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ORIGINAL RESEARCH / *ÖZGÜN ARAŞTIRMA*

Factors Affecting Mortality in COVID-19

COVID-19'da Mortaliteyi Etkileyen Faktörler

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ABSTRACT

Objective: Determining the factors affecting mortality may be pivotal in terms of improving survival in the coronavirus disease-2019 (COVID-19). The aim of this study was to determine the demographic, clinical and laboratory characteristics of COVID-19 patients and the factors affecting intensive care unit (ICU) mortality.

Materials and Methods: It was designed as a retrospective cohort study in which patients with a diagnosis of COVID-19 hospitalized in the ICU. The clinical and laboratory parameters were compared between cohorts with mortality and those with survival cohorts. Univariate and multivariate logistic regression analyses were performed for the effect profiles of the parameters on mortality.

Results: The mortality of 58.6% was similar for the three pandemic waves or selected time intervals (p=0.245). Presence of comorbid disease, age, COVID-19 related complications, admission, acute physiology and chronic health evaluation II (APACHE II) and sequential organ failure assessment (SOFA) scores were significantly higher in the mortality cohort (p<0.001). The factors influencing mortality according to the multivariate logistic regression model were hypertension, malignancy (solid and hematologic), neurological illness, age, APACHE-II and SOFA scores, and neutrophil to lymphocyte ratio.

Conclusion: The patients with these risk factors should be monitored with greater caution in terms of the timing and duration of ICU care.

Keywords: COVID-19, mortality, intensive care unit

ÖZ

Amaç: Mortaliteyi etkileyen faktörlerin belirlenmesi, koronavirüs hastalığı-2019'da (COVID-19) sağkalımın iyileştirilmesi açısından çok önemlidir. Bu çalışmanın amacı, COVID-19 hastalarının demografik, klinik ve laboratuvar özelliklerini ve yoğun bakım ünitesi (YBÜ) mortalitesini etkileyen faktörleri belirlemektir.

Gereç ve Yöntem: Bu çalışma YBÜ'deki COVID-19 tanılı hastaların dahil edildiği retrospektif bir kohort çalışması olarak tasarlandı. Klinik ve laboratuvar parametreleri mortalite ve sağkalım kohortları arasında karşılaştırıldı. Parametrelerin mortalite üzerindeki etki profilleri için tek değişkenli ve çok değişkenli lojistik regresyon analizleri yapıldı.

Bulgular: Mortalite %58,6 olup üç pandemi dalgası veya seçilen zaman aralıkları için benzerdi (p=0,245). Komorbid hastalık varlığı, yaş, COVID-19 ile ilişkili komplikasyonlar, başvurudaki akut fizyoloji ve kronik sağlık değerlendirmesi II (APACHE II) ve sıralı organ yetmezliği değerlendirmesi (SOFA) skorları mortalite kohortunda anlamlı olarak daha yüksekti (p<0,001). Çok değişkenli lojistik regresyon modeline göre mortaliteyi etkileyen faktörler hipertansiyon, malignite (solid ve hematolojik), nörolojik hastalık, yaş, APACHE-II ve SOFA skorları ve nötrofil/lenfosit oranıdır.

Sonuç: Bu risk faktörlerine sahip hastalar, YBÜ bakımının zamanlaması ve süresi açısından daha dikkatli izlenmelidir.

Anahtar Kelimeler: COVID-19, mortalite, yoğun bakım ünitesi

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Introduction

The coronavirus disease-2019 (COVID-19), recognized by the reports informing pneumonia cases of unknown etiology at the end of 2019 in Wuhan, China, has spread worldwide, causing millions of deaths (1). Although clarification on the clinical manifestation and pathophysiology of the disease has grown over the past three years, it continues to be an important public health problem. In Türkiye, where the first case of COVID-19 was detected on March 11, 2020, more than 17 million cases of COVID-19 and 101,419 deaths were reported to the World Health Organization (WHO) until October 8, 2023 (2). The crisis of the pandemic dissolved as the disease transformed into a mild respiratory tract infection with substantially less short-term mortality. However, long-term complications and survival are still a matter of debate.

The cumulative rise in the number of critically ill patients during this pandemic increased the demand for intensive care units (ICUs). For this reason, ICU capacity and the number of staff were rapidly expanded, while the quality of the ICU care was diminished in many countries. Similarly, in various periods of the pandemic in Türkiye, the capacity of many ICUs had to be increased. The rates of admission to the ICU and mortality differed greatly among hospitals due to various factors, such as ICU bed capacity, the time between the occurrence of ICU admission criteria and ICU admission, patient characteristics, staff availability, and applied treatment protocols. Determining the factors that may be associated with mortality is important for guiding and improving the ICU follow-up of patients with COVID-19. Several reports investigating the clinical course, mortality, and morbidity related to COVID-19 published from many countries and hospitals revealed that genetic substructure, race, lifestyle, treatment opportunity in hospitals, and staff availability influenced the survival of the patients (3-5). There is limited information focusing on the characteristics and prognosis of Turkish patients with COVID-19 admitted to the ICU, as well as the impact of the disparity of sequential pandemic waves on patient prognosis. The aim of this study was to determine the demographic, clinical, and laboratory characteristics of COVID-19 patients and the factors affecting ICU mortality in Akdeniz University Medical Faculty Hospital, Antalya, Türkiye throughout the pandemic.

Materials and Methods

The current study was carried out in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Akdeniz University Faculty of Medicine, Antalya, Türkiye (approval no: KAEK-335, date:11.05.2022). In addition, this study is retrospectively registered in the ClinicalTrials.gov clinical trials registry (no. NCT06043115).

It was designed as a retrospective cohort study in which patients diagnosed with COVID-19 who were hospitalized in the ICU between 11 March 2020 and 31 March 2022 were included. At the beginning of the pandemic, 8 beds were reserved for COVID-19 patients in our hospital, and while the pandemic progressed, the bed capacity was increased to 30 beds. The data of the patients were obtained from the patient file database and the observation results noted in the patient ICU charts. Patient informed consent was waived due to the retrospective study design. Researchers analyzed only anonymized data.

Patients ≥18 years old with a confirmed diagnosis of the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection, by a positive real-time reverse-transcription polymerase chain reaction test (RT-PCR) performed via nasopharyngeal swab or endotracheal aspirate were included in the present study. Criteria for admission to the ICU included oxygen saturation (SpO_2) below 90% in room air, ratio of partial oxygen pressure to fraction of inspired oxygen (PaO_2/FiO_2) less than 300, respiratory rate of more than 30 breaths per minute or lung infiltrates more than 50% of lung image on tomographic examination, and viral pneumonia with life-threatening conditions such as hemodynamic insufficiency or septic shock. Patients who had a negative SARS-CoV-2 RT-PCR test and whose chest computed tomography findings or symptoms were not compatible with COVID-19 were not included in the study.

Demographic and clinical data derived and analyzed included age, sex, body mass index (BMI), smoking history, comorbidities, vaccination status, acute physiology and chronic health evaluation II (APACHE II) and sequential organ failure assessment (SOFA) scores at admission, blood gas analysis, method of oxygen delivery, ICU and hospital length of stay and COVID-19 related complications. Laboratory findings recorded were blood cell count, fibrinogen, D-dimer, C-reactive protein (CRP), ferritin, creatinine, procalcitonin, and microbial culture results. Additional adjunctive support, including extracorporeal membrane oxygenation (ECMO), prone positioning, renal replacement therapy (RRT) were noted by date. Information on patient-specific therapies, such as administration of antivirals, convalescent plasma and plasmapheresis was also obtained.

Patients were managed following the institutional protocol (Figure 1). Acute respiratory distress syndrome (ARDS) was diagnosed and classified according to The Berlin Definition (6). A lung-protective ventilation strategy was used for all

Figure 1: Institutional COVID-19 protocol

COVID-19: coronavirus disease-19, SpO_2: oxygen saturation, PaO_2: arterial partial oxygen pressure, FiO_2: fraction of inspired oxygen, COPD: chronic obstructive pulmonary disease, ARDS: acute respiratory distress syndrome, AKI: acute kidney injury, DIC: disseminated intravascular coagulation, SARS-CoV-2: severe acute respiratory syndrome coronavirus-2, RT-PCR: real-time reverse-transcription polymerase chain reaction test, CRP: C-reactive protein

patients. Prone positioning was a part of management in all patients if not contraindicated. Patients with a PaO_2/FiO_2 ratio of less than 150 mmHg and a FiO_2 ≥60%, despite positive end-expiratory pressure optimization, were placed in the prone position, (12-16 hours). Patients with severe COVID-19 (as defined by the current WHO COVID-19 clinical management guideline) (7) requiring supplemental oxygen (including high-flow nasal oxygen) or non-invasive ventilation were placed in the awake prone position in 4-hour periods, with a total prone time of 12-16 hours daily. Sepsis-3 criteria were used for the diagnosis of sepsis/septic shock (8). Acute kidney injury (AKI) was defined according to Kidney Disease: Improving Global Outcomes (KDIGO) criteria (9). Co-existing infection was defined as clinical signs of systemic infection with a positive culture of a pathogen other than SARS-CoV-2 obtained from blood or body fluid specimens. Therapeutic dosing anticoagulation (low-molecular weight heparin) was applied to all patients who did not have risk or clinical manifestation of bleeding disorders during the ICU follow-up period. Patients received methylprednisolone at a dose of 1-2 mg/kg/day intravenously for an average of 5-10 days, as described by the current WHO COVID-19 clinical management guidelines (7).

The primary objective of the study was to determine the factors affecting mortality in COVID-19 patients in our ICU. The secondary outcome was to determine whether the pandemic waves had distinct characteristics in terms of factors affecting mortality. Based on the number of COVID-19 cases reported nationally to WHO during the pandemic in Türkiye, the period when the weekly incidence risk exceeds 30 per 100,000 people is defined as a wave (2,10). According to this definition, we examined the pandemic in three consecutive waves (first wave: 11 March 2020 to 31 January 2021, second wave: 1 February 2021 to 30 June 2021, third wave: 1 July 2021 to 31 March 2022).

Statistical Analysis

Statistical analysis was performed using SPSS version 18 statistical software (SPSS Inc., Chicago, Illinois, USA). A value of $p<0.05$ was considered statistically significant. The distribution of the continuous variables was tested using the Kolmogorov-Smirnov test. Frequencies and percentages were calculated for categorical variables. Baseline characteristics were presented as mean ± standard deviation (SD) and median with interquartile range (IQR) for continuous variables and as numbers with percentages for categorical variables. Pearson chi-square test or Fisher exact test were used in the analysis of categorical variables for outcome comparisons between survivors and non-survivors, and the Mann-Whitney U test was used for continuous variables. We used multivariate and univariate logistic regression models to identify risk factors of mortality. Variables that were found to be significant ($p<0.05$) during the univariate analysis were included in the multivariate regression model. The results are expressed as odds ratios (ORs) with 95% confidence intervals (95% CIs). The receiver operating characteristic (ROC) curves were used to determine the distinctive performance of laboratory parameters in predicting mortality in patients. The analysis results, which include the area under the curve (AUC) and cut-off value, were presented along with the sensitivity, specificity, and 95% CIs. The optimal cut-off values of the parameters were calculated with the Youden index.

Results

During the study period, a total of 985 patients with suspected COVID-19 were admitted to the ICU; the data of 619 patients who met the inclusion criteria were analyzed (Figure 2). All patients were discharged or died prior to data collection.

Among the study patients, 256 (41.4%) survived (survival cohort), and 363 (58.6%) died (mortality cohort). Clinical and demographic characteristics of patients are presented in Table 1. The mean age of the patients was 64.2±16.2 years and 69.7% were male. The majority of the study population was male, but the sex distribution was similar between the two mentioned cohorts, while the difference in terms of age

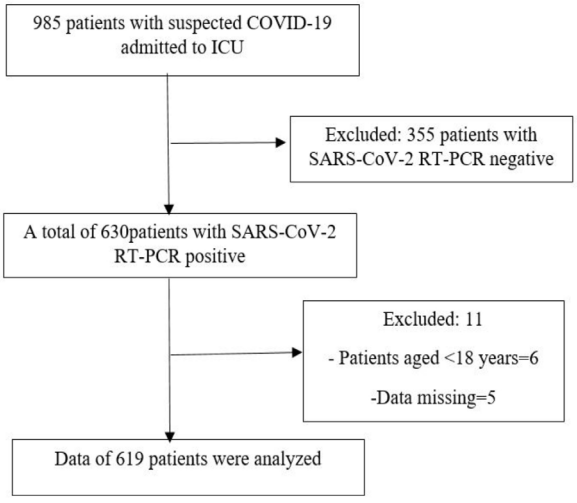

Figure 2: Study flow diagram

COVID-19: coronavirus disease-19, SARS-CoV-2: severe acute respiratory syndrome coronavirus-2, RT-PCR: real-time reverse-transcription polymerase chain reaction test

Table 1. Comparison of the quantitative and qualitative parameters regarding prognosis status (mortality)

Parameters	Overall	Mortality	Survival	p-value	Parameters	Overall	Mortality	Survival	p-value	Parameters	Overall	Mortality	Survival	p-value
Distribution*														
Age, (years) mean ± SD[a]	64.2±16.2	68.3±14.8	58.4±16.4	**<0.001**	**CAD[c]**	146	86 (23.7)	60 (23.4)	0.942	**Malignancy -solid[c]**	75	52 (14.3)	23 (9)	**0.045**
Apache-II score, IQR[b]	12 (0-45)	15 (2-45)	9 (0-38)	**<0.001**	**Obesity Groups(BMI)[c]**					**Malignancy-hematologic[c]**	53	38 (10.5)	15 (5.9)	**0.044**
SOFA score, IQR[b]	4 (0-17)	5 (0-17)	4 (0-13)	**<0.001**	<30	421	236 (65)	185 (72.3)		**IMV duration (day), IQR[b]**	2 (0-103)	6 (0-103)	0 (0-61)	**<0.001**
BMI(kg/m²), mean ± SD[a]	28.5±5.9	28.8±5.9	28.0±5.8	0.125	30-35	120	80 (22)	40 (15.6)	0.187	**Tracheotomy[d]**	8	3 (0.8)	5 (2.0)	0.285
Age groups[c]					35-40	51	32 (8.8)	19 (7.4)		**LOSH-ICU (day), IQR**	8 (1-225)	9 (1-225)	6 (1-64)	**<0.001**
18-55 years	155	62 (17.1)	93 (36.3)		>40	27	15 (4.1)	12 (4.7)		**LOSH (Total) (day), IQR**	16 (1-225)	14 (1-225)	18 (1-182)	**<0.001**
56-63 years	112	54 (14.9)	58 (22.7)	**<0.001**	**CKD[c]**	73	45 (12.4)	28 (10.9)	0.579	**ECMO support[c]**	13	12 (3.3)	1 (0.4)	**0.013**
64-68 years	79	49 (13.5)	30 (11.7)		**Transplantation[c]**	44	30 (8.3)	14 (5.5)	0.183	**Duration of ECMO (day)**	0 (0-64)	0 (0-64)	0 (0-19)	**0.013**
≥69 years	273	198 (54.5)	75 (29.3)		**Neurological illness[c]**	112	77 (21.2)	35 (31.3)	0.016	**Prone possition [c]**	291	126 (34.7)	93 (36.3)	0.679
Gender[c]					**Chronic lung disease[c]**	118	79 (21.8)	39 (15.2)	0.042	**Clinical complications**				
Female	187	110 (30.3)	77 (30.1)	0.952	**Thyroid disease**	44	25 (6.9)	19 (7.4)	0.799	Pneumothorax[c]	47	43 (11.8)	4(1.6)	**<0.001**
Male	432	253 (69.7)	179 (69.9)		**Pregnancy[d]**	10	3 (0.8)	7 (2.7)	0.102	Hemothorax[d]	6	3 (0.8)	3 (1.2)	0.695
Cigarette use[c]					**Reason of ICU admission[c]**					Pulmonary edema[d]	8	3 (0.8)	5 (2.0)	0.285
None	266	158 (43.7)	108 (42.2)	0.104	Respiratory Failure (RF)	420	240 (66.1)	180 (70.3)	**<0.001**	AKI[c]	281	221 (60.9)	60 (23.4)	**<0.001**
Smoker	107	53 (14.7)	54 (21.1)		Sepsis	17	10 (2.8)	7 (2.7)		Requirement of RRT[c]	60	50 (13.8)	10 (3.9)	**<0.001**
Exsmoker	244	150 (41.6)	94 (36.7)		Septic shock	15	8 (2.2)	7 (2.7)		DIC[c]	13	12 (3.3)	1 (0.4)	**0.013**
Vaccination status[c]					Myocardial infarction	12	7 (1.9)	5 (2)		Sepsis[c]	372	304 (83.7)	68 (26.6)	**<0.001**
None	473	299 (82.4)	174 (68)	**<0.001**	RF+septic shock	74	63 (17.4)	11 (4.3)		Septic shock[c]	346	296 (81.5)	50 (19.5)	**<0.001**
Sinovac	81	34 (9.4)	47 (18.4)		Other	81	35 (9.6)	46 (18)		Myocardial infarction[d]	10	7 (1.9)	3 (1.2)	0.535
Biontech	29	12 (3.3)	17 (6.6)		**Oxygen management[d]**					Cardiac arrhythmiad	162	126 (34.7)	36 (14.1)	**<0.001**
Sinovac+Biontech	36	18 (5)	18 (7)		Low flow †	472	252 (69.4)	220 (85.9)	**<0.001**	Thrombosis (DVT, emb.)[c]	24	20 (5.5)	4 (1.6)	**0.012**
Comorbidity[c]	552	339 (93.4)	213 (83.2)	**<0.001**	High flow	5	5 (1.4)	0 (0)		Bleeding[c]	63	49 (13.5)	14 (5.5)	**0.001**
Comorbidity count[c]					NIV	4	4 (1.1)	0 (0)		**PaO_2/ FiO_2(mmHg)** IQR[b]	100 (21-900)	90 (21-550)	125 (40-900)	**<0.001**
None	67	24 (6.6)	43 (16.8)	**<0.001**	IMV	138	102 (28.1)	36 (14.1)		**ARDS[c]**				
1	143	76 (20.9)	67 (26.2)		**IMV duration[c]**					None	52	18 (5.0)	34 (13.4)	**<0.001**
2	158	103 (28.4)	55 (21.5)		0-6 days	431	196 (54.0)	235 (91.8)	**<0.001**	Mild	66	28 (7.8)	38 (15.0)	
3 and over	251	160 (44.1)	91 (35.5)		7-9 days	64	59 (16.3)	5 (2.0)		Moderate	162	82 (22.7)	80 (31.5)	
HT[c]	281	182 (50.1)	99 (38.7)	0.005	10-17 days	71	64 (17.6)	7 (2.7)		Severe	335	233 (64.5)	102 (40.2)	
DM[c]	201	116 (32)	85 (33.2)	0.74	≥18 days	53	44 (12.1)	9 (3.5)						

*:Parameters showing a normal distribution pattern are expressed as mean, standard deviation (SD), and non-normally distributed parameters are expressed as median, as minimum, and as maximum (IQR). Categorical variables were expressed as frequency (N) and percentage (%). The general distribution of the parameter is summarized under the overall title.

†:Includes non-rebreather mask, venturi mask and nasal prongs, [a]:Indepentent-t test, [b]:Mann-Whitney U test, [c]:Pearson's chi-squared test, [d]:Fisher's exact test

HT: hypertension, DM: diabetes mellitus, CAD: coronary artery disease,CKD: chronic kidney disease, DVT: deep venous trombosis, BMI: body mass index, ICU: intensive care unit, IMV: invasive mechanic ventilation, NIV: non-invasive mechanic ventilation, LOSH: lenth of stay in hospital, ECMO: extracorporeal membrane oxygenation, AKI: acute kidney injury, RRT: renal replacement therapy, DIC: disseminated intravascular coagulation, APACHE-II: acute physiology and chronic health evaluation II, SOFA:sequential organ failure assessment, IQR: interquartile range, SD: standart deviation

was significant (p<0.001). The most common comorbidities were hypertension (45.4%), diabetes mellitus (32.4%) and obesity (BMI >30) (32%). One or more comorbidities were detected in 552 (89%) patients. In addition, the presence of comorbid disease was significantly higher in the mortality cohort (p<0.001). Hypertension, chronic lung disease, neurological illness, solid and hematologic organ malignancy were more frequent in patients who died (p=0.005, p=0.042, p=0.016, p=0.045 and p=0.044, respectively). A hundred and ten (17.8%) patients were vaccinated with either Sinovac (13.1%) or BioNTech (4.7%) and with both vaccines (5.8%). The proportion of unvaccinated patients was significantly lower in the survival group (p<0.001). The median APACHE II and SOFA scores were 12 (0-45) and 4 (0-17), respectively, being higher in the mortality cohort (p<0.001). Respiratory failure was the most common cause of ICU admission. 472 patients (76.3%) were on low flow oxygen, which includes non-rebreather mask, venturi mask, and nasal prongs; 138 (22.2%) were on invasive mechanical ventilation (IMV), and 9 (1.4%) were on non-invasive ventilation or high flow nasal oxygen. During the follow-up, 323 out of 472 patients who were receiving low-flow oxygen (<5L/min) required high-flow oxygen or non-invasive ventilation. Likewise, 264 out of 481 patients who did not need IMV on admission needed IMV during ICU follow-up. The median duration of IMV was 2 (0-103) days, which was longer in the mortality cohort (p<0.001). Successful weaning from IMV was achieved in only 7% of patients (29 of 402 patients). The median length of ICU and hospital stay was 8 (1-225) and 16 (1-225) days, respectively. Patients who died had longer ICU stay (9 (1-225) vs. 6 (1-64) days, p<0.001). A large number of patients had moderate to severe ARDS (80.2%) at ICU admission, and most of these patients took part in the mortality cohort (p<0.001). The prone position was applied to 47% of the patients with severe or moderate ARDS, a substantial proportion. Prone position could not be applied to 328 patients for various reasons, such as haemodynamic instability, anatomical difficulty, and increased intracranial pressure. Patients received veno-venous ECMO according to the "ECMO to Rescue Lung Injury in Severe ARDS (EOLIA) criteria" (11). ECMO support was applied in 13 patients, with survival achieved in one. The clinical complications such as sepsis/septic shock (p<0.001), AKI (p<0.001), pneumothorax (p<0.001), disseminated intravascular coagulation (p=0.013), cardiac arrhythmia (p<0.001), thrombosis (p=0.012), and bleeding (p=0.001) were observed more in the mortality cohort.

The neutrophil-to-lymphocyte (N/L), monocyte-to-lymphocyte (M/L), and neutrophil-to-platelet (N/Plt) ratios; eosinophil count; serum creatinine; procalcitonin; CRP; and ferritin values were significantly higher, whereas hemoglobin, platelet, and lymphocyte count values were significantly lower in the mortality cohort. Table 2 depicts the comparison of all laboratory parameters between cohorts. ROC analysis was performed to determine the predictive values and effect levels of parameters regarding mortality, and the results are presented in Table 3 and Figure 3. Univariate and multivariate logistic regression analysis were performed for the effect profiles of the parameters on mortality. Age, SOFA and APACHE II scores, duration of IMV, comorbidity status, hypertension, chronic lung disease, malignancy (solid and hematologic), neurological illness, hemoglobin, lymphocyte count, CRP, N/L, M/L, and N/plt ratio were associated with mortality in the univariate regression analysis. The multivariate model included the parameters that were found to be related to mortality in the univariate analysis. Another analysis was performed to check whether all parameters met the Box-Tidwell assumption. Duration of IMV and lymphocyte count parameters were excluded from the multivariate logistic regression model as they did not meet the assumptions. The factors influencing mortality according to the multivariate-logistic-regression model were hypertension, malignancy (solid and hematologic), neurological illness, age, APACHE-II and SOFA scores, and N/L ratio (Tables 4,5). The cut-off values affecting mortality were >65.5 years for age (sensitivity 64.5% and specificity 63.7%), >11.5 for APACHE-II score (sensitivity 68.4% and specificity 66.4%), >4.5 for SOFA score (sensitivity 61.8% and specificity 71.5%), and >18.45 for N/L ratio (sensitivity 51.5% and specificity 71.9%) (Table 3).

The percentage of COVID-19 patients per pandemic waves was 30% (n=186) in the 1st wave, 18.7% (n=116) in the 2nd wave, and 51.2% (n=317) in the 3rd wave in our study. Mortality was 62.6% in the 1st wave, 58.6% in the 2nd wave, and 56.1% in the 3rd wave period. Mortality was similar for the three pandemic waves (p=0.245). In all pandemic wave periods, mortality was higher over the age of 69. Obesity was found to be a risk factor for mortality in the patients admitted during the 3rd wave period. The number of comorbidities in the 1st and 3rd wave period, the rate of IMV in the 2nd wave period, and the number of unvaccinated patients in the 3rd wave period, were higher in the mortality cohort. Moreover, the rate of severe ARDS was found to be higher in the mortality cohort in all pandemic wave periods (Table 6).

Table 2. Comparison of quantitative and categorical variables according to prognosis (mortality) status				
	Prognosis			**p-value**
	Overall	**Mortality (n=363, %58.6)**	**Survival (n=256, %41.6)**	
Parameters	**Distribution**			
Mean ±SD[1]				
Hemoglobin (g/dL)	11.56±2.27	11.37±2.35	11.84±2.14	**0.011**
Median (IQR)[2]				
CRP (mg/L)	92 (0.89-433)	98.0 (1.74-433)	78.0 (0.89-397)	**0.002**
D-dimer (mg/L)	1.89 (0.13-155.0)	2.19 (0.13-155)	1.69 (0.17-42.4)	0.078
Ferritin (μg/L)	692.5 (3.84-100000)	771.0 (3.84-100000)	572.0 (14.68-85867)	**0.001**
Fibrinogen (mg/dL)	520 (33-4758)	520.0 (33-4319)	506.0 (136-4758)	0.384
Leukocyte count (10^3/μL)	10.46 (0.97-228.6)	10.8 (10.0-228.6)	10.2 (0.97-133.3)	0.728
Platelet count (10^3/μL)	224.5 (16-980)	208.0 (16.0-980.0)	243.5 (24.0-688.0)	**<0.001**
Neutrophil count (10^3/μL)	89.7 (2.6-98)	90.8 (2.6-98)	87.85 (18.2-97.5)	**<0.001**
Lymphocyte count (10^3/μL)	5.8 (0-95.3)	4.8 (0-95.3)	7.35 (1.0-83.0)	**<0.001**
Monocyte count (10^3/μL)	3.7 (0-67)	3.5 (0-67.0)	4.25 (0-26.0)	**<0.001**
Eosinophil count (10^3/μL)	0 (0-32.4)	0 (0-32.4)	0 (0-8.0)	**<0.001**
Neutrophil/Lymphocyte ratio	15.5 (0-271)	18.7 (0-271)	12.05 (0.79-106)	**<0.001**
Monocyte/Lymphocyte ratio	0.63 (0-18.2)	0.73 (0-18.2)	0.53 (0-5.03)	**<0.001**
Neutrophil /Platelet ratio	0.0004 (0.00003-0.0048)	0.0006±0.0006	0.0004±0.0003	**<0.001**
Creatinine (mg/dL)	0.9 (0.17-13.5)	1.04 (0.17-10.09)	0.8 (0.19-13.5)	**<0.001**
Procalcitonin (μg/L)	0.33 (0.01-100)	0.46 (0.01-100.0)	0.19 (0.01-100.0)	**<0.001**
n (%)				
Positive culture result (general)	340	264 (77.6)	76 (22.4)	**<0.001[3]**
Blood culture				
None or <2 positive result	590	342 (94.2)	248 (96.9)	0.177[3]
≥2 positive result(polymicrobial)	29	21 (5.8)	8 (3.1)	
Urine culture				
None or <2 positive result	584	336 (92.6)	248 (96.9)	**0.035[3]**
≥2 positive result(polymicrobial)	35	27 (7.4)	8 (3.1)	
Trachea/sputum culture				
None or <2 positive result	489	253 (69.7)	236 (92.2)	**<0.0013**
≥2 positive result(polymicrobial)	130	110 (30.3)	20 (7.8)	

1: Independent t-test, [2]: Mann-Whitney U test, [3]: Pearson chi-squared test or Fisher's exact test, *: Parameters showing a normal distribution pattern are expressed as mean ± SD, and non-normally distributed parameters are expressed as median, minimum and maximum (IQR). Categorical variables were expressed as frequency (N) and percentage (%). The general distrubition of the parameter is summerised under the overall title.
CRP: C-reactive protein, SD: standard deviation

Table 3. Predictive values and affect levels of parameters regarding mortality

Variable	AUC (95% CI)	p-value	Cut-off	Sensitivity (%)	Specificity (%)
Age (years)	0.679 (0.637-0.722)	**<0.001**	>65.5	64.5	63.7
BMI (kg/m²)	0.546 (0.500-0.592)	**0.049**	>28.35	50.4	60.2
Apache-II score	0.722 (0.682-0.763)	**<0.001**	>11.5	68.4	66.4
SOFA score	0.722 (0.681-0.762)	**<0.001**	>4.5	61.8	71.5
CRP (mg/L)	0.572 (0.526-0.619)	**0.002**	>51.5	73.3	39.2
Lymphocyte count ($10^3/\mu L$)	0.649 (0.606-0.692)	**<0.001**	<496.84	46.9	76.6
Procalcitonin (μg/L)	0.613 (0.562-0.664)	**<0.001**	>0.20	70.1	52.2
D-dimer (mg/L)	0.548 (0.495-0.601)	0.078	>2.49	47.7	62.1
Ferritin (μg/L)	0.595 (0.543-0.648)	**0.001**	>552	65.4	48.9
Fibrinogen (mg/dL)	0.525 (0.470-0.579)	0.384	>519.5	50.4	50.3
Neutrophil/Lymphocyte ratio	0.637 (0.593-0.681)	**<0.001**	>18.45	51.5	71.9
Monocyte/Lymphocyte ratio	0.604 (0.559-0.648)	**<0.001**	>0.605	58.8	58.6
Neutrophil /Platelet ratio	0.594 (0.549-0.639)	**<0.001**	>0.0004	56.1	56.3

CRP: C-reactive protein, BMI: body mass index, APACHE-II: acute physiology and chronic health evaluation II, SOFA: sequential organ failure assessment, AUC: area under curve, CI: confidence interval

Discussion

The results of our study revealed that hypertension, along with identified malignancies (solid and hematologic), neurological illness, age, APACHE-II and SOFA scores, and N/L ratio were independently associated with mortality. However, the sensitivity or specificity percentiles of the factors determined with ROC analysis revealed that none of the cut-off values was solely sufficient for predicting mortality in COVID-19 patients. Mortality was 58.6% and was similar across the three pandemic waves. However, incidence of comorbidity in the 1st and 3rd wave period, IMV in the 2nd wave period, and unvaccinated patients in the 3rd wave period were higher in the mortality cohort.

The reported mortality of critically ill COVID-19 patients varied between centers, with a wide range of 15% to 81.9% (12,13). Differences in the characteristics of the patient population included in the study (ethnicity, comorbidity status, etc.), ICU admission criteria, treatment approach, SARS-CoV-2 variants and ICU resources encountered may be the factors accounting for the disparity of the results. Studies reported from Türkiye indicate that the mortality varied between 36% and 66.5% in critically ill COVID-19 patients (14-19). Most of these reports reflected a short duration of the pandemic, which lasted over 3 years, and some studies included SARS-CoV-2 RT-PCR negative patients with suspicious clinical findings in their study cohort (14,16-18). We included 619 SARS-CoV-2 RT-PCR positive, critically ill patients in our study and mortality was 58.6%. Among the studies reported from Türkiye, our single-center study included a relatively high number of SARS-CoV-2 RT-PCR positive patients admitted to the ICU over a period of two years, covering three pandemic waves.

Multiple waves of pandemics and new variants have emerged since SARS-CoV-2 was first detected in 2019, which may alter patient characteristics and mortality. In a study reporting the data of 2493 COVID-19 ICU patients in Australia, the third wave revealed the highest hospital mortality of the three pandemic waves. Additionally, during the 3rd wave, the most frequent reason for ICU admission was COVID-19 related complications, and the average age of the patients was lower than in the first two waves (20). Sargın Altunok et al. (21) reported similar mortality in hospitalized COVID-19 patients with severe/critical illness for the first and second waves in Türkiye. However, the study covered only the first 8 months of the pandemic, and the basis on which the wave periods were defined was not specified. Apart from this study, there have been no data regarding the clinical course and mortality of ICU patients reflecting the three pandemic waves from Türkiye. In our study, we examined the pandemic process in three consecutive waves over a wide period of time, consisting of the whole pandemic episode. Although mortality was similar in all three wave periods, the number of COVID-19 patients admitted to ICU, and incidence of unvaccinated patients were higher in the third wave period compared with other waves. Additionally, mortality in patients aged 69 and over, was higher in the third wave than in former waves. Older age was pointed out to have an impact on mortality in COVID-19 patients due to increased incidence of comorbidities and systemic

complications (22,23). Univariate and multivariate logistic regression analysis revealed that a cut-off age greater than 65.5 years was significant for the prediction of mortality for COVID-19 in this study. This finding was in agreement with previous studies (24,25). Evidence of one or more comorbidities was identified as a risk factor for death among COVID-19 patients, but it is not completely clear which comorbidity affects mortality more (26,27). Some investigations reported that pre-existing chronic conditions, such as diabetes mellitus, chronic pulmonary disease, kidney disease, hypertension, obesity, cancers, and neurological diseases, were associated with ICU admission and death (28,29). The majority of the patients had one or more comorbidities in our study. The most common comorbidities were hypertension, diabetes mellitus, obesity and coronary artery disease. Additionally, having one or more comorbidities, such as hypertension, malignancy (both solid and hematological), and neurological disease, was determined as an independent risk factor for mortality in multivariate logistic regression analysis. The impact of obesity on mortality in COVID-19 patients is controversial. While

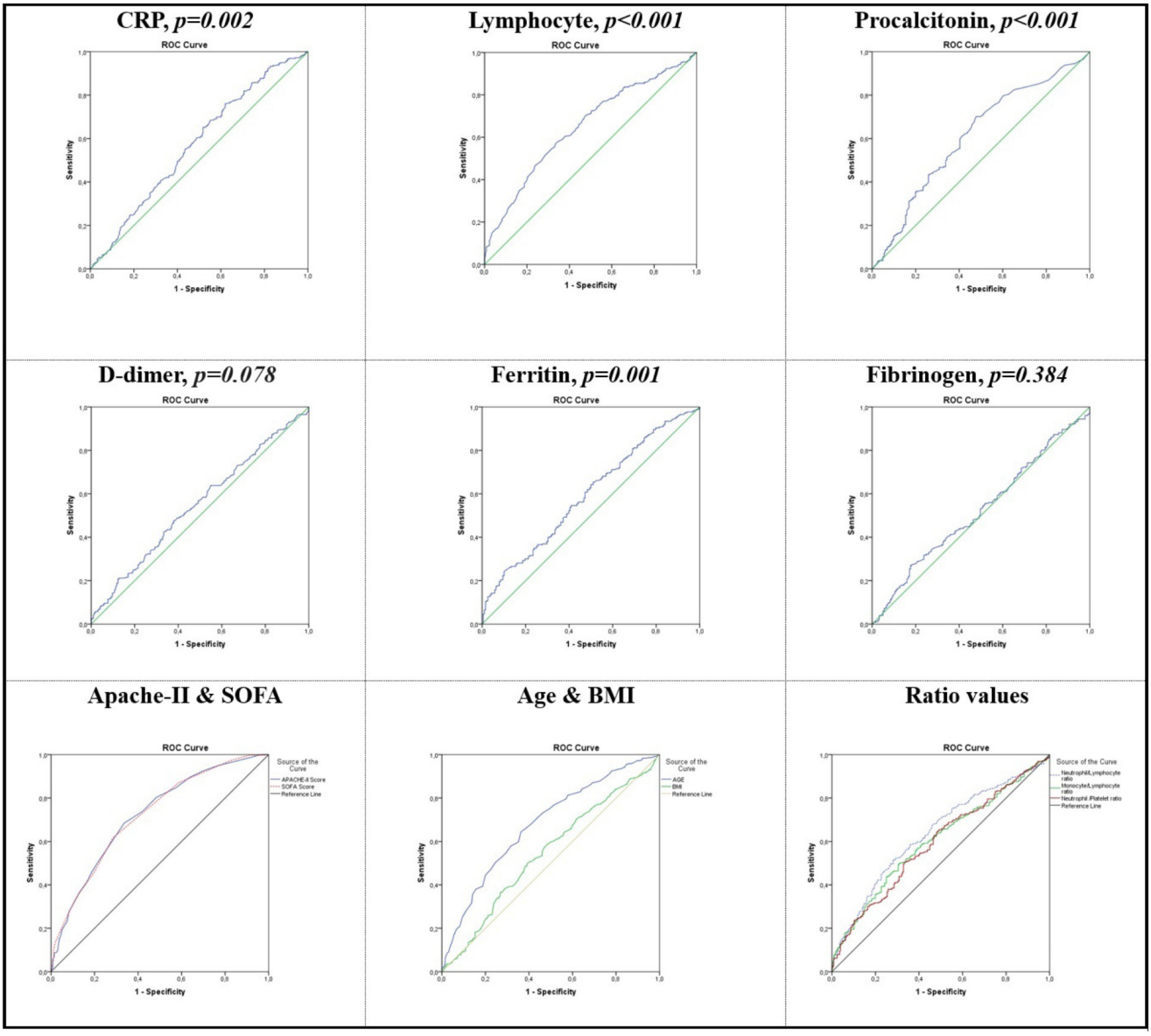

Figure 3. ROC analysis figures of Apache-II score, SOFA score, demographic variables, ratio values regarding laboratory results and laboratory parameters

APACHE-II: acute physiology and chronic health evaluation II, SOFA: sequential organ failure assessment, BMI: body mass index, CRP: C-reactive protein

various studies indicated that obesity was associated with mortality and that the need for hospitalization and mechanical ventilation were high in obese patients (30,31), others reported no risk in terms of mortality in obese patients (22,32). In our study, mortality was higher in patients with a BMI of 30 and above only in the third wave period. This finding may result from the characteristics of SARS-CoV-2 variants encountered or relatively high numbers of obese patients admitted to ICU during the third wave of the pandemic.

Table 4. Univariate and multivariate logistic regression analysis and effect profiles of parameters on mortality

Variables*	Univariate LR		Multivariate LR†	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age (years)	1.041 (1.030-1.53)	**<0.001**	0.965 (0.953-0.978)	**<0.001**
BMI (kg/m^2)	1.022 (0.994-1.051)	0.126	-	
Duration IMV (days)*	0.829 (0.793-0.867)	**<0.001**	-	
Apache-II score	0.888 (0.863-0.913)	**<0.001**	0.954 (0.923-0.986)	**0.005**
SOFA score	0.708 (0.562-0.769)	**<0.001**	0.797 (0.72-0.883)	**<0.001**
Hemoglobin (g/dL)	1.097 (1.021-1.178)	**0.012**	0.989 (0.909-1.077)	0.807
Lymphocyte(10^3/μL)*	1.031 (1.011-1.050)	**0.002**	-	
CRP (mg/L)	0.997 (0.995-0.999)	**0.013**	1 (0.997-1.002)	0.766
Neutrophil/Lymphocyte ratio	0.974 (0.964-0.984)	**<0.001**	0.985 (0.972-0.998)	**0.021**
Monocyte/Lymphocyte ratio	0.547 (0.416-0.720)	**<0.001**	0.784 (0.562-1.093)	0.151
Neutrophil /Platelet ratio	0.339 (0.240-0.664)	**<0.001**	0.741 (0.435-1.261)	0.269
Procalcitonin (μg/L)	0.996 (0.983-1.008)	0.482	-	
D-dimer (mg/L)	0.981 (0.961-1.001)	0.060	-	
Ferritin (μg/L)	1.000 (0.999-1.000)	0.180	-	
Fibrinogen (mg/dL)	1.000 (0.999-1.001)	0.915	-	

*: The multivariate model includes the significant parameters identified in the univariate analyses. Analysis was conducted to determine whether all parameters met the Box-Tidwell assumption. IMV duration and lymphocyte parameters that did not meet the assumptions were excluded from the multivariate LR model. †: -2LL=659.133 Nagelkerke R2=0.323, Hosmer and Lemeshow test assumption has been met for the model.
BMI: body mass index, APACHE-II: acute physiology and chronic health evaluation II, SOFA: sequential organ failure assessment, CRP: C-reactive protein, IMV: invasive mechanic ventilation, CI: confidence interval

Table 5. Univariate and multivariate logistic regression analysis and effect profiles of parameters on mortality

Variables	Univariate LR		Multivariate LR	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Comorbidity	2.852 (1.682-4.835)	**<0.001**	1.738 (0.967-3.123)	0.065
HT	1.595 (1.152-2.207)	**0.005**	1.463 (1.024-2.089)	**0.036**
DM	1.058 (0.753-1.489)	0.744	-	
CAD	0.986 (0.676-1.438)	0.942	-	
CKD	0.868 (0.526-1.433)	0.580	-	
Thyroid disease	1.084 (0.584-2.013)	0.799	-	
Chronic lung disease	1.548 (1.015-2.361)	**0.043**	1.426 (0.921-2.208)	0.112
Malignancy-solid	1.694 (1.008-2.847)	**0.047**	1.855 (1.076-3.196)	**0.026**
Malignancy-hematologic	1.879 (1.010-3.494)	**0.046**	1.975 (1.043-3.738)	**0.037**
Neurological illness	1.700 (1.099-2.630)	**0.017**	1.59 (1.013-2.495)	**0.044**

The multivariate model includes the significant parameters identified in the univariate analyses, HT: hypertension DM: diabetes mellitus CAD: coronary artery disease CKD: chronic kidney disease, CI: confidence interval

Table 6. Analysis of demographic and clinical characteristics according to mortality during COVID periods						
Variables	**COVID periods**					
	1st wave		**2nd wave**		**3rd wave**	
	Mortalite, n (%)		**Mortalite, n (%)**		**Mortalite, n (%)**	
	Mortality (n=69)	**Survival (n=117)**	**Mortality (n=68)**	**Survival (n=48)**	**Mortality (n=178)**	**Survival (n=139)**
Age groups						
18-55 years	17 (24.6)	17 (14.5)	16 (33.3)	9 (13.2)	60 (43.2)	36 (20.2)
56-63 years	17 (24.6)	12 (10.3)	20 (41.7)	15 (22.1)	21 (15.1)	27 (15.2)
64-68 years	14 (20.3)	17 (14.5)	5 (10.4)	9 (13.2)	11 (7.9)	23 (12.9)
≥69 years	21 (30.4)	71 (60.7)	7 (14.6)	35 (51.5)	47 (33.8)	92 (51.7)
p-value	**0.001**		**<0.001**		**<0.001**	
Gender						
Female	17 (24.6)	35 (29.9)	13 (27.1)	20 (29.4)	47 (33.8)	55 (30.9)
Male	52 (75.4)	82 (70.1)	35 (72.9)	48 (70.6)	92 (66.2)	123 (69.1)
p-value	0.545		0.948		0.582	
Obesity						
No	52 (75.4)	81 (69.2)	33 (68.8)	43 (63.2)	100 (71.9)	112 (62.9)
Yes	17 (24.6)	36 (30.8)	15 (31.2)	25 (36.8)	39 (28.1)	66 (37.1)
p-value	0.467		0.677		0.090	
Obesity groups (BMI kg/m²)						
<30	52 (75.4)	81 (69.2)	33 (68.8)	43 (63.2)	100 (71.9)	112 (62.9)
30-35	13 (18.8)	21 (17.9)	10 (20.8)	15 (22.1)	17 (12.2)	44 (24.7)
35-40	3 (4.3)	11 (9.4)	3 (6.2)	5 (7.4)	13 (9.4)	16 (9)
>40	1 (1.4)	4 (3.4)	2 (4.2)	5 (7.4)	9 (6.5)	6 (3.4)
p-value	0.564		0.917		0.031	
Smoking						
None	28 (40.6)	56 (47.9)	20 (41.7)	29 (42.6)	60 (43.2)	73 (41)
Active smoker	16 (23.2)	15 (12.8)	9 (18.8)	15 (22.1)	29 (20.9)	23 (12.9)
Exsmoker	25 (36.2)	46 (39.3)	19 (39.6)	23 (33.8)	50 (36)	81 (45.5)
Unknown	0 (0)	0 (0)	0 (0)	1 (1.5)	0 (0)	1 (0.6)
p-value	0.181		0.902		0.103	
Vaccination status						
None	110 (94.0)	68 (98.6)	67 (98.5)	44 (91.6)	122 (68.5)	62 (44.7)
Sinovac	3 (2.6)	1 (1.4)	1 (1.5)	3 (6.3)	30 (16.9)	43 (30.9)
Biontec	1 (0.8)	0 (0)	-	-	11 (6.2)	17 (12.2)
Sinovac+Biontec	3 (2.6)	0 (0)	0 (0)	1 (2.1)	15 (8.4)	17 (12.2)
p-value	0.681		0.207		**<0.001**	
Comorbidity						
No	7 (6.0)	13 (18.8)	7 (10.3)	10 (20.8)	10 (5.6)	20 (14.4)
Yes	110 (94.0)	56 (81.2)	61 (89.7)	38 (79.2)	168 (94.4)	119 (85.6)
p-value	**0.006**		0.114		**0.008**	
Oxygen support						
No	24 (20.5)	4 (5.8)	22 (32.4)	1 (2.1)	54 (30.3)	7 (5.0)
Yes	93 (79.5)	65 (94.2)	46 (67.6)	47 (97.9)	124 (69.7)	132 (95.0)
p-value	**0.007**		**<0.001**		**<0.001**	
IMV						
No	6 (5.1)	54 (78.3)	5 (7.4)	37 (77.1)	11 (6.2)	104 (74.8)
Yes	111 (94.9)	15 (21.7)	63 (92.6)	11 (22.9)	167 (93.8)	35 (25.2)
p-value	**<0.001**		**<0.001**		**<0.001**	
ARDS						
None	7 (6.0)	9 (13.0)	2 (2.9)	6 (12.5)	9 (5.1)	19 (13.9)
Mild	74 (63.3)	27 (39.1)	47 (69.1)	21 (43.7)	112 (63.7)	54 (39.4)
Moderate	28 (23.9)	25 (36.2)	14 (20.6)	12 (25.0)	40 (22.7)	43 (31.4)
Severe	8 (6.8)	8 (11.7)	5 (7.4)	9 (18.8)	15 (8.5)	21 (15.3)
p-value	**0.014**		**0.017**		**<0.001**	

Pearson's chi-squared analysis or Fisher's exact tests, BMI: body mass index, IMV: invasive mechanic ventilation, ARDS: acute respiratory distress syndrome

Following the discovery and marketing of COVID-19 vaccines, CoronaVac (Sinovac, Beijing, China; starting January 14, 2021) and BNT162b2 (BioNTech, Mainz, Germany; starting April 2, 2021) were widely used in Türkiye. Studies have shown that all vaccine types were effective in protecting against COVID-19, reducing the severity and mortality of the disease (33,34). The present study found that 82.4% of our mortality cohort was unvaccinated. Moreover, the number of ICU admissions and unvaccinated patients was higher in the 3rd wave period. Some studies have reported that the BNT162b2 vaccine reduced mortality more than the CoronaVac vaccine (35,36). Most of the patients admitted to our ICU had been vaccinated with CoronaVac only (n=81), and a small number of patients had a history of BNT162b2 vaccination (n=29). Relatively less incidence of BNT162b2 vaccination in patients admitted to ICU may reflect the efficacy of the vaccine in terms of reducing morbidity or mortality of SARS-COV-2 however our data was not sufficient to make a strong assumption as most of the patients were unvaccinated of vaccinated with CoronaVac.

SOFA and APACHE II scores are the well-known scoring systems that have long been used to estimate disease severity of ICU patients. Previous studies revealed distinct scoring values to predict mortality in COVID-19 patients (37,38). Higher values of mean APACHE II and SOFA scores in non-survivors and significant differences in ICU admission scores between study cohorts (cut off values for predicting mortality; APACHE II >11.5 and SOFA >4.5) have proven the availability of these scoring systems in predicting ICU mortality. Beigmohammadi et al. (39) reported alike cut off values of APACHE II and SOFA scores for mortality in ICU Patients with COVID-19 as 13 and 5 respectively.

The laboratory parameters associated with mortality in logistic regression analysis were CRP, procalcitonin, ferritin, N/L, M/L, and N/Plt ratio. However, using multivariate logistic regression analysis, only the N/L ratio was independently associated with mortality. Elevated N/L ratio may be a key indicator of mortality in COVID-19 (40). The N/L ratio correlates with the systemic inflammatory status and the disease activity. Neutrophilia may result from inflammation or steroid use in COVID-19 patients (41). The ratio of neutrophils to lymphocytes increases due to the frequently coexisting lymphopenia. The threshold for the N/L ratio was 18 according to the Youden Index, with a 71.9% specificity in our study. There has been no consensus on the optimal cut-off value for N/L ratio to predict mortality, especially for COVID-19. Various studies have reported threshold values for N/L ratio ranging from 3.2 to 27 (41,42). Although the mean fibrinogen and D-dimer values obtained at ICU admission were higher than normal ranges, there was no difference between patients who survived and those who did not. We did not analyze the fibrinogen or D-dimer values during ICU follow-up. Insufficiency of these parameters in predicting mortality in our study may be related to the time of analysis which coincided with the onset of severe respiratory failure.

SARS-CoV-2 causes various serious clinical conditions. It has been reported that development of complications such as ARDS, arrhythmia, myocardial infarction, sepsis/septic shock, AKI, thrombosis, disseminated intravascular coagulation, pneumothorax due to COVID-19, led to an increase in mortality (31,43). The incidence of clinical complications such as severe and moderate ARDS, sepsis/septic shock, AKI, pneumothorax, disseminated intravascular coagulation, cardiac arrhythmia, thrombosis and bleeding was higher in the mortality cohort of our study. Most of the patients had moderate to severe ARDS (80.2%) at admission. The need for IMV was indicated in 64.9% of the patients during ICU admission or follow-up. Prone positioning was reported to improve oxygenation and decrease mortality in non-COVID-19 intubated patients with moderate to severe ARDS (44,45). During the COVID-19 outbreak, the practice of awake prone positioning has also become widespread in terms of improving oxygenation, and reducing the necessity of intubation. However, it was controversial whether prone positioning had a significant effect on mortality in patients who did not receive mechanical ventilation. In a recent systematic review and meta-analysis in COVID-19 patients (intubated and non-intubated), it was stated that the prone position improved oxygenation and reduced the risk of intubation in non-intubated patients, but did not reduce the risk of mortality (46). In this study, the majority of the patient population had moderate to severe ARDS. The prone position was applied to 47% of the patients (awake and intubated) and, in line with the literature, no effect on mortality was observed. ECMO is used as rescue treatment in patients with severe ARDS. Studies have reported that mortality related to ECMO was high and that ECMO had no effect on reducing mortality in COVID-19 patients (47,48). In our study, veno-venous ECMO was performed in 13 patients who had refractory hypoxemia and/or hypercapnia despite mechanical ventilation optimization according to EOLIA criteria (11) and only 1 patient survived.

During the COVID-19 outbreak, the first drugs reported to reduce mortality were corticosteroids (49). Methylprednisolone treatment was reported to be associated with decreased mortality in a single-center observational study from China at the beginning of the pandemic (50). A concurrent preprint

observational study suggested that low-dose (1-2 mg/kg/day) and short-term (5-7 days) methylprednisolone treatment provided faster recovery of clinical symptoms (51). Afterwards, the RECOVERY trial showed that dexamethasone (6 mg/day for 10 days) therapy reduced 28-day mortality in patients who received invasive or non-invasive oxygen therapy (49). Corticosteroids were administered to our patient population throughout all the pandemic waves, and methylprednisolone (1-2 mg/kg/day) was preferred. There are several reasons for preference for methylprednisolone. Firstly, methylprednisolone has high penetration in lung tissue with a longer residence time than dexamethasone, which may be more effective in lung injury (52). Secondly, previous studies have shown the effectiveness of methylprednisolone in treating SARS (53,54). Thirdly, the conventional corticosteroid dose for ARDS was 1-2 mg/kg/day methylprednisolone in past studies (55,56). Finally, reports from China at the beginning of the pandemic showed that methylprednisolone treatment could reduce mortality (50,51). Because methylprednisolone was used as standard therapy in our study population, its effect on mortality could not be evaluated. Corticosteroids are known to play a role in suppressing lung inflammation. However, corticosteroid treatment may also cause suppression of the immune system, which may lead to bacterial/fungal infection and delayed clearance of viruses (57). Co-infections were observed in 54.9% of patients, and polymicrobial infections were detected in 194 (31.4%) patients in our study. Moreover, the mortality was higher in patients with co-infection. Based on data in the literature, the percentage of COVID-19 patients with coinfection or secondary infection is highly variable (ranging between 7.2% and 66.3%) (58,59). The development of co-infection or secondary infection can be affected by many factors such as the nurse/patient ratio, the availability of isolated rooms for a single patient, and the immunosuppressive treatments applied. In our study, there was no control group, in terms of corticosteroids. For this reason, an analysis could not determine whether the corticosteroid increased the co-infection rate or not.

Study Limitations

Our study has several limitations. The first limitation is the absence of external validation due to its retrospective nature. Secondly, the SARS-CoV-2 variant type was missing in the majority of patients, and therefore, the effects of different variants on mortality were not analyzed.

Conclusion

In conclusion, ICU mortality was 58.6% in COVID-19 patients throughout all pandemic waves. Hypertension, malignancy (solid and hematologic), neurological illness, age, APACHE-II and SOFA scores, N/L ratio led to the prediction of mortality with good accuracy, and these parameters were independently associated with mortality. The findings of our study may guide clinicians in taking essential measures in patients who have risk factors associated with mortality.

Ethics

Ethics Committee Approval: This study protocol was reviewed and approved by the Institutional Ethics Committee of Akdeniz University Faculty of Medicine, Antalya, Türkiye (approval no: KAEK-335, date:11.05.2022). The trial was also retrospectively registered at ClinicalTrials.gov (identifier: NCT06043115).

Informed Consent: Patient informed consent was waived due to the retrospective study design. Researchers analyzed only anonymized data.

Footnotes

Author Contributions

Surgical and Medical practice: Ü.A.Y., H.T., Concept: B.Ö., M.Y., Design: M.C., M.Y., Data Collection and Process: B.Ö., H.T., Analysis or Interpretation: Ü.A.Y., A.S.K., Literature Search: B.Ö., A.S.K., Writing: Ü.A.Y., M.C., M.Y.

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

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Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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