4)	2/12 (16.7)	4/16 (25.0)	0.673
Peripheral artery disease	2/28 (7.1)	0/12 (0.0)	2/16 (12.5)	0.492
Chronic renal failure (eGFR <60 ml/min)	5/28 (17.9)	3/12 (25.0)	2/16 (12.5)	0.624
Previous smoker	7/28 (25.0)	5/12 (41.7)	2/16 (12.5)	0.103
Current smoker	0/28 (0.0)	-	-	-
COPD (all stages)	6/28 (21.4)	0/12 (0.0)	6/16 (37.5)	0.024
CIRS points	9.9 (5.1)	9.3 (4.2)	10.3 (5.7)	0.592
Questionnaires / Assessments				
6-MWT, meters at entry [mean (SD)]	230.9 (153.6)	241.3 (154.4)	223.1 (157.7)	0.764
6-MWT, meters at discharge [mean (SD)]	360.9 (134.6)	386.7 (135.7)	341.6 (134.7)	0.391
6-MWT, meters change [mean (SD)]	130.0 (78.0)	145.4 (59.1)	118.5 (89.8)	0.376
FT, points at entry [median (IQR)]	40.0 (40.0;55.0)	45.0 (40.0;50.0)	40.0 (31.3;60.0)	0.536
FT, points at discharge [median (IQR)]	80.0 (67.5;84.0)	80.0 (75.0;90.0)	70.0 (60.0;80.0)	0.066
FT, points change [median (IQR)]	30.0 (22.5;40.0)	30.0 (25.0;40.0)	30.0 (20.0;40.0)	0.434
CRQ, score points [median (IQR)]	4.0 (3.4;4.9)	4.3 (3.0;5.5)	4.0 (3.4;4.9)	0.877
FIM, total points [median (IQR)]	107.0 (103.0;122.0)	106.0 (103.0;122.0)	113.5 (103.0;122.8)	0.451
HADS A, points [median (IQR)]	4.0 (1.0;7.0)	4.5 (2.5;6.8)	3.0 (0.0;8.0)	0.779
HADS D, points [median (IQR)]	4.0 (1.0;7.0)	4.0 (3.0;7.8)	1.0 (0.0;7.0)	0.281
Laboratory values [mean				

(SD)]				
CRP, mg/L	122.4 (94.6)	171.9 (107.7)	85.2 (64.6)	0.024
Leucocytes, G/L	7.9 (3.2)	10.3 (3.4)	6.3 (1.7)	0.002
Creatinine, µmol/ml	91.6 (74.4)	116.8 (106.4)	72.6 (28.0)	0.185
Hemoglobin, g/L	116.7 (21.7)	108.8 (22.9)	122.6 (19.3)	0.096
Creatine kinase, U/L	114.0 (79.8)	136.0 (79.2)	94.2 (78.9)	0.266
D-Dimere, ng/ml	4.1 (3.5)	4.3 (3.5)	3.9 (3.7)	0.785

BMI, body mass index; ICU, intensive care unit; COPD, chronic obstructive pulmonary disease; 6-MWT, 6-minute walk test; FT, Feeling Thermometer; CIRS, Cumulative illness rating Scale; CRQ, Chronic Respiratory Questionnaire; FIM, Functional Independence Measure; HADS A, Hospital Anxiety and Depression Scale Anxiety; HADS D, Hospital Anxiety and Depression Scale Depression; CRP, c-reactive protein; extern, referred to CPR;

in-house infected, infection occurred during rehabilitation.

*p-value for the comparison with the total group of the extern cohort.

Table 2: respiratory parameters of COVID-19 patients before discharge from rehabilitation

	Total group N=28	+ ventilation N=12	- Ventilation N=16	p value
Respiratory parameters				
BGA pO2, kPa [mean (SD)]	9.4 (2.9)	9.9 (3.5)	8.9 (2.3)	0.451
BGA pCO2, kPa [mean (SD)]	4.9 (1.2)	4.7 (0.8)	5.1 (1.4)	0.460
SpO2 Admission, % [mean (SD)]	92.7 (2.7)	92.4 (2.2)	92.9 (3.1)	0.665
SpO2 Discharge, % [mean (SD)]	96.0 (2.3)	96.0 (2.8)	96.1 (2.1)	0.946
O2 Therapy at admission, n [%]	21/28 (75.0)	11/12 (91.7)	10/16 (62.5)	0.184
O2 Therapy at discharge, n [%]	7/28 (25.0)	4/12 (33.3)	3/16 (18.8)	0.418
NIV at admission, n [%]	3/27 (11.1)	2/11 (18.2)	1/16 (6.3)	0.549
Obstruction				
None, n [%]	8/21 (38.1)	3/9 (33.3)	5/12 (41.7)	1.000
Mild, n [%]	2/21 (9.5)	0/9 (0.0)	2/12 (16.7)	0.486
Moderate, n [%]	0/21 (42.9)	-	-	-
Severe, n [%]	0/21 (4.8)	-	-	-
Very severe, n [%]	1/21 (4.8)	0/9 (0.0)	1/12 (8.3)	1.000
Restriction				
Non, n [%]	8/21 (38.1)	2/9 (22.2)	6/12 (50.0)	0.367
Mild, n [%]	2/21 (9.5)	1/9 (11.1)	1/12 (8.3)	1.000
Moderate, n [%]	9/21 (42.9)	6/9 (66.7)	3/12 (25.0)	0.087
Severe, n [%]	1/21 (4.8)	0/9 (0.0)	1/12 (8.3)	1.000
CO-Diffusion				
Normal, n [%]	1/21 (4.8)	0/9 (0.0)	1/12 (8.3)	1.000
Mild, n [%]	8/21 (38.1)	4/9 (44.4)	4/12 (33.3)	0.673
Moderate, n [%]	7/21 (33.3)	4/9 (44.4)	3/12 (25.0)	0.397
Severe, n [%]	4/21 (19.0)	1/9 (11.1)	3/12 (25.0)	0.603

BGA, blood gas analysis; NIV, non invasive ventilation; extern, referred to CPR; in-house infected, infection occurred during rehabilitation.

*p-value for the comparison with the total group of the extern cohort.