Retrospective Clinical Research Report

Journal of INTERNATIONAL MEDICAL RESEARCH

Journal of International Medical Research
2022, Vol. 50(11) 1–12

DOI: 10.1177/03000605221138843
journals.sagepub.com/home/imr
SAGE

Evaluation of the predictive factors of the short-term effects of a multidisciplinary rehabilitation in COVID-19 survivors

Valentina Barbieri[1,2], Luca Scarabel[1,3], Laura Bertella[1], Federica Scarpina[4,5], Nicola Schiavone[3], Laura Perucca[2,6] and Paolo Rossi[1]

Abstract

Objective: Functional impairments after coronavirus disease 2019 (COVID-19) constitute a major concern in rehabilitative settings; however, evidence assessing the efficacy of rehabilitation programs is lacking. The aim of this study was to verify the clinical characteristics that may represent useful predictors of the short-term effectiveness of multidisciplinary rehabilitation.

Methods: In this real-practice retrospective pre–post intervention cohort study, the short-term effectiveness of a multidisciplinary patient-tailored rehabilitation program was assessed through normalized variations in the Functional Independence Measure in post-acute care patients who had overcome severe COVID-19. Biochemical markers, motor and nutritional characteristics, and the level of comorbidity were evaluated as predictors of functional outcome. Length of stay in the rehabilitation ward was also considered.

Results: Following rehabilitation, all participants ($n = 53$) reported a significant decrease in the level of disability in both motor and cognitive functioning. However, neither motor and nutritional characteristics nor comorbidities played a significant role in predicting the overall positive change registered after rehabilitation.

[1]Clinica Hildebrand, Centro di Riabilitazione Brissago, Brissago, Switzerland
[2]IRCCS Istituto Auxologico Italiano, U.O. di Riabilitazione Neuromotoria Auxologico 'Capitanio', Milan, Italy
[3]Cliniche di Riabilitazione Ente Ospedaliero Cantonale (CREOC), Novaggio and Faido, Switzerland
[4]'Rita Levi Montalcini' Department of Neurosciences, University of Turin, Turin, Italy
[5]IRCCS Istituto Auxologico Italiano, U.O. di Neurologia e Neuroriabilitazione, Ospedale San Giuseppe, Piancavallo (VCO), Italy
[6]Department of Biomedical Sciences for Health, University of Milan, Milan, Italy

Corresponding author:
Valentina Barbieri, Clinica Hildebrand, Centro di Riabilitazione Brissago, Via Crodolo 18, 6614 Brissago, Switzerland.
Email: v.barbieri@clinica-hildebrand.ch

Conclusions: The results support the existing sparse evidence addressing the importance of an early rehabilitation program for patients who received intensive care and post-acute care due to severe COVID-19.

Keywords
COVID-19, multidisciplinary rehabilitation, Functional Independence Measure, post-acute care, functional impairment, rehabilitation effectiveness.

Date received: 13 June 2022; accepted: 12 October 2022

Introduction

Coronavirus disease 2019 (COVID-19) is a multisystemic disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The respiratory tract remains the first and foremost involved apparatus in many affected individuals. Nevertheless, in the acute phase of the disease, alterations in the cardiocirculatory, haemopoietic, endocrinological, muscular, and nervous systems are reported.[1,2] COVID-19-related long-term sequelae are far from fully understood, although preliminary evidence suggests residual impairments in cardiorespiratory and neurological functions.[3,4] COVID-19 has different degrees of severity, ranging from the absence of symptoms to the need for long periods of hospitalization in the intensive care unit (ICU), with or without the need of invasive mechanical ventilatory support and prone positioning, in some cases for long hours and many days in a row. Invasive ventilation procedures combined with prolonged immobilization may contribute to the development of critical illness, myopathy and neuropathy, often associated with dysphagia, neck, shoulder and back pain, and difficulties in sitting, standing, and walking.[5,6] The psychological profile is also affected, with many patients describing a reduced quality of life and emotional distress.[3] Thus, most survivors of severe COVID-19 need multidisciplinary rehabilitation after the ICU, to restore the functioning in daily living as well as an acceptable quality of life after discharge,[7] also in consideration of pre-existing comorbidities.[8]

To date, evidence regarding the effectiveness of rehabilitation programs in COVID-19 survivors remains rare and inconclusive.[9–11] Piquet et al.[9] reported substantial functional, motor, and cardiorespiratory improvement after an early rehabilitation program in patients who had been affected by the severe-acute form of the disease. However, impaired autonomy in daily life activities and motor weakness persisted at discharge. The authors also observed that motor disability at discharge correlated with the amount of time spent in ICU.

The primary aim of the present study was to identify possible outcome predictors of a short-term multidisciplinary patient-tailored rehabilitation program and its effectiveness in reducing the level of COVID-19 disability in two Swiss rehabilitation clinics.

Patients and methods

This real-practice retrospective study was conducted in a cohort of post-acute care patients who overcame severe COVID-19, and who were included in a rehabilitation

protocol at the Clinica Hildebrand, Centro di Riabilitazione Brissago, and the Clinica Novaggio, both part of the ReHa Ticino in Switzerland. Participants were recruited between April 2020 and June 2020. Because of the pandemic, a clinical trial of a rehabilitation group versus 'sham rehabilitation' control group was not considered feasible and ethical. Thus, the study was conducted with a quasi-experimental pre–post design without a separate control group. The study was approved by the Swiss Association of Research Ethics Committees (Project ID 2021-02106 - Rif. CE3969), and data collected for the present research had been obtained as part of the included institutions' clinical procedures. Verbal and/or written informed consent was obtained from study participants, in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki), and all patient details were de-identified. The reporting of this study conforms to STROBE guidelines.[12]

Study population

Patients were consecutively admitted for the rehabilitation protocol (and for study inclusion) according to the following criteria. For patients with a SARS-CoV-2-positive nasopharyngeal swab: (1) a recent chest computed tomography or X-ray with evidence of significant improvement versus baseline (e.g. reduction of lesion load by at least 50%, improvement of the ground-glass picture); (2) arterial oxygen partial pressure (PaO2)/fractional inspired oxygen (FiO2) ratio >300 with FiO2 35%; (3) apyretic for ≥3 days; and (4) 90 mmHg <systolic blood pressure <140 mmHg; 60 mmHg <diastolic blood pressure <90 mmHg. For patients with a negative nasopharyngeal swab for SARS-CoV-2: (1) apyretic for ≥3 days; and (2) at least two consecutive negative swabs with at least a 48-h interval between swabs. All included patients came directly from an acute care setting, which might be an ICU, a respiratory high-dependency care unit, or an infectious diseases unit of a local hospital.

Patients under existing prescription for psychotropic drugs, those with COVID-19 encephalitis, or with signs of dementia, were excluded.

Baseline clinical assessment

Prior to starting rehabilitative intervention, several clinical and functional measurements were obtained from each patient regarding nutritional, functional, and motor domains, as well as the number and degree of pre-existing comorbidities. Nutritional status was recorded at 24 h following admission into the rehabilitation program. Body mass index (BMI) was calculated (presented as kg/m^2), and patients were assessed using the Nutritional Risk Screening-2002 (NRS-2002) system.[13] NRS-2002 allows the patient's level of malnutrition to be scored, with a total score ranging from 0 (absent) to 6 (severe): a patient with a score ≥3 is considered to be malnourished. Serum albumin level was also included as a marker of the visceral protein reserve, plus electrolyte levels, as baseline abnormalities appear to be related to poor prognosis in the acute phase of COVID-19.[14] Functional assessment of the motor apparatus, focusing on articular range of motion and segmental muscular strength of the upper and lower limbs, was performed using the Manual Muscle Test evaluation,[15] and the Oxford Medical Research Council (MRC) muscle strength evaluation, with a score ranging from 0 (no muscle movement) to 5 (normal strength). Functional strength of the lower extremities was assessed by the 30-s sit-to-stand test (according to the Shirley Ryan AbilityLab; www.sralab.org/rehabilitation-measures/30-second-sit-stand-test). Upper limb coordination and grip strength for both hands were assessed with

a Patterson Medical Jamar hand dynamometer.[16] Strength of pinch and hand grip were measured qualitatively (Oxford Scale [MRC 1–5]), while coordination was assessed using classical clinical manoeuvres, such as finger to nose test and evaluation of dysdiadochokinesia. Moreover, patients were asked to rate the subjective level of perceived pain from 0 (no pain) to 10 (the worst pain) on a visual analogue scale.

The presence and cumulative severity of pre-existing pathologies was assessed using the version provided by Mistry et al.[17] of the Cumulative Illness Rating Scale (CIRS).[18] The scale consists of fourteen health-related domains. Each item is scored on a 5-point ordinal scale, ranging from a score of 0 (no impairment to that organ or system) to 4 (extremely severe problem and/or immediate treatment required and/or organ failure and/or severe functional impairment). The Severity Index was computed as the number of items ranking three or four in disease severity, and the Comorbidity Index was computed as the sum of items (except for the psychiatric category), in which participants reported a score $\geq$3 (higher score 13). The score relative to the psychiatric domain was independently reported.

The rehabilitation program

The rehabilitation program was built consistently according to the indications of Crisafulli et al.,[19] using different strategies in patients who were either positive or negative for SARS-CoV-2. This was necessary in order to avoid further risk of contagion, particularly during respiratory rehabilitation sessions, typically characterized by a greater production of droplets. Regarding respiratory function, sessions were initially aimed at reducing breathing difficulties and perception of dyspnoea, as well as reducing the incidence of complications, such as bacterial superinfections of the airways. Sessions proceeded in parallel with weaning from oxygen therapy or, when this was not feasible, sessions were aimed at obtaining the greatest possible oxygen therapy reduction, optimizing the flows for home therapy. Patients who remained positive for SARS-CoV-2 underwent a rehabilitative protocol that included respiratory exercises such as deep, slow breathing, and chest expansion combined with shoulder expansion in order to reduce the spread of droplets. Breathing exercise helped patients to fully re-expand the lungs and to further the progression of airway secretions from small to large airway, thus reducing alveolar dead space. Once negative for SARS-CoV-2, aerosol therapy was introduced and active breathing, as well as training with positive expiratory pressure, were started. The rehabilitation sessions occurred daily, with a duration ranging from 30 to 45 min, according to individual tolerance.

For the neuromotor domain, the rehabilitation was aimed at preserving joint mobility and the prevention of muscle wasting. Oxygen saturation was constantly monitored during each session. The rehabilitation developed through a progressive course, with training in the passage from supine position to sitting, bed to wheelchair transfer, and sitting to standing. The intervals of time spent standing were gradually increased and, when the standing position was deemed safe, gait training was started, initially with assistance and aids, and afterwards independently. The last steps of the motor rehabilitation process, also useful for evaluating improvement in respiratory performance, comprised training in climbing and descending stairs and proprioceptive exercises to improve balance and postural reactions. The program included daily sessions of about 30 min, delivered 5 days per week. The rehabilitation setting changed as the recovery progressed: the initial sessions were at the patient's bed, then in the rehabilitation gym.

Finally, patients received psychological support to address the emotional and traumatic issues related to the disease itself, and to the prolonged isolation faced before and during hospitalization. The number of sessions per week varied according to individual needs from a clinical and social perspective.

Primary outcome: the Functional Independence Measure (FIM)

A normalized score based on the Functional Independence Measure (FIM) was used to verify the short-term effect of multidisciplinary rehabilitation.[20,21] FIM measured at admission predicts functional ability during rehabilitation periods,[22] and consists of an 18-item, seven-level, ordinal scale that is sensitive to changes over the course of a comprehensive inpatient medical rehabilitation program. The 18 items are grouped into two subscales: motor and cognitive. The motor subscale includes eating, grooming, bathing, dressing the upper body, dressing the lower body, toileting, bladder management, bowel management, bed/chair/wheelchair transfers, toilet transfers, bath/shower transfer, walk/wheelchair and stairs. Each item is scored on a 7-point ordinal scale, ranging from 1 (total assistance/not testable) to 7 (complete independence). The motor subscale is the sum of the individual motor subscale items, with a value ranging between 13 and 91. The cognition subscale includes comprehension, expression, social interaction, problem-solving, and memory. Each item is scored on a 7-point ordinal scale, ranging from 1 (total assistance/not testable) to 7 (complete independence). The sum of the individual cognition subscale items results in the cognition subscale score, with a value ranging between 5 and 35. The total FIM score (the sum of the two subscale scores) ranges between 18 and 126. The higher the score, the higher the individual level of functional independence.

Statistical analyses

Changes in the motor and cognition subscale scores, and the total FIM score, were investigated by comparing the scores reported at baseline (T0) and after treatment (T1) within the present sample, using Wilcoxon signed–rank test. Successively, for each FIM subset score, the Rehabilitation Effectiveness (REs) index was computed, which represents the percentage of the potential functional improvement eventually achieved after the rehabilitation program.[23] The REs index for each FIM score was computed as:

$$REs = 100\% \ x\frac{DC(x) - adm(x)}{Max(x) - adm(x)}$$

where x was the score; DC represents the discharge time-point; adm, the admission time-point; and max, the maximum possible score. The rehabilitation efficiency score (DREs), was also computed by dividing the REs index value by the rehabilitation length of stay (in days).

Potential associations between changes in FIM scores observed after the rehabilitation program (T1) and participants' baseline characteristics at admission were assessed through linear regression analysis.[24] Thus, the correlation and directionality of the data were investigated in a preliminary analysis to formulate the statistical model, using Pearson's correlation coefficient (Pearson's r) for continuous data and Spearman's rank correlation coefficient (Spearman's ρ) for categorical data. Variables that were found to be significantly associated (P-value ≤ 0.05) with the main outcome score were further investigated with a linear regression model, in which goodness-of-fit was reported as R^2. Also, the significance of the model was evaluated by F-value and P-value. Finally, the relative contribution of the factors included in the statistical model with the dependent variable (the outcome score) were verified. The variance inflation

factor (VIF), as a measure of multicollinearity, was reported for each factor.

Data are presented as mean ± SD (or range), and *n* (%) prevalence, and were analysed using SPSS software, version 18.0 (SPSS Inc., Chicago, IL, USA). A *P*-value ≤0.05 was considered to be statistically significant.

Results

Participants

A total of 53 patients (16 females and 37 males) were included in the study. All patients received ventilatory (i.e., non-invasive or invasive mechanical ventilation) support. Baseline patient characteristics are summarised in Table 1.

Regarding nutritional status, and specifically BMI, no participant reported a BMI score below the threshold of 18.5 kg/m^2 (i.e., under-weight) at admission; instead, 20 patients (37.73% of the cohort) reported a BMI over the threshold of 30 kg/m^2 (i.e., obese). In terms of the Kondrup scale, 30 patients (56.61%) reported a score over the threshold of 3, suggesting that they were malnourished, in ranging degrees of severity. A total of 38 patients (71.69%) were found to have a serum albumin concentration below the threshold of 38 g/l. Regarding sodium, four patients (7.54%) were found to have a concentration below the threshold of 136 mmol/l, while no patient reported a value over the threshold of 149 mmol/l. Six patients (11.32% of the entire sample) could not perform the 30-s sit-to-stand test, and one patient (1.88%) was not assessed for the passive knee extension test. Finally, 11 patients (20.75%) could perform the grip strength assessment. The study sample

Table 1. Baseline characteristics in 53 patients following severe coronavirus disease 2019, who were admitted for rehabilitation therapy.

Characteristic	Total study population (*n* = 53)
Age, years	67.9 ± 8.73 (49–92)
Duration of the rehabilitation treatment, days	31.81 ± 20.37 (9–136)
Body mass index, kg/m^2	28.92 ± 6.53 (19–54)
Albumin, g/l	35.36 ± 3.67 (29–42)
Sodium, mmol/l	138.83 ± 2.58 (131–145)
Kondrup Index	3.92 ± 1.35 (2–6)
30 s sit-to-stand test, *n* repetitions	3.72 ± 3.56 (0–11)
Passive knee extension, °	
Right	3.85 ± 0.78 (2–5)
Left	3.82 ± 0.81 (2–5)
Overall (the mean of right and left knee)	3.84 ± 0.78 (2–5)
Grip strength	
Right hand, kg	19.37 ± 9.49 (0–42)
Left hand, kg	18.27 ± 9.35 (0–40)
Overall (mean of right and left hand), kg	18.82 ± 8.96 (2–41)
Pain VAS, categorical scale from 0 to 10	2.0 ± 2.47 (0–8)
Cumulative Illness Rating Scale	
Severity Index	1.51 ± 0.48 (0.61–2.61)
Comorbidity Index	6.69 ± 2.39 (2–12)

Data presented as mean ± SD (range).
VAS, visual analogue scale.

prevalence of comorbidity levels within 14 different organ systems are shown in Table 2.

Primary outcome

After the rehabilitation program, the study population were found to have higher scores in the FIM scale, suggesting an increased level of physical and cognitive functioning (Table 3). The relationship between REs and DREs scores computed for the FIM scales and clinical parameters in the study population is summarised in Table 4.

According to correlational analyses, older age as well as severe malnutrition measured through the Kondrup Index were related to lower outcomes in FIM. The performance at the sit-to-stand test, and mean scores for knee extension and hand grip strength were significantly related to the motor scale and the total scale REs scores and DREs. Thus, these statistically significant factors were included in the linear regression models as potential predictors of REs scores and DREs for motor function, and REs scores and DREs for total FIM.

The four regression models were all significant. Grip strength and knee extension significantly predicted the DREs for motor function ($P \leq 0.05$), with no other statistically significant results (Table 5). The regression model relative to DREs for cognitive function, including age as predictor, was significant ($R^2 = 0.01$; $F[1,52] = 5.76$; $P = 0.02$): age significantly predicts also the DREs cognitive score, with an inverse correlation ($B = -0.5$; $t = -2.41$; $P = 0.02$; $VIF = 1$).

Discussion

The present study provides evidence of a short-term decrease in the level of disability in COVID-19 survivors after a multidisciplinary rehabilitative program in Swiss rehabilitation clinics. A secondary aim of the study was to find parameters, consistent

Table 2. Relative pre-existing comorbidity levels (scored from 0 to 4) in different organ systems, according to the CIRS, in 53 patients following severe coronavirus disease 2019.

	Score				
Organ system	0	1	2	3	4
Heart	29 (54.7)	2 (3.8)	7 (13.2)	12 (22.6)	3 (5.7)
Haematopoiesis	7 (13.2)	7 (13.2)	27 (50.9)	12 (22.6)	0 (0)
Eyes, ears, nose, and throat	6 (11.3)	2 (3.8)	18 (34)	22 (41.5)	5 (9.4)
Lower gastrointestinal tract	1 (1.9)	0 (0)	2 (3.8)	25 (47.2)	25 (47.2)
Renal	31 (58.5)	8 (15.1)	12 (22.6)	0 (0)	2 (3.8)
Bone and skin	31 (58.5)	9 (17)	6 (11.3)	6 (11.3)	1 (1.9)
Endocrine and breast	28 (52.8)	11 (20.8)	8 (15.1)	3 (5.7)	3 (5.7)
Vascular	22 (41.5)	12 (22.6)	14 (26.4)	5 (9.4)	0 (0)
Respiratory	31 (58.5)	5 (9.4)	6 (11.3)	7 (13.2)	4 (7.5)
Upper gastrointestinal tract	33 (62.3)	6 (11.3)	9 (17)	3 (5.7)	2 (3.8)
Liver, gallbladder, and pancreas	1 (1.9)	3 (5.7)	15 (28.3)	26 (49.1)	8 (15.1)
Genitourinary tract	17 (32.1)	7 (13.2)	15 (28.3)	11 (20.8)	3 (5.7)
Neurological	21 (39.6)	4 (7.5)	18 (34)	8 (15.1)	2 (3.8)
Psychiatric	16 (30.2)	16 (30.2)	15 (28.3)	5 (9.4)	1 (1.9)

Data presented as *n* (%) prevalence in each severity level, where 0 (no impairment) to 4 (extremely severe problem and/or immediate treatment required and/or organ failure and/or severe functional impairment).
CIRS, Cumulative Illness Rating Scale.

Table 3. Functional Independence Measure (FIM) scores at baseline (T0) and after rehabilitation (T1), and REs and DREs in 53 patients following severe coronavirus disease 2019.

FIM score	T0	T1	Statistical significance[a]	REs	DREs
Motor score					
Mean	45.9	76.3	$Z = 1378$;	70.45	2.78
SD	19.75	16.84	$P < 0.001$;	26.52	1.78
Range	13–88	13–91	$\eta 2 = 3.25$	0–100	0–9.09
Cognitive score					
Mean	28.62	30.86	$Z = 460.5$;	36.31	1.21
SD	6.62	5.68	$P < 0.001$;	40.34	1.61
Range	8–35	8–35	$\eta 2 = 8.52$	0–100	0–6.25
Total score					
Mean	74.52	107.16	$Z = 1378$;	68	2.68
SD	24.28	21.7	$P < 0.001$;	26.06	1.74
Range	21–123	21–126	$\eta 2 = 3.25$	0–100	0–9.09

DREs, rehabilitation efficiency score; REs, Rehabilitation Effectiveness; SD, standard deviation.
[a]T1 versus T0 (Wilcoxon signed–rank test).

with the individual clinical characteristics at admission to the rehabilitation program, that may play a predictive role in patient outcome.

After rehabilitation, the patient cohort showed a significant decrease in the level of disability measured through the FIM scale; specifically, a significant improvement in both motor and cognitive functioning was observed. These results were in support of the limited previously published evidence addressing the efficacy of early rehabilitation programs for patients who have spent time in ICU and post-acute care.[9–11] Nevertheless, as a sham-treated control group was not included in the present study, the role of a spontaneous recovery could not be evaluated. Moreover, the relatively small sample size may have affected the results, including the relevance of the results to the general population.

Nutritional, motor and comorbidity factors were not individually found to play a significant predictive role in the overall positive change following rehabilitation. However, the positive change in motor functional outcome was significantly predicted by baseline increased hand coordination and grip strength, as well as leg joint range of motion and quality of movement. Crucially, this result emerged only when the duration of rehabilitation care was considered when computing the DREs score, thus pointing towards a better efficiency of the rehabilitative process in those patients with higher scores.[23] The significant change in cognitive functional outcome after the rehabilitation program was predicted only by age, when the duration of treatment was considered: a higher amelioration was observed for younger individuals. Nevertheless, the results may be limited by two factors. First, a neuropsychological assessment of patients' cognitive abilities was not performed through standardized tests at admission. However, some preliminary evidence suggests the presence of long-lasting cognitive difficulties, particularly in the domains of attention, executive function, and memory, after infection with SARS-CoV-2; nevertheless, the severity of cognitive alterations seemed to be not strictly

Table 4. Associations between the three Functional Independence Measure (FIM) scales (motor, cognitive, and total) and patient characteristics.[a]

	Rehabilitation effectiveness			Rehabilitation efficiency score		
Characteristic	Motor	Cognitive	Total	Motor	Cognitive	Total
Age	$r = -0.39$	$r = -0.19$	$r = -0.4$	$r = -0.039$	$r = 0.31$	$r = -0.39$
	$P = 0.003$	NS	$P = 0.002$	$P = 0.004$	$P = 0.02$	$P = 0.004$
Sex	$\rho = 0.19$	$\rho = 0.07$	$\rho = 0.17$	$\rho = 0.16$	$\rho = 0.09$	$\rho = 0.14$
	NS	NS	NS	NS	NS	NS
BMI	$r = -0.04$	$r = 0.25$	$r = -0.03$	$r = -0.16$	$r = 0.14$	$r = -0.15$
	NS	NS	NS	NS	NS	NS
Albumin	$r = 0.12$	$r = 0.12$	$r = 0.14$	$r = 0.21$	$r = 0.22$	$r = 0.23$
	NS	NS	NS	NS	NS	NS
Sodium	$r = -0.19$	$r = 0.18$	$r = -0.18$	$r = -0.26$	$r = 0.03$	$r = -0.25$
	NS	NS	NS	NS	NS	NS
Kondrup Index	$\rho = -0.43$	$\rho = -0.1$	$\rho = -0.47$	$\rho = -0.46$	$\rho = -0.16$	$\rho = -0.47$
	$P = 0.001$	NS	$P < 0.001$	$P = 0.001$	NS	$P < 0.001$
Sit-to-stand	$r = 0.52$	$r = -0.51$	$r = 0.53$	$r = 0.72$	$r = 0.15$	$r = 0.73$
	$P < 0.001$	NS	$P < 0.001$	$P < 0.001$	NS	$P < 0.001$
Knee extension	$\rho = 0.38$	$\rho = 0.009$	$\rho = 0.39$	$\rho = 0.57$	$\rho = 0.09$	$\rho = 0.57$
	$P = 0.005$	NS	$P = 0.004$	$P < 0.001$	NS	$P < 0.001$
Grip strength	$r = 0.64$	$r = 0.2$	$r = 0.61$	$r = 0.6$	$r = 0.27$	$r = 0.6$
	$P < 0.001$	NS	$P < 0.001$	$P < 0.001$	NS	$P < 0.001$
pain VAS	$r = 0.21$	$r = 0.03$	$r = 0.2$	$r = -0.08$	$r = -0.07$	$r = -0.08$
	NS	NS	NS	NS	NS	NS
Cumulative Illness Rating Scale						
Severity index	$r = 0.05$	$r = -0.08$	$r = 0.02$	$r = -0.04$	$r = -0.1$	$r = -0.06$
	NS	NS	NS	NS	NS	NS
Comorbidity index	$r = -0.03$	$r = 0.03$	$r = -0.05$	$r = -0.23$	$r = -0.08$	$r = -0.24$
	NS	NS	NS	NS	NS	NS
Psychiatric component	$\rho = 0.14$	$\rho = -0.001$	$\rho = 0.08$	$\rho = -0.06$	$\rho = -0.2$	$\rho = -0.08$
	NS	NS	NS	NS	NS	NS

[a]Correlation analyses using Pearson's correlation coefficient (Pearson's r) for continuous data and Spearman's rank correlation coefficient (Spearman's ρ) for categorical data.
NS, no statistically significant correlation ($P > 0.05$).

predicted by the severity of acute illness.[25] Moreover, the cognitive domain was not specifically treated during the rehabilitation.

The present study describes a residential multidisciplinary rehabilitation programme that was longer than described in the study by Piquet et al.,[9] who reported a length of rehabilitation of 9.8 ± 5.6 days, and was more in line with the programme reported by Curci et al.[10] (31.97 ± 9.06 days). It may be useful to underline that in the present study, patients were discharged when the achieved level of function and independence mirrored the individual's premorbid functionality. Since the length of rehabilitation programs, as well as their goals, might be different between local health systems, we strongly recommend assessing after-effects taking into account the duration of rehabilitation therapy, as was done in the present study, to increase data comparability between studies.

Table 5. Results from analyses of linear regression models to predict REs scores and DREs for motor function score and total FIM score after rehabilitation in 53 patients following severe coronavirus disease 2019.

	Motor domain		Total FIM	
Variable	REs score	DREs score	REs score	DREs score
	$R^2 = 0.38$; $F(5,33) = 3.55$; $P = 0.013$	$R^2 = 0.58$; $F(5,33) = 7.72$; $P < 0.001$	$R^2 = 0.4$; $F(5,33) = 3.79$; $P = 0.009$	$R^2 = 0.59$; $F(5,33) = 8.36$; $P < 0.001$
Age	B = –0.68;	B = –0.04;	B = –0.61;	B = –0.03
VIF = 1.26	t = –1.58; NS	t = –1.23; NS	t = –1.43; NS	t = –1.11; NS
Kondrup Index	B = –1.7;	B = –0.03	B = –2.72	B = –0.09
VIF = 1.74	t = –0.63; NS	t = –0.16; NS	t = –1.02; NS	t = –0.46; NS
Sit-to-stand	B = –0.98;	B = 0.5	B = 0.72	B = 0.15
VIF = 2.29	t = 0.82; NS	t = –1.63; NS	t = 0.61; NS	t = 1.69; NS
Knee Extension	B = –1.89;	B = –0.46	B = –0.18	B = 0.44
VIF = 2	t = –0.34; NS	t = –2.61; $P = 0.01$	t = –0.03; NS	t = 1.04; NS
Grip strength	B = 0.7;	B = 0.07	B = 0.65	B = 0.07
VIF = 1.86	t = 1.51; NS	t = 2.04; $P = 0.05$	t = 1.42; NS	t = –1.95; NS

REs, Rehabilitation effectiveness; DREs, Rehabilitation efficiency score; FIM, Functional Independence Measure; VIF, variance inflation factor.
NS, no statistically significant correlation ($P > 0.05$).

Conclusions

The present evidence may support the importance of guaranteeing rehabilitation for patients who have been hospitalized in the ICU, independent of age, especially regarding motor functionality, after acute COVID-19 infection. The present study included a set of functional tools that may be administered at admission before the onset of rehabilitation. These tests may prove useful in tailoring rehabilitative interventions, and as a guide in the formulation of a rehabilitative prognosis in terms of length of stay in the case of COVID-19. However, the results may be limited by the relatively small study population and their clinical heterogeneity, as well as the absence of a control group, and should be regarded with caution. Future research may highlight the role of other untested factors in predicting functional outcomes in COVID-19 survivors.

Acknowledgments

The Authors thank Tommaso Roveda, Antonella Mascetti, Giulia Gabbi, Renate Siegenthaler, and Alessia Albini for their assistance in data collection, and Elisa Galimberti for her technical support during the study conception.

Author contributions

Valentina Barbieri, Nicola Schiavone, Laura Perucca, and Paolo Rossi have given substantial contributions to study design and conception; Valentina Barbieri, Luca Scarabel, and Laura Bertella contributed to the data collection; Federica Scarpina and Luca Scarabel performed the statistical analyses; Federica Scarpina, Valentina Barbieri, Nicola Schiavone, and Paolo Rossi interpreted the results; Valentina Barbieri and Federica Scarpina drafted the article. Laura Perucca contributed to study supervision; Federica Scarpina contributed to study submission. All authors read and approved the final version of the manuscript.

Data accessibility statement

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

ORCID iD

Federica Scarpina https://orcid.org/0000-0003-4326-1596

References

1. Gupta A, Madhavan MV, Sehgal K, et al. Extrapulmonary manifestations of COVID-19. *Nat Med* 2020; 26: 1017–1032.
2. Thakur V, Ratho RK, Kumar P, et al. Multi-organ involvement in COVID-19: beyond pulmonary manifestations. *J Clin Med* 2021; 10: 446.
3. Barker-Davies RM, O'Sullivan O, Senaratne KPP, et al. The Stanford Hall consensus statement for post-COVID-19 rehabilitation. *Br J Sports Med* 2020; 54: 949–959.
4. Simpson R and Robinson L. Rehabilitation after critical illness in people with COVID-19 infection. *Am J Phys Med Rehabil* 2020; 99: 470–474.
5. Bagnato S, Boccagni C, Marino G, et al. Critical illness myopathy after COVID-19. *Int J Infect Dis* 2020; 99: 276–278.
6. Printza A, Tedla M, Frajkova Z, et al. Dysphagia severity and management in patients with COVID-19. *Curr Health Sci J* 2021; 47: 147–156.
7. Kiekens C, Boldrini P, Andreoli A, et al. Rehabilitation and respiratory management in the acute and early post-acute phase. 'Instant paper from the field' on rehabilitation answers to the COVID-19 emergency. *Eur J Phys Rehabil Med* 2020; 56: 323–326.
8. Demeco A, Marotta N, Barletta M, et al. Rehabilitation of patients post-COVID-19 infection: a literature review. *Int J Med Res* 2020; 48: 0300060520948382.
9. Piquet V, Luczak C, Seiler F, et al. Do patients with COVID-19 benefit from rehabilitation? Functional outcomes of the first 100 patients in a COVID-19 rehabilitation unit. *Arch Phys Med Rehabil* 2021; 102: 1067–1074.
10. Curci C, Negrini F, Ferrillo M, et al. Functional outcome after inpatient rehabilitation in postintensive care unit COVID-19 patients: findings and clinical implications from a real-practice retrospective study. *Eur J Phys Rehabil Med* 2021; 57: 443–450.
11. Puchner B, Sahanic S, Kirchmair R, et al. Beneficial effects of multi-disciplinary rehabilitation in postacute COVID-19: an observational cohort study. *Eur J Phys Rehabil Med* 2021; 57: 189–198.
12. Von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. *Ann Intern Med* 2007; 147: 573–577.
13. Kondrup J, Rasmussen HH, Hamberg O, et al. Nutritional risk screening (NRS 2002): a new method based on an analysis of controlled clinical trials. *Clin Nutr* 2003; 22: 321–336.
14. Tezcan ME, Dogan Gokce G, Sen N, et al. Baseline electrolyte abnormalities would be related to poor prognosis in hospitalized coronavirus disease 2019 patients. *New Microbes New Infect* 2020; 37: 100753.
15. Ciesla N, Dinglas V, Fan E, et al. Manual muscle testing: a method of measuring extremity muscle strength applied to critically ill patients. *J Vis Exp* 2011; 50: 2632.
16. Bohannon RW. Hand-grip dynamometry predicts future outcomes in aging adults. *J Geriatr Phys Ther* 2008; 31: 3–10.
17. Mistry R, Gokhman I, Bastani R, et al. Measuring medical burden using CIRS in older veterans enrolled in UPBEAT, a psychogeriatric treatment program: a pilot study. *J Gerontol A Biol Sci Med Sci* 2004; 59: M1068–M1075.

18. Miller MD and Towers A. *A manual of guidelines for scoring the cumulative illness rating scale for geriatrics (CIRS-G)*. Pittsburgh, PA: University of Pittsburgh, 1991.
19. Crisafulli E, D'Abrosca F, Delicati O, et al. Italian recommendations on rehabilitation pneumology. Scientific evidence and clinical-practical messages: Summary article by a group of experts. *Rassegna di Patologia dell'Apparato Respiratorio* 2015; 30: 250–263 [In Italian].
20. Keith RA, Granger CV, Hamilton BB, et al. The functional independence measure: a new tool for rehabilitation. *Adv Clin Rehabil* 1987; 1: 6–18.
21. Linacre JM, Heinemann AW, Wright BD, et al. The structure and stability of the Functional Independence Measure. *Arch Phys Med Rehabil* 1994; 75: 127–132.
22. Meyer MJ, Pereira S, McClure A, et al. A systematic review of studies reporting multivariable models to predict functional outcomes after post-stroke inpatient rehabilitation. *Disabil Rehabil* 2015; 37: 1316–1323.
23. Koh GC, Chen CH, Petrella R, et al. Rehabilitation impact indices and their independent predictors: a systematic review. *BMJ Open* 2013; 3: e003483.
24. Myers RH, Montgomery DC, Vining GG, et al. *Generalized linear models: with applications in engineering and the sciences*. 2nd ed. Hoboken, NJ: John Wiley & Sons, 2012.
25. Vanderlind WM, Rabinovitz BB, Miao IY, et al. A systematic review of neuropsychological and psychiatric sequalae of COVID-19: implications for treatment. *Curr Opin Psychiatry* 2021; 34: 420–433.