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Factors Affecting the Mortality of Patients in Critical Condition with Coronavirus Disease 2019 in the Intensive Care Unit

Coronavirus 2019 Nedeniyle Yoğun Bakım Ünitesinde Yatan Kritik Hastalarda Mortaliteye Etki Eden Faktörler

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ABSTRACT *Objective:* This study aimed to determine the factors affecting the mortality of patients in critical condition with Coronavirus disease 2019 (COVID-19) in the intensive care unit (ICU).
Materials and Methods: We included a total of 445 patients who are admitted in the ICU due to COVID-19. Patients were divided into two groups-those who survived and those who died during the ICU follow-up-and their demographic, clinical and laboratory characteristics were compared. Factors affecting mortality were also determined.
Results: Older age, high Kidney Disease: Improving Global Outcome (KDIGO) stage and Sequential Organ Failure Assessment (SOFA) scores at first admission to the ICU, high neutrophil/lymphocyte ratio, high D-dimer levels, low bicarbonate (HCO3) values and high lactate dehydrogenase (LDH) and creatinine levels were determined as independent risk factors for mortality in patients in critical condition with COVID-19 admitted in the ICU. Particularly, a substantial relationship was observed between the KDIGO stage and mortality during the ICU admission.
Conclusion: Age, KDIGO stage and SOFA scores at first admission, neutrophil/lymphocyte ratio and D-dimer, HCO3, LDH and creatinine levels were independent risk factors for mortality in patients in critical condition with COVID-19 admitted in the ICU.
Keywords: Coronavirus disease 2019, ICU, Kidney Disease: Improving Global Outcome, Mortality, Sequential Organ Failure Assessment score

ÖZ *Amaç:* Bu çalışmada yoğun bakım ünitesinde yatan kritik coronavirus disease 2019 (COVID-19) hastalarını demografik, klinik ve laboratuvar özellikleri açısından karşılaştırıp mortaliteye etkili olan faktörleri saptamayı amaçladık.
Gereç ve Yöntem: Çalışmaya yoğun bakım ünitesinde COVID-19 nedeniyle yatan 445 hasta dahil edildi. Hastalar yoğun bakım ünitesinde takipleri sırasında mortalite gelişmeyenler ve mortalite gelişenler olarak iki gruba ayrılıp demografik, klinik ve laboratuvar özellikleri açısından karşılaştırıldı ve mortaliteye etki eden faktörler saptanmaya çalışıldı.
Bulgular: İleri yaş, yoğun bakım ünitesine ilk yatıştaki yüksek Kidney Disease: Improving Global Outcome (KDIGO) evresi ve Sequential Organ Failure Assessment (SOFA) skorları, yüksek nötrofil lenfosit oranı, yüksek D-dimer düzeyleri düşük bikarbonat (HCO3) değerleri, yüksek laktat dehidrogenaz (LDH) düzeyleri ve yüksek kreatinin düzeyleri yoğun bakım ünitesinde yatan kritik COVID-19 hastalarında mortalite için bağımsız risk faktörleri olarak saptandı. Özellikle yoğun bakım ünitesine başvuru esnasındaki KDIGO evresiyle mortalite arasındaki ilişki dikkat çekiciydi.
Sonuç: Yoğun bakım ünitesinde yatan kritik COVID-19 hastalarında yaş, ilk yatıştaki KDIGO ve SOFA skorları, nötrofil lenfosit oranı, D-dimer, HCO3, LDH ve kreatinin mortalite için bağımsız risk faktörleridir.
Anahtar Kelimeler: Coronavirus disease 2019; Kidney Disease: Improving Global Outcome; mortalite; Sequential Organ Failure Assessment score; yoğun bakım ünitesi

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Introduction

Based on the data published by the World Health Organization (WHO) on December 12, 2020, the coronavirus disease 2019 (COVID-19) pandemic, in which 69.5 million individuals were infected and 1,582,674 individuals have died, continues to be an issue worldwide [1]. Although vaccination studies, which have recently accelerated, are a hope, approximately 15% of the patients with COVID-19 develop critical illnesses requiring oxygen support. In approximately 5% of the patients, respiratory failure secondary to acute respiratory distress syndrome (ARDS) as well as numerous complications including sepsis and septic shock, thromboembolism, renal failure, and cardiac damage, may further develop into a critical illness [2]. The disease mortality can be extremely high, particularly due to the complications that may develop in the critical patient group. In the initial publications, it was stated that in-hospital mortality due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was approximately 28% [3]2019, Wuhan, China, has experienced an outbreak of coronavirus disease 2019 (COVID-19. Moreover, it was emphasized that mortality was higher in critically ill patients (76%) hospitalized in the intensive care unit (ICU) [4].

When the publications on mortality in patients with COVID-19 were examined, there were reportedly numerous factors that could affect the clinical course and patient mortality [3,5–12]coronavirus disease (COVID-19. Among these factors, patient characteristics, male sex, advanced age, obesity, smoking, and comorbid diseases (particularly diabetes and hypertension) as well as Acute Physiology and Chronic Health Evaluation II (APACHE II) and Sequential Organ Failure Assessment (SOFA) score and several laboratory values are reportedly associated with mortality in patients with COVID-19 [4,12–14]disease diagnosis is essential for optimal management and timely isolation of infected cases in order to prevent further spread. The aim of this study was to systematically review the assessment of risk and model the predictors of mortality in COVID-19 patients. Methods: A systematic search was conducted of PubMed, Scopus, Embase, Google Scholar, and Web of Science databases. Variables associated with hospital mortality using bivariate analysis were included as potential independent predictors associated with mortality at the $p < 0.05$ levels. Results: We included 114 studies accounting for 310,494 patients from various parts of the world. For the purpose of this analysis, we set a cutoff point of 10% for the mortality percentages. High mortality rates were defined as higher than 10% of confirmed positive cases and were given a score of two, while low mortality (<10%.

Currently, no effective treatment has been discovered for managing the COVID-19 epidemic, which has affected the world to a substantial extent [15]. Determining the factors that affect mortality remains an important concern in terms of decreasing mortality due to the disease. In the current study that was planned with considering this notion, we aimed to perform a comparative assessment of critical patients with COVID-19 who were followed up in ICUs in our region since the beginning of the pandemic in terms of demographic, clinical, and laboratory characteristics and to determine the factors that affect mortality in this patient group.

Materials and Methods

Study Design, Population, and Data

Critical patients hospitalized due to COVID-19 in ICU of the University of Health Sciences Turkey, Diyarbakır Gazi Yaşargil Training and Research of Hospital between March 22 and September 1, 2020, were included in this study. The study was approved by the Ethics Committee of University of Health Sciences Turkey, Diyarbakır Gazi Yaşargil Training and Research of Hospital (No: 550, 11.09.2020). The trial was registered with clinicaltrials.gov (NCT04659876). This retrospective cohort study was conducted in accordance with the 2008 Declaration of Helsinki criteria.

Critical patients diagnosed with COVID-19 on the dates specified, followed up in ICU, aged >18 years, in serious need of oxygen support according to WHO [2] and the temporary guidelines of T.C. Science Board of the Ministry of Health [presence of fever, muscle/joint pain, cough, and sore throat; tachypnea (30 breaths/min) or dyspnea; use of extra respiratory muscles; SpO_2 level below of ≤90% in room air; bilateral diffuse pneumonia symptom detected on chest radiography or computerized tomography (CT); and PaO_2/FiO_2 ratio of <300], and developed or had complications including severe pneumonia, ARDS, sepsis/septic shock, and acute renal failure were included in the study. Patients with COVID-19 aged <18 years with mild-to-moderate symptoms, no respiratory distress, and no signs of diffuse pneumonia on chest X-ray or CT as well as ICU patients

excepted from COVID-19 diagnosis were excluded from the study. In addition, patients whose complete data could not be accessed from the hospital system or the patient file records were excluded. When the patients were admitted to ICU for the first time, their clinical conditions were evaluated with APACHE II and SOFA scores, and the degree of renal failure was evaluated using the Kidney Disease: Improving Global Outcomes (KDIGO) classification [17].

Age; sex; comorbidity; ABO and Rh blood groups; APACHE II and SOFA scores and KDIGO stage during admission to ICU; hemogram parameters [white blood cell (WBC), neutrophil, lymphocyte, neutrophil/lymphocyte (N/L) ratio, hemoglobin, hematocrit, and platelet count]; blood gas values [pH, partial oxygen pressure (PO_2), partial carbon dioxide pressure (PCO_2), bicarbonate (HCO_3), and lactate]; coagulation parameters [prothrombin time (PTZ) and D-dimer]; blood biochemistry results [creatine kinase (CK), lactate dehydrogenase (LDH), C-reactive protein (CRP), urea, creatinine, alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin, direct bilirubin, and indirect bilirubin]; and procalcitonin (PCT) and ferritin levels of the patients were recorded. Moreover, the length of stay in ICU and whether the patient died or survived were recorded. Patient data were rechecked for erroneous information before the last data entry and entered into a computerized database.

Patients were divided into two groups—those who survived (Survivors) and those who died (Non-survivors) during ICU follow-up. Both groups were compared in terms of clinical characteristics; APACHE II and SOFA scores and KDIGO stage; and laboratory values at the first admission to ICU. We attempted to determine the factors that affect mortality in critically ill patients hospitalized in ICU with COVID-19 diagnosis.

Statistical Analysis

SPSS 16.0 software for Windows (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Continuous data were expressed as means (SD or minimum–maximum), and categorical data were expressed as frequencies with percentages. Comparison of categorical data in the groups was performed using chi-square and Fisher's exact test, and the results were presented as n%. Kolmogorov–Smirnov test was used to determine whether the numerical data fit the normality distribution. Data conforming to the normality distribution were evaluated using Student t-test, and Mann–Whitney U and Kruskal–Wallis tests were employed to compare data that did not fit the normality distribution. Binary logistic regression was performed for the risk factors that were found to be significant in the univariate analysis. Odds ratio (OR) with 95% confidence interval (CI) was used to report the association between mortality and exposure to the risk factors. In all comparisons, P value of <0.05 was considered significant.

Results

Overall, data of 474 patients were accessed in the study. According to the exclusion criteria, 29 patients were excluded, and the study was completed with 445 patients. The mean (SD) age of the patients was 68.5 (15.1) years; 232 (52.1%) patients were male and 213 (47.9%) were female. Of the patients included in the study, 338 (76%) had at least one comorbid disease. The most common comorbid diseases were hypertension (40.2%) and diabetes (28.5%). Further, 296 patients died during their follow-up period in ICU and mortality was 66.5%. The mean (SD) length of stay of patients in ICU was 11.2 (10.7) days. The demographic, clinical, and laboratory characteristics of patients are detailed in Table 1.

Univariate Analysis

Patients were divided into two groups—those who survived (Survivors = 149, 33.5%) and those who died (Non-survivors = 296, 66.5%) during ICU follow-up—and compared. In terms of demographic and clinical characteristics, the mean patient age of the Non-survivor group was higher (71.4 vs. 62.7 years; $P < 0.001$). Mortality was higher than survival in male patients (56.1% vs. 43.9%; $P = 0.019$). Patients with KDIGO Stage 1, 2, and 3 showed higher mortality than expected ($P < 0.001$). Further, patients who died were found to have higher APACHE II and SOFA scores ($P < 0.001$; $P < 0.001$) (Table 1).

On comparing both groups in terms of laboratory values at the first admission to ICU, the Non-survivors showed a significant higher N/L ratio, WBC, neutrophil, PTZ, D-dimer, lactate, LDH, CK, CRP, urea, creatinine, AST, direct bilirubin, procalcitonin, and ferritin values and lower lymphocyte, hemoglobin, hematocrit, platelet, pH, and HCO_3 values. Details and significance values of the comparison between both groups are shown in Table 1.

Table 1. Demographic, clinical, and laboratory characteristics of patients hospitalized in the intensive care unit due to COVID-19				
Characteristic	All patients (n = 445) Mean (min-max)	Survivors (n = 149) Mean (min-max)	Non-survivors (n = 296) Mean (min-max)	p value
Age (year)	68.5 (18-100)	62.7 (22-95)	71.4 (18-100)	**<0.001**
Sex				**0.019**
Female	213 (47.9%)	83 (55.7%)	130 (43.9%)	
Male	232 (52.1%)	66 (44.3)	166 (56.1%)	
Blood group				0.48
A	225 (50.6%)	74 (49.7%)	151 (51%)	
B	71 (16%)	21 (14.1%)	50 (16.9%)	
AB	33 (7.4%)	9 (6%)	24 (8.1%)	
0	116 (26.1%)	45 (30.2%)	71 (24%)	
Rh factor				0.87
Negative	61 (13.7%)	21 (12.7%)	42 (14.2%)	
Positive	384 (86.3%)	130 (87.3)	254 (85.8%)	
Comorbidities				
No	107 (24%)	42 (28.2%)	65 (22%)	0.14
Yes	338 (76%)	107 (71.8%)	231 (78%)	
Diabetes	127 (28.5%)	38 (25.5%)	89 (30.1%)	0.31
Hypertension	179 (40.2%)	64 (43%)	115 (38.3%)	0.53
COPD	45 (10.1)	19 (12.8%)	26 (8.8%)	0.19
CKD	34 (7.6%)	12 (8.1%)	22 (7.4%)	0.81
CVD	66 (14.8%)	19 (12.8%)	47 (15.9%)	0.38
KDIGO score				**<0.001**
0	189 (42.4%)	113 (75.8%)	76 (25.6%)	
1	83 (18.7%)	17 (11.4%)	66 (22.3%)	
2	79 (17.8%)	12 (8.1)	67 (22.6%)	
3	94 (21.1%)	7 (4.7)	87 (29.4%)	
APACHE II score	16.61 (2-49)	13.1 (2-33)	18.3 (2-49)	**<0.001**
SOFA score	4.34 (1-17)	3.3 (1-12)	4.8 (1-17)	**<0.001**
Laboratory				
White blood cells (× 103 / uL)	11.33 (1.13-57.4)	10.6 (2.95-42.7)	11.6 (1.13-57.4)	**0.032**
Neutrophil (× 103 / uL)	9.51 (0.66-37.5)	8.75 (1.3-37.5)	9.9 (0.66-34.4)	**0.004**
Lymphocyte (× 103 / uL)	0.98 (0.14-3.59)	1.1 (0.19-3.59)	0.93 (0.14-3.5)	**<0.001**
Neutrophil lymphocyte ratio	12.8 (0.12-87.14)	9.4 (0.33-60.04)	14.5 (0.12-87.14)	**<0.001**
Hemoglobin (g / dl)	12.8 (5.6-19.2)	13.06 (5.9-17)	12.6 (5.6-19.2)	**0.015**
Hematocrit (%)	40.61 (17.8-61.6)	41.2 (20.2-55.9)	40.2 (17.8-61.6)	**0.039**
Platelet (× 103 / uL)	242.5 (30-671)	253.4 (84-671)	237.03 (30-628)	**0.048**
Prothrombin time (s)	13.83 (9.7-34.6)	13.3 (9.9-22.5)	14.1 (9.7-54.9)	**0.011**
D-dimer (ng / ml)	2019.2 (8.4-44498)	954.5 (75-16948)	2564.4 (8.4-44498)	**<0.001**

Table 1. contiuned

pH	7.36 (6.82-7.55)	7.38 (6.91-7.54)	7.36 (6.82-7.55)	**0.01**
PO_2 (mmHg)	41.37 (13.5-206)	42.14 (17.9-162)	40.3 (13.5-198)	0.76
PCO_2 (mmHg)	38.61 (20-115)	39.1 (16.9-108)	38.2 (20-115)	0.12
HCO_3 (mmol / L)	21.78 (5.3-32.1)	23.02 (5.9-31.5)	21.16 (5.3-32.1)	**<0.001**
Lactate (mmol / L)	2.76 (0.6-26)	2.2 (0.6-8.2)	3.04 (0.7-26)	**<0.001**
Lactate dehydrogenase (U / L)	514.9 (99-4500)	406.7 (139-1079)	569.4 (99-4500)	**<0.001**
Creatine kinase (IU / L)	314.05 (0.32-14952)	204.4 (11-2949)	369.4 (0.32-14952)	**<0.001**
C-reactive protein (mg / L)	141.2 (2-350)	120.4 (2-350)	151.7 (2-350)	**<0.001**
Blood urea nitrogen (mg / dl)	64.1 (8-280)	47.6 (8-267)	72.5 (13-280)	**<0.001**
Creatinine (mg / dl)	1.55 (0.36-21.8)	1.28 (0.44-10.4)	1.68 (0.36-21.8)	**<0.001**
ALT (U / L)	42.6 (6-1254)	32.2 (6-442)	47.9 (6-1254)	0.13
AST (U / L)	67.9 (7-3444)	40.8 (9-518)	81.5 (7-3444)	**<0.001**
Total bilirubin (mg / dl)	0.73 (0.12-6.8)	0.68 (0.14-3.69)	0.75 (0.12-6.8)	0.20
Direct bilirubin (mg / dl)	0.38 (0.1-4.7)	0.34 (0.1-2.31)	0.4 (0.1-4.7)	**0.02**
Indirect bilirubin (mg / dl)	0.33 (0.01-2)	0.33 (0.03-1.86)	0.33 (0.01-2)	0.93
Procalcitonin (ng / ml)	3.19 (0.02-100)	1.39 (0.02-62.8)	4.13 (0.03-100)	**<0.001**
Ferritin (µg / L)	854.8 (5.86-2000)	673.8 (5.86-2000)	951.5 (16.6-2000)	**<0.001**
Length of stay in the intensive care unit (day)	11.2 (1-91)	13.02 (1-91)	10.3 (1-79)	**0.004**

COPD = Chronic obstructive pulmonary disease; CKD = Chronic kidney disease; CVD = Cardiovascular disease; KDIGO = Kidney Disease: Improving Global Outcomes score; APACHE II = Acute Physiology and Chronic Health Evaluation II score; SOFA = Sequential Organ Failure Assessment score; PO_2 = Partial oxygen pressure; PCO_2 = Partial carbon dioxide pressure; HCO_3 = Bicarbonate; ALT = Alanine aminotransferase; AST = Aspartate aminotransferase

Risk Factors for Mortality in ICU Patients with COVID-19

Results of the binary logistic regression are shown in Table 2. Advanced age (OR, 1.03; 95% CI, 1.008–1.055), KDIGO Stage 1 (OR, 5.23; 95% CI, 2.490–10.97), KDIGO Stage 2 (OR, 7.07; 95% CI, 2.9–17.24), KDIGO Stage 3 (OR, 33.98; 95% CI, 8.860–130.3), high SOFA score (OR, 1.194; 95% CI, 1.007–1.416), high N/L ratio (OR, 1.069; 95% CI, 1.006–1.137), high D-dimer levels (OR, 1.000; 95% CI, 1.0–1.001), low HCO_3 values (OR, 0.888; 95% CI, 0.802–0.983), high LDH levels (OR, 1.004; 95% CI, 1.002–1.006), and elevated creatinine levels (OR, 0.499; 95% CI, 0.368–0.676) were identified as independent risk factors for mortality in critical COVID-19 patients hospitalized in ICU.

Discussion

In the present study that evaluated the factors affecting mortality in critical patients with COVID-19 followed up in ICU, the mortality was determined to be 66.5%. Moreover, advanced age; high KDIGO stage and SOFA scores at the first admission to ICU; N/L ratio; D-dimer, LDH, and creatinine levels; and low HCO3 value were determined as independent risk factors affecting mortality in this critical patient group.

Most studies conducted on patients with COVID-19 have emphasized that advanced age is an independent risk factor for mortality [6,7,9,11,18–20]. With increasing age, compared with young individuals, stronger host innate responses to viral infections, decreased type 1 interferon expression, age-related defects in T and B cell functions, and excessive type 2 cytokine production result in deficient response to viral infections and prolonged proinflammatory responses, which are considered as the causes of increased mortality risk in older aged patients with COVID-19 [3]. In the present study, mean patient age of the Non-survivors was 71.4 (18–100) years, and similar to previous studies, advanced age was determined as an independent risk factor for COVID-19.

Table 2. Risk factors for mortality in critical patients with COVID-19 in the intensive care unit				
Characteristic	**Mean (SD)**	**Odds ratio**	**95% CI OR**	**p value**
Age (year)	68.5 (15.1)	1.03	1.008-1.055	**0.009**
Male (%)	232 (52.1)	1.13	0.570-2.230	0.7
KDIGO score (%)				
1	83 (18.7%)	5.23	2.490-10.97	**<0.001**
2	79 (17.8%)	7.07	2.900-17.24	**<0.001**
3	94 (21.1%)	33.98	8.860-130.3	**<0.001**
APACHE II score	16.6 (7.23)	1.023	0.960-1.090	0.49
SOFA score	4.34 (2.59)	1.194	1.007-1.416	0.041
Laboratory				
White blood cells (× 103 / uL)	11.33 (6.42)	0.995	0.918-1.079	0.91
Neutrophil (× 103 / uL)	9.51 (5.19)	0.950	0.831-1.087	0.45
Lymphocyte (× 103 / uL)	0.98 (0.57)	1.284	0.593-2.780	0.52
Neutrophil lymphocyte ratio	12.8 (11.36)	1.069	1.006-1.137	**0.031**
Hemoglobin (g / dl)	12.8 (2.05)	0.694	0.373-1.292	0.25
Hematocrit (%)	40.61 (6.12)	1.062	0.867-1.300	0.56
Platelet (× 103 / uL)	242.5 (100.3)	0.998	0.995-1.001	0.27
Prothrombin time (s)	13.83 (2.76)	1.052	0.925-1.198	0.44
D-dimer (ng / ml)	2019.2 (4887.1)	1.000	1.000-1.001	**0.007**
pH	7.36 (0.1)	5.381	0.052-554.0	0.47
HCO_3 (mmol / L)	21.78 (4.34)	0.888	0.802-0.983	0.02
Lactate (mmol / L)	2.76 (2.35)	1.010	0.813-1.254	0.92
Lactate dehydrogenase (U / L)	514.9 (413.07)	1.004	1.002-1.006	**<0.001**
Creatine kinase (IU / L)	314.05 (841.9)	1.000	1.000-1.001	0.17
C-reactive protein (mg / L)	141.2 (89.01)	1.003	0.999-1.006	0.10
Blood urea nitrogen (mg / dl)	64.1 (48.2)	1.000	0.991-1.010	0.91
Creatinine (mg / dl)	1.55 (1.76)	0.499	0.368-0.676	**<0.001**
AST (U / L)	67.9 (214.3)	1.000	0.993-1.007	0.95
Direct bilirubin (mg / dl)	0.38 (0.36)	0.619	0.288-1.332	0.22
Procalcitonin (ng / ml)	3.19 (10.08)	1.026	0.978-1.077	0.29
Ferritin (µg / L)	854.8 (635.2)	1.000	1.000-1.001	0.79

KDIGO = Kidney Disease: Improving Global Outcomes score; APACHE II = Acute Physiology and Chronic Health Evaluation II score; SOFA = Sequential Organ Failure Assessment score; HCO_3 = Bicarbonate; AST = Aspartate aminotransferase

Numerous studies have reported that male patients with COVID-19 exhibit a more severe disease, and the mortality risk in the male sex is higher [9,14,20,21]. The high mortality in males has been attributed to higher chronic comorbidities, such as cardiovascular disease, hypertension, and lung disease, and smoking rate [20]. In the present study, the patient group with a mortal course of the disease exhibited a predominance of male population, in accordance with the literature. However, as a result of the logistic regression analysis, it was determined that male gender is not an independent risk factor for critical COVID-19 patients hospitalized in the ICU. This unexpected result contradicts the studies in the literature. This result may be due to the single-center nature of our study and the limited number of patients.

On literature review, another risk factor that can affect the clinical course of the disease in patients with COVID-19 is the presence of comorbidities. In the meta-analysis by Martins-Filho et al., the authors emphasized that the presence of comorbidities in patients with COVID-19 resulted in a 1.6

times increase in the in-hospital mortality [6]. In a study conducted by Schmidt et al. wherein they examined 4244 critical patients with COVID-19, the presence of a history of diabetes mellitus led to a 1.51 times increase in the 90-day mortality [7]. By contrast, in the present study, the presence of comorbidities did not affect mortality in critical patients with COVID-19 hospitalized in ICU. We believe that this result can be attributed to the patient population of our study. The mean patient age in this study was considerably high [68.5 (15.1) years], and most patients (76%) reported at least one comorbid disease. We believe that these factors led to the result observed.

APACHE II and SOFA are scoring systems that are frequently used during the follow-up examination of critically ill patients for assessing disease severity and mortality [22]. Some studies have stated that these scoring systems can be used to determine the disease course in patients with COVID-19 and that high APACHE II and SOFA scores are associated with poor prognosis and mortality [4,22,23]. In the present study, it was observed that Non-survivor patients showed higher APACHE II and SOFA scores during their first admission to ICU. However, only a high SOFA score was determined as a risk factor for mortality in critical patients with COVID-19 in ICU.

One of the important organs that is affected besides the respiratory system in patients with COVID-19 is the kidneys. Although renal manifestations specific to COVID-19 have not clearly been defined, acute renal damage may reportedly develop in 0.5%–29% of the patients with COVID-19 and the incidence of acute renal damage is higher in patients experiencing severe disease or death [11,23–25]. In the present study, patients with a mortal course showed higher KDIGO stages on the first day of admission to ICU. In addition, it was found that with the increase in the KDIGO stage of the patient, there was an increase in the mortality risk. These results indicate that a high KDIGO stage at the time of the first admission to ICU is an independent risk factor for mortality. Urgent application of appropriate treatments to patients with high KDIGO stage at admission will contribute to a substantial reduction in mortality risk.

Characteristic laboratory findings observed in critical patients with COVID-19 are reportedly low lymphocyte, albumin, and PaO2 levels and high WBC, neutrophil, LDH, CRP, urea, creatinine, PTZ, activated partial thromboplastin time (aPTT), ferritin, and PCT levels [12,26]. Linli et al. evaluated 192 critical patients with COVID-19 and stated that abnormal CRP, WBC, AST, and pH values were associated with high mortality and that CRP values should be closely monitored in these patients [27]. Cummings et al., evaluating 257 critically ill patients, stated that high D-dimer levels were an independent risk factor for in-hospital mortality [11]. In the present study, high WBC, neutrophil, N/L ratio, PTZ, D-dimer, lactate, LDH, CK, CRP, urea, creatinine, AST, direct bilirubin, PCT, and ferritin levels as well as low lymphocyte, hemoglobin, hematocrit, platelet, pH, and HCO3 levels were detected. High N/L ratio, D-dimer, LDH, and creatinine values and low HCO3 value were identified as independent risk factors for mortality in critical patients with COVID-19. Careful monitoring of these values in critical patients with COVID-19 hospitalized in ICU may act as a caution sign for mortality.

Conclusion

As a result of present study, it has been determined that the demographic characteristics of critical COVID-19 patients hospitalized in the ICU, as well as the clinical situation at the first admission to the ICU and some laboratory values are independent risk factors for mortality. In particular, the relationship between high KDIGO stages and mortality at the first admission to the ICU was noteworthy. We believe that monitoring these factors during the follow-up period of critical patients with COVID-19 in ICU can help predict the clinical course of the disease and reduce mortality.

Limitations

The most important limitation of this study was that it is retrospective and single centered. Conducting studies on critical patients with COVID-19 hospitalized in ICU with multicenter and large patient series across the country or the world will provide more precise information. Another study limitation is that the parameters such as obesity and regional and ethnic differences mentioned in some studies were not included. There was no information about these features in the data we obtained.

Ethics

Ethical Commite Approval: The study was approved by the Ethics Committee of University of Health Sciences Turkey, Diyarbakır Gazi Yaşargil Training and Research of Hospital (No: 550, 11.09.2020).

Informed Consent: This retrospective cohort study was conducted in accordance with the 2008 Declaration of Helsinki criteria.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: O.U., C.K.K., M.E.E., M.S.G., M.A., Z.K., Ö.C., Concept: O.U., C.K.K., M.E.E., M.S.G., Z.K., Ö.C., Design: O.U., C.K.K., M.E.E., M.A., Data Collection and Process: O.U., C.K.K., M.E.E., M.S.G., M.A., Z.K., Ö.C., Analysis or Interpretation: O.U., C.K.K., M.E.E., M.A., Ö.C., Literature Search: O.U., C.K.K., M.E.E., M.S.G., M.A., Z.K., Ö.C., Writing: O.U., C.K.K.

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