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Original Research

A First View of the Effect of a Trial of Early Mobilization on the Muscle Strength and Activities of Daily Living in Mechanically Ventilated Patients With COVID-19

Manabu Nankaku, PT, PhD [a], Ryosuke Ikeguchi, MD, PhD [a,b], Tomoki Aoyama, MD, PhD [c], Gakuto Kitamura, PT, MS [a], Ayumi Otagaki, PT, BS [a], Ryota Hamada, PT, MS [a], Takuma Yuri, OTR, PhD [a], Shuichi Matsuda, MD, PhD [a,b]

[a] *Rehabilitation Unit, Kyoto University Hospital, Kyoto, Japan*
[b] *Department of Orthropedic Surgery, Faculty of Medicine, Kyoto University, Kyoto, Japan*
[c] *Human Health Sciences, Graduate School of Medicine, Kyoto University, Kyoto, Japan*

KEYWORDS
Activities Of Daily Living;
Covid-19;
Early Ambulation;
Muscle Strength;
Rehabilitation;
Respiration

Abstract *Objective:* To retrospectively investigate the effect of early mobilization on the muscle strength and activities of daily living in patients with COVID-19 under mechanical ventilation.
Design: This was a single-center, retrospective, observational study.
Setting: Inpatient rehabilitation care in Japan.
Participants: The study subjects were divided based on the onset of mobilization: under mechanical ventilation (n=17; aged 68.5±11.9, 13 male) and after extubation (n=11; aged 59.7±7.1, 6 male; N=28).
Interventions: Mobilization, including dangle sitting, standing, walking, and muscle strengthening exercises.
Main Outcome Measures: The outcome measures were Barthel Index, Medical Research Council Manual Muscle Test, and intensive care unit Mobility Scale.
Results: The difference in the Barthel Index, Medical Research Council Manual Muscle Test, and intensive care unit Mobility Scale scores pre- and postintervention were not statistically significant between the 2 groups, but all significantly improved after the intervention.

List of abbreviations: ADLs, activities of daily living; Covid-19, coronavirus disease 2019; ICU, intensive care unit; MRC, Medical Research Council Manual Muscle Test.
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Conclusion: This small sample size study found no difference in the functional recovery of patients with severe COVID-19 who underwent early mobilization under mechanical ventilation relative to when it was begun after extubation.

COVID-19 has been declared a global pandemic. Its complications vary according to age, sex, and comorbidities,[1] with some patients developing severe pneumonia or acute respiratory distress syndrome and requiring mechanical ventilation in the intensive care unit (ICU).[2,3]

In the clinical setting, mechanically ventilated patients often develop skeletal muscle dysfunction, such as ICU-acquired weakness.[4] Prolonged periods of mechanical ventilation are significantly related to adverse psychosocial and physical outcomes.[5] A previous study also reported that patients with severe COVID-19 had prolonged stays in the ICU, which might lead to a high incidence of muscle weakness and decline in activities of daily living (ADLs).[6] Therefore, the improvement in physical function through early mobilization is essential for patients with severe COVID-19.

Early mobilization has been recommended for patients with mechanical ventilation to prevent ICU-acquired weakness.[7,8] On the other hand, some systematic reviews reported that there is a lack of evidence concerning the benefits of early mobilization in patients with mechanical ventilation.[9,10] Thus, it is not clear whether rehabilitation should be started during or after ventilator insertion in the acute phase. Moreover, there is currently no literature that has systemically investigated the effect of mobilization during and after ventilator insertion, particularly in mechanically ventilated patients with COVID-19.

This study aimed to investigate whether early mobilization in patients with COVID 19 with mechanical ventilation affects the recovery of ADLs, muscle strength, and functional mobility.

Methods

Study design and participants

This was a single-center, retrospective, observational study. We consecutively enrolled 73 patients who were diagnosed with COVID-19 and had been hospitalized at Kyoto University Hospital between May 2020 and October 2021. The inclusion and exclusion criteria are shown in figure 1. The final analysis included 28 patients. This study was approved by the ethics committee of Kyoto University Graduate School and the Faculty of Medicine and was conducted in accordance with the World Medical Association Declaration of Helsinki. The patients provided written informed consent before participating.

Rehabilitation

The multidisciplinary team, composed of medical doctors, physical therapist, nurses, and so on, discussed initiation of the rehabilitation. Rehabilitation was begun once the multidisciplinary team requested the initiation of rehabilitation to improve functional outcomes. The rehabilitation programs were performed by a physical therapist and 2 nurses wearing a full set of personal protective equipment in an isolated room in the ICU. These were conducted throughout the patients' hospitalization. When sedation had been reduced, mobilization, including dangle sitting, standing, walking, and muscle strengthening exercises, was performed, depending on the patient's condition and physical function. Each rehabilitation session was performed for approximately 20-40 min/day.

For the patients without rehabilitation during ventilation, the nurses minimally positioned and passively moved their extremities.

Outcome measurements

The period of mechanical ventilation, number of rehabilitation sessions performed during hospitalization, and outcome at discharge (discharge home or transfer to another hospital) were retrospectively retrieved from the medical records of each patient. All outcomes were measured by the therapists on the day intervention began and the day before hospital discharge.

We used the Barthel Index (range 0-100) to measure patients' abilities to perform ADLs. This consists of 10 items on mobility and self-care, and a higher score indicates a greater ability to function independently. The Barthel Index has been used as the assessment tool for the inpatient irrespective of illness.[11]

The sum score of the Medical Research Council Manual Muscle Test (MRC) was assessed by experienced physical therapists. The total score ranges from 0 to 60, and ICU-acquired weakness has been defined as a score of <48/60.[12]

To assess the functional mobility of patients within the ICU setting, the ICU Mobility Scale was used, which is an 11-item categorical scale (range 0-10). A higher score indicates a higher level of functional mobility.

Statistical analyses

The patients were divided into the mobilization with mechanical ventilation group and the mobilization after extubation group. The normality of the data was assessed using the Shapiro-Wilk test. The unpaired *t* test, chi-square test, or Mann-Whitney U test was used to examine the differences between the 2 groups. The paired *t* test or Wilcoxon signed-rank test was also used to examine the differences in each parameter pre- and postintervention. The analyses were performed using SPSS for Windows v17.0.[a] Statistical significance was set at $P<.05$.

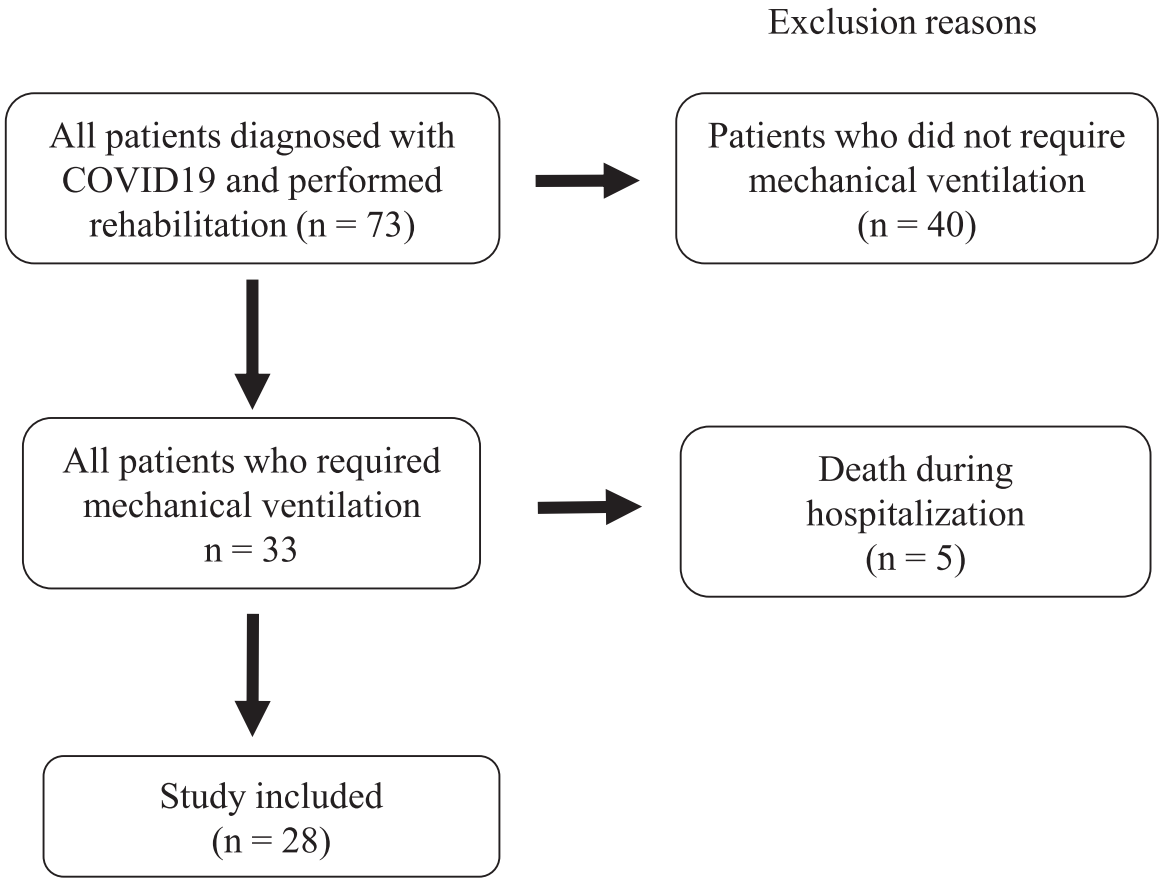

Fig 1 Flow diagram of the study participants.

The post hoc power analysis was conducted with an α of .05 using G*Power v3.1.[b]

Results

In this study, serious adverse events requiring additional treatment were not observed during rehabilitation. In addition, none of the medical staff involved in the rehabilitation program was infected.

There were 17 patients in the mechanical ventilation group (61%) and 11 patients in the extubation group (39%). The measurements of the 2 groups are summarized in table 1. The age of the extubation group was significantly lower than that of the mechanical ventilation group. The period of mechanical ventilation, period of hospitalization, number of rehabilitations performed during hospitalization, and outcomes at pre- and postintervention were not significantly different between the 2 groups.

Figure 2 shows a comparison of the measured parameters before and after the intervention. In both groups, the postintervention Barthel Index, MRC, and ICU Mobility Scale scores significantly improved compared with the pre-intervention scores. The powers for the Barthel Index analysis were 0.98 in the ventilation group and 0.72 in the extubation group. Those for the MRC were 0.66 and 0.52, respectively, and those for the ICU Mobility Scale were 0.99 and 0.95, respectively. The mean improvements between pre- and postintervention in Barthel Index score were 36.5 in the mechanical ventilation group and 31.8 in the extubation group.

Discussion

It is important to clarify when rehabilitation should be initiated to maximize the effectiveness of early mobilization in the ICU. Several studies recommended early mobilization for patients with severe COVID-19.[13,14] However, to our knowledge, there is little information in the literature regarding the effectiveness of early mobilization in patients with severe COVID-19; therefore, we retrospectively investigated the effect of early mobilization on the functional outcomes in patients with COVID-19 with mechanical ventilation. It should be noted that this study had a small sample size and missing confounders. However, the most important finding of this study was that the recovery process for patients who started rehabilitation during intubation and after extubation was similar. This finding may allow us to determine the optimal timing for the early mobilization of patients with severe COVID-19.

The current treatments for patients with severe COVID-19 include long-term sedation, insufflation management, and the use of neuromuscular blocking agents for lung protection.[15,16] Particularly, the extended administration of neuromuscular blocking agents results in skeletal muscle

Table 1 Comparison of the measured parameters between the 2 groups

	With Ventilation Group (n=17)	After Extubation Group (n=11)	*P* Value	Power
Age	68.5±11.9	59.7±7.1	.036	0.730
Sex (male/female)	13/4	6/5		
Period of mechanical ventilation (d)	9.3±6.1	6.4±4.9	.194	0.370
Period of hospitalization (d)	24.7±12	20.0±7.3	.255	0.218
Number of rehabilitation sessions performed during hospitalization	6.8±5.6	3.8±2.4	.106	0.540
Discharge to home/Transfer to another hospital	2/15	2/9		
Pre-intervention evaluation				
Barthel Index	3.2±13.3	12.3±29.1	.351	0.260
Medical Research Council Manual Muscle Test	32.9±24.2	38.5±12.8	.433	0.170
ICU Mobility Scale	1.2±1.7	2.4±2.9	.245	0.350
Postintervention evaluation				
Barthel Index	39.7±31.9	44.1±41.3	.768	0.090
Medical Research Council Manual Muscle Test	48.5±11.5	46.5±10.8	.648	0.110
ICU Mobility Scale	5.9±2.1	6.3±3.0	.713	0.100

dysfunction and increases the risk of developing ICU-acquired weakness.[17,18] In this study, the average intubation period was 9.3 days in the with-ventilation group and 6.4 days in the after-extubation group. Additionally, the pre-intervention MRC score was lower than 48 points, which is the cutoff for ICU-acquired weakness,[12] suggesting that muscle dysfunction progressed during intubation. Our data support the importance of strengthening the muscles to obtain good clinical outcomes in patients with severe COVID-19.

In our study, the Barthel Index score, muscle strength, and functional mobility after rehabilitation improved significantly compared to those at baseline. Castiglia et al reported that the minimal clinically important change in Barthel Index was 35.[11] This is comparable with our improvement between pre- and postintervention in Barthel Index. Saito et al reported that the mean Barthel Index score of healthy elderly people in Japan was 99.[19] However, Barthel Index scores postintervention in our study were 39.7 in the ventilation group and 44.1 in the extubation group, which indicates that most patients with COVID-19 were functionally not independent at discharge. The results of the present study are consistent with those reported by Musheyev et al.[6] It was also reported that remaining dysfunction due to weakness acquired in the ICU impedes the complete recovery of independent daily life and social activities.[20] In view of these findings, long-term rehabilitation should be continued for patients with severe COVID-19.

During the pandemic, the number of rehabilitation sessions performed at our hospital varied widely among patients based on the regional hospitals that can be transferred. In addition, many patients had to be transferred without sufficient recovery, which may have contributed to the lack of difference in recovery between the 2 groups.

Study limitations

This study had several limitations. First, this was a single-center, retrospective observational study with a small sample size. The baselines of the age are different between our 2 groups. These limitations might influence the outcomes of

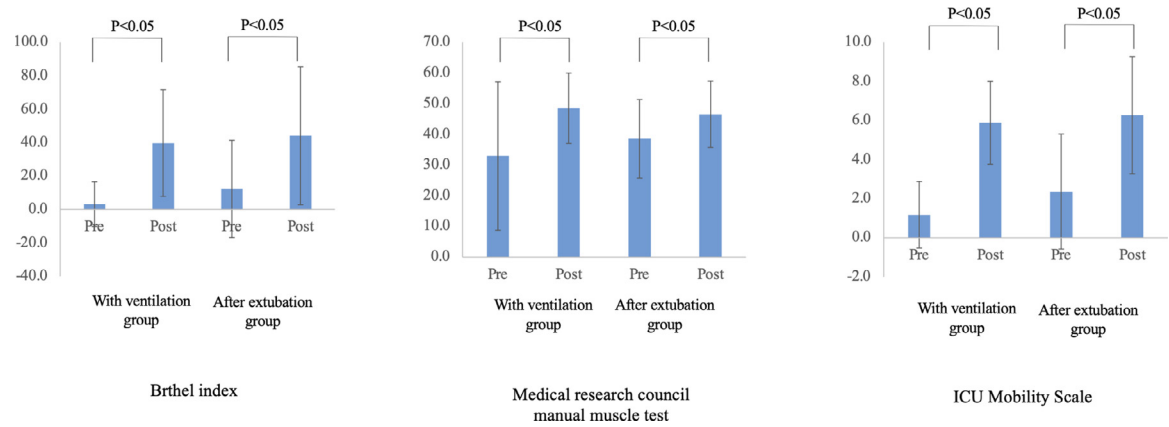

Fig 2 Comparison between the pre- and postintervention Barthel Index, Medical Research Council Manual Muscle Test, and ICU Mobility Scale scores.

mobilization. Multicenter joint studies with a greater number of patients and constructive study design, such as randomized control studies, are needed to generalize the results of the present study. Second, only limited information regarding rehabilitation was collected because of an increase in the number of patients requiring urgent and intensive care during the pandemic. Other factors, such as when the rehabilitation center received orders to mobilize a patient, might affect the outcome. In addition, this study does not include data on multimorbidities and patient vaccination, as well as whether or not it's the first time the patients in this study have experienced these symptoms. Another limitation of this study was the lack of long-term follow-up. Although this study was useful in identifying the time of rehabilitation initiation, the lack of long-term outcomes limits its conclusions.

Conclusions

This study revealed that the functional recovery in patients with COVID-19 who started rehabilitation during intubation was comparable to that in patients who started rehabilitation after extubation. These results might help determine the optimal timing for the initiation of early mobilization in the acute phase of COVID-19.

Suppliers

a. SPSS for Windows v17.0, IBM.
b. G*Power v3.1, Heinrich Heine University.

Corresponding author

Ryosuke Ikeguchi MD, PhD, Rehabilitation Unit, Kyoto University Hospital, 54 Kawahara-cho, Shogoin, Sakyo-ku Kyoto 606-8507, Japan. *E-mail address:* ikeguchi@kuhp.kyoto-u.ac.jp.

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