



Investigation of the Effect of Demographic and Clinical Characteristics on Mortality of COVID-19 Patients Treated in the Intensive Care Unit: A Retrospective Study

Yoğun Bakım Ünitesinde Tedavi Edilen COVID-19 Hastalarının Demografik ve Klinik Özelliklerinin Mortalite Üzerine Etkisinin İncellenmesi: Retrospektif Çalışma

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Abstract

Aim: COVID-19 can cause clinical pictures ranging from asymptomatic to severe respiratory failure and sudden death. The severity of the disease varies depending on many factors such as comorbidity, vaccination status, as well as demographic characteristics such as age and gender. In this study, it was aimed to investigate the independent risk factors that have an effect on mortality in COVID-19 patients.

Material and Method: In the study, records of 140 patients with a diagnosis of COVID-19 followed in the intensive care unit between 01.01.2021 and 01.01.2022 were examined. Demographic characteristics such as age and gender, comorbidity, vaccination status and clinical course of the patient were investigated and recorded.

Results: In our study, a statistically significant difference was found between mortality and age, and the number of days of total invasive/noninvasive mechanical ventilation support ($p=0.01$, $p=0.25$, $p<0.001$, respectively). It was found that mortality increased statistically significantly with the increase in the CO-RADS score ($p=0.03$). In addition, a statistically significant correlation was found between the vaccination status of the patients and mortality ($p=0.03$).

Conclusion: In conclusion, the findings of the study showed that the mortality rate increased as age, duration of invasive or noninvasive mechanical ventilation support and lung involvement increased. It was also found that COVID-19 vaccines reduce mortality in patients hospitalized in intensive care.

Keywords: COVID-19, intensive care, comorbid disease, COVID-19 vaccine, mortality

Öz

Amaç: COVID-19, asemptomatikten ciddi solunum yetmezliği ve ani ölüme kadar değişen klinik tablolara sebep olabilmektedir. Hastalığın şiddeti yaş, cinsiyet gibi demografik özellikler yanında, komorbidite, aşı durumu gibi birçok faktöre bağlı değişiklik gösterir. Bu çalışmada COVID-19 hastalarında mortalite üzerine etkisi olan bağımsız risk faktörlerinin ortaya konması amaçlandı.

Gereç ve Yöntem: Çalışmada 01.01.2021 ile 01.01.2022 tarihleri arasında yoğun bakım ünitesinde takip edilen COVID-19 tanılı toplam 140 hasta kayıtları incelendi. Hasta yaş, cinsiyet gibi demografik özellikler yanında, komorbidite, aşı durumu ve klinik seyri araştırılarak kaydedildi.

Bulgular: Çalışmamızda mortalite ile yaş, toplam invaziv/noninvaziv mekanik ventilasyon desteği aldığı gün sayısı arasında istatistiksel olarak anlamlı bir ilişki bulunmuştur (sırasıyla $p=0,01$, $p=0,25$, $p<0,001$). CO-RADS skorunun artmasıyla mortalitenin istatistiksel olarak anlamlı derece arttığı bulundu ($p=0,03$). Ayrıca hastaların aşı durumu ile mortalite arasında istatistiksel olarak anlamlı bir ilişki bulundu ($p=0,03$).

Sonuç: Sonuç olarak çalışmanın bulguları yaş, invaziv ya da noninvaziv mekanik ventilasyon desteği aldığı toplam gün ve akciğer tutulumu arttıkça mortalitenin de arttığını gösterdi. Ayrıca COVID-19 aşısının yoğun bakımda yatan hastalardaki mortaliteyi azalttığı bulundu.

Anahtar Kelimeler: COVID-19, yoğun bakım, komorbid hastalıklar, COVID-19 aşı, mortalite



INTRODUCTION

The disease (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first detected on December 31, 2019 in Wuhan, China and spread rapidly around the world, becoming a global problem and recognized as a pandemic by the World Health Organization (WHO). COVID-19 has similar symptoms to severe acute respiratory syndrome (SARS-CoV), which occurred in China between 2002-2003, and Middle East respiratory syndrome (MERS-CoV), which was detected in the Middle East in 2012, but the rate of spread is quite high.^[1] COVID-19 is a pathogen that can cause serious health problems by attacking the respiratory tract, digestive tract, liver, kidneys, and central nervous system.^[1,2] The disease primarily affects the respiratory system and is manifested by fever, dry cough, and difficulty breathing. If the disease progresses, it can lead to death from pneumonia and acute respiratory distress syndrome.^[1,2] Transmission of COVID-19 occurs mainly through droplets in the air we breathe (coughing or sneezing), close contact with an infected person, and touching surfaces or objects exposed to the droplets. As a result, most affected countries have taken numerous measures to contain the spread of infection, such as restricting social activities and travel, quarantining suspected persons, and isolating infected individuals.

Despite numerous global efforts, COVID-19, which is highly contagious, continues to spread rapidly and cause serious illness and death.^[3] Various measures have been taken to prevent transmission, and vaccines have been produced, but a specific and effective treatment for infected individuals has not been found to date.^[3]

COVID-19 can lead to clinical pictures ranging from asymptomatic to severe respiratory failure and sudden death.^[1,2] The severity of the disease can vary depending on many factors such as comorbidity, vaccination status, and demographic characteristics such as age and sex. Some studies have found that chronic lung disease such as asthma and chronic obstructive pulmonary disease (COPD); diabetes; hypertension; renal, hepatic, and cardiac disease; a history of smoking and drug use; age older than 60 years; and male sex cause an increase in morbidity and mortality.^[1,3] Some studies have found that chronic lung disease such as asthma and chronic obstructive pulmonary disease (COPD), diabetes, hypertension, organ failure (renal, hepatic, and cardiac), a history of smoking and drug use, age older than 60 years, and male sex cause an increase in morbidity and mortality.^[1,3] People with one or more of these characteristics often have a weakened immune system that increases their risk for infection, severe disease, and death. It has been reported that the admission rate of COVID-19 patients to the intensive care unit ranges from 3% to 90%, and the mortality rate ranges from 6% to 86%.^[3,4] Many factors such as patient demographic characteristics, comorbidity, and vaccination status affect the wide range of intensive care unit (ICU) admission and mortality rate. For this reason, it is very important to know

the independent risk factors, identify those at risk for severe illness, and determine the necessary precautions and treatment methods.

The factors affecting the clinical course in COVID-19 patients have been investigated in many studies, and conflicting results have been reported, so further studies are needed. It is very important to study the risk factors of patients treated in the ICU, especially to determine their effects on mortality and morbidity. In this study, we aimed to retrospectively investigate the impact of demographic characteristics, coordination, and vaccination status of patients admitted to the ICU with a diagnosis of COVID-19 in the last year.

MATERIAL AND METHOD

This retrospective observational study was performed on patients admitted to the intensive care unit because of COVID-19. Institutional review board approval (22-KAEK-025) was obtained from the clinical research ethics committee before starting the study. The study was carried out in accordance with the principles of the Helsinki Declaration. In our study, the records of 140 patients treated in the intensive care unit of COVID-19 between 01/01/2021 and 01/01/2022 01.01.2021 and 01.01.2022 were retrospectively analyzed. Demographic characteristics such as age and sex, comorbidity, vaccination status, and clinical course of the patient were examined and recorded. Non COVID-19 patients treated in the intensive care unit or suspected patients with an unconfirmed diagnosis of COVID-19 were not included in the study.

Nasal high-flow oxygenation, time of onset and duration of noninvasive mechanical ventilation (MV), developing complications, developing organ failure, length of ICU stay, and outcome were recorded on the day patients were admitted to the ICU for COVID-19 from the onset of symptoms. In addition, patient's chest computed tomography (CT) was assessed and recorded when they were admitted to the ICU according to the COVID-19 reporting and data system (CO-RADS) classification.^[5]

In the classification of CO-RADS: CO-RADS 1: Very unlikely. CT is normal or there are noninfectious findings suggestive of disease such as congestive heart failure, sarcoidosis, histoplasmosis, malignancy, fibrotic changes. CO-RADS 2: Suspicion is low. No typical COVID-19 symptoms. The CT picture shows bronchiectasis and thickening of the bronchial walls, and there are no obvious opacities. CO-RADS 3: Uncertain. There are central baseline opacities, interlobular septal thickening suggestive of pulmonary edema, or pleural effusions. CO-RADS 4: Suspicion is high. Suspicious CT findings are present. Unilateral vitreous multifocal consolidations without other typical findings are findings suspicious for COVID-19 an underlying lung disease. CO-RADS 5: Most likely. Bilateral and multifocal consolidations or base line vitreous opacities are typically present at COVID-19. CO-RADS 6: Certainly. Patient with bilateral ground-glass areas with positive PCR and CT.

Biostatistical Analysis

Statistically, the conformity of data to the normal distribution was assessed using the Kolmogorov-Smirnov test for one sample. Qualitative data were presented as numbers and percentages, normally distributed quantitative data as mean and standard deviation, and non-normally distributed quantitative data as median (minimum-maximum). The chi-square test was used to analyze qualitative data when comparisons were made between groups. Student's t test was used when quantitative data were normally distributed and Mann-Whitney U test when they were not. The relationship between demographic variables and mortality was analyzed by logistic regression analysis. The Statistical Package for Social Sciences (version 20.0, SPSS Inc, Chicago, IL, USA) was used to analyze all data. The statistical significance value was accepted as $p < 0.05$ in the analysis of the data.

RESULTS

140 patients were evaluated for the study. Of the 140 patients, 79 (56.4%) were female and 61 (43.6%) were male. The age of the patients ranged from 23 to 96 years and the mean was 76 years. Hypertension in 82 (58.6%) patients, diabetes in 59 (42.1%), cardiovascular disease in 44 (31.4%) patients and chronic respiratory disease in 23 (16.4%) patients, 18 (12.9%) had cancer and 10 (7.1%) had cerebrovascular disease (Table 1).

	Yes (%)	No (%)	Mortality (p)
Hypertension	82 (58.6)	58 (41.4)	0.08 ^a
Diabetes	59 (42.1)	81 (57.9)	0.58 ^a
Cardiovascular disease	44 (31.4)	96 (68.6)	0.11 ^a
Chronic lung disease	23 (16.4)	117 (83.6)	0.10 ^a
Cancer	18 (12.9)	122 (87.1)	0.45 ^a
Cerebrovascular disease	10 (7.1)	130 (92.9)	0.56 ^a
Gender: male (43.6%), female (56.7%)			0.66 ^a
CO-RADS score			0.03 ^{a*}
Immunisation status			0.04 ^{a*}

CO-RADS: COVID-19 Reporting and Data System, a: Pearson Chi-Square test ($p < 0.05$ was considered significant), *: Statistically significant.

In our study, a statistically significant difference was found between patients' age and mortality ($p = 0.01$), (Table 2). Mortality was found to statistically increase with increasing age ($p = 0.01$).

Clinically, 137 (97.9%) patients had respiratory symptoms and 3 (2.1%) had gastrointestinal symptoms. The thorax CT classification of patients before admission to the ICU is shown in Table 3. The CO-RADS score was 4 in 74 (52.9%) patients, 5 in 32 (22.9%) patients, and 3 in 28 (20%) patients (Table 3). The outcome of patients according to the CO-RADS score is shown in Table 4. It was found that mortality increased statistically significantly with the increase in CO-RADS score ($p = 0.03$), (Table 1).

	Minimum	Maximum	Median	Mortality (p)
Age	23	96	76	0.01 a *
Days of hospitalization in the ICU (after diagnosis)	1	21	3	0.3 a
Total days of ICU stay	3	21	9	0.1 a
Pulse prednol start day	1	16	4	0.5 a
Noninvasive MV start day	0	21	3	
Invasive MV start day	0	36	6	
Total days of noninvasive MV support	0	14	4	0.02 a *
Total days of invasive MV support	0	36	4	<0.001 a *

ICU: intensive care unit, MV: mechanical ventilation, a: Mann-Whitney U test ($p < 0.05$ was considered significant), *: Statistically significant.

CO-RADS Score	Person	Percent (%)
CO-RADS 1	1	0.7
CO-RADS 2	2	1.4
CO-RADS 3	28	20
CO-RADS 4	74	52.9
CO-RADS 5	32	22.9
CO-RADS 6	3	2.1

CO-RADS: COVID-19 Reporting and Data System

CO-RADS Score	Person (percent)		
	Discharged to Service	Exitus	Total Person
CO-RADS 1	1 (100%)	0	1 (100%)
CO-RADS 2	1 (50%)	1 (50%)	2 (100%)
CO-RADS 3	16 (57.1%)	12 (42.9%)	28 (100%)
CO-RADS 4	32 (43.2%)	42 (56.8%)	74 (100%)
CO-RADS 5	8 (25%)	24 (75%)	32 (100%)
CO-RADS 6	0	3 (100%)	3 (100%)

CO-RADS: COVID-19 Reporting and Data System

Patients in our study were hospitalized in the intensive care unit between days 1 and 21 after diagnosis, with a median of 3 days (Table 2). Invasive MV support was required in 58 (41.4%) patients and 82 (58.6%) patients, respectively (Table 2). Noninvasive MV support was found to be used between days 1 and 21 (median value=4) and invasive MV support was used between days 1 and 24 (median value=8) after COVID-19 diagnosis (Table 2). Patients remained in the ICU for 1 to 39 days (median=9) (Table 2). fifty-eight (41.6%) patients were admitted to the emergency department, and 82 (58.4%) died.

In our study, a statistical difference was found between the duration of non-invasive or invasive MV support and mortality ($p = 0.02$, $p < 0.001$), (Table 2). It was found that with increasing duration of MV support, mortality rate increased statistically significantly.

The vaccination status of the patients is shown in **Table 5**. 60 (42.9%) of the patients had not received vaccination. The outcome of patients according to their vaccination status is shown in **Table 6**. A statistically significant difference was found between the vaccination status of the patients in our study and mortality ($p=0.03$), (**Table 1**).

Vaccination	Person	Percent (%)
Yok	60	42.9
Sinovac (1 dose)	9	6.4
Sinovac (2 dose)	35	25
Sinovac (3 dose)	16	11.4
Biontech (1 dose)	1	0.7
Biontech (2 dose)	12	8.6
Sinovac (1 dose), Biontech (1 dose)	2	1.4
Sinovac (2 dose), Biontech (1 dose)	5	3.6

Vaccination	Person (%)		
	Discharged to Service	Exitus	Total
No	16 (26.7%)	44 (73.3%)	60 (100%)
Sinovac (1 dose)	3 (33.3%)	6 (66.6%)	9 (100%)
Sinovac (2 dose)	17 (48.6%)	18 (51.4%)	35 (100%)
Sinovac (3 dose)	10 (62.5%)	6 (37.5%)	16 (100%)
Biontech (1 dose)	0	1 (100%)	1 (100%)
Biontech (2 dose)	7 (58.3%)	5 (41.7%)	12 (100%)
Sinovac (1 dose), Biontech (1 dose)	1 (50%)	1 (50%)	2 (100%)
Sinovac (2 dose), Biontech (1 dose)	4 (80%)	1 (20%)	5 (100%)

	B	S.E	Wald	Df	Sig.	Eks(B)
Gender (female)	-20.689	7795.265	.000	1	.998	.000
Age	.039	.016	5.825	1	.016*	1.040
Vaccination status (yes)	1.076	0.404	7.021	1	.008*	2.934
Hypertension	11.634	7922.580	.000	1	.999	112823.157
Diabetes	-22.699	6705.220	.000	1	.997	.000
Cardiovascular disease	-40.611	4995.517	.000	1	.994	.000
Chronic respiratory disease	6.058	27754.303	.000	1	1.000	427.696
Cerebrovascular disease	10.821	43358.827	.000	1	1.000	50068.808
Cancer	6.446	17658.745	.000	1	1.000	630.460
Sinovac (1 dose)	43.016	75562.892	.000	1	1.000	4.805E+18
Sinovac (2 dose)	-10.203	77930.097	.000	1	1.000	.000
Sinovac (3 dose)	20.221	77389.412	.000	1	1.000	605434579.732
Sinovac (1 dose), Biontech (1 dose)	43.360	72914.581	.000	1	1.000	6.777E+18
Sinovac (2 dose), Biontech (1 dose)	18.656	522817.071	.000	1	1.000	126590021.112
Biontech (1 dose)	-31.195	74967.863	.000	1	1.000	.000
Biontech (2 dose)	55.011	79937.998	.000	1	.999	7.782E+23
Cough	45.282	50020.755	.000	1	.999	4.632E+19
Dyspnea	4.376	28024.497	.000	1	1.000	79.528
Temperature	69.038	50482.488	.000	1	.999	9.616E+29
CO-RADS 1	58.504	814169.143	.000	1	1.000	2.558E+25
CO-RADS 2	41.240	38971.552	.000	1	.999	8.132E+17
CO-RADS 3	61.415	33287.888	.000	1	.999	4.700E+26
CO-RADS 4	31.124	33395.694	.000	1	.999	3.290E+13
Pulse prednol day	.106	1334.990	.000	1	1.000	1.112

CO-RADS: COVID-19 Reporting and Data System, Logistic Regression Analysis, *: Statistically significant.

When the relationship between logistic regression analysis and demographic data on mortality was examined in our study, it was found that age and vaccination were important factors. (**Table 7**).

DISCUSSION

Many factors such as patient demographic characteristics and concomitant diseases affect the severity of COVID-19. The presence of various factors such as increasing age, smoking, hypertension, diabetes, cardiovascular disease, chronic respiratory disease, renal disease, malignancy has been associated with disease severity, need for critical care, morbidity, and mortality.^[4-6] In addition, high levels of white blood cells, neutrophils, D-dimers, ferritin, and low levels of platelets and lymphocytes in the blood have been shown to influence mortality.^[6] While some studies have found an association between gender, body mass index, and cerebrovascular disease and mortality, other studies have reported that this association does not exist.^[4-8]

Susceptibility to infections in males has been shown to be increased in association with the X chromosome, which plays an important role in immunity.^[8] Male sex has been reported to significantly increase mortality in COVID-19 patients.^[1,9] In our study, 79 (56.4%) of 140 patients were female and 61 (43.6%) were male. However, no statistically significant association was found between gender and mortality in our study.

The age of the patients in our study ranged from 23 to 96 years, and the median age was 76 years. Advanced age has been shown to increase morbidity and mortality in COVID-19 patients.^[1,10] In addition to the occurrence of many comorbidities with advancing age, the decline in the functions of cells such as T and B cells, which play a role in immunity, also affects the course of COVID-19 disease.^[4,11] Our study confirms this, and we found that age is a statistically significant risk factor for mortality.

The two most common comorbidities in patients admitted to the ICU with a diagnosis of COVID-19 were hypertension (47.7%) and diabetes (26.9%), followed by cardiovascular disease (12.9%), chronic respiratory disease (5%, 5), renal disease (5.3%), and liver disease.^[1,3-6] Similar to the literature, the most common comorbidities in our patients were hypertension and diabetes. Hypertension in 82 (58.6%) patients, diabetes in 59 (42.1%), cardiovascular disease in 44 (31.4%) patients and chronic respiratory disease in 23 (16.4%) patients, 18 (12.9%) had cancer and 10 (7.1%) had cerebrovascular disease. Hypertension and diabetes are also the most common comorbidities in patients treated in the ICU for reasons other than COVID-19.^[12,13] For this reason, the incidence might be increased in COVID-19 patients hospitalized in the ICU. However, hypertension can suppress the immune system by decreasing the level of angiotensin converting enzyme 2 (ACE2).^[14,15] It has been reported to increase morbidity and mortality rates by increasing the infectivity and susceptibility of COVID-19.^[14,16] On the other hand, diabetes has been reported to increase susceptibility to acute respiratory distress syndrome (ARDS) and to increase the risk of hospitalization of COVID-19 patients in the intensive care unit and follow-up with invasive MV.^[2]

Fever (78.8%), cough (53.9%), and malaise (37.9%) are the most common symptoms in COVID-19 patients.^[17] In contrast to other viral respiratory infections, rhinorrhea (7.5%) is less common.^[17] The frequency of gastrointestinal symptoms ranged from 3% to 39.6%, with diarrhea in 7.5% to 18.1% of patients, nausea 4.5% to 8.3%, vomiting 1.3% to 5.9%, abdominal pain in 0.5% to 4.53%.^[17-19] Shortness of breath occurs in about half (48.96%) of severe cases and only in 13.6% of cases with mild symptoms.^[17] While the patients in our study were admitted to the ICU, most (97.9%) had respiratory symptoms and some (2.1%) had gastrointestinal symptoms. While the patients in our study were admitted to the ICU, most had respiratory symptoms.

It has been reported that severe disease develops in 22.9% of COVID-19 patients, leading to death in approximately 5.6%.^[17] It has been shown that mortality in hospitalized COVID-19 patients is 17.62%.^[15] It was reported that 10.96% of COVID-19 patients were admitted to the intensive care unit and 7.1% required support MV.^[17] It has been reported that mortality in COVID-19 patients admitted to the ICU varied regionally from 10.6% to 61.9%, with an average of 41.6%.^[7] In contrast, some studies report mortality rates in ICU patients, particularly in underdeveloped countries, to be much higher than the

reported rates.^[20] The mortality rate in COVID-19 patients treated in the intensive care unit in Turkey ranges from 27% to 84%.^[21,22] The mortality rate in our study was 58.4% and was similar to the mortality rate of COVID-19 patients treated in the intensive care unit in Turkey.

Many studies have reported that mortality rates are higher in COVID-19 patients who require MV support.^[4,12,22] In addition, it has been reported that the mortality rate increases with increasing duration of MV support.^[1,7,23] Similar to the literature, our study also found that the need for MV support was significantly higher in the mortality group, regardless of whether it was non-invasive or invasive support. Mortality rates have been shown to increase with lung involvement (CO-RADS) in COVID-19 patients admitted to the ICU on the chest CT.^[4,13,22,23] Our study was also similar to the literature. Although no association with mortality was found in logistic regression analysis, it showed that mortality was statistically significantly higher when CO-RADS score increased ($p=0.039$), (**Table 4**). The CO-RADS score is useful for identifying patients at risk and has been reported to be a good guide for predicting mortality in the early phase.^[22,23]

One of the most important steps in the fight against COVID-19 is vaccination. Vaccines have been produced that provide effective protection in a short time, and the results are satisfactory.^[24] There are many vaccines that have been approved by WHO based on studies. In our country, the vaccines used are Sinovac, Biontech, and Turkovac. Biontech is an mRNA vaccine that does not contain antigen but provides the genetic information for the antigen and is synthesized in the cells of those vaccinated with antigen. Sinovac is an inactivated vaccine that confers cellular immunity with a non-replicating viral antigen. mRNA vaccines have only recently been used in humans, but inactivated vaccines have been used for years to prevent many diseases and their safety has been extensively studied. The Biontech vaccine, based on the new mRNA technology, has been shown to be superior to Sinovac in preventing symptomatic disease. However, it has been reported that there is no significant difference between the two vaccines in terms of effective protection against severe disease.^[24] In another study, the whole vaccine was found to provide 95% effective protection with Biontech and 65.7% with Sinovac.^[25] Overall, a single dose of vaccine for COVID-19 provided effective protection of 41% for infection prevention, 52% for symptomatic illness, 66% for hospitalization, 45% for ICU admission, and 53% for mortality. Two doses of vaccine provided effective protection of 85% for infection prevention, 97% for symptomatic illness, 93% for hospitalization, 96% for ICU admission, and 95% for mortality.^[25] This demonstrates the importance and necessity of full-dose vaccination.^[25] There are many studies that have investigated vaccines, and the general opinion is that mRNA vaccines are more effective than inactivated virus vaccines.^[25-28] In accordance with the literature, a statistically significant correlation was found between the vaccination status of the patients in our study and mortality ($p=0.03$). In our study, relation between the vaccination status and mortality was similar to the literature.

CONCLUSION

We found that mortality increased with the total number of days of mechanical ventilatory support and pulmonary involvement in patients followed up in the ICU because of COVID-19, regardless of age, invasive or noninvasive course, and that vaccination with COVID-19 decreased mortality in patients treated in the ICU. We believe that patients of advanced age are at risk for mortality associated with COVID-19 and that prophylactic vaccination is important. However, we believe this should be confirmed with more patient populations.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Tokat Gaziosmanpaşa University Clinical Research Ethics Committee (Date: 04.03.2022, Decision No: 22-KAEK-025).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

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