

1 **- ONLINE SUPPLEMENTARY MATERIAL -**
2 **Benefits of pulmonary rehabilitation in COVID-19 –**
3 **a prospective observational cohort study**
4
5
6
7

8 **Authors:** Rainer Gloeckl PhD^{1,2}, Daniela Leitl MSc* ^{1,2}, Inga Jarosch^{1,2}, Tessa Schneeberger^{1,2},
9 Christoph Nell PhD³, Nikola Stenzel PhD⁴, Claus F. Vogelmeier MD⁵, Klaus Kenn MD^{1,2}, Andreas R.
10 Koczulla MD^{1,2,6}

11
12
13
14 **Affiliations:**

15 ¹ Department of Pulmonary Rehabilitation, Philipps-University of Marburg, Member of the
16 German Center for Lung Research (DZL), Marburg, Germany

17 ² Institute for Pulmonary Rehabilitation Research, Schoen Klinik Berchtesgadener Land –
18 Schoenau am Koenigssee; Germany

19 ³ Department of Pulmonology, Philipps-University Marburg, Germany

20 ⁴ Psychologische Hochschule Berlin (PHB), Berlin

21 ⁵ Department of Medicine, Pulmonary and Critical Care Medicine, University Medical Centre
22 Giessen and Marburg, Philipps-Universität Marburg, Germany. Member of the German
23 Center for Lung Research (DZL), Marburg, Germany

24 ⁶ Teaching hospital, Paracelsus Medical University, Salzburg, Austria

25 **Additional information on the comparison group of idiopathic pulmonary fibrosis**
 26 **(IPF) patients:**

27 The comparison group consisted of 17 IPF patients that were recruited for a randomized,
 28 controlled trial, investigating the benefits of pulmonary rehabilitation. These 17 patients
 29 belonged to the control group and received usual care (without pulmonary rehabilitation).
 30 Results from this study were recently published by our working group (Jarosch et al. J Clin
 31 Med 2020; 9, 1567). COVID-19 patients in the current study showed restrictive lung pattern
 32 similar to patients with chronic fibrotic lung diseases. Since the current study was not a
 33 randomized, controlled trial we draw an indirect comparison by using these IPF patients as
 34 a non-PR comparison group.

35 Description of baseline characteristics can be found in table S1. Furthermore, a comparison
 36 of changes following 3-weeks of rehabilitation in COVID-19 patients versus the outcomes of
 37 usual care in IPF patients after 2 months can be found in table S2.

38
 39 Table S1. Baseline characteristics post-COVID-19 patients on admission of pulmonary rehabilitation (PR) and
 40 the comparison group of non-PR-patients with idiopathic pulmonary fibrosis (IPF)

	Mild/moderate COVID-19	Severe/critical COVID-19	Non PR IPF group	p-value
General				
n	24	26	17	
Age, ys	52*** [47 - 56]	66 [60 - 71]	65 [58 - 75]	<0.001
Sex, female (%)	20 (83%)***	8 (31%)	3 (18%)	<0.001
BMI, kg/m ²	24.7 [22.0 - 29.8]	26.9 [24.2 - 29.2]	26.8 [24.8 - 28.8]	0.13
Oxygen therapy, n (%)	0* (0%)	7 (27%)	6 (35%)	0.007
Respiratory parameters				
PaO ₂ , mmHg	73.1 [63.6 - 77.4]	73.2 [62.7 - 77.6]	65.0 [74.0 - 47.1]	0.10
PaCO ₂ , mmHg	35.0 [32.6 - 38.5]	35.5 [31.8 - 36.9]	37.4 [34.6 - 40.3]	0.25
DLCO, %predicted	57.0* [50.0 - 65.5]	55.8 [37.2 - 63.0]	32.0 [20.0 - 48.0]	0.043
TLC, %predicted	82.2 [65.3 - 88.9]	80.9 [64.4 - 88.6]	65.5 [58.1 - 78.5]	0.24
FVC, %predicted	80.0 [59.2 - 90.9]	75.1 [59.8 - 90.6]	71.1 [62.2 - 88.5]	0.91
FEV ₁ , %predicted	83.3 [65.5 - 101.1]	79.1 [65.8 - 99.7]	82.9 [61.0 - 91.2]	0.65
FRC, %predicted	113.0*** [95.0 - 127.0]	82.6 [70.3 - 97.4]	73.2 [55.3 - 100.1]	<0.001
Exercise performance				
6MWD, m	509 [426 - 539]	344* [244 - 392]	416 [278 - 483]	<0.001
6MWD, %predicted	70.1 [57.8 - 80.2]	52.5 [42.4 - 58.3]	51.5 [40.4 - 70.5]	0.003
6MWT SpO ₂ nadir, %	96*** [94 - 97]	92* [88 - 94]	81 [71 - 90]	<0.001
End-6MWT dyspnea, Borg scale	4 [3 - 5]	5 [4 - 6]	3 [2 - 7]	0.16
Quality of life				
SF-36 physical component sum score, points	31.8 [26.2 - 35.7]	30.2* [22.7 - 36.8]	39.7 [30.5 - 46.9]	0.023
SF-36 mental component sum score, points	48.6 [37.2 - 53.8]	38.5 [30.1 - 52.8]	49.0 [35.4 - 52.8]	0.35

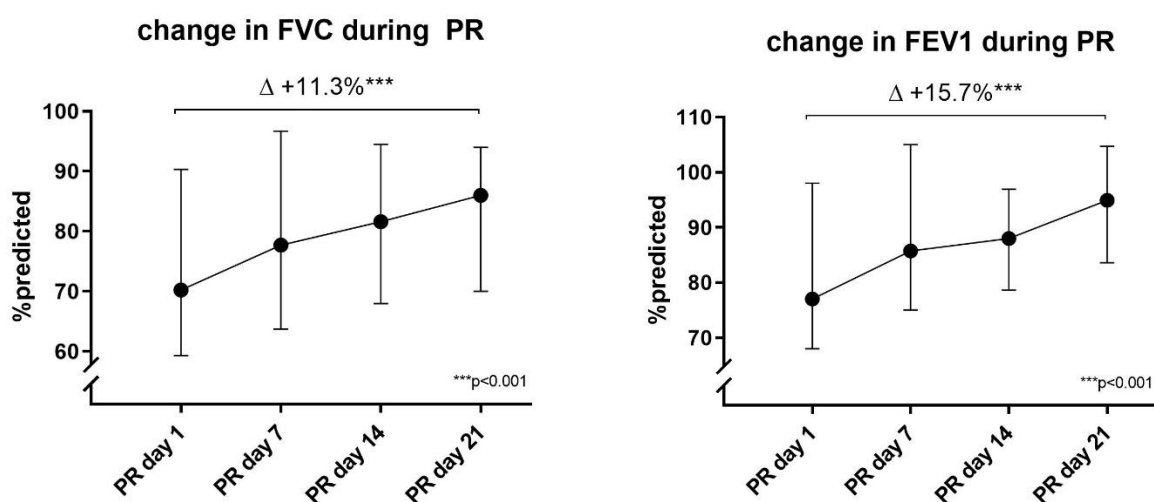
41 Data are presented as median and percentage or median and interquartile range.
 42 Significance between COVID-subgroup and IPF comparison group: *p<0.05; **p<0.01; ***p<0.001
 43 Abbreviations: 6MWD – 6-minute walk distance, 6MWT – 6-minute walk test, BMI: Body Mass Index, COVID-19: Corona Virus
 44 Disease 2019, DLCO – diffusion lung capacity for carbon monoxide, FEV₁ – forced expiratory volume in 1 second, FVC –
 45 forced vital capacity, O₂: oxygen, PaCO₂ – partial carbon dioxide pressure, PaO₂ – partial oxygen pressure, SpO₂ – oxygen
 46 saturation, TLC – total lung capacity

47 Table S2. Outcomes of a comprehensive inpatient pulmonary rehabilitation (PR) in 50 post-acute
 48 COVID-19 patients and a comparison group of 17 non-PR patients with idiopathic pulmonary fibrosis
 49 (IPF)

	<i>mild/moderate COVID-19 (n=24)</i>	<i>severe/critical COVID-19 (n=26)</i>	<i>non-PR IPF group (n=17)</i>	<i>p-value</i>
Respiratory parameters				
PaO ₂ , mmHg	2.7 [-0.9 - 10.8]	2.5 [-1.2 - 10.5]	0.6 [-6.5 - 5.7]	0.38
PaCO ₂ , mmHg	-1.2 [-2.7 - 2.5]	-0.2 [-2.9 - 2.7]	1.3 [-1.9 - 2.0]	0.37
DLCO, %predicted	4.5 [-1.8 - 16.5]	3.7* [-0.5 - 12.7]	-1.0 [-3.6 - 3.5]	0.038
TLC, %predicted	-1.1 [-4.7 - 10.7]	0.1 [-4.3 - 10.5]	0.0 [-4.0 - 1.8]	0.69
FVC, %predicted	7.7 [1.0 - 17.8]	11.3 [1.0 - 16.9]	1.0 [-4.1 - 7.3]	0.06
FEV ₁ , %predicted	11.8** [3.3 - 18.1]	15.7** [3.7 - 17.5]	0.5 [-4.0 - 4.5]	0.002
FVC, %predicted	0.0 [-5.0 - 11.0]	2.0 [-6.5 - 9.1]	-1.6 [-9.3 - 9.6]	0.882
Exercise performance				
6MWD, m	48** [35 - 113]	124*** [75 - 145]	-8 [-40 - 30]	<0.001
6MWD, %predicted	10.9** [4.7 - 14.6]	18.0*** [11.2 - 23.1]	-4.1 [-5.9 - 4.5]	<0.001
6MWT SpO ₂ nadir, %	0.0 [-2.0 - 1.0]	1.0 [-1.0 - 2.5]	0.5 [-3.0 - 7.3]	0.45
End-6MWT dyspnea, Borg scale	0 [-1 - 1]	0 [-2 - 1]	0 [-2 - 1]	0.98
Quality of life				
SF-36 physical component sum score, points	-0.1 [-4.0 - 9.9]	4.5* [0.5 - 9.5]	-1.4 [-4.2 - 3.2]	0.019
SF-36 mental component sum score, points	5.6 [1.4 - 9.2]	14.4 [-0.6 - 24.5]	-6.3 [-1.0 - 4.4]	0.099

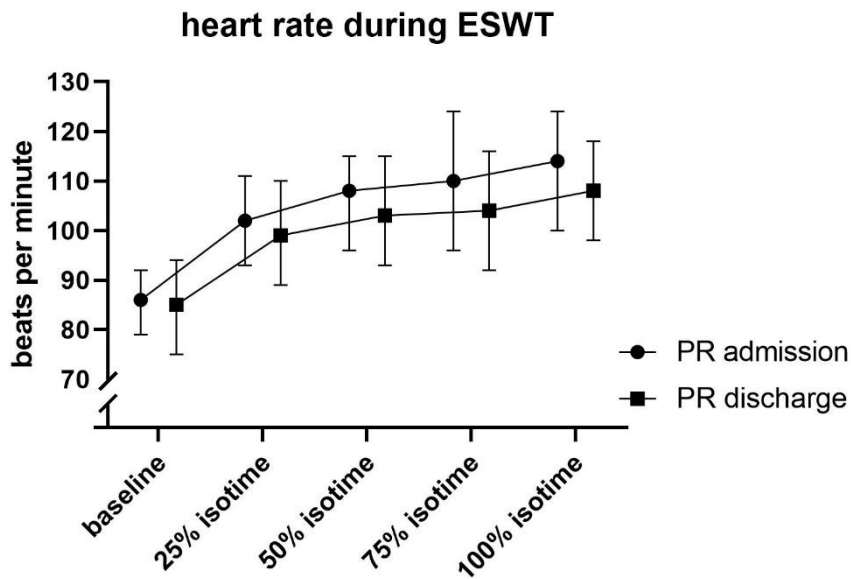
50 Data are presented as median and percentage or median and interquartile range.
 51 Abbreviations: 6MWD – 6-minute walk distance, 6MWT – 6-minute walk test, DLCO – diffusion lung capacity for carbon
 52 monoxide, FEV₁ – forced expiratory volume in 1 second, FVC – forced vital capacity, PaCO₂ – partial carbon dioxide pressure,
 53 PaO₂ – partial oxygen pressure, SpO₂ – oxygen saturation, TLC – total lung capacity

54
55
56
57



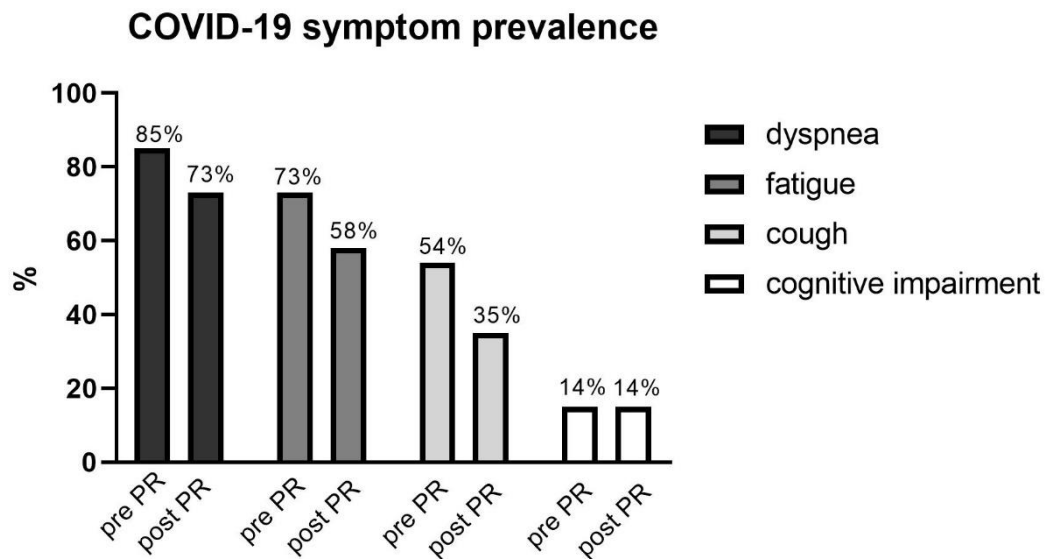
58 Figure S1. Change in forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV₁)
 59 during pulmonary rehabilitation (PR) in 26 patients with post-acute severe to critical COVID-19.
 60 Data are presented as median and interquartile range.
 61
 62

63
64



65
66 Figure S2. Development of heart rate during endurance shuttle walk test (ESWT) from
67 baseline to isotime in 26 patients with post-acute severe to critical COVID-19 before and
68 after pulmonary rehabilitation (PR). Data are presented as median and interquartile range.

69
70
71



72
73 Figure S3. Prevalence of COVID-19 symptoms in 26 patients with severe to critical COVID-19 pre and
74 post a 3-week comprehensive inpatient pulmonary rehabilitation. Symptoms were assessed by
75 interviewing patients. Therefore, a list of typical COVID-19 symptoms was read to them and patients
76 were asked to rate yes or no if they perceive any of the symptoms. None of the changes was
77 significantly different.

78