



## Research

# The Relationship Between Blood Transfusions and Mortality and Length of Stay in Patients Followed up with a Diagnosis of COVID-19 in Intensive Care Units

COVID-19 Tanısıyla Yoğun Bakım Ünitelerinde Takipli Hastalarda Kan Transfüzyonlarının Mortalite ve Yoğun Bakımda Kalış Süreleri ile İlişkisi

Gülsen Keskin, Melis Sumak Hazır, Dilek Ünal, Jülide Ergil

University of Health Sciences Turkey, Dışkapı Yıldırım Beyazıt Training and Research Hospital, Clinic of Anesthesiology and Reanimation, Ankara, Turkey

## ABSTRACT

**Objective:** The number of studies investigating the requirement for red blood cell (RBC) transfusions and the effects of transfusions on mortality in intensive care unit (ICU) patients with coronavirus disease-2019 (COVID-19) is limited. This study investigated the relationship between RBC transfusions and the prognostic laboratory criteria of COVID-19, ICU length of stay, and mortality in ICU patients with a diagnosis COVID-19.

**Methods:** This retrospective study included 401 patients aged 18 years and older who were followed up and treated in the ICU with a positive real-time polymerase chain reaction test result for COVID-19 between September 01, 2020 and January 31, 2021. After obtaining the ethics committee approval, the demographic data, clinical data, and laboratory results of the patients included in the study were screened from the electronic medical record system and recorded in data-recording forms.

**Results:** The mean age of the 393 patients included in the analyses was  $69.42 \pm 12.90$  years, and 52.7% were male. Eighty-eight percent ( $n=346$ ) of the patients had comorbidities, with 35.9% having three or more comorbidities. Forty (10.2%) patients who received transfusion had higher values of Acute Physiology and Chronic Health Evaluation score ( $p<0.05$ ), ICU length of stay ( $p<0.001$ ), D-dimer ( $p<0.05$ ), brain natriuretic peptide ( $p=0.001$ ), lactate dehydrogenase (LDH) ( $p<0.05$ ), and creatinine ( $p=0.001$ ) than those without transfusion. The lowest hemoglobin value ( $p<0.001$ ) and LDH value ( $p<0.05$ ) were found to be factors effective in transfusion status. The mortality rate was higher in patients who required RBC transfusions (72.5%) than in patients without transfusion requirements (45.9%) ( $p=0.001$ ). The rate of having three or more diseases was higher in patients with transfusions (55.0%) than in patients without transfusions (33.7%) ( $p<0.05$ ).

**Conclusion:** This retrospective study demonstrated the association of RBC transfusions with an increase in ICU length of stay and mortality. The decision of transfusion for the critically ill group followed up in the COVID-19 ICU should be individualized, and unnecessary transfusions should be avoided.

**Keywords:** COVID-19, mortality, transfusion, intensive care

## ÖZ

**Amaç:** Koronavirüs hastalığı-2019 (COVID-19) nedeniyle yoğun bakım ünitelerinde (YBÜ) takip edilen hastalarda eritrosit süspansiyonu (ES) transfüzyonu ihtiyacı ve transfüzyonların mortalite üzerine etkilerini araştıran çalışmalar yetersizdir. Bu çalışmada, yoğun bakımlarda COVID-19 tanısı ile takip edilen hastalarda ES transfüzyonlarının COVID-19 prognostik laboratuvar kriterleri YBÜ'de kalış süreleri ve mortalite ile ilişkisinin araştırılması amaçlandı.

**Gereç ve Yöntem:** Retrospektif olarak planlanan bu çalışmaya 01.09.2020-31.01.2021 tarihleri arasında, YBÜ'de takip ve tedavi edilen 18 yaş ve üzeri, gerçek zamanlı polimeraz zincir reaksiyonu testi pozitif olan 401 hasta alındı. Etik kurul onayı sonrasında, dahil edilen hastaların demografik verileri, klinik verileri ve laboratuvar sonuçları elektronik tıbbi kayıt sisteminden hasta kayıtları taranarak veri kayıt formları dolduruldu.

**Address for Correspondence:** Gülsen Keskin, University of Health Sciences Turkey, Dışkapı Yıldırım Beyazıt Training and Research Hospital, Clinic of Anesthesiology and Reanimation, Ankara, Turkey

Phone: +90 533 413 35 24 E-mail: drgulsenkeskin@gmail.com ORCID ID: orcid.org/0000-0002-9990-5533

**Cite as:** Keskin G, Sumak Hazır M, Ünal D, Ergil J. The Relationship Between Blood Transfusions and Mortality and Length of Stay in Patients Followed up with a Diagnosis of COVID-19 in Intensive Care Units. Med J Bakirkoy 2022;18:356-363

**Presented in:** This study was presented as an oral presentation at the 25<sup>th</sup> Uludag Winter Symposium on February 25-26, 2022.

**Received:** 20.07.2022

**Accepted:** 21.09.2022

**Bulgular:** Analizlere dahil edilen 393 hastanın %52,7'i erkek, hastaların yaş ortalaması  $69,42 \pm 12,90$  idi. Hastaların %88'inin (346) yandaş hastalığı vardı ve bunların %35,9'unda 3 ve üzeri ek hastalık saptandı. Transfüzyon yapılan 40 (%10,2) hastanın Akut Fizyoloji ve Kronik Sağlık Değerlendirmesi skoru ( $p<0,05$ ), yoğun bakımda kalış süresi ( $p<0,001$ ), D-dimer ( $p<0,05$ ), beyin kaynaklı natriüretik peptid ( $p=0,001$ ), laktat dehidrogenaz (LDH) ( $p<0,05$ ) ve kreatinin ( $p=0,001$ ) değeri transfüzyon yapılmayan hastalara göre yüksek bulundu. En düşük hemoglobin değeri ( $p<0,001$ ) ve LDH değeri ( $p<0,05$ ) transfüzyon yapılmaya durumu üzerinde etkili faktörler olarak saptandı. ES transfüzyonu yapılan hastalardaki ölüm oranı (%72,5), transfüzyon yapılmayan hastalardakine göre (%45,9) daha yüksek bulundu ( $p=0,001$ ). Transfüzyon yapılan hastalardaki 3 ve üzeri hastalığa sahip olma oranı (%55,0), transfüzyon yapılmayan hastalara göre (%33,7) daha yüksek bulundu ( $p<0,05$ ).

**Sonuç:** Bu retrospektif çalışma sonucunda ES transfüzyonlarının artmış YBÜ kalış süresi ve mortalite ile ilişkisi gösterilmiştir. COVID-19 YBÜ'de takip edilen kritik hasta grubunda transfüzyon kararının hasta düzeyinde özelleştirilmesi ve gereksiz transfüzyonlardan kaçınılması gereği her zaman göz önünde bulundurulmalıdır.

**Anahtar Kelimeler:** COVID-19, mortalite, transfüzyon, yoğun bakım

## INTRODUCTION

Many patients diagnosed with coronavirus disease-2019 (COVID-19) pneumonia caused by severe acute respiratory syndrome coronavirus-2 are followed up in intensive care units (ICU). Studies have reported a higher mortality rate in the advanced age group with comorbidities (1).

ICU patients require blood component transfusions due to both COVID-19-related complications and comorbidities (2). Anemia is the most common reason for red blood cell (RBC) transfusion requirements among ICU patients. Anemia is common in ICU patients as an iatrogenic-induced condition due to chronic disease, iron deficiency, and repetitive sampling (2). Although the transfusion rate has been reported as 38.3% in non-COVID-19 patients in ICUs (3), a recent study found a RBC transfusion rate of 41.01% in COVID-19 patients in ICUs and associated this with increased mortality (4).

Blood transfusions have been shown to be associated with morbidity and mortality, such as prolonged length of hospital and ICU stay, the requirement for mechanical ventilation, and multiorgan failure (5). Prolonged ICU length of stay (LOS) causes both an increase in the cost of healthcare services and the inability of patients with an ICU requirement to receive appropriate healthcare (6).

Despite the published guidelines on blood transfusions, the decision of patient blood management is currently left to the clinician, and there is no consensus among clinicians in this respect (7,8). Moreover, the number of studies investigating the relationship between blood transfusions and other laboratory parameters with ICU LOS and mortality in patients with COVID-19 in the ICU is limited. A better understanding of the factors associated with mortality may allow for better management of these patients (9).

Therefore, we investigated the effects of RBC transfusions on ICU LOS and mortality in ICU patients with COVID-19.

## METHODS

The study was approved by the University of Health Sciences Turkey, Dışkapı Yıldırım Beyazıt Training and Research

Hospital Clinical Research Ethics Committee (decision no: 109/14, date: 19.04.2021). We retrospectively evaluated the records of patients aged 18 years and older who were followed up in the level 3 COVID-19 ICU affiliated with the anesthesiology and reanimation clinic between September 01, 2020 and January 31, 2021, and who had a positive COVID-19 reverse transcriptase-polymerase chain reaction test result.

Demographic data, clinical data, and laboratory data (complete blood count, coagulation parameters, inflammatory parameters) of the patients included in the study were screened from an electronic medical record system and recorded in data-recording forms. Hypertension (HT), cardiovascular disease (CVD), chronic obstructive pulmonary disease, chronic kidney disease (CKD), cerebrovascular disease, diabetes mellitus, and cancer were noted as comorbidities. Blood and blood product transfusions, Acute Physiology and Chronic Health Evaluation-II (APACHE-II) scores, drugs used [steroid, low-molecular-weight heparin (LMWH), acetylsalicylic acid (ASA)], length of intensive care and hospital stay, and discharge status (discharged to the ward/exodus) of the patients were recorded.

## Statistical Analysis

We calculated the descriptive properties of the variables (mean, median, number, and percentage). Numerical variables were checked to determine whether they followed a normal distribution. In two-group comparisons, the Student's t-test was used for normally distributed numerical variables, while the Mann-Whitney U test was used for non-normally distributed numerical variables. The comparison of categorical variables was performed using the chi-square test. We performed univariate logistic regression while conducting a risk factor analysis for mortality. This was followed by a multivariate logistic regression test by adding all variables. A p-value of  $<0.05$  was considered significant. The Statistical Package for the Social Sciences version 17 (Chicago, USA) software was used to evaluate the results.

## RESULTS

The study included 401 patients. Two patients were excluded from the study for treatment refusal, two patients who was referred to another hospital, one patient for being transferred to the non-COVID-19 ICU, two patients who received only fresh frozen plasma transfusions, and one patient who received only platelet transfusions. Statistical analysis was performed on 393 patients.

The median age of the 393 patients included in the analysis was 71 [minimum (min)-maximum (max): 19-95] years, and 52.7% of the patients were male and 47.3% were female. Of these patients, 346 (88.0%) had comorbidities. Of those with comorbidities, 64.7% had two or more comorbidities. The median APACHE-II score was 15 (min-max: 1-41). The number of patients who received RBC transfusions was 40 (10.2%). The median ICU LOS was 7 (min-max: 1-49) days. The number of patients transferred to the ward was 200 (50.9%), and the number of patients who died was 193 (49.1%) (Table 1).

The mean age, male-to-female ratios, APACHE-II scores, and drug use (steroid, LMWH, ASA), transfusion rates, and transfusion status were statistically similar ( $p>0.05$ ). The transfusion group had a higher rate of having three or more diseases than the non-transfusion group ( $p<0.008$ ). Patients with transfusion had higher admission hemoglobin (Hb) and lowest Hb values and longer ICU LOS than those without transfusion ( $p<0.001$ ). Patients who received RBC transfusion had a higher mortality rate than non-transfusion patients ( $p<0.003$ ) (Table 2).

According to multivariate logistic regression analysis, the lowest Hb value and lactate dehydrogenase (LDH) value were factors effective in transfusion status ( $p<0.001$ ;

**Table 1. Demographic data and clinical characteristics**

Variables	
Age (years), Median (min-max)	71 (19-95)
Gender (female/male) n (%)	186 (47.3)/207 (52.7)
APACHE-II score Median (min-max)	15 (1-41)
ICU length of stay (days) Median (min-max)	7 (1-49)
Transfusion (yes/no) n (%)	40 (10.2)/353 (89.8)
Exitus n (%)	193 (49.1)

APACHE-II: Acute Physiology and Chronic Health Evaluation-II, ICU: Intensive care unit, min-max: Minimum-maximum

$p<0.020$ ) (Table 3). The use of antithrombotic agents, a low lowest Hb value, and high brain natriuretic peptide (BNP) levels increased the risk of ICU stay of more than 7 days. A high APACHE-II score was found to be an independent risk factor for a LOS of more than 30 days ( $p<0.009$ ) (Table 4).

ICU LOS, APACHE-II score, LDH, creatinine, international normalized ratio (INR), procalcitonin, thrombocytopenia, and lymphopenia were found to be factors affecting mortality (Table 5).

## DISCUSSION

This retrospective study investigating RBC transfusion and mortality and ICU LOS in ICU patients with COVID-19 revealed an association between RBC transfusions and increased ICU LOS and mortality. The results of this study showed that patients with RBC transfusions had higher D-dimer, BNP, LDH, and creatinine values and that the lowest Hb and LDH values were predictive of transfusion in COVID-19 patients.

Some studies have reported mild anemia in critically ill COVID-19 patients (7). The causes of anemia in COVID-19 patients may include impaired iron metabolism secondary to a cytokine storm, the shortened lifespan of RBCs by inflammation, direct infection of blood cells by the virus, and iatrogenic phlebotomy (2). The analysis of admission Hb values of the patients in this study showed that the values were within the normal range in the non-transfusion group, whereas the mean value was 9.4 g/dL in the transfusion group, which supports the results of mild anemia reported in previous studies. The transfusion rate in our study was 10.2%, which was lower than the 41.9% reported by Grandone et al. (4) in 179 patients followed up in the ICU. Mortality rates in the ICU patients who were transfused were 76.7% in this study and 72.5% in our patient group. Although the studies looked similar in terms of demographic characteristics, the transfusion Hb threshold values, APACHE scores and LOS in the ICU were not reported. The difference in transfusion and mortality rates may be due to our use of restrictive transfusion strategies. Indeed, restrictive transfusion strategies have been shown to significantly reduce patient mortality (2).

As there are no published guidelines on blood transfusions for COVID-19 patients, current guidelines are also used for the decision of transfusion in COVID-19 patients. According to the American Association of Blood Banks blood transfusion guidelines published in 2016, the Hb threshold value for RBC transfusion is 7 g/dL for patients who are not expected to have active bleeding, including critically ill patients (10). However, it is recommended that each patient be evaluated individually during transfusion.

**Table 2.** Demographic and clinical data of patients with and without transfusion

Variables	Transfusion group n=40	Non-transfusion group n=353	p
Age (years) Median (min-max)	72.00 (44.00-92.00)	71.00 (19.00-95.00)	0.215
Gender (M/F), n (%)	17/23 (42.5/57.5)	190/163 (53.8/46.2)	0.174
Comorbidity, n (%)	No comorbidity ≥3 comorbidities	2 (5.0) 22 (55.0)	45 (12.7) 119 (33.7)
Hypertension	29 (72.5)	215 (61.3)	0.22
Diabetes	16 (40)	132 (37.6)	0.90
CKD	11 (27.5)	23 (6.6)	<0.001
Cardiovascular disease	10 (25)	77 (21.9)	0.81
Neurological disease	6 (15)	50 (14.2)	1.00
Malignancy	5 (12.5)	21 (6)	0.17
COPD	3 (12)	62 (23.5)	0.28
Others	5 (12.5)	40 (11.4)	0.79
APACHE-II score Median (min-max)	16.00 (7.00-41.00)	11.00 (6.00-6.20)	0.49
Admission Hb (g/dL) Median (min-max)	8.65 (6.00-19.10)	12.30 (7.40-7.20)	<0.001
Lowest Hb (g/dL) Median (min-max)	6.70 (3.90-8.80)	11.00 (6.00-6.20)	<0.001
ΔHb Median (min-max)	2.25 (2.00-3.20)	1.00 (1.35-1.40)	<0.001
ICU length of stay (days) Median (min-max)	11.50 (1.00-37.00)	7.00 (1.00-49.00)	<0.001
Discharge status from ICU n (%)	Exitus Ward	29 (72.5) 11 (27.5)	164 (46.5) 189 (53.5)
Drug use, n (%)	Steroid LMWH ASA	34 (85.0) 38 (95.0) 26 (65.0)	322 (91.2) 349 (98.9) 234 (66.3)

APACHE-II: Acute Physiology and Chronic Health Evaluation-II, COPD: Chronic obstructive pulmonary disease, CKD: Chronic kidney disease, ICU: Intensive care unit, LMWH: Low-molecular-weight heparin, ASA: Acetylsalicylic acid, ΔHb: Admission Hb value-lowest Hb value, Hb: Hemoglobin, min-max: Minimum-maximum

For the critically ill patient group followed up in the ICU, the Hb value, oxygenation, intravascular volume, and comorbidities play an important role in the decision of blood transfusion (7). Unnecessary transfusion may increase the patient's inflammatory markers, progression in lung damage, deterioration in oxygenation, and coagulopathy, along with transfusion-related complications such as transfusion associated circulatory overload and transfusion related lung injury (11,12). To reduce lung damage in COVID-19 patients, the number of transfusions and the number of different donors should be limited, and oxygenation should be improved with non-transfusion methods (7,13).

In the advanced restrictive transfusion approach, the patient's general condition may worsen due to deterioration in the peripheral circulation, impaired oxygenation, and increased cardiac and respiratory workload. Oxygenation, which is impaired secondary to acute respiratory distress syndrome, may become even worse when a very restrictive transfusion approach is preferred in the group of patients with advanced age and comorbidities followed up in the COVID-19 ICU (2).

In our study, the mean threshold value for Hb transfusion was found to be 6.7 g/dL. Among the parameters examined in the data, the lowest Hb level was found to be effective in

**Table 3.** Factors affecting to RBC transfusion

Variables	OR	95% CI Lower threshold	95% CI Upper threshold	p
Hb (g/dL)	1.040	0.768	1.408	0.799
Lowest Hb (g/dL)	0.074	0.026	0.208	<0.001
ΔHb	0.135	0.072	0.254	<0.001
APACHE-II score	0.968	0.884	1.059	0.474
Length of ICU stay (days)	1.057	0.987	1.132	0.112
D-dimer	0.958	0.818	1.123	0.598
BNP	1.000	1.000	1.000	0.747
LDH	1.002	1.000	1.003	0.024
Creatinine	1.250	0.877	1.781	0.216
Platelet	0.996	0.990	1.002	0.179
2≥ comorbidities	1.298	0.325	5.181	0.712

RBC: Red blood cells, Hb: Hemoglobin, APACHE-II: Acute Physiology and Chronic Health Evaluation-II; BNP: Brain natriuretic peptide, LDH: Lactate dehydrogenase, OR: Odds ratio, CI: Confidence interval, ICU: Intensive care unit

transfusion decisions. Given these observations, we consider that the restrictive blood transfusion approach should be adopted among clinicians in the ICU where the study was conducted in accordance with the guidelines. In this retrospective study, the data on the patients' oxygenation and intravascular volumes could not be evaluated since they were not complete. Moreover, although the lowest Hb value of patients in the ICU affected their transfusion status, we did not find it to be a risk factor for mortality. Therefore, we can speculate that the total effect of comorbid conditions is more important than the effect of isolated anemia and transfusion in terms of prognosis.

Advanced age, smoking, HT, diabetes, CVD, respiratory diseases, kidney disease, and malignancies have been associated with ICU mortality among COVID-19 patients (14). Our study demonstrated that the presence of comorbidities affected the requirement for and decision of transfusion and that the patient population with three or more comorbidities received more RBC transfusions compared with the group without comorbidity. The separate analysis of comorbidities showed that the presence of CKD was higher in the transfusion group.

Routine biochemical, hematological, and immunochemical laboratory tests have been widely used to evaluate disease severity, select appropriate treatments, and monitor treatment responses in COVID-19 patients. Previous studies have reported the prognostic value of increased LDH, D-dimer, and creatinine levels, along with lymphopenia and thrombocytopenia (15). The results of our study revealed that APACHE-II score, ICU LOS, INR, lymphopenia,

thrombocytopenia, LDH, and creatinine levels were risk factors for mortality.

Studies have shown an association between advanced age, comorbid diseases, APACHE-II scores, elevated levels of urea and creatinine, and prolonged ICU LOS. Prolonged ICU LOS has not been clearly defined, and different durations (>7, >14, >21, >30 days) have been used depending on subjective evaluations (16-19). Susceptibility to anemia has been reported to be increased by an increased LOS, which is associated with morbidity and mortality. Our study revealed longer LOS and higher mortality rates in the transfusion group compared to the non-transfusion group.

This study investigated transfusion-related mortality and ICU LOS in patients followed up in the COVID-19 ICU, but it has several limitations. First, there was no standardized protocol for transfusion, and only previous transfusions were analyzed in this retrospective study. Because of the lack of data, pre-transfusion oxygenation and intravascular volume could not be evaluated. Additionally, the study included only patients who received RBC transfusions, while other blood component transfusions were excluded due to the limited number of patients.

Based on the results of this study, we suggest that there is a need for multicenter prospective studies with transfusion protocols that also evaluate the oxygenation and intravascular status, as well as the Hb values and comorbid conditions of patients. Moreover, examining large patient populations and transfusions of other non-RBC blood and blood products will also guide clinicians.

**Table 4.** Multivariate analysis for ICU stay of more than 7 days and more than 30 days

Variables	Univariate		Multivariate	
	OR (95% CI)	p	OR (95% CI)	p
<b>Risk analysis for ICU stay of more than 7 days</b>				
Hypertension	1.228 (0.679-2.222)	0.497	-	-
CKD	0.756 (0.206-2.776)	0.010	-	-
APACHE-II score	1.086 (1.020-1.156)	0.010	-	-
Anticoagulants	1.970 (0.121-31.992)	0.634	-	-
Antithrombotics	2.483 (1.306-4.721)	0.006	2.730 (1.843-5.529)	0.005
Admission Hb (g/dL)	1.272 (1.066-1.517)	0.008	-	-
Lowest Hb (g/dL)	1.416 (1.179-1.700)	0.000	1.569 (1.277-1.926)	<0.001
ΔHb	1.218 (0.975-1.522)	0.082	-	-
LDH	1.730 (0.777-3.851)	0.179	-	-
Creatinine	0.710 (0.287-1.757)	0.459	-	-
Ferritin	0.417 (0.162-1.073)	0.070	-	-
BNP	0.619 (0.330-1.164)	0.137	0.378 (0.182-0.786)	0.009
D-dimer	2.004 (0.962-4.177)	0.064	-	-
INR	0.717 (0.377-1.363)	0.310	-	-
Procalcitonin	0.456 (0.196-1.061)	0.068	-	-
PLT	1.217 (0.445-3.324)	0.702	-	-
Lymphocyte	1.107 (0.612-2.004)	0.736	-	-
RBC transfused	3.263 (0.572-18.619)	0.183	-	-
<b>Risk analysis for ICU stay of more than 30 days</b>				
Hypertension	2.741 (0.555-13.540)	0.216	-	-
CKD	6.464 (1.153-36.231)	0.034	-	-
APACHE-II score	1.153 (1.035-1.283)	0.009	1.153 (1.035-1.283)	0.009
Anticoagulants	77750116.39 (0-)	0.999	-	-
Antithrombotics	3.2 (0.391-26.202)	0.278	-	-
Admission Hb (g/dL)	1.046 (0.721-1.517)	0.814	-	-
Lowest Hb (g/dL)	0.826 (0.603-1.132)	0.234	-	-
ΔHb	1.408 (0.977-2.030)	0.067	-	-
LDH	90870450.6 (0-)	0.998	-	-
Creatinine	2.414 (0.469-12.426)	0.292	-	-
Ferritin	92020777.43 (0-)	0.998	-	-
BNP	0 (0-)	0.997	-	-
D-dimer	1.818 (0.22-15.012)	0.579	-	-
INR	0 (0-)	0.997	-	-
Procalcitonin	1.947 (0.236-16.057)	0.536	-	-
Platelet	0 (0-)	0.998	-	-
Lymphocyte	0.979 (0.255-3.759)	0.975	-	-
RBC transfused	0 (0-)	0.998	-	-

CKD: Chronic kidney disease, ICU: Intensive care unit, APACHE-II: Acute Physiology and Chronic Health Evaluation-II, ΔHb: Admission Hb value-lowest Hb value, LDH: Lactate dehydrogenase, BNP: Brain natriuretic peptide, INR: International normalized ratio, RBC: Red blood cell, PLT: Platelet, OR: Odds ratio, CI: Confidence interval, Hb: Hemoglobin

**Table 5.** Analysis of risk factors for mortality

Variables	Univariate			Multivariate			p
	OR	CI	p	OR	CI	p	
>70 years	1.744	1.166	2.607	0.007	-	-	-
Hypertension	1.589	1.052	2.402	0.028	-	-	-
CKD	2.670	1.241	5.745	0.012	-	-	-
Duration of ICU	0.946	0.918	0.975	0.000	0.955	0.921	0.991 0.014
APACHE-II score	1.149	1.104	1.196	0.000	1.095	1.042	1.151 0.000
Anticoagulants	0.384	0.074	2.002	0.256	-	-	-
Antithrombotics	0.555	0.364	0.847	0.006	-	-	-
Admission Hb (g/dL)	0.916	0.833	1.007	0.068	-	-	-
Lowest Hb (g/dL)	0.921	0.841	1.009	0.076	-	-	-
ΔHb	1.002	0.886	1.133	0.978	-	-	-
LDH	10.868	3.252	36.322	0.000	9.961	2.425	40.908 0.001
Creatinine	10.602	6.260	17.957	0.000	4.650	2.482	8.712 0.000
Ferritin	2.800	1.392	5.631	0.004	-	-	-
BNP	4.682	3.049	7.192	0.000	-	-	-
D-dimer	4.067	1.956	8.454	0.000	-	-	-
INR	2.408	1.584	3.660	0.000	1.786	1.026	3.108 0.040
Procalcitonin	22.68	5.388	95.476	0.000	9.298	2.074	41.677 0.004
Platelet	3.458	1.977	6.047	0.000	2.570	1.184	5.579 0.017
Lymphocyte	3.914	2.537	6.038	0.000	3.493	1.997	6.110 0.000

CKD: Chronic kidney disease, ICU: Intensive care unit, APACHE-II: Acute Physiology and Chronic Health Evaluation-II, ΔHb: Admission Hb value-lowest Hb value, LDH: Lactate dehydrogenase, BNP: Brain natriuretic peptide, INR: International normalized ratio, Hb: Hemoglobin, OR: Odds ratio, CI: Confidence interval

## CONCLUSION

The results of this retrospective study investigating the effects of RBC transfusions in the COVID-19 ICU on mortality and ICU LOS showed an association between RBC transfusions and prolonged ICU LOS and increased mortality in ICU patients with COVID-19. The results also revealed that the admission Hb level affected transfusion decisions in ICU patients, but it had no effect on mortality. This study demonstrated that the transfusion decisions of ICU patients should be individualized, and unnecessary transfusions should be avoided.

## ETHICS

**Ethics Committee Approval:** The study was approved by the University of Health Sciences Turkey, Dışkapı Yıldırım Beyazıt Training and Research Hospital Clinical Research Ethics Committee (decision no: 109/14, date: 19.04.2021).

**Informed Consent:** Retrospective study.

## Authorship Contributions

Surgical and Medical Practices: G.K., M.S.H., Concept: D.Ü., J.E., Design: G.K., D.Ü., Data Collection or Processing: M.S.H., D.Ü., Analysis or Interpretation: M.S.H., J.E., Literature Search: G.K., M.S.H., Writing: G.K., J.E.

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

**Financial Disclosure:** The authors declare that this study received no financial support.

## REFERENCES

1. Armstrong RA, Kane AD, Cook TM. Outcomes from intensive care in patients with COVID-19: a systematic review and meta-analysis of observational studies. *Anaesthesia* 2020;75:1340-9.
2. Beverina I, Borotto E, Novelli C, Radizzani D, Brando B. Iatrogenic anaemia and transfusion thresholds in ICU patients with COVID-19 disease at a tertiary care hospital. *Transfus Apher Sci* 2021;60:103068.
3. Shehata N, Forster AJ, Lawrence N, Ducharme R, Fergusson DA, Chassé M, et al. Transfusion Patterns in All Patients Admitted

- to the Intensive Care Unit and in Those Who Die in Hospital: A Descriptive Analysis. *PLoS One* 2015;10:e0138427.
4. Grandone E, Pesavento R, Tiscia G, De Laurenzo A, Ceccato D, Sartori MT, et al. Mortality and Transfusion Requirements in COVID-19 Hospitalized Italian Patients According to Severity of the Disease. *J Clin Med* 2021;10:242.
  5. Vincent JL, Baron JF, Reinhart K, Gattinoni L, Thijs L, Webb A, et al. Anemia and blood transfusion in critically ill patients. *JAMA* 2002;288:1499-507.
  6. Kiray G, İnal MT, Memiş D, Turan FN. Investigation of the Factors Affecting Prolonged Intensive Care Unit. *Turk J Intensive Care* 2020;18:84-90.
  7. Baron DM, Franchini M, Goobie SM, Javidroozi M, Klein AA, Lasocki S, et al. Patient blood management during the COVID-19 pandemic: a narrative review. *Anaesthesia* 2020;75:1105-13.
  8. Fan BE, Ong KH, Chan SSW, Young BE, Chong VCL, Chen SPC, et al. Blood and blood product use during COVID-19 infection. *Am J Hematol* 2020;95:E158-60.
  9. Taylor EH, Hofmeyr R, Torborg A, Tonder CV, Boden R, Earle E, et al. Risk factors and interventions associated with mortality or survival in adult COVID-19 patients admitted to critical care: a systematic review and meta-analysis. *South Afr J Anaesth Analg* 2020;26:116-27.
  10. Carson JL, Guyatt G, Heddle NM, Grossman BJ, Cohn CS, Fung MK, et al. Clinical Practice Guidelines From the AABB: Red Blood Cell Transfusion Thresholds and Storage. *JAMA* 2016;316:2025-35.
  11. Vlaar APJ, Toy P, Fung M, Looney MR, Juffermans NP, Bux J, et al. A consensus redefinition of transfusion-related acute lung injury. *Transfusion* 2019;59:2465-76.
  12. Yoshida T, Prudent M, D'alessandro A. Red blood cell storage lesion: causes and potential clinical consequences. *Blood Transfus* 2019;17:27-52.
  13. Vincent JL, Jaschinski U, Wittebole X, Lefrant JY, Jakob SM, Almekhlafi GA, et al. Worldwide audit of blood transfusion practice in critically ill patients. *Crit Care* 2018;22:102.
  14. Martin CM, Hill AD, Burns K, Chen LM. Characteristics and outcomes for critically ill patients with prolonged intensive care unit stays. *Crit Care Med* 2005;33:1922-7; quiz 1936.
  15. Pourbagheri-Sigaroodi A, Bashash D, Fateh F, Abolghasemi H. Laboratory findings in COVID-19 diagnosis and prognosis. *Clin Chim Acta* 2020;510:475-82.
  16. Zampieri FG, Ladeira JP, Park M, Haib D, Pastore CL, Santoro CM, et al. Admission factors associated with prolonged (>14 days) intensive care unit stay. *J Crit Care* 2014;29:60-5.
  17. Chalfin DB. Length of intensive care unit stay and patient outcome: the long and short of it all. *Crit Care Med* 2005;33:2119-20.
  18. Çevik B, Geyik FD. Prolonged Stay in Intensive Care Unit: Retrospective Analysis of Predisposing Factors and Outcome. *Turk J Intens Care* 2019;17:96-101.
  19. Oliveira AB, Dias OM, Mello MM, Araújo S, Dragosavac D, Nucci A, et al. Factors associated with increased mortality and prolonged length of stay in an adult intensive care unit. *Rev Bras Ter Intensiva* 2010;22:250-6.