e-ISSN: 2459-1467

OTSBD Online Türk Sağlık Bilimleri Dergisi

Online Turkish Journal of Health Sciences 2021;6(3):382-390

Online Türk Sağlık Bilimleri Dergisi 2021;6(3):382-390

# COVID-19 Nedeniyle İnterne Edilen Geriatrik Hastalarda Malnütrisyon Riski ile Prognoz Arasındaki İlişki

## The Relationship between Malnutrition Risk and Prognosis in Geriatric Patients Hospitalized for COVID-19

<sup>1</sup>Beytullah GUNER, <sup>2</sup>Rıdvan SIVRITEPE, <sup>1</sup>Sema Ucak BASAT

<sup>1</sup>Department of Internal Medicine, University of Health Sciences Umraniye Education and Research Hospital, Istanbul, Turkey <sup>2</sup>Department of Internal Medicine, Istanbul Medipol University, Faculty of Medicine, Pendik Hospital, Istanbul, Turkey

> Beytullah Güner: https://orcid.org/0000-0002-8499-7762 Rıdvan Sivritepe: https://orcid.org/0000-0003-0547-1883 Sema Uçak Basat: https://orcid.org/0000-0002-6479-1644

#### ÖZ

Amaç: Çalışmamızda COVID-19 hastalığı nedeniyle hastaneye yatırılan geriatrik hastalarda nutrisyon durumunun hastalığın prognozuna olan etkisini değerlendirdik.

Materyal ve Metot: Bu prospektif tek merkezli çalışmaya pandemi servisimize yatırılan 65 yaş üstü 110 COVID-19 tanılı hasta dâhil edildi. Malnutrisyon riski Nutrityonel Risk Taraması 2002 (NRS 2002) ile değerlendirildi. Hastalar NRS 2002 skoruna göre  $\geq$ 3 puan (1. grup) ve <3 puan (2. grup) olacak şekilde iki gruba ayrıldı. Hastaların prognoz belirteçleri kaydedildi. Tüm bu parametreler bu iki grup arasında değerlendirildi. İstatistiksel anlamlılık düzeyi p<0,05 olarak belirlendi.

**Bulgular:** Çalışmaya toplam 110 hasta (Erkek/ Kadın:51/59) dahil edildi. 1.grupta yatış süresi, tomografi tutulumu, entübasyon ve yoğun bakıma sevk oranları, lökosit, C reaktif proteini (CRP), ferritin, d-dimer düzeyleri 2. gruba göre daha yüksekti (p<0,05). 1.gruptaki 35 olgu taburcu, 18 olgu 1. basamak yoğun bakıma sevk, 2 olgu 3. basamak yoğun bakıma sevk edildi. 2. Grupta ise 53 olgu taburcu, 2 olgu 1. basamak yoğun bakıma sevk edildi. NRS2002 skoru ile yaş, solunum sayısı, lökosit, üre, kreatinin, CRP, d-dimer ve yattığı gün sayısı arasında pozitif yönde anlamlı bir ilişki saptandı (p<0,05).

**Sonuç:** COVID-19 tanısı ile hastaneye yatırılan geriatrik hastalarda nutrisyonel durumun hastalığın prognozunu etkilediğini gösterdik. Malnütre hastaların prognostik belirteçleri daha kötü, hastanede yatış süresi daha uzundur ve yoğun bakım ihtiyacı belirgin olarak artmıştır.

Anahtar Kelimeler: COVID-19, geriatri, malnütrisyon, NRS 2002

#### ABSTRACT

**Objective:** We evaluated the effect of nutritional status on the prognosis of the disease in geriatric patients hospitalized due to COVID-19 disease.

**Materials and Methods:** 110 patients over 65 years old were included. Malnutrition risk was assessed by Nutritional Risk Screening 2002 (NRS 2002). The patients were divided into two groups according to the NRS 2002 score ( $\geq$ 3 as group-1, <3 as group-2). Prognosis markers of the patients were recorded. Statistical significance level was set at p<0.05.

**Results:** The study was conducted 110 patients (Man/ Woman:51/59). In group-1, duration of hospitalization, tomography involvement, intubation rate and referral to intensive care, respiratory rate, leukocyte count, C reactive protein (CRP), ferritin, d-dimer levels were higher than group-2 (p<0.05). In group 1; 35 cases were discharged, 18 cases were transferred to 1st level intensive care, and 2 cases were transferred to 3rd level intensive care. In the group 2, 53 cases were discharged, and 2 cases were transferred to 1st level intensive care unit. There was a significant positive correlation between NRS 2002 score and age, respiratory rate, leukocyte, CRP, d dimer and days of hospitalization score (p<0.05).

**Conclusion:** Malnourished patients have higher poor prognostic markers, longer hospital stay and more intensive care needs.

Keywords: COVID-19, geriatrics, malnutrition risk, NRS 2002

Sorumiu Yazar / Corresponding Author:	Yayin Bilgisi / Article Info:
Rıdvan Sivritepe	Gönderi Tarihi/ Received: 13/03/2021
Bahcelievler Quarter, Adnan Menderes Boulevard No:31-33 Pendik	Kabul Tarihi/ Accepted: 05/07/2021
Istanbul/ Turkey	Online Yayın Tarihi/ Published: 05/09/2021
Tel: +90 (545)2605957	
E-mail: dr.ridvansivritepe@gmail.com	

Attf / Cited: Güner B and et al. The Relationship between Malnutrition Risk and Prognosis in Geriatric Patients Hospitalized for COVID-19. Online Türk Sağlık Bilimleri Dergisi 2021;6(3):382-390. doi: 10.26453/otjhs.892552

## INTRODUCTION

Six coronavirus strains, including Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) and Middle East Respiratory Syndrome Coronavirus (MERS-CoV), are known to cause respiratory diseases in humans.<sup>1</sup> SARS-CoV and MERS CoV are corona viruses that can cause severe respiratory failure in humans.<sup>2</sup> COVID-19 disease occurred in Wuhan, China in December 2019, and then spread to many countries of the world, including Turkey was declared a pandemic.<sup>3-5</sup> In COVID-19 disease, the prognosis is worse and mortality rates are higher in older adults, those with low body resistance and polymorbid individuals.<sup>6,7</sup> Although more than 159 million people are infected worldwide due to COVID-19 disease, an effective antiviral treatment has still not been found.<sup>5,8</sup> Nutrition is one of the important elements of healthcare. Nutritional deficiency and imbalance play a direct or indirect role in the pathophysiology of many diseases. Malnutrition increases the risk of developing the disease in individuals, extends the duration of hospital stay, and increases post-discharge mortality and rehospitalizations.9 Although these bad effects of malnutrition are known in other diseases, there is not enough data on the effects of COVID-19. For this purpose, the present study was planned in the vulnerable group in epidemic diseases and individuals over 65 years of age who are at risk for malnutrition. We aimed to investigate the relationship between the risk of malnutrition and the prognosis of the disease in patients over 65 years infected by COVID-19.

#### MATERIALS AND METHODS

The study was designed as a cross-sectional study and has been approved by the Ethics Committee of Umraniye Education and Research Hospital (Date: 14.04.2020; decision no: B.10.1.TKH.4.34.H.GP.0.01/107). For the power analysis, the study titled 'Prognostic significance of malnutrition for long-term mortality in communityacquired pneumonia: a propensity scores matched analyses' was taken as reference. Considering the correlation coefficient between long-term clinical outcomes and nutritional status r: 0.86 p<0.001, the sample size per group was calculated as minimum 55, with a Type 1 error of 0.05 and the strength of the study being 80%. With a 20% loss, a total of 110 patients (55 patients for the first group and 55 patients for the second group) were incorporated in the study. Since the first detection of SARS-COV 2 infection on 03/10/2020 in Turkey, a total of 110 patients, 51 males and 59 females, who were over 65 years of age admitted to our hospital's pandemic services, were included in the study according to the order of hospitalization. Patients under 65 years of age and with a history of malignancy that could lead to malnutrition were not included in the study. A detailed history was taken from all patients and their physical examinations were performed. Biochemical blood tests (urea, creatine, C-reactive protein (CRP), procalcitonin, d-dimer, ferritin, calcium, lactate dehydrogenase, albumin, leukocyte, lymphocyte, hemoglobin, thrombocyte, neutrophil lymphocyte ratio, partial arterial oxygen pressure (PaO2), oxygen saturation (SaO2), computed tomography findings, duration of hospitalization, clinical discharge, intensive care transfer and intubation rates were recorded. The blood samples of the patients were taken between 08.00 and 10.00 on an empty stomach. Blood samples were collected into SST II, LH PST II and EDTA tubes and analyzed simultaneously.

Metabolic Parameters: Plasma glucose by the enzymatic test method, calcium, phosphorus, alanine transaminase, aspartate transaminase, gamma glutamyl transferase, alkaline phosphatase, amylase, albumin and triglyceride concentration by enzymatic colorimetric test, creatinine by Jaffe' method, CRP by immunoassay, blood urea nitrogen by spectrophotometer, potassium, sodium, and chlorine level with ion-selective electrode analysis was measured with Architect plus c4000 (Abbott, USA). D-dimer was measured by immunoturbidimetric method with STA-Liatest device (Asnières-sur-Seine, France). Hemogram parameters were measured with the Mindray MC6800 device (Shenzhen, P. R. China.) by the electrical impedance method. Procalcitonin was measured by the ELFA method with the Biomerieux screw device (Hennigsdorf, Germany). Blood gas measurements were measured with ABL800 FLEX device (Bronshoj, Denmark).

*Nutrition assessment:* Nutritional Risk Screening 2002 (NRS 2002) questionnaire was used in the nutritional evaluation of the patients. Patients with a NRS 2002 score  $\geq$ 3 were defined as increased malnutrition risk. Those with a score below 3 points were considered as normal nutritional status.<sup>10</sup> The patients were divided into two groups according to the NRS 2002 score. Those with NRS 2002  $\geq$ 3 was included in group 1 and those with NRS 2002 <3 was included in group 2. All parameters were compared between these two groups.

*Statistical Analysis:* Statistical analyzes in the study were analyzed using the Statistical Package for the Social Sciences 25.0, IBM, Armonk, NY, United States (SPSS 25.0) program. Distribution of data was found to be normal with the Kolmogorov Smirnov test. While evaluating the study data, besides descriptive statistical methods (mean, standard deviation, frequency), t-test and One Way Anova test were used for parametric data. Pearson correlation analysis was performed to determine the relationship between quantitative data, and regression analysis was used to determine the associated parameters. Significance was evaluated at p<0.05 levels for all values.

#### RESULTS

The study was conducted between 01.04.2020 and 01.06.2020 with a total of 110 patients (51 males and 59 females) aged  $75.1\pm7.6$  years. The general characteristics of the patients are summarized in Table 1. When patients were compared according to NRS 2002 scores, mean age, respiratory rate per minute, white blood cell (WBC), urea, creatinine, CRP, ferritin, D-dimer, and the mean number of days of lying were higher in group 1 than group 2. Arterial blood PaO2 value, Sp02, albumin levels were found to be lower in group 1 compared to group 2 (Table 2). In the correlation analysis, a positive significant correlation was found between NRS 2002 score and age, urea, crp, respiratory rate, WBC, creatine, d-dimer, and duration of hospitaliza-

tion. There was also an inversely significant correlation between NRS 2002 score and arterial blood po2, Spo2, albumin and hemoglobin values. No statistically significant relationship was found between lymphocyte, thrombocyte, neutrophil lymphocyte ratio, procalcitonin, ferritin, calcium, LDH and CT findings (Table 3). According to the regression analysis results, the parameters affecting the NRS 2002 score were age, albumin, arterial blood p02 and spo2 values (Table 3).

Of the 110 patients participating in the study, 88 were discharged, 20 were transferred to the 1st level intensive care unit, and 2 were transferred to the 3rd level intensive care unit. No statistically significant relationship was found between gender and type of discharge (p: 0.394). In addition, no statistically significant correlation was found between CT findings and the type of discharge (p: 0.583). When the relationship between the comorbidity and the type of discharge was examined, it was found that 15 of the 17 patients without additional disease were discharged and 2 were transferred to intensive care. Diabetes and cardiovascular disease were present in one of the patients who was transferred to intensive care unit and intubated. The other patient had respiratory system, cardiovascular system, and neurological system diseases.

A statistically significant relationship was found between the respiratory rate, arterial blood p02 value, spo2, neutrophil lymphocyte ratio, albumin, urea, creatine, crp, ferritin, d-dimer and calcium

		1	1
		Ν	%
	Male	51	46.4
Gender	Woman	59	53.6
	≥3	55	50
Nutritional Risk Screening 2002	<3	55	50
	Light	58	52.7
Involvement Severity on Tomography	Middle	30	27.3
	Heavy	22	20
T-ma of incolution and an doma manhar	Unilateral	19	17.3
Type of involvement on tomography	Bilateral	91	82.7
	Discharge	88	80
Type of discharge	ICU / Extubate	20	18.2
	ICU / Intubate	2	1.8
	SARS COV-2	17	15.4
	Nrs2002≥3	16	29
Mortality	Nrs2002<3	1	1.8

Table 1. Demographic data, and clinical parameters.

ICU / Extubate: Extubated and transferred to the intensive care unit; ICU / Intubate: Intubated and transferred to the intensive care unit; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus-2; Nrs2002: Nutritional Risk Screening 2002.

**Table 2.** Comparison of all parameters according the NRS 2002 score.

	NRS 2002	Mean	Standard deviation	Mini- mum	Maxi- mum	P value*	
Hagnitalization Day	Group 1	9.35	5.948	1	27	0.006	
Hospitalization Day	Group 2	6.47	4.826	1	25	0.000	
	Group 1	77.33	7.732	65	93	0.002*	
Age (years)	Group 2	72.91	6.859	65	95	0.002*	
	Group 1	23.13	3.991	16	40	0.011*	
<b>Respiratory Rate (/min)</b>	Group 2	21.47	2.508	17	28	0.011*	
Partial oxygen pressure	Group 1	80.25	18.02	45	129	0.042*	
(80-100 mmHg)	Group 2	85.93	9.388	50	123	0.042	
Oxygen Saturation (%	Group 1	93.62	4.403	77	100	0.01.6*	
95-100)	Group 2	95.35	2.823	87	100	0.016*	
Leukocyte (4.1-8.9 103 /	Group 1	8.2693	3.60333	1.8	17	0.020*	
ul)	Group 2	6.9907	2.75769	2.8	17	0.039*	
Lymphocyte (1.2-5.2	Group 1	3.0647	12.3778	0.48	93	0.306	
103 /ul)	Group 2	1.64	0.6985	0.23	3.3	0.390	
Hemoglobin (12.4-14.8	Group 1	11.902	1.918	7.9	15.6	0.132	
g/l)	Group 2	12.416	1.6287	7.6	17.1	0.152	
Neutrophil lymphocyte	Group 1	6.112	5.66806	1.17	29	0.081	
ratio	Group 2	3.9647	7.03454	0.97	52	0.001	
Albumin (3.5-5.5 g/dl)	Group 1	32.89	9.739	18	44	0.000*	
	Group 2	38.07	3.42	29	44	0.000	
$U_{max}$ (5.11 mg/dl)	Group 1	69.95	44.325	23	254	0.002*	
Orea (5-11 mg/ul)	Group 2	47.98	30.372	19	194	0.003	
Creatinin (<1 mg/dl)	Group 1	1.4744	1.30756	0.5	8.1	0.046*	
Creatinin ( (1 mg/ui)	Group 2	1.0655	0.73541	0.5	5.6	0.040	
C-reactive protein (3mg/	Group 1	12.33	8.901	0	37	0*	
l)	Group 2	4.93	4.88	0	22	0	
Procalcitonine (< 0.50	Group 1	2.9605	14.9474	0.05	109	0.025	
ng/mL)	Group 2	3.8815	26.9569	0.05	200	0.823	
Ferritine (20-500 ml/ng)	Group 1	570.35	1093.32	16	7668	0.02*	
	Group 2	212.96	260.08	7	1192	0.02	
D-Dimer (0-550 µg/mL)	Group 1	3544.78	4485.97	9	20000	0.004*	
	Group 2	1447.65	2909.61	200	20000		
Calcium (8.5 ile 1.03 mg/	Group 1	8.684	0.7396	6.3	10.8	0.506	
dL)	Group 2	8.769	0.5947	7.9	7.9		
Lactate Dehydrogenase	Group 1	398.8	173.064	113	1045	0.524	
(90-250 U/L)	Group 2	354.87	478.06	134	3686	0.521	

Nrs2002: Nutritional Risk Screening 2002; \*: Mann Whitney U test.

	NRS 2002	P value	
	Pearson Correlation		
Age (years)	0.408**	0	
Respiratory Rate (min)	0.201*	0.035	
Partial oxygen pressure (80-100 mmHg)	-0.247**	0.009	
Oxygen Saturation (%95-100)	-0.239*	0.012	
Leukocyte (4.1-8.9 103 /ul)	0.219*	0.021	
Lymphocyte (1.2-5.2 103 /ul)	0.026	0.785	
Hemoglobin (12.4-14.8 g/l)	-0.201*	0.035	
Neutrophil Lymphocyte Ratio	0.176	0.065	
Albumin (3.5-5.5 g/dl)	-0.385**	0	
Urea (5-11 mg/dl)	0.358**	0	
Creatinin (<1 mg/dl)	0.251**	0.008	
C-reactive protein (<3mg/l)	0.405**	0	
Procalcitonine (< 0.50 ng/mL)	-0.011	0.913	
Ferritine (20-500 ml/ng)	0.179	0.061	
D-Dimer (0-550 μg/mL)	0.255**	0.007	
Calcium (8.5 ile 1.03 mg/dL)	-0.047	0.623	
Lactate Dehydrogenase (90-250 U/L)	0.104	0.28	
Hospitalization day	0.295**	0.002	

Table 3. The correlation analysis between the NRS 2002 with other parameters.

Nrs2002: Nutritional Risk Screening 2002.

Table 4. Com	parison of all	parameters accordin	g to the ty	pe of discharge.
			~ ~ ~	

		Mean	Standard deviation	p value	Pearson correlation	p value
	D' 1	74.22	147			
Age (years)	Discharge	74.32	14./	_		
	ICU / extubate	/9.2	11.5	0.010	0.156	0.102
	ICU / intubate	69.5	3.6	0.019	0.156	0.103
Descionation Details	total	/5.12	27.10			
Respiratory Rate (/min)		21.94	/.3	_		
	ICU / extubate	24.1	4.2	0.022	0.157	0 101
	total	20.1	0.1	0.025	0.137	0.101
Dential company and second (90	Discharge	22.5	1.3			
Partial oxygen pressure (80-		84.81	1.11	_		
100 mmHg)	ICU / extubate	/5./	20.1	0.04	0.212*	0.026
	ICU / Intubate	81.5	1.4	0.04	-0.212	0.020
	total	83.09	4.12			
Oxygen Saturation (%95-	Discharge	4.4	16.3			
100)	ICU / extubate	92.05	1.10			
· ·	ICU / intubate	5.4	14.11	0.005	-0.226*	0.018
	total	94.48	9.5			
Lymphocyte (1.2-5.2 103 /ul)	Discharge	27.7	2.2			
	ICU / extubate	29.8	0.86011			
	ICU / intubate	1.2	23.2	0.84	-0.043	0.657
	total	27.5	17.2			
Neutrophil lymphocyte ratio	Discharge	9.3	2.10			
	ICU / extubate	26.11	14.6			
	ICU / intubate	1.6	11.8	0.016	0.205*	0.031
	total	10.12	28.7			
C-reactive protein (<3mg/l)	Discharge	1.7	29.5			
	ICU / extubate	14.14	26.11			
	ICU / intubate	7.3	13.3	0.003	0.261**	0.006
	total	1.8	17.1			
Procalcitonine (< 0.50 ng/	Discharge	2.4	27.5			
mL)	ICU / extubate	17.5	17.2			
	ICU / intubate	0.24	0.19799	0.252	0.123	0.2
	total	13.5	17.2			
D-Dimer (0-550 µg/mL)	Discharge	1684.15	2090.51			
	ICU / extubate	6119.7	7103.6			
	ICU / intubate	1992.5	2164.45	0.1	0.362**	0.1
	total	2496.22	3908.11			
Hospitalization day	Discharge	1.8	5.6			
	ICU / extubate	5.5	25.1			
	ICU / intubate	4.5	0.707	0.022	-0.255**	0.007
	total	1.7	12.4			

ICU / Extubate: Extubated and transferred to the intensive care unit; ICU / Intubate: Intubated and transferred to the intensive care unit; Nrs2002: Nutritional Risk Screening 2002; \*: One-way ANOVA p values; \*\*: Spearman's rho.

value and the type of discharge of the patients (p<0.05). While this relationship was positive with NLR, urea, creatine, crp, ferritin, d-dimer, it was negative with arterial blood p02, sp02, albumin, calcium value (Table 4).

## DISCUSSION AND CONCLUSION

We examined the relationship between malnutrition risk and prognosis of the patients in this study. At the end of the study, we found that poor nutritional status prolonged the length of stay in COVID-19 patients, and the rates of intubation, intensive care transfer rate referral and mortality were higher in these patients.

Malnutrition causes many adverse metabolic events that affect the immune system and hinder the body's ability to adapt, heal, and survive. The susceptibility of malnourished individuals to bacterial and parasitic infections and especially respiratory tract infections has been found. Saunders et al. clearly revealed the relationship between malnutrition and airway functions in their study.<sup>11</sup> It has been reported that COVID-19 can infect human respiratory epithelial cells by interacting with the human ACE2 receptor.<sup>12,13</sup>

Malnutrition can delay recovery and prolong hospital stay, increase susceptibility to infection, reduce the quality of life, and even increase the mortality rate in most patients.<sup>9</sup> The present study has once again revealed the relationship between malnutrition and length of stay in hospital, in concordant to other studies. Since malnutrition disrupts the functions of the organs, it causes the prolongated hospitalization, development of complications, recurrent hospital admissions, and decreased life expectancy.<sup>14</sup>

When looking at the relationship between gender and NRS 2002 score, malnutrition risk was found in 47% of men and 52% of women. According to this result, there was no significant difference between gender and malnutrition risk.

It has been shown that malnutrition is associated with increased mortality in acute conditions.<sup>15</sup> Matthay et al. found that patients with diabetes, hypertension, coronary heart disease, chronic obstructive pulmonary disease, cerebro vascular disease and kidney disease exhibited worse clinical outcomes when infected with SARS-CoV-2 than those without additional disease.<sup>16</sup> In the present study, NRS 2002 score was found to be higher in patients with comorbid diseases. It was observed that 15 of 17 patients without any additional disease were discharged. These results were consistent with other publications in terms of the relationship between comorbidity and disease severity.

In a study conducted by Chen et al., they showed that 75% of the patients had bilateral pneumonia and the remaining 25% had unilateral pneumonia in chest X-ray and CT imaging.<sup>17</sup> In the present study, we found that 83% of 110 patients had bilateral pneumonia and 17% had unilateral pneumonia. Our results in terms of lung involvement were consistent with other studies in the world in this age group.

According to the results obtained from the case studies of the European Center for Disease Prevention and Control, it was found that 80% of COVID-19 patients had mild pneumonia, 14% more severe pneumonia and 6% were critically ill.<sup>18</sup> In the present study, 80% patient was discharged from the hospital. 18% patient was transferred to the 1st level intensive care unit without being intubated. 1.8% patient was intubated and transferred to the 3rd level intensive care unit. In present study, while the mortality rate of patients who were followed up for COVID-19 disease was 15.4%, this rate was quite high with 29% in the group with NRS 2002 $\geq$ 3. When the computed tomography findings were examined, moderate and severe involvement was found to be significantly higher in the NRS 2002≥3 group. These data are consistent with the data of other studies in terms of the severity of the disease. A retrospective study conducted during the corona virus epidemic found that only 6% of patients infected with SARS-CoV developed acute kidney damage, and approximately 92% of patients with SARS with acute kidney damage died.<sup>19</sup> A recent prospective study involving 701 patients with moderate or severe disease showed that 43.9% of patients had proteinuria and 26.7% hematuria, and approximately 13% had elevated levels of serum creatinine, blood urea nitrogen, or both. In the present study, we found a significant relationship between high creatine and blood urea nitrogen levels and NRS score and the type of discharge. Urea and creatinine levels were found to be higher in patients who transferred to intensive care.

In the study conducted by Qin et al., serum ferritin levels were found to be high in critically ill patients in the intensive care unit.<sup>20</sup> In the present study, it was concluded that the risk of malnutrition was higher in patients with high ferritin levels and the prognosis of these patients was worse. The CRP level was found to be high in COVID-19 patients and it was shown to be associated with the severity of the disease.<sup>21</sup> Luo et al. suggest that the CRP level may be important in grading the severity of the disease.<sup>22</sup> Consistent with these data, it was found in our study that patients with high CRP levels had higher NRS 2002 scores and were hospitalized for a longer time. Regarding procalcitonin, there was no significant relation neither in terms of malnutrition nor in terms of prognosis of the patients in our study. In the retrospective cohort study of Zhou F et al., it was found that increased d-dimer levels were associated with increased in-hospital mortality.<sup>23</sup> In our study, a statistically significant relationship was found between d-dimer and the prognosis and malnutrition status.

In the present study, we tried to evaluate the effect of malnutrition risk on the prognosis of the disease during the SARS COV-2 pandemic process in elderly patients.

Our study is valuable because it is one of the first studies evaluating the effect of malnutrition risk on COVID-19 in the elderly. Malnutrition is known to increase susceptibility to other infections and especially respiratory infections in the elderly. However, there is not enough information about the effect of malnutrition in COVID-19 on the course of the disease.

As a result of our study, the duration of stay was longer in elderly patients at risk of malnutrition. Intensive care referral rates, intubation rates and mortality were higher in these patients. Among the laboratory findings that can be considered as prognostic, WBC, urea, creatine, CRP, ferritin, and ddimer were found to be higher in this group. The limitation of our study is this was a cross-sectional study and did not obtain direct evidence of causal relationship. Secondly, the patients' NRS 2002, and laboratory measurements were evaluated at a single time point. Thirdly, our study was a single center study, so our results may not be representative of all patients with COVID-19.

*Ethics Committee Approval:* The Ethics Committee of Umraniye Education and Research Hospital (Date: 14.04.2020; decision no: B.10.1.TKH.4.34.H.GP.0.01/107).

*Conflict of Interest:* No conflict of interest was declared by the authors.

*Author Contributions:* Concept – SBU; Supervision-SBU; Materials – BG; Data Collection and/or Processing – BG, RS; Analysis and/or Interpretation –SBU; Writer – SBU, BG, RS.

Peer-review: Externally peer-reviewed.

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