

Do Patients With COVID-19 Benefit from Rehabilitation? Functional Outcomes of the First 100 Patients in a COVID-19 Rehabilitation Unit

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Do Patients with Covid-19 Benefit from Rehabilitation?

Functional outcomes of the first 100 patients in a Covid-19 rehabilitation unit

Violaine Piquet^{1,2}, MBS, Cédric Luczak^{1,2}, MBS, Fabien Seiler^{1,2}, PT, Jordan Monaury^{1,2}, PET,

Alexandre Martini^{1,2}, MD, Anthony B Ward³, MD, Jean-Michel Gracies^{1,2}, MD, Damien

Motavasseli^{1,2}, MD; on behalf of the Covid Rehabilitation Study Group

1) AP-HP, Service de Rééducation Neurolocomotrice, Unité de Neurorééducation, Hôpitaux

Universitaires Henri Mondor, Créteil F-94010 France

2) UR 7377 BIOTN, Laboratoire Analyse et Restauration du Mouvement, Université Paris Est Créteil

(UPEC), France

3) North Staffordshire Rehabilitation Centre, Haywood Hospital, High Lane, Burslem, Stoke on Trent,

UK-ST6 7AG, United Kingdom

Corresponding author for review and publication:

Damien Motavasseli, MD Service de Rééducation Neurolocomotrice AP-HP, Hôpitaux Universitaires Henri Mondor 51 Avenue du Maréchal de Lattre de Tassigny 94000 Créteil, France Phone: +33-1-49-81-38-80 Fax : +33-1-49-81-30-69 E-mail: damien.motavasseli@aphp.fr

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1	Do Patients with Covid-19 Benefit from Rehabilitation?
2	Functional outcomes of the first 100 patients in a Covid-19 rehabilitation unit
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4	
5 6	ABSTRACT (274/275 words)
7	Objective: To determine the benefits associated with brief inpatient rehabilitation for Covid-
8	19 patients.
9	Design: Retrospective chart review.
10	Setting: A newly created specialized rehabilitation unit in a tertiary care medical center
11	Participants: Consecutive sample of the first 100 patients with Covid-19 infection admitted
12	to rehabilitation.
13	Intervention: Inpatient rehabilitation for post-acute care Covid-19 patients
14	Main Outcome Measures: Measurements, at admission and discharge, comprised a Barthel
15	Activities of Daily Living Index (including baseline value before Covid-19 infection), time to
16	perform 10 sit-to-stands with associated cardio-respiratory changes, and grip strength
17	(dynamometry). Correlations between these outcomes and the time spent in ICU were
18	explored.
19	Results: Patient characteristics upon admission to rehabilitation were: men 66%, age 66±22
20	years, mean delay from symptom onset 20.4±10.0 days, BMI 26.0±5.4 kg/m ² , hypertension
21	49%, diabetes 29%, with 26% having >50% pulmonary damage on CT-scans. Mean length of
22	rehabilitation stay was 9.8±5.6 days. From admission to discharge, the Barthel index (/100)
23	increased from 77.3 \pm 26.7 to 88.8 \pm 24.5 (p<0.001), without recovering baseline values
24	(94.5±16.2; p <0.001). There was a 37% improvement in sit-to-stand frequency (0.27±0.16 to
25	0.37±0.16 Hz; p<0.001), a 13% decrease in post-test respiratory rate (30.7±12.6 to 26.6±6.1;
26	p=0.03), and a 15% increase in grip strength (18.1±9.2 to 20.9±8.9 kg; $p<0.001$). At both

1/21

27	admission and discharge, Barthel score correlated with grip strength (rho= $0.39-0.66$; $p<0.01$),
28	which negatively correlated with time spent in ICU (rho=-0.57 to -0.49, p <0.05).
29	Conclusions: Inpatient rehabilitation for Covid-19 patients was associated with substantial
30	motor, respiratory and functional improvement, especially in severe cases, even though there
31	remained mild persistent autonomy loss upon discharge. Following acute stages, Covid-19,
32	primarily a respiratory disease, might convert into a motor impairment correlated with the
33	time spent in intensive care.
34	
35	Keywords: Covid-19, Pandemic, Rehabilitation
36	
37	List of abbreviations:
38	CT-scan: Computerized Tomography scan
39	D14: Day 14
40	D24: Day 24
41	ICU: Intensive Care Unit
42	IQ: InterQuartile
43	PM&R: Physical Medicine and Rehabilitation
44	PT: Physical Therapy
45	RNA: Ribonucleic Acid
46	RT-PCR: Reverse Transcriptase Polymerase Chain Reaction
47	

INTRODUCTION

50	The Covid-19 pandemic forced healthcare systems to rapidly adjust to constantly evolving
51	situations. Traditional acute care units were converted into Covid-19 units with concerns
52	about overwhelming hospital capacities. The rapid development of specific rehabilitation
53	units was essential in response to the high level of dependence observed in many patients and
54	the need to prevent outbreaks in other departments. Several authors have highlighted the need
55	to prepare for post-acute care, but few functional outcomes after Covid rehabilitation have
56	been reported. [1-7]
57	Covid-19 rehabilitation not only needs to address cardiorespiratory and motor deconditioning,
58	as seen in acute respiratory distress syndrome, but also neurological deterioration, aggravation
59	of comorbidities, and consequences of prolonged bed rest. [8-11]
60	
61	In this work, we quantified the changes in functional parameters from admission to discharge,
62	for the first 100 patients of a specifically designed Covid-19 rehabilitation unit, comparing
63	non-intensive care unit (ICU) with post ICU patients and those after short vs long prior stay in
64	acute care.
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67	MATERIAL AND METHODS
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69	Creation of the unit - Target patients
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72	A unit of thirty-five single rooms dedicated to Covid rehabilitation was opened to meet the
73	needs of our hospital group during the Spring 2020 epidemic wave, all patients coming from
74	its acute care units. Admission criteria in the rehabilitation unit comprised:
75	-positive RT-PCR or CT-scan supporting Covid-19 infection (as RT-PCR sensitivity has been
76	reported to range from 66% to 80%, patients having highly evocative clinical signs and CT-
77	scans were considered as Covid-19 patients, as in acute care departments) [12];
78	-no >6 liters/min oxygen requirement (patients requiring more than 6 liters/min of oxygen
79	were deemed unstable and remained under acute care);
80	-clinical impression of stability;
81	-no current endotracheal intubation or tracheotomy;
82	-and need for rehabilitation and/or extensive social work to optimize a return home.
83	
84	Nursing and medical care
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87	The ward was organized into sub-units of 8-9 patients, each operated by a team of two
88	physicians, one nurse, two nursing assistants, and two physical therapists. Full personal
89	protective equipment were donned by the staff for patients <14 days after symptom onset.
90	Patients remained in their room at all times, including for their rehabilitation treatments.
91	Following evidence suggesting the persistence of viral RNA on nasopharyngeal swabs for
92	over 20 days, rehabilitation stays were extended up to D24 and further. [13] For >D14
93	patients, less strict prevention procedures were implemented, involving the sole use of

94

96 Logistics and Equipment

medical masks and hand disinfection with hydro-alcoholic gel.

98

A physiotherapy space was arranged at the floor level for the >D14 patients to minimize patient transportations and to ease access to therapy activities. In addition, individual rehabilitation equipment was made available in each patient room, including dumb-bells, training bands, pedal-boards, hand-cycles, and chairs of standardized height. Eight bicycleergometers were available: five for the \leq D14 patient rooms and three for the >D14 physiotherapy space.

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106 Organization of the rehabilitation activities

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109 Two physical therapy (PT) sessions per day were provided for each patient but were kept 110 short (<20 minutes) given the compromised cardio-respiratory condition and high levels of 111 fatigability in post Covid patients. The therapy program primarily included overall motor 112 strengthening with body weight exercises (sit-to-stand, tiptoe stands, squats), elastics and 113 weights, with about three series of ten repetitions for each exercise, according to the patient 114 abilities. Respiratory rehabilitation exercises were associated, including controlled 115 diaphragmatic breathing, with work on the inspiratory and expiratory times. Aerobic work 116 included bicycle-ergometer sessions at submaximal intensity, with monitoring of vital 117 parameters. Finally, an individualized self-rehabilitation program was taught to patients, who 118 were strongly advised to pursue these exercises after discharge, using specific workbooks.

In addition to this PT work, a physical education teacher organized small group sessions for >D14 patients who had become able to handle one-hour long workshops (4 patients at a time, at least 4 meters apart). Two occupational therapists, one speech therapist, and one psychologist were also dedicated to the 35-bed unit. To be medically authorized, speech therapy sessions had to be provided beyond D24, after two consecutive negative RT-PCR tests. The psychologist also cared for the staff.

- 126
- 127 Discharge process
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- 129

130 To consider discharge home, patients had to be >D14 from symptom onset and no longer 131 symptomatic for Covid-19 infection for at least 48h. Suitable home accommodation with 132 temporary possibility of a private space was also required, as well as personal assistance if 133 needed, and no at-risk relative at home. A specific mobile discharge team comprising one 134 PM&R physician, one social worker and one occupational therapist helped detect early and 135 solve any social issues encountered towards returning home. The physician of the mobile 136 discharge team systematically provided tele-consultations after discharge. In addition, a 137 dedicated physiotherapist insured proper execution of the self-rehabilitation exercises by 138 visio-consultations. When discharge home was not possible at D24 from symptom onset, a 139 Covid-free rehabilitation unit was sought.

- 140
- 141 *Ethics*
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- 143

144	The local ethics committee approved the study (UPEC IRB 0011558 n°2020-064). Non-
145	opposition to utilization of patient data was systematically pursued.
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147	Study design and participants

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A retrospective chart review of the first 100 patients admitted to the Covid-19 rehabilitationdepartment was conducted since its opening on March 25, 2020.

152

153 Inclusion criteria included age ≥ 18 years, and the ability and willingness to participate in two 154 daily PT sessions five days a week. Among included patients, functional outcome criteria 155 were analyzed for lengths of stay ≥ 72 hours.

156

Demographics and clinical characteristics were recorded, including age, sex, date of admission, medical history, Covid-19 severity factors, clinical signs, biological and radiological data from the acute stay, drug treatments, date of discharge, length of stay, destination at discharge, and personal assistance at home if any. The following outcomes were assessed by only two physiotherapists to limit variability:

Barthel Index of Activities of Daily Living (also retrospectively assessed before the Covid
episode by questioning the patient or family); [14,15]

164 - Time to perform 10 full sit-to-stands as quickly as possible from a standardized 40-cm
165 height chair, arms folded over the chest, with respiratory rate, oxygen saturation, heart rate,
166 and Borg scale of perceived exertion, recorded before and after. [16-18] When 10 sit-to167 stands could not be completed, the number of completions in one minute was collected;

- Hand grip strength, using dynamometry. The forearm was resting on the thigh, palm
upwards, elbow to the body at 90° flexion. The best result of two tries was kept for each side.
[19,20]

171 Changes in these outcomes from admission to discharge were measured in all patients, and172 then compared between:

173 - Patients who stayed in ICU *versus* patients who did not.

Patients who stayed in acute care longer than the median length of stay *versus* those whostayed less.

176 Correlations between outcomes were also explored.

- 177
- 178 Data analysis

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180

181 Descriptive statistics were used for quantitative continuous variables using mean±SD or median (IQ). Qualitative data were compared using χ^2 -tests. Comparisons between admission 182 183 and discharge values were carried out by paired sample *t*-tests or Wilcoxon signed ranked 184 tests. Correlations between Barthel total score and other functional tests, and between 185 functional scores and time spent in acute care were explored by Spearman or Pearson tests. 186 Between-group comparisons were made using independent samples *t*-tests or Mann-Whitney 187 U tests. Patients with missing data, upon admission or discharge, were excluded from the 188 statistical analysis for the relevant parameter. All statistical analyses were performed 189 according to conditions of normality on Shapiro-Wilk tests. SPSS v25 software was used, 190 with a significance set at 0.05.

- 191
- 192 **RESULTS**
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195 **Population description**

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The descriptive characteristics of the 100 patients are presented in Table 1. On admission, median age was 66 (41% were >70) with 66% men; mean BMI was 26 kg/m²; mean delay post-onset was 20.4 \pm 10.0 days. At the time of diagnosis, the main clinical symptoms were dyspnea with fever and 26% had >50% pulmonary damage on CT-scans. There was a high prevalence of hypertension (48%) and diabetes (29%). In terms of prior drug treatment, 37% had received hydroxychloroquine, 9% had received liponavir, 5% had received tocilizumab and 6% had received corticosteroids.

205 23% of patients had been admitted to intensive care and 77% had needed oxygen. Upon 206 admission in rehabilitation, 58% still required oxygen, administered with nasal cannula (Table 207 2). The severity of admitted patients worsened over the course of the epidemic wave as the 208 proportion of ICU and intubated patients gradually increased to reach 60% and 50% 209 respectively by May 15, 2020, the date of the admission of the 100th patient. Of note, there 210 was a discrepancy between the number of patients hospitalized in intensive care and those 211 who were intubated (Supplemental Figure 1). Indeed, the general consensus was to limit 212 orotracheal intubation to a strict minimum to avoid complications related to this procedure. 213 [21] In parallel, the number of days since the onset of infection at admission also gradually 214 increased (Supplemental Figure 1A). The number of weekly admissions followed the spring 215 pandemic's curve, peaking at 25 (Supplemental Figure 1B & 2).

The mean length of stay in the rehabilitation unit was 9.8 ± 5.6 days, with 79% of discharges home or to a relative's and 15% transfers to Covid-free units for further inpatient rehabilitation. The proportion of patients needing personal assistance at home increased by 26% (p<0.001) as compared with before the infection, and 3% of patients still needed oxygen
at discharge (*Table 2*).

221

222 **Overall functional outcomes**

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224

- The total Barthel score improved from admission to discharge (77.3 \pm 26.7 vs 88.8 \pm 24.5 respectively; p<0.001), in particular in terms of personal care and motor skills (transfers, walking, and use of stairs). However, independence for personal tasks of daily living at discharge remained lower than prior to infection (88.8 \pm 24.5 vs 94.5 \pm 16.2 respectively; p=0.001) (*Figure 1*).

230 - Sit-to-stand frequency increased by 37% (0.27±0.16 to 0.37±0.16 Hz; *p*<0.001; *Figure 2A*);

231 - Post sit-to-stand test respiration rate dropped by 9% (30.1±12.0 to 28.0±7.5; *p*=0.029;
232 *Figure 2A*);

233 - Borg exertion score after the sit-to-stand test improved by 30% (3.0 \pm 2.4 to 2.1 \pm 1.5; 234 *p*=0.023; *Figure 2B*);

- Grip strength among right-handed people (92% of patients) increased by 15% (18.1±9.25 to
20.9±8.9 kg, *p*<0.001; *Figure 2C*).

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238 Correlations between length of acute stay, motor parameters and functional autonomy

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Barthel total score correlated with sit-to-stand frequency, both at admission and discharge (rho=0.66, p<0.001 and rho=0.53, p<0.001 respectively; *Figure 3A*) and with grip strength both at admission and discharge (rho=0.43, p=0.003 and rho=0.39, p=0.007 respectively; *Figure 3B*). Grip strength was negatively correlated with the number of days spent in ICU, both at admission and discharge (rho=-0.49, p=0.053 and rho=-0.57, p=0.021 respectively; *Figure 3C*), as was post-test Borg at discharge (rho=-0.51, p=0.042).

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248 Between-group comparisons

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251 Prior to admission into rehabilitation, the median length of stay in acute care was 14 days. 252 The patient groups considered for comparison were therefore: 1) ICU versus non-ICU stays; 253 2) ≥ 14 days versus <14 in acute care. The mean length of stay in the Covid rehabilitation 254 department was not different between these groups: post-ICU patients (n=23) had spent 255 9.4±4.2 days in our unit versus 9.9±5.3 days in non-ICU patients (n=77) (p=0.86), and 256 patients who spent ≥ 14 days in acute care (n=50) had spent 10.1±5.1 days in our unit versus 257 9.5 \pm 5.0 days for those who spent <14 days in acute care (n=50) (p=0.54). There was also no 258 difference in functional parameters upon admission into rehabilitation between these same 259 groups, including for grip strength and Barthel index. Yet, comparisons of changes in 260 functional outcomes from admission to discharge revealed two differences between the 261 groups:

- Grip strength improved more in post-ICU patients (+3.3±3.1 kg; n=13) versus patients who
did not require ICU (+0.99±3.7 kg; n=31; p=0.049; data not shown);

- The score for transfers on the Barthel Index improved more in patients who stayed ≥14 days
in acute care (+30.0±60.7%; n=45) than in patients who stayed <14 days (+8.7±22.3%, n=45; *p*=0.041; data not shown).

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271

In this retrospective study on the first 100 patients with Covid-19 infection admitted into a specialized rehabilitation unit, inpatient therapy was associated with substantial functional, motor, and cardio-respiratory improvement, particularly in those patients who had undergone severe acute disease. Nonetheless, loss of autonomy and motor weakness persisted at discharge, which occurred about a month after the onset of Covid-19.

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278 Usefulness of a Covid rehabilitation unit

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281 To our knowledge, the present article is the first to report quantified, systematically collected 282 data on rehabilitation effects in such a large cohort of Covid patients. It is worth mentioning 283 that this work came in the midst of a trend to convert many rehabilitation facilities into acute 284 departments in several countries. [22] In that context, the present study still suggests the 285 importance of early inpatient Covid rehabilitation, within 3 weeks of disease onset, including 286 sustained motor exercises. Our findings confirmed early reports from around the world: a 287 recent Japanese case report showed a comparable improvement on grip strength and Barthel 288 index in one patient with early rehabilitative care, while an Italian review of post Covid 289 clinical status upon admission into rehabilitation also observed low Barthel Index total scores 290 (<50, see below). [23,24] More recently, two studies compared functional data between 291 admission and discharge from a specialized rehabilitation unit, from smaller sample sizes. The 292 first study mainly provided respiratory data for 23 subjects, while the second provided other 293 functional data for 41 patients. As in the present work, both studies showed an improvement

in Barthel index and suggested that the neurological consequences of Covid infection couldbe long-lasting. [6,7]

296

297 In this study, most patients admitted to the rehabilitation unit were elderly, male, with a high 298 prevalence of cardiovascular comorbidities, all characteristics consistent with Covid-19 299 infection risk and severity factors previously reported. [25-27] The estimated Barthel index 300 prior to the episode was >90/100, showing that these patients were free of prior limitation of 301 daily activities. Barthel at admission in rehabilitation was thus notably low (77.3±26.7), 5% 302 of the patients having even lost all autonomy for daily activities (i.e. Barthel <30). Upon 303 admission, there was marked motor weakness in this non-geriatric population mostly free of 304 pre-morbid neurological disability, with a mean grip strength and a sit-to-stand frequency 305 both at 80% of normal values in that age range. At discharge, mean grip strength remained 306 10% below normal. [17,18,28] Therefore, in this study much of the post-acute functional 307 consequences seemed to be motor. The question may arise as to whether such motor 308 impairment may be attributable to sole deconditioning in patients who were hospitalized for 309 several days, or to direct Covid-19 aggression of neurological pathways. [29-33]

310

Any impact of Covid-19 on the nervous system is being scrutinized in the literature. A literature review with meta-analysis outlines possible neurological symptomatology. [34] The sole known neurological disorders observed in the present series were probable ICU-acquired weakness – unfortunately however, electroneuromyography was not systematically performed in the present cohort – and few post-intubation swallowing disorders. We did not note any emerging confusion related to the Covid-19 infection in a context where some of our patients did have pre-existing cognitive impairments. One patient suffered from an acute stroke for 318 which he was initially hospitalized and was then incidentally diagnosed with Covid-19. In the 319 presence of other risk factors, this stroke was not attributed to the ongoing Covid infection.

320 Most of the rehabilitative therapy involved motor exercises and few pure respiratory 321 exercises. Accordingly, motor progression was dramatic during the hospital stay and 322 functional autonomy highly correlated with motor performance. This made sense since the sit-323 to-stand test and grip strength have been shown to correlate with overall strength and global 324 physical functioning, thus assumingly with the Barthel Index. [15,17] The mean length of 325 rehabilitation stay (9.8±5.0 days) was notably shorter than in a traditional inpatient 326 rehabilitation setting. This may have resulted from both the intensity of the rehabilitative care 327 provided and the effectiveness of the mobile team specifically dedicated to accelerate the 328 discharge process.

Recovery was incomplete at discharge, which may imply the need to continue with outpatient rehabilitation beyond discharge. To this end, since outpatient physiotherapy was forbidden during the spring pandemic, patients were taught guided self-rehabilitation exercises and were provided with a workbook containing an individualized program, similarly to what exists in other indications [35]. A more prolonged stay might have allowed a more complete recovery.

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335 Effect of motor rehabilitation on severe Covid cases

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The findings suggest that an ICU or longer acute stay did not hamper responsiveness to rehabilitation. In fact, responsiveness was even enhanced for some outcomes in these severely affected patients. Admittedly, motor function may have started from lower values in these cases, even though differences upon admission into rehabilitation were not statistically significant between the groups. Nevertheless, these findings are reassuring, since they support the reversibility of much of the motor consequences of longer stays in acute care or of ICUstays.

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346 Study limitations

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349 The present study is not controlled. In the context of the health crisis of the Spring 2020, it 350 was not considered ethical to carry out a clinical trial of rehabilitation versus a "sham 351 rehabilitation" control group. The lack of hindsight in this disease and the emergencies that 352 professionals were faced with also made it impossible to design a control group with a real 353 but different rehabilitation protocol. Another limitation was the proportion of missing 354 functional data (see Tables & Figures). Due to rapid patient turnover, functional assessments 355 could not be always carried out. Data were however sufficient to show pre-post and between-356 group statistical differences. Respiratory data was also incomplete although these would have allowed to better characterize and follow up patients: spirometry was not assessed as there 357 358 was concern about the infectious risk of its use, and Pa/FiO2 measurements were not possible 359 since patients admitted in rehabilitation were not ventilated, as per inclusion criteria.

360

361 Conclusions

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363

When the Covid-19 health crisis began, a number of reports emphasized the need to be prepared for post-acute care management. [1-5] The objective, quantified functional improvement from admission to discharge suggests the usefulness of rehabilitation in a specialized unit after Covid-19 infection, with even greater improvement for some outcomes

368	in patients who had undergone ICU or stayed longer in acute care. However, the
369	consequences of severe Covid-19 infection on dependence appear to be long lasting and
370	predominantly related to motor limitation. Once the acute hospital situation has subsided,
371	prospective and randomized blinded studies comparing the effectiveness of different types of
372	rehabilitation and including specific respiratory assessments may further knowledge on Covid
373	rehabilitation.
374	
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384	The authors declare no competing interests.
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485 Figure 1. Changes in Barthel index (n=89)

486 A. Barthel index items; Items laid out in order to highlight motor tasks. B. Barthel index total

487 score. Data expressed in mean±SEM.

488 * p<0.05; ** p<0.01; *** p<0.001

489

490 Figure 2. Functional data upon admission and at discharge

491 A. Sit-to-stand parameters; B. Borg scale before and after Sit-to-stand test; C. Grip strength in

492 right-handed patients. Data expressed in mean±SEM.

493 * p<0.05; ** p<0.01; *** p<0.001

494

- 495 Figure 3. Correlations between motor/functional tests and Barthel index or number of
- 496 ICU days
- 497 **A.** Barthel total score and Sit-to-stand frequency at admission and at discharge.
- 498 **B.** Barthel total score and mean grip strength at admission and at discharge.
- 499 C. Grip strength and the number of days spent in ICU at admission and at discharge.
- 500 Spearman or Pearson tests were used according to conditions of normality on Shapiro Wilk
- 501 tests. Outliers beyond 2SD on Z-tests were excluded.









Admission

Discharge

TABLE 1 Population characteristics (n=100)

n≥95 for all collected data. Delays expressed in days. n [%] unless specified otherwise.

Demographics		
Age [median±IQ]	66±22	
Sex (Male)	66 [66%]	
Mean delay post-onset at admission	20.4±10.0	
Mean delay post-onset at discharge	32.7±10.7	
BMI [mean±SD]	26.0±5.4	
Clinical characteristics at time of diagnosis		
Dyspnea	79 [79%]	
Asthenia	76 [76%]	
Fever	73 [73%]	
Cough	64 [64%]	
Myalgia	33 [33%]	
Diarrhea	25 [25%]	
Ageusia	16 [16%]	
Headache	14 [14%]	
Anosmia	13 [13%]	
Pulmonary embolism	4 [4%]	
Thrombosis	1 [1%]	
Background and comorbidities		
High blood pressure	48 [48%]	
Age >70	41 [41%]	
Diabetes	29 [29%]	
BMI >30	17 [17%]	

BMI >30	17 [17%]
Renal failure	13 [13%]
Coronaropathy	1 [1%]
Stroke	9 [9%]
Immunosuppression	3 [3%]

TABLE 2 Characteristics of hospital stays (n=100)

 $n \ge 99$ for all collected data. Duration and lengths of stay expressed in days. n [%] unless specified otherwise.

Acute care		
Prior intensive care	23 [23%]	
Intubation	13 [13%]	
Duration of intubation [mean±SD]	8.2±8.5	
Nasal O2 at admission	77 [77%]	
Nasal O2 at discharge	58 [58%]	
Overall length of stay in acute care [mean±SD]	14.4±8.7	
In intensive care [mean±SD]	13.8±9.0	
In acute care after ICU [mean±SD]	10.22±4.87	
In acute care if no ICU stay [mean±SD]	11.65±6.48	
Rehabilitation care		
Length of stay [mean±SD]	9.8±5.1	
Deaths	2 [2%]	
At discharge		
Overall duration of O2 dependency [mean±SD]	17.4±11.1	
O2 dependency at discharge	3 [3%]	
Discharge home	75 [75%]	
Discharge to a relative's home	4 [4%]	
Transfer to a Covid-free rehabilitation unit	15 [15%]	
Transfer to acute care	8 [8%]	
Personal assistance before Covid	19 [19%]	
Personal assistance after Covid	24 [24%]	