

# EARLY INPATIENT REHABILITATION FOLLOWING INTENSIVE CARE UNIT DISCHARGE IN ACUTE RESPIRATORY DISTRESS SYNDROME DUE TO COVID-19

✉Mahir Topaloğlu, ✉Zeynep Turan, ✉Özden Özyemişçi Taşkıran

Koç University School of Medicine, Department of Physical Medicine and Rehabilitation, Istanbul, Türkiye

## ABSTRACT

**Objective:** COVID-19 presents with varying severities, with about 5% of patients requiring intensive care unit (ICU) admission due to acute respiratory distress syndrome (ARDS). This severe condition often leads to ICU-acquired weakness (ICUAW) and muscle atrophy, affecting long-term functional recovery. Early physical therapy may mitigate these outcomes, though evidence remains inconclusive. This observational study aimed to evaluate functional outcomes at hospital discharge in COVID-19 patients who underwent early rehabilitation post-ICU discharge.

**Material and Method:** Patients aged  $\geq 18$  with COVID-19-induced ARDS transitioned from ICU to quarantine wards were enrolled from March 2021 to March 2022. Clinical assessments included oxygen saturation, heart rate, blood pressure, muscle strength (MRC Scale). Individualized exercise programs and neuromuscular electrical stimulation (NMES) sessions were administered daily in quarantine wards.

**Results:** Twenty-one patients (14 males, 7 females; median age  $71 \pm 15.77$  years) were included, undergoing 186 rehabilitation sessions. Muscle strength assessments showed 4 patients with MRC scores  $< 48$ , indicating significant muscle weakness. By discharge, 12 patients could walk independently, 4 patients could sit without assistance, and others had varying degrees of mobility limitations. Oxygen requirements decreased for most, with 15 patients not needing respiratory support at discharge. Rehabilitation interventions were well-tolerated without significant complications.

**Conclusion:** Early, tailored rehabilitation, including physical therapy and NMES, significantly improves functional outcomes in COVID-19 ARDS survivors. Findings highlight the importance of individualized rehabilitation programs in enhancing recovery and quality of life. Future research should focus on establishing comprehensive rehabilitation guidelines for critically ill COVID-19 patients.

**Keywords:** COVID-19, acute respiratory distress syndrome, ICU-acquired weakness, early rehabilitation, neuromuscular electrical stimulation.

<b>C</b>	<b>CORRESPONDING AUTHOR:</b> Mahir Topaloğlu Maltepe Mahallesi, Davutpaşa Caddesi No. 4, Zeytinburnu, İstanbul, Türkiye mahir_topaloglu@hotmail.com
<b>ORCID</b>	<b>MT</b> <a href="https://orcid.org/0000-0002-9364-4512">https://orcid.org/0000-0002-9364-4512</a> <b>ORCID</b> <b>ZT</b> <a href="https://orcid.org/0000-0001-8142-3467">https://orcid.org/0000-0001-8142-3467</a> <b>ORCID</b> <b>ÖÖTT</b> <a href="https://orcid.org/0000-0002-2052-6072">https://orcid.org/0000-0002-2052-6072</a>
<b>✓</b>	<b>DELIVERING DATE:</b> 17 / 07 / 2024 • <b>ACCEPTED DATE:</b> 26 / 07 / 2024

## YOĞUN BAKIM TABURCULUĞU SONRASI COVID-19 NEDENLİ AKUT SOLUNUM SIKINTISI SENDROMUNDA HASTANE İÇİ ERKEN REHABİLİTASYON

### ÖZET

**Amaç:** Değişen şiddetlerde ortaya çıkmakla birlikte COVID-19 hastalarının yaklaşık %5'inin Akut Solunum Sıkıntısı Sendromu (ARDS) nedeniyle yoğun bakım ünitesine yatırılması gerekmektedir. Bu ciddi durum genellikle yoğun bakım ünitesinde edinilen zayıflığa ve kas atrofisine yol açarak uzun vadeli fonksiyonel iyileşmeyi etkiler. Erken fizik tedavi bu sonuçları hafifletebilir, ancak kanıtlar kesin değildir. Bu gözlemsel çalışma, yoğun bakım ünitesinden taburcu olduktan sonra erken rehabilitasyona tabi tutulan COVID-19 hastalarında hastaneden taburculuktaki fonksiyonel sonuçları değerlendirmeyi amaçladı.

**Materyal ve Metot:** Mart 2021 ile Mart 2022 arasında yoğun bakım ünitesinden karantina servislerine geçiş yapan, COVID-19 kaynaklı ARDS tanılı 18 yaş ve üzeri hastalar dahil edildi. Klinik parametreler arasında oksijen saturasyonu, kalp hızı, kan basıncı ve kas gücü (MRC Ölçeği) değerlendirildi. Bireyselleştirilmiş egzersiz programları ve nöromüsküler elektriksel stimülasyon (NMES) tedavisi karantina servisinde günlük olarak uygulandı.

**Bulgular:** Toplamda 186 rehabilitasyon seansına katılan 21 hasta (14 erkek, 7 kadın; medyan yaş 71±15,77 yıl) çalışmaya dahil edildi. Kas gücü değerlendirmesinde önemli kas zayıflığı gösteren 4 hastanın MRC skoru <48 olarak değerlendirildi. Taburcu olduktan sonra 12 hasta bağımsız olarak yürüyebiliyordu, 4'ü yardımsız oturabiliyordu ve diğerlerinde değişen derecelerde hareket kısıtlılığı vardı. Taburculuk sırasında çoğu hastanın oksijen ihtiyacı azalmıştı; 15 hasta ek solunum desteğine ihtiyaç duymuyordu. Rehabilitasyon çalışmaları tüm hastalarda önemli komplikasyon olmaksızın iyi tolere edildi.

**Sonuç:** Fizik tedavi ve NMES'i içeren erken, kişiye özel rehabilitasyon, ARDS'den sağ kalan COVID-19 hastalarında fonksiyonel sonuçları önemli ölçüde iyileştirmektedir. Bulgular, iyileşmeyi ve yaşam kalitesini artırmada bireyselleştirilmiş rehabilitasyon programlarının önemini vurgulamaktadır. Gelecekteki araştırmalar, kritik durumdaki COVID-19 hastaları için kapsamlı rehabilitasyon kılavuzları oluşturmayı amaçlamalıdır.

**Anahtar kelimeler:** COVID-19, akut solunum sıkıntısı sendromu, yoğun bakım ünitesinden kaynaklanan güçsüzlük, erken rehabilitasyon, nöromüsküler elektriksel stimülasyon.

### INTRODUCTION

COVID-19 can present itself across a large spectrum of symptoms. While some individuals experience mild infections, others may suffer from severe respiratory complications, necessitating ventilator support and intensive care unit (ICU) admission for approximately 5% of all infected patients.<sup>1</sup> It has been shown that bedridden patients undergoing acute respiratory distress syndrome (ARDS) may manifest the signs of muscle atrophy as early as 10 days into their illness.<sup>2</sup> Patients in ARDS could develop muscle weakness, known as ICU-acquired weakness (ICUAW), which is characterized by atrophy in both upper and lower extremity muscles, with immobilization identified as a contributing risk factor.<sup>3</sup>

The catabolic state resulting in muscle loss during ARDS can be induced by sepsis, acute inflammation, multiple organ failure, and medical therapy (i.e., steroids and neuromuscular blocking agents).<sup>4-6</sup> It has been discussed that ARDS survivors often face a significant decline in physical function over a prolonged period, typically observed up to 5 years post-ICU discharge. Older age and pre-existing comorbidities prior to ICU admission are recognized as prominent risk factors contributing to this decline. ICU-acquired weakness (ICUAW), encompassing critical illness polyneuropathy and

myopathy, frequently manifests in ARDS patients, further complicating their recovery trajectory.<sup>7,8</sup>

Despite these challenges, there is growing evidence supporting the positive impact of early physical therapy, including passive and active range of motion exercises with respiratory muscle training, during ICU stays.<sup>9</sup> Such interventions aim to mitigate muscle atrophy and improve functional outcomes among ARDS survivors. Exercise rehabilitation following ICU discharge might be beneficial for recovery from critical illness, especially regarding functional capacity, however there is currently no literature review within the Cochrane format supporting this.<sup>10</sup>

Despite the lack of conclusive evidence on its effectiveness, neuromuscular electrical stimulation (NMES) has emerged as a promising adjunct therapy. It may delay muscle wasting and help preserve muscle mass in critically ill ARDS patients, particularly those experiencing immobilization-related denervation.<sup>11</sup> Integrating these rehabilitative approaches early in the treatment continuum not only aims to mitigate immediate physical decline but also holds promise for enhancing long-term recovery outcomes and overall health-related quality of life in ARDS survivors.

The aim of this observational study was to evaluate functional outcomes at the time of hospital discharge in COVID-19 patients who received rehabilitation during early inpatient care following their ICU discharge.

## MATERIAL AND METHOD

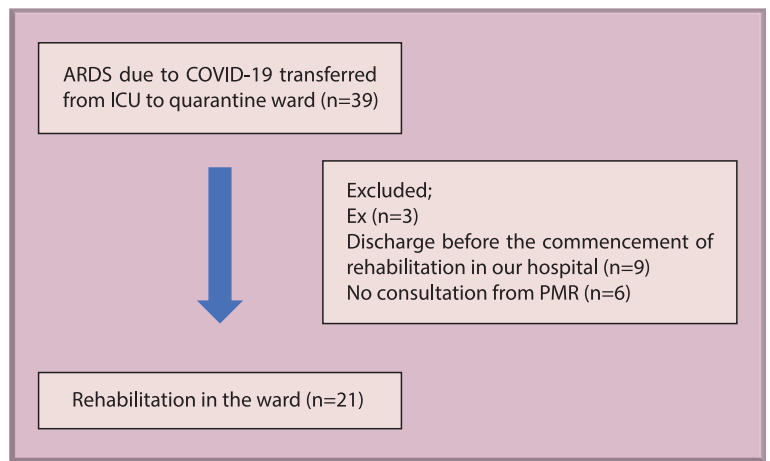
Patients over the age of 18 who developed ARDS due to COVID-19 and were admitted to the ICU followed by the quarantine ward between March 2021 and March 2022 were enrolled in the rehabilitation program until discharge from the hospital. The criteria for transfer from ICU to quarantine ward were clinical stability, absence for the need of vasopressors  $\geq 24$  hours following weaning of the mechanical ventilation, and oxygen saturation  $\geq 92\%$ .

Under adequate protective measures, physiatrists evaluated these patients for vital signs such as oxygen saturation, heart rate, blood pressure, fever, as well as Physical Medicine and Rehabilitation specific measurements such as range of motion in all extremity joints and restrictions to movement. Manual muscle strength was evaluated using the Medical Research Council (MRC) Scale, with clinically significant muscle weakness defined as an MRC sum-score  $< 48$  out of 60 points across three muscle groups in each limb.<sup>12,13</sup> Functional assessments focused on evaluating sitting, standing, and walking abilities, as feasible.<sup>14</sup>

Each patient was prescribed an individualized exercise program based on the physiatrists' evaluation. Prescribed exercises and NMES were performed daily under the supervision of physiotherapists.

Passive range of motion exercises were performed with patients that were unable to follow simple commands. The rehabilitation program progressed gradually towards active-assistive range of motion (ROM), active ROM, sitting and ambulation exercises per patient tolerance. Each joint in the upper and lower extremities underwent 10-15 repetitions during passive ROM exercises. In terms of sitting exercises, balance training at the edge of the bed and sit to stand exercises were performed. Patients were mobilized in their rooms with a 3-meter-distance from the bed to the door in accordance with isolation measures. Oxygen support levels were adjusted for patients experiencing desaturation during walking or other exercises. The exercise sessions were conducted for approximately 15 minutes per day, six days a week. Physiologic parameters such as oxygen saturation, heart rate, and blood pressure were monitored continuously. Symptoms such as dyspnea, exertion and tachypnea were noted during the sessions by the therapists.

Neuromuscular electrical stimulation (NMES), (using the Compex Rehab 400, Switzerland) was applied bilaterally to the quadriceps femoris and tibialis anterior muscles.



**Figure.** The flowchart of the study

ARDS: Acute respiratory distress syndrome, ICU: intensive care unit, PMR: physical medicine and rehabilitation

The stimulation parameters were adjusted based on the observed contraction level of the patients, with an amplitude of 20-25 mA, symmetrical biphasic square waves with a 6-second duration of contraction, and a frequency of 50 Hz.<sup>15</sup> The sessions lasted for a total of 52 minutes, during which visible muscle contractions were achieved.

This study was approved by Koç University Ethics Committee with the Approval No. 2024.268.IRB2.118.

## RESULTS

A total of 21 patients who were diagnosed with ARDS due to COVID 19 and transferred from the ICU to quarantine ward were enrolled in the rehabilitation program. Flow chart of the patients is depicted in Figure. The study group consisted of 14 male and seven female patients with ages ranging from 28 years to 90 years of age. Median age was  $71 \pm 15.77$  years. In total, 186 sessions of rehabilitation were conducted by therapists in the quarantine ward. Demographic information as well as factors impacting disease severity such as comorbidities, length of hospitalization, need for mechanical ventilation, presence of a tracheostomy, and number of sessions are provided in Table.

Among 21 patients, 19 showed no restriction or pain during passive ROM exercises. Two patients exhibited limitations: one had restricted phalangeal flexion, and the other had limitations in the hip, knee, and shoulder joints due to preexisting neurological sequelae.

The muscle strength of 17 cooperative patients was assessed with an MRC sum-score totaling 60 points. Four patients had an MRC sum-score of less than 48 points, indicating significant muscle weakness. Among these, diagnoses included brachial plexopathy and foot drop. Resting oxygen saturations were above 92%.

Table. Demographic characteristics of participants in the study (n=171)							
Patients	Age (years)	Gender	Systemic comorbidities	Mechanical ventilation duration (days)	Total length of stay in hospital (days)	Tracheostomy	Number of sessions
#1	49	M	-	19	20	-	2
#2	64	M	-	18	18	-	6
#3	83	F	CHF	6	12	-	4
#4	77	M	HT	5	10	-	4
#5	79	M	-	7	17	-	6
#6	55	M	DM	10	15	-	11
#7	71	F	ILD, RA, HT	17	25	-	7
#8	77	F	CAD, AF, DM, HT	24	24	+	12
#9	74	M	COPD, AF	21	30	+	22
#10	67	F	Stroke, CAD, HT	23	23	+	21
#11	82	M	Dementia, immobility	0	8	-	1
#12	72	M	HT, DM, AF, CHF	8	20	-	2
#13	51	F	DM	11	18	-	3
#14	76	M	COPD	10	23	-	2
#15	84	M	HT, CAD	36	42	+	6
#16	90	F	HT	23	45	-	8
#17	64	M	HT, COPD, AF	29	47	-	13
#18	51	M	-	60	77	+	24
#19	62	M	DM, AF, Lung cancer, GI hemorrhage	64	70	+	20
#20	42	M	-	7	19	-	3
#21	28	F	Pregnancy	25	13	-	9

M: Male, F: female, CHF: congestive heart failure, HT: hypertension, DM: diabetes mellitus, ILD: interstitial lung disease, RA: rheumatoid arthritis, CAD: coronary artery disease, AF: atrial fibrillation, COPD: chronic obstructive pulmonary disease, CHF: chronic renal failure, GI: gastrointestinal

Throughout the rehabilitation sessions, there were no significant instances of hemodynamic instability or complications observed. The oxygen requirements of patients exhibited a gradual increase during the sessions: eight patients experienced desaturation, seven did not desaturate, and six were unable to walk independently.

Fatigue was a prominent symptom in all cooperative patients: two of the patients had dyspnea and another two reporting coughing. There were no issues noted with sputum production. All patients were discharged after 72 hours after clinical stability.

At the time of discharge, the functional status of patients was categorized as follows: twelve were able to walk independently, four could sit without assistance, two were bedridden due to cerebrovascular accident, one had severe chronic obstructive pulmonary disease, one had severe coronary artery disease, and one had previous immobility.

Respiratory support and oxygen requirements of the patients prior to discharge were noted as follows: fifteen patients required no respiratory support, while six patients needed oxygen supplementation. Among

these, four patients relied on mechanical ventilation via tracheostomy, and two received intermittent nasal oxygen support.

## DISCUSSION

The findings of this study underline the diverse rehabilitation needs among COVID-19 patients, ranging from those able to mobilize shortly after ICU discharge to others who have been immobile for an extended period. This aligns with previous research highlighting the importance of individualized rehabilitation doses for critically ill patients, suggesting that a one-size-fits-all approach may not be effective.<sup>16,17</sup>

A case of upper trunk brachial plexopathy was observed in a patient with shoulder muscle strength graded at 3/5, likely due to severe ARDS necessitating prone positioning. Prone positioning is helpful for the treatment of hypoxia in ARDS and has been used in 11.5% of patients with ARDS associated with COVID-19.<sup>18</sup> The development of plexopathy in this patient may be linked to either the prone positioning itself or the positional stretching of the brachial plexus during patient repositioning maneuvers.

Current guidelines for early rehabilitation after ICU are not well established in COVID-19 patients. Articles published on the rehabilitation of COVID-19 patients are often based on expert opinions from the management of critically ill patients with conditions other than COVID-19. However, emerging evidence suggests that greater rehabilitation exposure early in the ICU is associated with improved physical function at hospital discharge, emphasizing the need for further research and standardized protocols.<sup>17</sup>

The present study is limited by the heterogeneity of the population in terms of risk factors and ICU admission circumstances, as well as the low number of patients. Nonetheless, the significant improvements in mobility and daily activities observed in patients undergoing acute rehabilitation underscore its potential benefits, supporting findings from other studies that report positive outcomes with interdisciplinary rehabilitation interventions in severe COVID-19 cases.<sup>19</sup>

## CONCLUSION

This case series highlights the critical importance of individualized rehabilitation programs for COVID-19 patients recovering from ARDS, particularly following ICU discharge. Early, tailored rehabilitation

interventions, including structured physical therapy and neuromuscular electrical stimulation (NMES), can significantly improve functional outcomes and overall recovery of the patients. Many patients regained significant functional abilities, supporting the necessity for personalized approaches. Notably, complications such as brachial plexopathy associated with prone positioning highlight the complexities and specific risks involved in ARDS rehabilitation, emphasizing the need for careful management and targeted interventions.

For patients likely to stay in the ICU for extended periods, such as those with ARDS, early intervention and initiation of physical therapy in the ICU are crucial. Early rehabilitation efforts can mitigate immediate physical decline and contribute significantly to better long-term recovery outcomes and overall health-related quality of life. This study contributes valuable insights to the clinical setting, supporting the integration of early, individualized rehabilitation programs in the care of critically ill COVID-19 patients, and emphasizes the need for further research to establish comprehensive rehabilitation guidelines.

\*The authors declare that there are no conflicts of interest.



## REFERENCES

1. Shan C, Yao YF, Yang XL, et al. Infection with novel coronavirus (SARS-CoV-2) causes pneumonia in Rhesus macaques. *Cell Res* 2020; 30: 670-677.
2. de Andrade-Junior MC, de Salles ICD, de Brito CMM, et al. Skeletal Muscle Wasting and Function Impairment in Intensive Care Patients with Severe COVID-19. *Front Physiol* 2021; 12: 640973.
3. Reid CL, Campbell IT, Little RA. Muscle wasting and energy balance in critical illness. *Clin Nutr* 2004; 23: 273-280.
4. Berg HE, Eiken O, Miklavcic L, et al. Hip, thigh and calf muscle atrophy and bone loss after 5-week bedrest inactivity. *Eur J Appl Physiol* 2007; 99: 283-289.
5. Gruther W, Benesch T, Zorn C, et al. Muscle wasting in intensive care patients: ultrasound observation of the M. quadriceps femoris muscle layer. *J Rehabil Med* 2008; 40: 185-189.
6. Svanberg E, Frost RA, Lang CH, et al. IGF-I/IGFBP-3 binary complex modulates sepsis-induced inhibition of protein synthesis in skeletal muscle. *Am J Physiol Endocrinol Metab* 2000; 279: 1145-1158.
7. Herridge MS, Moss M, Hough CL, et al. Recovery and outcomes after the acute respiratory distress syndrome (ARDS) in patients and their family caregivers. *Intensive Care Med* 2016; 42: 725-738.
8. Pfoh ER, Wozniak AW, Colantuoni E, et al. Physical declines occurring after hospital discharge in ARDS survivors: a 5-year longitudinal study. *Intensive Care Med* 2016; 42: 1557-1566.
9. Ambrosino N, Makhabah DN. Comprehensive physiotherapy management in ARDS. *Minerva Anestesiol* 2013; 79: 554-563.
10. Connolly B, Salisbury L, O'Neill B, et al. Exercise rehabilitation following intensive care unit discharge for recovery from critical illness: executive summary of a Cochrane Collaboration systematic review. *J Cachexia Sarcopenia Muscle* 2016; 7: 520-526.
11. Maffioletti NA, Roig M, Karatzanos E, et al. Neuromuscular electrical stimulation for preventing skeletal-muscle weakness and wasting in critically ill patients: a systematic review. *BMC Med* 2013; 11: 137.
12. Fan E. Critical illness neuromyopathy and the role of physical therapy and rehabilitation in critically ill patients. *Respir Care* 2012; 57: 933-944.
13. Turan Z, Topaloglu M, Ozyemisci Taskiran O. Medical Research Council-sumscore: a tool for evaluating muscle weakness in patients with post-intensive care syndrome. *Crit Care* 2020; 24: 562.
14. Curci C, Pisano F, Bonacci E, et al. Early rehabilitation in post-acute COVID-19 patients: data from an Italian COVID-19 Rehabilitation Unit and proposal of a treatment protocol. *Eur J Phys Rehabil Med* 2020; 56: 633-641.
15. Akar O, Günay E, Sarınc Ulasli S, et al. Efficacy of neuromuscular electrical stimulation in patients with COPD followed in intensive care unit. *Clin Respir J* 2017; 11: 743-750.
16. Carneiro I, Costa AJ, Lima A, et al. Protocol proposal to the initial assessment of the post-intensive care syndrome in COVID-19 patients, in an inpatient rehabilitation setting. *Rehabilitacion (Madr)* 2021; 55: 82.
17. Mayer KP, Haezebrouck E, Ginoza LM, et al. Early physical rehabilitation dosage in the IntensiveCare Unit predicts hospital outcomes after critical COVID-19. *Res Sq* 2024; 3.-4319133.
18. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med* 2020; 8: 475-481.
19. Elmer N, Reißhauer A, Brehm K, et al. Functional outcome after interdisciplinary, acute rehabilitation in COVID-19 patients: a retrospective study. *Eur Arch Psychiatry Clin Neurosci* Published online 2024.