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Original Research

COVID-19: Patient Characteristics in the First Phase of Postintensive Care Rehabilitation

Carolina M.H. Wiertz, MD [a], Wouter A.J. Vints, MD [a,b], Geert J.C.M. Maas, MSc [a,c], Sascha M.C. Rasquin, PhD [a], Yvette Y. van Horn, MD [a], Martijn P.M. Dremmen, MD [a,d], Bena Hemmen, MD, PhD [a,e], Jeanine A. Verbunt, MD, PhD [a,e,f]

[a] *Adelante Zorggroep, Hoensbroek, The Netherlands*
[b] *Department of Health Promotion and Rehabilitation, Lithuanian Sports University, Kaunas, Lithuania*
[c] *Department for Health and Technique, Physiotherapy, Zuyd University of Applied Sciences, Heerlen, The Netherlands*
[d] *Department of Rehabilitation Medicine, Zuyderland Medical Centre, Heerlen-Sittard, The Netherlands*
[e] *Department of Rehabilitation Medicine, Maastricht University Medical Centre, Maastricht, The Netherlands*
[f] *Department of Rehabilitation Medicine Research School CAPHRI, Maastricht University, Maastricht, The Netherlands*

KEYWORDS
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Abstract *Objective:* To describe clinical characteristics of patients after intensive care unit (ICU) treatment for coronavirus disease 2019 (COVID-19) who were admitted for inpatient rehabilitation.
Design: A cross-sectional design.
Setting: Inpatient rehabilitation care in the Netherlands.
Participants: All post-ICU patients with COVID-19 admitted to the rehabilitation center between April 2 and May 13, 2020, were invited to participate in the study. Included were patients older than 18 years needing inpatient rehabilitation after ICU treatment for COVID-19 (N=60; mean age, 59.9y; 75% male).
Interventions: Not applicable.

List of abbreviations: ARDS, acute respiratory distress syndrome; COVID-19, coronavirus disease 2019; CRRT, continuous renal replacement therapy; ECMO, extracorporeal membrane oxygenation; HHD, handheld dynamometer; ICU, intensive care unit; ICU-AW, intensive care unit–acquired weakness; MRC, Medical Research Council; MV, mechanical ventilation; NRS, Numeric Rating Scale; PE, pulmonary embolism; PICS, postintensive care syndrome; ROM, range of motion; SARS, severe acute respiratory syndrome.
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Main Outcome Measures: The following information was collected in the first week of inpatient rehabilitation care: (1) demographics; (2) ICU stay parameters; (3) medical, physical, and functional characteristics; and (4) self-reported symptoms.
Results: The most important findings for rehabilitation were the following: in the first week after discharge to the rehabilitation center, 38.3% of all patients experienced exercise-induced oxygen desaturation, in 72.7% muscle weakness was present in all major muscle groups, and 21.7% had a reduced mobility in 1 or both shoulders. Furthermore 40% had dysphagia, and 39.2% reported symptoms of anxiety.
Conclusion: Post-ICU patients with COVID-19 display physical and anxiety symptoms as reported in other post-ICU patient groups. However, this study showed some remarkable clinical characteristics of post-ICU patients with COVID-19. Rehabilitation programs need to anticipate on this. Long-term follow-up studies are necessary.

Since December 2019 a novel coronavirus (severe acute respiratory syndrome [SARS] coronavirus 2) has spread rapidly throughout the world. An infection with this virus most typically causes respiratory tract illness, which is called coronavirus disease 2019 (COVID-19).[1] The clinical spectrum ranges from asymptomatic infection to mild upper respiratory tract illness, severe viral pneumonia, respiratory failure, or death.[2] Atypical presentations with nausea, diarrhea, and acute abdominal pain are possible.[1,3] In the Netherlands approximately 2% of all confirmed cases eventually developed respiratory failure requiring admission to an intensive care unit (ICU).[4,5]

Previous studies showed that critical illness can have a major effect on all areas of participation.[6,7] The impairments in physical, cognitive, and/or mental health resulting from critical illness are described as postintensive care syndrome (PICS).[8] One year after ICU discharge, 56% of all patients experience 1 or more problems related to PICS.[9] Identification of PICS and rehabilitation needs may help prevent chronic disability.[10]

In addition to PICS, post-ICU patients with COVID-19 might be prone to (irreversible) pulmonary dysfunctions. Although long-term data on pulmonary consequences in patients with COVID-19 are not yet available, clinical characteristics might be similar to those seen with SARS or acute respiratory distress syndrome (ARDS). SARS and ARDS patients had a spectrum of residual symptoms such as ICU-acquired weakness (ICU-AW), moderate to severe dyspnea, reduced exercise capacity, fatigue, multiorgan impairment, and cognitive and mental health problems.[11-14]

At this moment information on long-term characteristics of post-ICU patients with COVID-19 is still incomplete. Information about physical, mental, and cognitive health in the acute phase after ICU discharge is needed to assess whether current multidisciplinary rehabilitation programs are suitable for this patient group. Therefore, the aim of this study is to describe clinical characteristics of post-ICU patients with COVID-19 in the first week after admission for inpatient rehabilitation.

Methods

Study design and participants

This cross-sectional study was performed at Adelante Zorggroep, a rehabilitation center in the South of the Netherlands. Inclusion criteria were patients (1) 18 years or older, (2) being referred for inpatient rehabilitation after ICU treatment for COVID-19 subsequent to ICU and hospital discharge, and (3) functioning independently before their COVID-19 infection. Excluded were all patients who did not fulfill the inclusion criteria. COVID-19 was diagnosed during hospital admission. All post-ICU patients with COVID-19 admitted to the rehabilitation center between April 2 and May 13, 2020, were invited to participate in the study. We started including from the first patient who was admitted to the rehabilitation center. Twenty-five beds were available for post-ICU patients with COVID-19. One of the wards was completely isolated as a quarantine ward. As soon as patients tested negative for COVID-19, they were transferred to another ward within the rehabilitation center. Zuyderland METC (METCZ20200086) and the Local Ethics Commission Adelante approved this study. Participants consented to medical record data related to their admission being used for research purposes.

Data collection

ICU-specific data were collected retrospectively, attained from medical transfer letters. All other data were collected in the first week after admission. Medical and functional characteristics and self-reported symptoms were collected on the first day, and physical characteristics were collected during the first week after admission to the rehabilitation center as part of standard clinical care. In case of any missing or uncertain records, data were considered lost.

The following information was collected:

1. Demographic data: age, sex, and comorbidities. Comorbidities of interest were diabetes mellitus, hypertension, cardiovascular disease, lung disease, overweight (defined as a body mass index [calculated as weight in kilograms divided by height in meters squared] over 25), and psychiatric disorders. In addition, the use of immunosuppressive medication was registered.
2. ICU stay—specific parameters: length of ICU stay, mechanical ventilation (MV), duration invasive MV,

additional interventions during ICU admission (eg, tracheal cannula placement, continuous renal replacement therapy [CRRT], extracorporeal membrane oxygenation [ECMO], or thromboembolic complications). Thromboembolic complications were defined as pulmonary embolisms (PEs), deep vein thrombosis, or stroke. This information was retrieved from the admission information that the rehabilitation center received from the hospital.

3. During the first week of admission the following data from various domains of functioning were collected:

Medical characteristics: nasal oxygen use, amount of supplementary oxygen use, pressure ulcers, weight loss, and dysphagia.
Physical characteristics: Muscle strength, sensory neuropathy, and range of motion (ROM).

For the assessment of muscle strength, the Medical Research Council (MRC) Scale and a handheld dynamometer (HHD) were used. The MRC Scale is a categorical scale for measuring the entire range of muscle strength, from 0-5.[15,16] For patients with an MRC≥3, assessment with dynamometry is more sensitive for detecting weakness and progress in muscle strength.[17] Thus, for these muscles HHD was performed. The following muscle groups were assessed with the HHD: shoulder abduction, elbow flexion, wrist extension, hip flexion and knee extension, and bilateral. HHD values were measured in Newtons and percentages of the norm compared with healthy persons of the same sex, age, and weight.[18,19] As in previous studies, muscle weakness was defined as <80% of the norm score.[20,21] Sensory impairment was identified with the Erasmus modified Nottingham Sensory Assessment.[22,23] ROM was extracted from cervical spine, shoulders, elbows, wrists, hips, knees, and ankles. We defined contracture as a recorded ROM that did not reach the full range.[24]

Functional characteristics: Activities of daily living function was assessed by the Barthel Index. The Barthel Index is a well-established instrument that consists of 10 items measuring the extent to which a person can perform basic activities of daily living independently.[25,26]

Self-reported symptoms: Those indicating complaints of fear, dyspnea, or fatigue were scored on a Numeric Rating Scale (NRS) ranging from 0-10, with 0 indicating a total absence of any complaints and 10 indicating the worst imaginable fear, fatigue, or dyspnea.[27,28] Fear, dyspnea, and fatigue were scored separately. Because several patients had restricted possibility to fill in self-reported questionnaires in the first week of inpatient rehabilitation, the NRS was chosen instead of self-reported questionnaires.

Statistical analysis

Descriptive statistics were used to summarize the data; results are reported as means and SDs in case of a normal distribution or medians and interquartile ranges in case of a nonnormal distribution of the data. Categorical variables were summarized as counts and percentages. No imputation was made for missing data. Statistical analysis was performed using SPSS, 26.0.[a]

Results

Between April 2 and May 13, 2020, 60 patients were admitted for inpatient rehabilitation. Everyone provided informed consent about the use of their medical data and were included. The demographic characteristics are shown in table 1. ICU stay–specific parameters are shown in table 2. In 7 patients (11.7%) tracheostomy tube placement had been necessary in the ICU because of a problematic weaning process. However, in 6 the tube could be removed before admission to the rehabilitation center. Only 1 person was transferred to the rehabilitation center with a tracheostomy tube because of severe dysphagia. Five patients (8.3%) needed CRRT on the ICU. In 2 CRRT could be stopped, and in 3 CRRT was converted to hemodialysis during their ICU stay. Of the 3 latter patients, 1 became independent of hemodialysis while still on the ICU, and 1 was first transferred to a hospital ward for geriatric rehabilitation and was transferred to the rehabilitation center at the moment hemodialysis could be stopped. The third patient was admitted to the rehabilitation center while still dependent on hemodialysis. Thromboembolic complications were present in 14 patients (23.3%); 1 had PE as well as a stroke. Two patients developed a cardiac arrest because of massive PE on the ICU. One patient was transferred to the rehabilitation center with postinfectious encephalitis.

Medical and functional characteristics are shown in table 3. On admission to the rehabilitation center 20 persons (33.3%) still required nasal oxygen therapy because of low saturation (<93%) in rest. However, in 38.3% of all patients exercise-induced hypoxemia (<90%) was noted. Twenty-four

Table 1 Demographic characteristics

Characteristics	Patients, n (%) N=60
Age (y), mean ± SD	59.9±10.2
<40	3 (5)
40-49	6 (10)
50-59	15 (25)
60-69	26 (43)
>70	10 (17)
Sex	
Male	45 (75)
Female	15 (25)
Comorbidities	
Diabetes	9 (15)
Hypertension	19 (32)
Cardiovascular disease	18 (30)
Overweight (BMI>25)	50 (83)
Obstructive sleep apnea syndrome	11 (18)
Chronic obstructive pulmonary disease	3 (5)
Depression	1 (1.7)
Mild mental retardation	1 (1.7)
Use of immunosuppressive	9 (15)

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).

Table 2 ICU-related parameters

Parameters	Patients, n (%) N=60
Duration ICU (d), n=53, median (IQR)	15.0 (14.0)
Noninvasive mechanical ventilation	9 (15.0)
Invasive mechanical ventilation	51 (85.0)
Duration invasive MV (d), n=49, median (IQR)	12.0 (11.0)
Tracheal cannula placement	7 (11.7)
Thromboembolic complications	14 (23.3)
Pulmonary embolism	13 (21.7)
Deep vein thrombosis	1 (1.6)
Cerebrovascular accident	1 (1.6)
CRRT	5 (8.3)
ECMO	1 (1.6)

NOTE. Data presented as n (%) unless stated otherwise.
Abbreviation: IQR, interquartile range.

(40.0%) were admitted with dysphagia needing tube feeding or adapted feeding consistency. Furthermore, 6 patients (10%) received adapted feeding consistency because of severe fatigue. Pressure ulcers were seen mostly on face, sacrum, and heels.

Physical characteristics are described in table 4 and figure 1. Four patients (7.3%) had an overall muscle strength of MRC<3, and 3 had a muscle strength MRC<3 in 2-5 of the major muscle groups at the moment of admission to the rehabilitation center. The HHD values obtained in this population showed that there is a severely reduced muscle force compared with reference values. In the present study population 72.7% had a muscle weakness of <80% compared with reference values in at least 8 of 10 major muscle groups. Furthermore 13.3% had a drop foot, 7 unilateral and 1 bilateral. In 21.7% contractures were present. All of them had a reduced ROM in 1 or both shoulders, sometimes in combination with 1 or more other joints. In 16.6% a sensory neuropathy was present, varying in location. In 5 cases reduced sensibility was associated with a drop foot.

Self-reported symptoms are given in table 5. Twenty patients (39.2%) experienced anxiety complaints. Mostly feared recurrent COVID-19, infecting other people, isolation measures, or future functioning.

Table 3 Functional and medical characteristics

Characteristics	Patients, n (%) N=60
Oxygen therapy in rest, nasal	20 (33.3)
Amount of oxygen therapy, median (IQR)	2.0 L/min (1.0)
Dysphagia	24 (40.0)
Weight loss (kg), n=49, median (IQR)	10.0 (8.0)
Pressure ulcers	28 (46.7)
Barthel Index, mean ± SD	10.5±5.8

NOTE. Data presented as n (%) unless stated otherwise.
Abbreviation: IQR, interquartile range.

Table 4 Physical characteristics

Characteristics	Patients, n (%) N=60
Contractures	13 (21.7)
Shoulder	13 (21.7)
Ankle	1 (1.6)
Wrist	1 (1.6)
Neck	1 (1.6)
Sensory neuropathy	10 (16.7)

Discussion

The aim of this study is to describe clinical characteristics of post-ICU patients with COVID-19 admitted for inpatient rehabilitation. A percentage of 38.3% of all patients experienced exercise-induced oxygen desaturation. We found no reports describing this in the acute phase for post-ICU patients without COVID-19. Herridge et al[29] reported oxygen saturation levels during a 6-minute walk test with continuous oximetry below 88% in 6% of patients after 1 year and 15% of patients after 5 years in post-ICU patients with ARDS. In 72.7% of our patients, muscle weakness in all major muscle groups was found, which is high compared with other post-ICU groups. Earlier studies reported an ICU-AW in 46% of the patients without COVID-19 with an ICU stay for longer than 7 days and 60% of patients with ARDS with a minimal ICU stay of 2 weeks.[30,31] In addition, 21.7% had a reduced mobility in 1 or both shoulders. This finding seems to fit within the range of 11.3%-76% as reported before in patients without COVID-19 with an ICU stay for longer than 6 days.[32,33] Forty percent of all patients had dysphagia. In earlier studies the incidence ranged from 10.0%-62.0% for patients without COVID-19 with an ICU stay longer than 6 days and 32% in patients with ARDS.[34,35] Furthermore, 39.2% reported symptoms of anxiety in the first week after ICU discharge, whereas previous studies found a prevalence of 32% for anxiety symptoms 2-3 months after ICU discharge.[36] Comparisons have to be made cautiously because of variation in follow-up time post ICU.

Previous studies have reported clinical characteristics of patients with COVID-19 admitted to the ICU. Most patients (71%-75%) required MV, of whom 42%-75% required invasive MV, 0%-11.5% required ECMO, and 17% required CRRT.[37,38] In the first weeks of the COVID-19 pandemic, in the Netherlands, an incidence of thromboembolic complications of 49%-59% was found in ICU patients.[39,40] In the present study population the number of rehabilitation patients that needed ECMO or CRRT and/or had thromboembolic complications was lower than in studies that describe these numbers in a population of ICU patients before discharge. That could be because patients with multiorgan failure and/or thromboembolic events have lower odds of surviving ICU stay.[37,39,40]

At the moment of admission to the rehabilitation center, 33% of the patients still depended on oxygen therapy. An exercise-induced hypoxemia (<90%) was noted in 38.3% of all patients. It remains unclear why some post-ICU patients with COVID-19 experience exertional hypoxemia, while

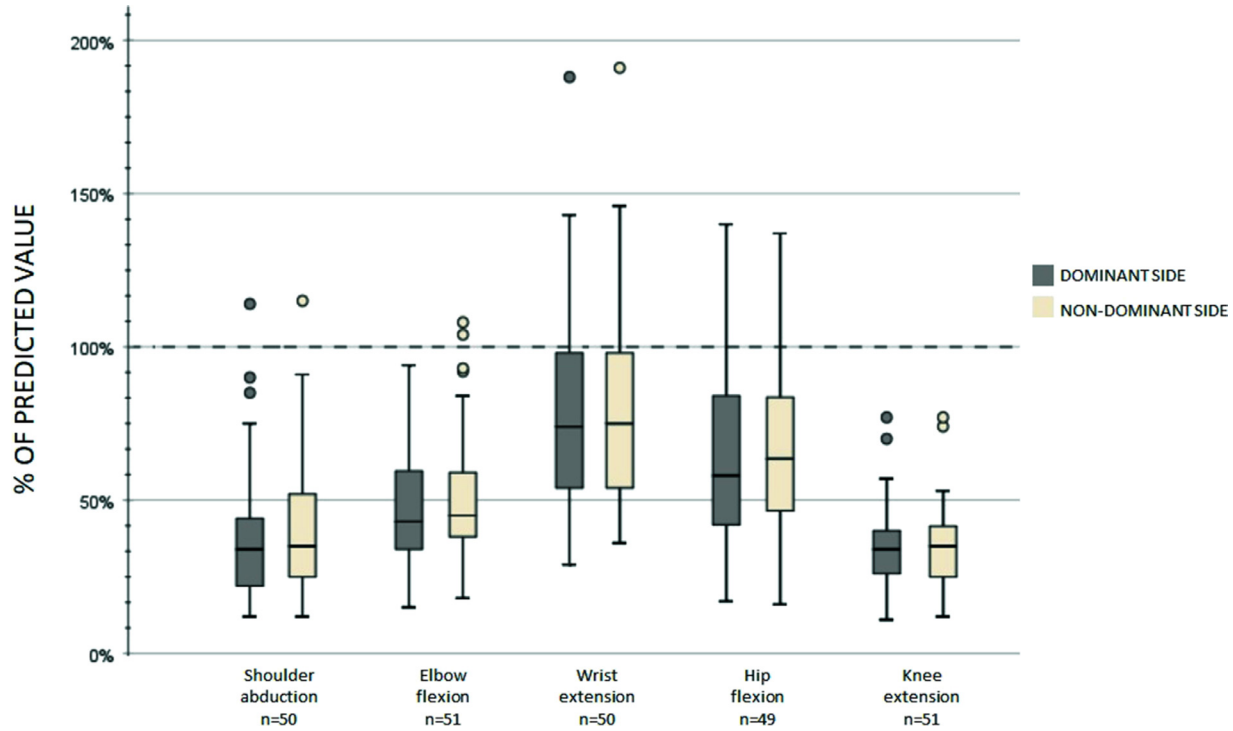

Fig 1 Box plot of the muscle strength measured with HHD, shown as median, interquartile range, and range (o=outliers). Percentages of predicted values are given as percentages of the norm (compared with healthy persons of the same sex, age, and weight). Muscle strength of patients with MRC values <3 was not measured.

others do not. Recent lung pathologic reports in COVID-19 found 3 main histologic patterns: reactive epithelial changes and diffuse alveolar damage, pulmonary microthrombi, and interstitial.[41] Further research is needed to find out to what degree these changes might contribute to long-term (exertional) hypoxemia and impaired cardiopulmonary function. Previous studies on SARS and ARDS reported a wide range (6%-58%) of patients with affected lung function.[14,42] Even though spirometry indicates a good recovery in terms of lung volumes, the diffusing capacity and exercise capacity seem to stay reduced 6-12 months after hospital or ICU discharge.[14,42] In case of an exercise-induced hypoxemia, oxygen therapy is indicated in patients with a blood oxygen saturation below 88%-90% or a relative reduction of 2%-5% during exercise lasting for 0.5-5.0 minutes.[43] Oxygen therapy will help patients meet elevated metabolic demands, prevent hypoxemia, and reduce pulmonary dynamic hyperinflation.[44] In this way training possibilities are increased.[43,44] In summary, we recommend a heightened awareness of exertional hypoxemia in patients with COVID-19 and the need to provide appropriate oxygen therapy and gradually increase exercise intensity over time starting with Borg Scale ≤4 while monitoring oxygen saturation.[44,45]

Table 5 Self-reported symptoms

Symptoms	Patients, n (%) N=60
Anxiety, n=51	20 (39.2)
NRS anxiety, mean ± SD	5.4±2.9
Fatigue, n=43	41 (95.3)
NRS fatigue, mean ± SD	6.5±1.7
Dyspnea, n=52	33 (63.5)
NRS dyspnea in rest, median (IQR)	2.0 (3)
NRS dyspnea while exercising, median (IQR)	5.0 (2)

NOTE. Data presented as n (%) unless stated otherwise.
Abbreviation: IQR, interquartile range.

The MRC and HHD values obtained in this population showed that patients have severely reduced muscle force compared with reference values. A serious shoulder weakness in almost all patients was found, with a median shoulder abduction strength of 35.0% of the norm. Weakness and atrophy of the shoulder muscles as a result of admission to an ICU and immobilization has a major effect on the stability of the shoulder, which eventually could even result in displacement of the humeral head and/or shoulder dysfunction.[33,46] Furthermore, prolonged use of neuromuscular blocking agents appears to have a negative influence on shoulder stability and muscle weakness.[33] According to Hosey and Needham,[47] there is a risk of developing brachial plexus injury because of repeated movements between supine and prone positions. However, this has not been demonstrated in the present study population.

Given the occurrence of shoulder weakness and reduced ROM in the post-ICU patients with COVID-19, shoulder rehabilitation should be considered as an important part of the multidisciplinary rehabilitation program, especially because previous studies have shown that ICU survivors could experience various shoulder impairments months after ICU

discharge. Battle et al[48] reported that 22% of the patients were experiencing shoulder pain 6 months after ICU discharge. Gustafson et al[33] reported an overall prevalence of shoulder impairment of 67%, whereas 46% of the patients presented upper limb dysfunction 6 months after ICU discharge. Next to shoulder impairment, knee extension appeared to be most limited. This is in accordance with literature on ultrasonography in ICU patients, which has shown that the vastus intermedius muscle shows the greatest change in muscle quality having a strong relationship with muscle strength. To a lesser extent the same applied for the rectus femoris.[49] Early rehabilitation started during ICU admission will lower the incidence of ICU-AW and improve short-term physical function in patients with critical illness.[50] Because of quarantine measures and prone position, multidisciplinary early rehabilitation interventions on the ICU were often not possible or were significantly limited, which may have led to an increased incidence of muscle weakness.

The present study found a median weight loss of 10 kg at the moment of intake for inpatient rehabilitation. Although good nutritional care is fundamental during post-ICU rehabilitation, previous studies suggest that nutritional deficits after ICU discharge are greater than during ICU stay.[51] Various factors, such as ICU-AW and anxiety/depression, could play a role in a decreased oral intake and malnutrition.[52] Furthermore patients with COVID-19 often display symptoms likely to affect oral intake, including loss of taste and smell.[53] Follow-up by a speech therapist and dietician is important to monitor dysphagia, asses the need to adjust feeding consistency, and monitor nutritional intakes.

Anxiety symptoms were found in 39.2% of all patients. Anxiety and depressive symptoms in the postacute phase after ICU discharge were previously found to be correlated with greater impairment in cognitive functioning 12 months after ICU admission.[54] Previous experience with post-ICU patients taught us that post-ICU patients often develop more mental and cognitive impairments weeks to months after ICU discharge. Whereas physical complaints seem to be more prominent in the acute phase, mental and cognitive impairments most of the time manifest later. Cognitive impairments are often noticed until returning to normal life. Follow-up of mental and cognitive impairments is therefore considered an important aspect of rehabilitation care because these can be a limiting factor in the rehabilitation process. Because of quarantine measures, family visits to the ICU and our rehabilitation center were nearly impossible. This might have affected these patients' mental health status and assessment of functional, cognitive, and behavioral changes relative to the preexistent situation. Therefore, a higher prevalence of mental and/or cognitive impairments in the post-ICU patients with COVID-19 and their families can be expected, which urges the need for follow-up.

Study limitations

Some limitations of the current study need to be considered. First, this study included patients referred to inpatient rehabilitation for a brief period from April until May 13, 2020. The complexity of the cases increased over time. The overall higher complexity of cases is probably associated with a longer ICU stay of patients who were referred for inpatient rehabilitation later on during the time frame of this research. Because we stopped inclusion after May 13, the values presented might therefore underestimate the actual total population of all post-ICU patients with COVID-19 referred to inpatient rehabilitation care. However, because of the urgent situation around COVID-19, it seems important to share information in this early stage. Further studies can update this information. Second, this study was situated in 1 rehabilitation center. However, patients were transferred to the rehabilitation center from 7 different hospitals in which they had been treated on the ICU (2 academic and 5 regional hospitals). In this way, this population represents transmural care for post-ICU patients with COVID-19 covered by 7 institutions. Third, cognitive and mental impairment are important domains within PICS, which makes cognitive testing important. However, in this acute phase directly after ICU discharge, the medical condition of patient hindered more extensive neuropsychological testing. The NRS was therefore chosen in this acute phase as a first representation of impairments of anxiety, fatigue, and dyspnea. Neuropsychological testing was included later on in the rehabilitation period. Fourth, this cross-sectional study only considers the clinical characteristics of post-ICU patients with COVID-19 in the first week after admission for inpatient rehabilitation. Further research is warranted, providing information on long term functioning of post-ICU patients with COVID-19.

Conclusions

This study showed a remarkable number of post-ICU patients with COVID-19 with exertional hypoxemia, severely reduced overall muscle force, shoulder problems, and dysphagia in the first week after discharge to the rehabilitation center. The presence of physical and anxiety symptoms as described in other post-ICU patients was confirmed. We therefore confirm the importance of being aware of PICS in post-ICU patients with COVID-19 and support the need for an early and effective multidisciplinary rehabilitation program.[55,56] Such a program can be based on existing programs for post-ICU patients but needs to be adapted to the specific needs of patients with COVID-19. Long-term follow-up studies are needed to reveal the long-term outcomes for physical, cognitive, and mental complaints.

Supplier

a. SPSS Statistics, version 26.0; IBM.

Corresponding author

Carolina M.H. Wiertz, MD, Adelante Zorggroep, P.O. Box 88, 6430 AB Hoensbroek, The Netherlands. *E-mail address:* c.wiertz@adelante-zorggroep.nl.

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