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Investigation of the Clinical Features and Long-Term Functional Status of Patients with a Diagnosis of Covid-19 Followed in the Intensive Care Unit

Yoğun Bakım Ünitesinde Takip Edilen Covid-19 Tanılı Hastaların Klinik Özelliklerinin ve Taburculuk Sonrası Uzun Dönem Fonksiyonel Durumlarının İncelenmesi

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Öz

Çalışma, kritik durumdaki COVID-19 hastalarının klinik özelliklerini, mortalite ile ilişkili faktörlerini ve hayatta kalanlarda uzun vadeli fonksiyonel durumlarını incelemeyi amaçlamaktadır. Mart 2020 ile Kasım 2020 tarihleri arasında yoğun bakım ünitemize başvuran tüm COVID-19 hastaları çalışmaya dahil edilmiştir. Mortalite ile ilişkili faktörler, tekli ve çoklu analizlerle incelenmiştir. Günlük yaşam aktiviteleri (Katz ADL ve Lawton IADL), beslenme (MNA-SF), kırılganlık (FRAIL indeksi) ve yaşam memnuniyeti testleri ile değerlendirilen uzun süreli fonksiyonel durumlar, hayatta kalan kritik COVID-19 hastalarında, taburculuk sonrası evdeki son durumları değerlendirilerek incelenmiştir. Çalışmaya toplam 203 COVID-19 hastası dahil edilmiştir (%55.2 erkek, medyan yaş 76 yıl, medyan yoğun bakım kalış süresi 7 gün, APACHE II skoru medyan 19 puan, mortalite oranı %81,8). İnvaziv mekanik ventilasyon gereksiniminin mortalite ile bağımsız ilişkili bir faktör olabileceği, çoklu regresyon analizlerinde gösterilmiştir. Yirmi iki (22/203, %11,0) hasta, telefon görüşmesi ile fonksiyonel durumlarına göre değerlendirilmiştir. Taburculuk sonrası ortanca takip süreleri 169 (97-324) gündü. Katz ADL, Lawton IADL, MNA-SF, FRAIL indeksi ve Yaşam Memnuniyeti Ölçeği puanlarının COVID-19 enfeksiyonundan önceki zamana kıyasla daha kötü olduğu tespit edilmiştir. Bu çalışmada, COVID-19 nedeniyle yoğun bakım ünitesine yatan hastalarda özellikle pandeminin ilk dönemlerinde mortalite oranlarının yüksek olabileceği, invaziv mekanik ventilasyon desteğinin mortalite için bağımsız bir ilişkili faktör olabileceği ve taburcu olabilen hastalarda COVID-19 enfeksiyonu öncesindeki durumlarına kıyasla yaşam aktiviteleri, beslenme durumları ve fiziksel performansları açısından aylarca sürebilen kötüleşme yaşanabileceği gösterilmiştir.

Anahtar Kelimeler: COVID-19, Yatış Süresi, Yoğun Bakım Ünitesi

Abstract

The study aims to examine the clinical features and mortality-related factors of COVID-19 patients in critical condition and their long-term functional status in survivors. All COVID-19 patients admitted to our intensive care unit (ICU) between March 2020 and November 2020 were included in the study. In the ICU, mortality-related parameters were evaluated using univariate and multiple analyses. The long-term functional status of daily living activities (Katz ADL and Lawton IADL), nutrition (MNA-SF), frailty (FRAIL index), and life satisfaction tests were evaluated by assessing the final status at home after discharge in critically ill COVID-19 patients. A total of 203 COVID-19 patients were included in the study (55.2% male, median age 76 years, median ICU stay 7 days, APACHE II score median 19 points, and mortality rate 81.8%). Invasive mechanical ventilation use was found to be an independent risk factor for ICU mortality in multiple regression models. Twenty-two (22/203, 11.0%) patients were evaluated by telephoneregarding their functional status. Median follow-up times after discharge were 169 days (97-324). The Katz ADL, Lawton IADL, MNA-SF, FRAIL index, and Life Satisfaction Scale scores were worse than before COVID-19 infection. In this study, it has been shown that mortality rates may be high, and invasive mechanical ventilation support was an independent risk factor for mortality in patients hospitalized in the intensive care unit due to COVID-19, especially in the early stages of the pandemic. Furthermore, patients who could be discharged may experience a deterioration in their life activities, nutritional status, and physical performance for months compared to their condition before COVID-19 infection.

Keywords: COVID-19, Length of Stay, Intensive Care Unit

Introduction

SARS-CoV-2 is transmitted mainly by droplets released by sick individuals through coughing and sneezing, which can infect others through contact with the mouth, nose, or eye mucosa after touching contaminated surfaces. Common signs of infection are respiratory symptoms, fever, cough, and dyspnea. In more severe cases, it causes pneumonia, acute respiratory distress syndrome (ARDS), multiple organ failure, and death (1). Studies examining different aspects of the COVID-19 disease worldwide continue, and the number of publications investigating the long-term effects of COVID-19 on activities of daily living in individuals with the disease is ongoing and published day by day; however, the pandemic has ended (2). Recent studies emphasize that, especially in elderly patients, critical situations such as the need for intensive care unit admission, and the mortality rates are higher in

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this population than in younger individuals. Additionally, post-COVID syndrome, which can last for a long time, may cause negative results in many aspects, especially in life activities, quality of life, cognitive functions, and nutritional status of patients. Studies on post-COVID syndrome are becoming increasingly essential and attracting attention (3). This study aims to examine the clinical features and mortality-related factors of COVID-19 patients (severe COVID-19 pneumonia) in our intensive care unit and to investigate the long-term clinical problems in patients who could be discharged from the intensive care unit.

Material and Method

Patients with a probable or definite diagnosis of COVID-19 who were hospitalized in the Internal Medicine Intensive Care Unit department at The Konya Education and Research Hospital between 30 March 2020 and 14 November 2020 were included in this study. All patients admitted to our intensive care unit with a probable or definite diagnosis of Covid-19 between these dates were included in the study. Our research is a retrospective, observational study with descriptive features. In addition, the long-term functional status of patients discharged from the ICU was evaluated prospectively. The data of all patients with definite-probable COVID-19 who were followed up in the Internal Diseases Clinic 3rd Stage ICU were scanned through the hospital's automation system within the specified periods. The co-investigator who conducted the study reviewed the patients' files in this list. Patients who could be discharged were called by phone between 23-26 February 2021 to examine their general functional characteristics after discharge. The patients were given detailed information about the study, and after verbal consent was obtained, their information was recorded after discharge. Incomplete patient data and refusal to participate in the survey for those discharged were accepted as the exclusion criteria.

The patients' data were recorded according to the form we prepared, which consists of two stages. First stage: It includes demographic data, chronic diseases, symptoms at admission, length of stay in hospital and ICU due to illness, clinical features in ICU follow-up, laboratory and imaging parameters, treatments given, and discharge status (discharge, referral, or death). In this stage, the mortality-related factors were evaluated.

In the second stage, the clinical conditions of the patients discharged from the hospital were examined. Whether they were still alive, whether they had experienced an acute illness, trauma, or surgery that required hospitalization/admission to the hospital/emergency department after discharge, their symptoms, life activities, nutritional status, and fragility were assessed.

As laboratory parameters, hemogram, international normalized ratio (INR), D-dimer, fibrinogen, ferritin, C-reactive protein (CRP), procalcitonin, erythrocyte sedimentation rate (ESR), alanine aminotransferase (AST), aspartate aminotransferase (ALT), lactate dehydrogenase (LDH), albumin, creatinine, and troponin values (at ICU admission and discharge days) were recorded. As treatment parameters, it was recorded whether they received hydroxychloroquine, favipiravir, steroids, vitamin C, tocilizumab, immune plasma, intravenous immunoglobulin (IVIG), and enoxaparin treatments during their intensive care stay. Acute Physiology and Chronic Health Evaluation II (APACHE II) score and respiratory support modalities (high-flow oxygen support, non-invasive mechanical ventilator, invasive mechanical ventilator) were recorded as clinical follow-up parameters.

Patients discharged from the hospital were called by phone. The death dates of the deceased patients were recorded. Those who were alive on the date of search and agreed to participate in the study:

- Life activities: - With Katz ADL (before and after COVID-19), and - With Lawton-Brody scale (before and after COVID-19)
- Nutritional status: - With MNA-SF test (before and after COVID-19) (0-7: Malnutrition, 8-11: Malnutrition risky, ≥12: Normal)
- Vulnerability states: - By FRAIL scale (before and after COVID-19) [0: Robust, 1-2: Pre-frail, ≥3: Frail]
- Life satisfaction perceptions: These were assessed with a life satisfaction scale (before and after COVID-19). The values of these questionnaires before and after COVID-19 pneumonia were compared.

The Katz activities of daily living (ADL) index determines the activities that provide the basic requirements necessary for life to continue. It is a measurement scored between 0 and 6 points, and increased scores are associated with increased independence (4).

The instrumental daily living activity (IADLs) index, developed by Lawton and Brody in 1969, determines individuals' instrumental daily living activities. It is a measure scored between 0 and 8 points, and increased scores are associated with increased independence. A Turkish validity and reliability study has been done on this scale before (5).

The mini-nutritional assessment form (MNA-SF) consists of six items. In this test, scoring is done by calculating whether the patient has changed in appetite, whether there has been weight loss in the last three months, mobility status, whether they have had psychological stress or acute illness in the previous three months, presence of neuropsychological problems, and body mass index. Getting 12-14 points from this scale, evaluated out

of fourteen points, can be called normal nutritional status, 8-11 points malnutrition risk, and 0-7 points malnutrition. It is a scale whose validity and reliability studies have been conducted in Turkish (6).

The FRAIL scale scores 0 or 1 according to the answers given by the patients and is evaluated as 0 points non-frail, 1-2 points pre-frail, and >2 points as frail (7).

The life satisfaction scale is a 7-point Likert-type self-report scale comprising five items. The scale includes a metric measure ranging from "(1) Strongly Disagree" to "(7) Agree." The scale can be applied to all individuals over the age of 16. Its application to individuals with cognitive impairment or disability should be done under the supervision of an observer. It is a measurement tool that assesses life satisfaction. Scores obtained from the content vary between 7-35. As the score obtained from the scale increases, life satisfaction increases (8).

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS, IBM, Armonk, NY, USA) version 27.0 program was used for statistical analysis. The Kolmogorov-Smirnov test was used to test the distributions of the numerical parameters. Categorical variables were presented as numbers (n) and percentages (%). Normally distributed numerical parameters were shown as mean ± standard deviation, while the skew-distributed ones were presented as median (minimum-maximum). The Student's t or Mann-Whitney U tests were used to compare the numerical parameters in two independent groups. The chi-square or Fisher's exact tests were used to compare categorical data between independent groups. Cox regression analyses were performed to identify factors associated with mortality. The receiver operating characteristics (ROC) curve analysis (with Youden index, area under the curve, sensitivity, specificity levels, and p-value) was used to obtain the optimum cut-off values of APACHE II, D-dimer, and age levels to predict mortality.The Wilcoxon test and paired sample t -test were used to compare numerical parameters (long-term functional assessment test scores) and McNemar test was used to compare categorical variables (frailty and nutritional statuses) between two dependent groups (for pre- and post-COVID periods).A p-value of less than 0.05 was accepted as statistical significance.

Results

General Characteristics

A total of 203 patients, with 91 (44.8%) females and 112 (55.2%) males, were included in the study. The patients' median age was 76 (23-97) years. Of the patients, 45 (22.2%) were young, and 158 (77.8%) were elderly. The most common complaint among the patients was dyspnea, reported by 58.1% (n=118).

Mortality-Related Factors

It was determined that 166 (81.8%) of the patients included in the study died in the ICU, while 37 (18.2%)were discharged from the ICU. The patients were divided into two groups: those who died and those who were discharged. Thegroups' clinical, laboratory, imaging features, and treatment modalities were compared. The median age of the deceased patients was significantly higher than the discharged ones (p=0.005). The median APACHE II score of the patients who passed away was significantly higher (19 vs. 17; p=0.001). Patients who died and those who were discharged were compared according to the treatment methods applied. While invasive MV was not used for any of the discharged patients, 98.8% of the patients who died had invasive MV (p<0.001). The rate of patients who received vitamin C was significantly higher in the discharged group than in those who died (94.6% vs. 72.3%; p=0.004). Additionally, the rate of patients given IVIG in the deceased group was significantly higher than in the discharged group (10.8% vs. 30.7%; p=0.014) (Table 1). As presented in Table 1, APACHE II score, ICU LOS, invasive MV, vitamin C, and IVIG usage rates were significantly different between patients who died and thosewho were discharged, when adjusted for age (all had p-value lower than 0.05).

Cox regression analysis evaluated the patients' mortality-related parameters during their ICU stay. In univariable analyses, age (HR: 1.038, p=0.008), APACHE II score (HR: 1.118, p=0.001), invasive MV use (HR: 83.00, p<0.001), and IVIG applications (HR: 3.659, p=0.020) were found to be positively associated factors, while vitamin C levels (HR: 0.149, p=0.011) were negatively associated with mortality.

In multiple analysis, among these parameters, invasive MV was found to be an independent indicator of mortality during the ICU stay (HR: 21.916, p<0.001) (Table 2)

Table 1. Comparison of demographic and clinical data of patients according to death status

Parameter	**Death (n=166)**	**Discharge (n=37)**	**p-value**	**p-value[1]**
General features, n (%)				
Gender,Female	73 (44)	18 (48.6)	0.605	0.371
Age, year	77 (34-97)	68 (23-95)	0.005	-
Comorbidities				
Hypertension	76 (45.8)	15 (40.5)	0.562	0.847
Coronary artery disease	54 (32.5)	9 (24.3)	0.329	0.568
DiabetesMellitus	44 (26.5)	10 (27)	0.948	0.578
Hyperlipidemia	10 (6)	3 (8.1)	0.709	0.624
Chronic kidney disease	27 (16.3)	6 (16.2)	0.994	0.910
Dementia	24 (14.5)	2 (5.4)	0.178	0.448
Cancer	10 (6)	3 (8.1)	0.709	0.572
APACHE II score	19 (2-46)	17 (7-25)	0.001	0.004
Length of hospital stay, days	9 (1-101)	10 (1-71)	0.231	0.246
ICU length of stay, days	7 (1-70)	8 (1-71)	0.239	0.043
Symptoms				
Shortness of breath	96 (57.8)	22 (59.5)	0.856	0.993
Fewer	7 (4.2)	4 (10.8)	0.118	0.065
Cough	14 (8.4)	4 (10.8)	0.748	0.790
Laboratory findings				
Hgb (g/dl)	12.1±2.3	12.3±2.7	0.642	0.680
WBC (10^3/µl)	10.6 (1.8-75.2)	9.7 (1.5-29)	0.380	0.428
Lymphocyte (10^3/µl)	0.62 (0.06-5.50)	0.72 (0.20-2.63)	0.295	0.917
Thrombocyte (10^3/µl)	202 (31-527)	196 (81-482)	0.934	0.801
Albumin (g/dl)	2.9±0.4	3.1±0.4	0.193	0.263
Creatinine (mg/dl)	1.2 (0.39-13.5)	0.95 (0.6-9.7)	0.067	0.990
ALT (ıU/l)	26 (2-3033)	23 (5-173)	0.184	0.182
CRP (mg/dl)	103 (2.5-383)	71.5 (5.8-344)	0.130	0.119
Procalcitonin (ng/ml)	0.45 (0.04-100)	0.24 (0.04-82)	0.102	0.845
INR	1 (0.8-4.8)	1 (0.8-4.8)	0.536	0.533
D-dimer (mg/l)	1.9 (0.3-36.5)	1 (0.2-10.6)	0.001	0.107
Applied Treatments, n (%)				
Hemodialysis	23 (13.9)	5 (13.5)	0.957	0.944
NIMV	72 (43.4)	10 (27.0)	0.067	0.237
InvasiveMV	164 (98.8)	0 (0)	<0.001	<0.001
Favipiravir	121 (72.9)	29 (78.4)	0.492	0.619
Hydroxychloroquine	95 (57.2)	24 (64.9)	0.394	0.542
Enoxaparin	151 (91.0)	34 (91.9)	0.857	0.537
Vitamin C	120 (72.3)	35 (94.6)	0.004	0.009
Methylprednisolone	115 (69.3)	23 (62.2)	0.402	0.539
Dexamethasone	36 (21.7)	8 (21.6)	0.993	0.924
PulseSteroid	40 (24.1)	5 (13.5)	0.161	0.179
Tocilizumab	24 (14.5)	1 (2.7)	0.054	0.137
IVIG	51 (30.7)	4 (10.8)	0.014	0.004
Immuno-plasma	45 (27.1)	7 (18.9)	0.302	0.104

APACHE-II: Acute Physiology and Chronic Health Evaluation II; ICU: Intensive care unit; Hgb: Hemoglobin; WBC: White blood cell; ALT: Alanine aminotransferase; CRP: C-reactive protein; INR: international normalized ratio; NIMV: Non-invasive mechanical ventilation; MV: Mechanical ventilation; IVIG: Intravenous immunoglobulin, Numerical parameters are expressed as median (minimum-maximum), 1 refers to age-adjusted p-valuesusing binary logistic regression analyses

Table 2. Examination of parameters related to mortality by regression analysis.

Parameters	Univariateanalysis			Multipleanalyzes		
	HR	95% CI	P	HR	95% CI	P
Model-1						
Age, years	1.038	1.010-1.067	**0.008**	0.994	0.980-1.009	0.455
APACHE-II, score	1.118	1.050-1.191	**0.001**	1.010	0.987-1.033	0.407
D-dimer, mg/L	1.225	0.987-1.520	0.066			
InvasiveMV usage	83.000	20.933-329.103	**<0.001**	21.916	5.355-89.693	**<0.001**
Vitamin C usage	0.149	0.034-0.645	**0.011**	1.062	0.740-1.525	0.742
IVIG usage	3.659	1.232-10.869	**0.020**	0.867	0.598-1.256	0.451
Model-2						
Age, Being older than 75 years	1.192	0.876-1.621	0.264			
APACHE-II, Being higher than 21 points	1.471	1.073-2.015	**0.016**	1.011	0.718-1.423	0.950
D-dimer, Being higher than 1.5 mg/L	1.116	0.801-1.555	0.516			
InvasiveMV usage	83.000	20.933-329.103	**<0.001**	22.711	5.546-93.008	**<0.001**
Vitamin C usage	0.149	0.034-0.645	**0.011**	1.077	0.751-1.544	0.687
IVIG usage	3.659	1.232-10.869	**0.020**	0.843	0.584-1.217	0.362

APACHE-II: Acute Physiology and Chronic Health Evaluation II; MV: Mechanical ventilation; IVIG: Intravenous immunoglobulin; HR: Hazard ratio; Model 1: Multiple analyses were used to evaluate mortality-related parameters during ICU stay using Cox regression analysis models. Parameters with significant differences ($p<0.05$) between deceased and discharged patients in univariate analyses were included in the regression analyses. Model 2: In these models, before starting the analyses, the best cut-off values of numerical variables given in this table were evaluated by Receiver Operating Characteristic (ROC) Curve analyses. Then, these continuous variables were categorized according to the cut-off values obtained from the ROC analyses. New univariate and multiple regression analyses were done using a methodology similar to Model 1 described above. The best cut-off value for APACHE-II score to differentiate death status from discharge was found >21 (Youden Index J= 0.313, AUC: 0.682, Sensitivity: 42%, Specificity: 89%, $p<0.001$). The best cut-off value for D-dimer to differentiate death status from discharge was found >1.5 (Youden Index J= 0.331, AUC: 0.683, Sensitivity: 60%, Specificity: 73%, $p<0.001$). The best cut-off value for Age to differentiate death status from discharge was found >75 (Youden Index J= 0.296, AUC: 0.648, Sensitivity: 57%, Specificity: 73%, $p=0.008$). Multi collinearity was tested using tolerance, variation inflation factor, correlation coefficients, and condition indexes between the parameters added to the multiple regression model.

Evaluations After Discharge

Thirty-seven patients discharged from the intensive care unit were called by phone. The median follow-up period after discharge was 169 days (97-324). Ten (27%) patients couldn't be reached via the phone numbers registered in the system. It was found that 5 (18.5%) patients died, and 22 (81.5%) patients were alive, as determined by the latest status obtained by phone. It was determined that patients who died on the1st, 4th, 6th, 17th, and 26th days after discharge (with a median value of 6 days). Of the patients alive and reached by telephone, 13 (59.1%) were female, 9 (40.9%) were male, and the mean age was 67.5 ± 14.3 years. Eleven (50%) of these patients were younger than 65. One (20%) of the deceased was female, and 4 (80%) were male, with a mean age of 75.6 ± 15. There was no significant difference between patients alive and those who died after discharge regarding age values and gender distributions ($p=0.271$ and $p=0.165$, respectively). The activities of daily living, nutritional status, frailty, and life satisfaction of the surviving patients were evaluated using five questionnaires. These questionnaires were assessed separately for the periods before and after COVID-19, to investigate whether there were any differences between these two periods. In the frailty scale, a significant increase was found in the post-COVID-19 period compared to the pre-COVID-19 period, while a significant decrease was noted in the other evaluated scales ($p<0.05$) (Table 3).

Table 3. Evaluations of the patients after discharge

Scale	Pre-COVID-19	Post-COVID-19	p-value
Katz ADL score	5.2±1.8	4.6±2.1	0.010
Lawton IADL score	6.5(0-8)	4.5(0-8)	0.002
Life satisfaction scale score	25.5(7-31)	21(7-33)	0.001
FRAIL score	1.5(0-5)	3(0-5)	0.001
Robust, n(%)	9(40.9)	4(18.2)	0.019
Pre-frail, n(%)	6(27.3)	4(18.2)	
Frail, n(%)	7(31.8)	14(63.6)	
MNA-SF score	13(2-14)	8(2-14)	<0.001
Malnutrition, n(%)	1(4.5)	10(45.5)	0.003
Malnutrition risk, n(%)	6(27.3)	7(31.8)	
Normal, n(%)	15(68.2)	5(22.7)	

ADL: Activities of daily living; MNA-SF: Mini-nutritional assessment-short form

Discussion

In this study, we examined the clinical features and long-term functional status of patients with COVID-19 who were followed in the ICU and found that more than 80% of the patients died. In multiple analysis, invasive MV was an independent predictor of mortality during the ICU stay. In the post-COVID-19 period (approximately six months after discharge), the frailty scale score was increased, and the basic and instrumental daily life activities, nutrition, and life satisfaction scale scores were substantially decreased compared to the pre-COVID period.

When we examined the laboratory findings of our patients in general, we found that white blood cell count, ferritin, D-dimer, fibrinogen, CRP, procalcitonin, troponin, and LDH values were high. In contrast, lymphocyte and albumin values were low. The difference was insignificant although

serum creatinine, CRP, procalcitonin, and ferritin levels were high in the deceased patients. In addition, D-dimer level was associated with mortality in univariable regression analysis. It has been reported that increased inflammatory status, liver and kidney dysfunction, malnutrition, hematological disorders, cardiac damage, coagulopathy, and a tendency to thrombosis may develop in patients with COVID-19 requiring follow-up in the intensive care unit, and laboratory indicators of these clinical conditions are associated with disease severity and mortality (9). In a meta-analysis by Taylor et al., increased white blood cell and neutrophil counts, high D-dimer and ferritin levels, and low platelet and lymphocyte counts were reported as laboratory findings associated with mortality (10).

In our study, the ICU mortality rate was 81.8%. Invasive MV was performed in 80.8% of the patients, and all of these patients died (100%). Invasive MV was applied to 98.8% of the patients who died, and one patient died before being connected to invasive MV. In multiple regression analysis, invasive MV was found to be an independent indicator of mortality during the ICU stay (HR: 21.9).Chang et al. reported one of the most comprehensive studies investigating the relationship between invasive MV application and mortality in COVID-19 patients in the intensive care unit, comparing these data with those from the beginning of the pandemic. Data from 28 studies involving 12,437 COVID-19 patients from 7 countries followed in the ICU were used in this meta-analysis. The invasive MV rate was 69%, the ICU mortality rate was 28.3%, and the invasive MV mortality rate was 43%. In addition, invasive MV was reported to be the most important factor associated with ICU mortality (OR: 12.4) (11).

In our study, the scale defined by Katz for evaluating basic daily living activities and the scale described by Lawton for instrumental activities were used, and the scores after discharge were calculated to be significantly lower than the pre-disease status. Studies examining different aspects of COVID-19 disease around the world continue to increase. However, the number of publications investigating the long-term effects of COVID-19 on activities of daily living in individuals with the disease still needs improvement.

In a prospective cohort study reported by Sathyamurthy et al., the functional status of 279 elderly patients older than 65 who were discharged from the COVID-19 inpatient service was compared to pre-disease status by phone on day 90. No significant difference was found in basic (Katz) and instrumental (Lawton) activities of daily living before and after discharge. The authors interpreted this result as indicating that elderly patients reached a functional state close to baseline 90 days after the disease was resolved (12).

In our study, the patients were evaluated approximately six months after they were discharged from the ICU. A significant decrease was found in MNA-SF scores when their nutritional status was compared with the pre-disease period. A substantial increase was found in the malnutrition rate (4.5% to 45.5%). COVID-19 is characterized by inflammation, decreased food intake, and increased muscle catabolism. It has been reported that a 30.1% loss in muscle volume occurred on the 10th day of ICU admission in severe COVID-19 patients (13). In a study reported by De Lorenzo et al., involving the nutritional evaluation of 126 COVID-19 patients treated in the hospital, a median of 21.5 days after discharge, the median MNA score was 11, with 4% of the patients being malnourished and 64.3% of them reported to be underweight, which is considered risky (14).Our results regarding long-term functionality assessments are generally similar to those in the literature, but a direct comparison may be misleading due to methodological differences.

In our study, a significant increase was found in the FRAIL scale score, where we evaluated frailty compared to the period before the COVID-19 disease, and the rate of being frail nearly doubled from 31.8% to 63.6%. Vulnerability describes the clinical condition in which an individual is more prone to dependence and/or mortality when exposed to a stressor. Frailty may develop due to many diseases and medical conditions (15-16).In a study reported by Greco et al., the frailty status of 76 nursing home residents who had COVID-19 was evaluated before and after two months using the Frail-NH scale and compared with 76 age-matched controls who did not have COVID-19. A 21% increase was found in the frailty score of those with COVID-19 compared to the control group. In multiple regression analysis, it was reported that having a disease increased the probability of developing frailty by four times. The authors suggested that the increased frailty they detected may develop as a result of the adverse effects of acute and chronic inflammation on muscle strength and performance that occur during the COVID-19 disease, and that decreased movement during the treatment and quarantine period may be related to the loss of muscle strength (17).

Our study found a significant decrease in the life satisfaction scale in discharged patients compared to pre-COVID-19 levels. The life satisfaction scale (scale) is a questionnaire evaluating participants' general satisfaction with life. Life satisfaction, on the other hand, is defined as the cognitive self-evaluation of an individual's sense of well-being in a series of activities carried out in school, work, family, and social life (18).In a study reported by Rogowska et al., a life satisfaction questionnaire was administered to 231 individuals during the first and second waves of the pandemic, and it was found that

the questionnaire scores obtained in the second wave were significantly lower ($p<0.001$) (19).

There are some limitations to this study. The five questionnaires used to compare with the pre-disease period were based on the patients' phrases, which may introduce bias. Patients with an average age of 67 were evaluated approximately 5.5 months after discharge, and the potential for patients' subjective answers due to incorrect recall during this process may have affected the results. Prospective studies can be planned with individuals residing where functional evaluations are routinely performed, such as nursing homes or elderly care centers, to avoid the assessment limitation through recollection of the pre-disease period.

Another limitation of our study is that patients were called only once after discharge. An acute illness during the search period may affect the results; therefore, conducting face-to-face evaluations at specific intervals after discharge would be beneficial to mitigate these situations. In this way, healthier and more objective data can be obtained regarding whether the deteriorations we generally detected in functional assessment were a result of severe COVID-19 disease that would require ICU admission.

The mortality rate was very high in this critically ill population during the severe period of COVID-19, and only 22 discharged patients could be reached. As a result, long-term data could only be presented for these 22 patients. Consequently, detailed comparisons could not identify independent factors related to long-term outcomes due to the patients' limited and small sample size.

Conclusion

Among the COVID-19 patients requiring follow-up in the intensive care unit, invasive MV application was identified as an independent indicator of mortality. In the ICU survivors, there was a significant decrease in the scores of the basic and instrumental daily life activity scales, the MNA-SF nutritional status scale, and the life satisfaction scale compared to the pre-disease period, along with a significant increase in the FRAIL frailty scale score. To prevent long-term functional losses in COVID-19 patients discharged from the intensive care unit, rehabilitation programs, including nutrition plans and physical and social activities, are essential.

Conflict of interest statement

The authors of this work have nothing to disclose.

Ethics Committee Approval: The study was started after the approval of the Konya Chamber of Commerce (KTO), Karatay University Faculty of Medicine, and the Non-Pharmaceutical and Medical Device Research Ethics Committee, with a decision dated 12.01.2021 and numbered E2021/045.

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