



# The Impact of CoronaVac Vaccination on 28-day Mortality Rate of Critically Ill Patients with COVID-19 in Türkiye

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**Background:** Vaccines against coronavirus disease-19 (COVID-19) have been effective in preventing symptomatic diseases, hospitalizations, and intensive care unit (ICU) admissions. However, data regarding the effectiveness of COVID-19 vaccines in reducing mortality among critically ill patients with COVID-19 remains unclear.

**Aims:** To determine the vaccination status and investigate the impact of the COVID-19 vaccine on the 28-day mortality in critically ill patients with COVID-19.

**Study Design:** Multicenter prospective observational clinical study.

**Methods:** This study was conducted in 60 hospitals with ICUs managing critically ill patients with COVID-19. Patients aged  $\geq 18$  years with confirmed COVID-19 who were admitted to the ICU were included. The present study had two phases. The first phase was designed as a one-day point prevalence study, and demographic and clinical findings were evaluated. In the second phase, the 28-day mortality was evaluated.

**Results:** As of August 11, 2021, 921 patients were enrolled in the

study. The mean age of the patients was  $65.42 \pm 16.74$  years, and 48.6% ( $n = 448$ ) were female. Among the critically ill patients with COVID-19, 52.6% ( $n = 484$ ) were unvaccinated, 7.7% ( $n = 71$ ) were incompletely vaccinated, and 39.8% ( $n = 366$ ) were fully vaccinated. A subgroup analysis of 817 patients who were unvaccinated ( $n = 484$ ) or who had received two doses of the CoronaVac vaccine ( $n = 333$ ) was performed. The 28-day mortality rate was 56.8% ( $n = 275$ ) and 57.4% ( $n = 191$ ) in the unvaccinated and two-dose CoronaVac groups, respectively. The 28-day mortality was associated with age, hypertension, the number of comorbidities, type of respiratory support, and APACHE II and sequential organ failure assessment scores ( $p < 0.05$ ). The odds ratio for the 28-day mortality among those who had received two doses of CoronaVac was 0.591 (95% confidence interval: 0.413-0.848) ( $p = 0.004$ ).

**Conclusion:** Vaccination with at least two doses of CoronaVac within six months significantly decreased mortality in vaccinated patients than in unvaccinated patients.

## INTRODUCTION

At the end of 2019, cases of unknown pneumonia caused by a new zoonotic virus called severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) emerged in Wuhan, China. This infectious disease was later identified as the novel coronavirus disease 2019 (COVID-19). In March 2020, the World Health Organization (WHO) declared the COVID-19 outbreak as a pandemic due to the rapid spread of the disease to other countries, making it a serious health concern worldwide. Although approximately 2 years have passed since then and hundreds of millions of people have been affected, COVID-19 continues to be a global public health problem.<sup>1-4</sup>

COVID-19 primarily affects the respiratory system, and the clinical spectrum can range from asymptomatic to severe disease requiring hospitalization. The viral replication of SARS-CoV-2 in target organs results in cellular damage, causing a systemic inflammatory response, cytokine storm, and organ dysfunction. Considering patients with “severe” COVID-19 as having viral sepsis describes the whole clinical picture more accurately based on the multisystemic clinical findings.<sup>1,5</sup> Approximately 5-32% of hospitalized patients with COVID-19 need to be admitted to the intensive care unit (ICU) due to acute respiratory distress syndrome requiring mechanical ventilation during their follow-up.<sup>2,3,6</sup> Although the overall hospital mortality rate is approximately 10-25% in hospitalized patients with COVID-19, the mortality rate is much higher in critically ill patients with COVID-19 admitted to the ICU, indicating an increase as the disease severity increases.<sup>1,3,7</sup>

Vaccination against infectious diseases is still considered the most effective method to prevent morbidity and mortality. Smallpox, one of history's most fatal disease, was eradicated via a successful vaccination program worldwide.<sup>4,8</sup> Different types of COVID-19 vaccines were developed by pharmaceutical industries, which were subsequently listed by WHO for emergency use.<sup>4,9,10</sup> Clinical trials demonstrated that these vaccines were highly effective in preventing symptomatic diseases, hospitalization, and ICU admissions and reduced disease transmission.<sup>10-16</sup> Consequently, the incidence of COVID-19 and its mortality rate dropped, as evidenced by real-world data. However, new variants of the SARS-CoV-2 especially the Delta variant might affect the efficacy of COVID-19 vaccines.<sup>10,13,15-17</sup>

To the best of our knowledge, there are limited data regarding the prevalence of patients in ICUs with SARS-CoV-2 variants and the effectiveness of the vaccines in reducing mortality among critically ill patients with COVID-19. In January 2021, the national COVID-19 vaccination campaign was initiated among healthcare professionals and at-risk groups in Türkiye. The primary aim of our study was to determine the prevalence of SARS-CoV-2 variants and the vaccination status by vaccine type in critically ill patients with COVID-19 who were admitted to the ICU in Türkiye. Additionally, we aimed to compare the 28-day mortality rate among vaccinated and unvaccinated patients with COVID-19 admitted to the ICU.

## MATERIALS AND METHODS

### Study design and participants

This was a national multicenter clinical study which used a hybrid design with two phases.

#### Phase 1

The first phase was designed as a one-day point prevalence study carried out on August 11, 2021. Sixty hospitals (state, university, and private hospitals) with ICUs managing patients with COVID-19 in Türkiye were invited to participate in the study. Data was collected by the ICU staff.

The following patients requiring ICU admission were included in the study: (i) those with a positive real-time polymerase chain reaction (PCR) (RT-PCR) assay for SARS-CoV-2 and (ii) those with a negative PCR assay but meeting the clinical criteria for COVID-19 with characteristic chest tomography findings. All patients aged  $\geq 18$  years who were admitted to the ICU were included. Patients with an unknown vaccination status or PCR result for COVID-19 were excluded from the study.

The following data were collected: age, sex, body mass index (BMI), smoking status, laboratory test results, radiological imaging results, intubation status, sequential organ failure assessment (SOFA) score and the presence of comorbidities such as hypertension, diabetes mellitus, coronary artery disease, congestive heart failure, chronic obstructive pulmonary disease, asthma, and chronic kidney disease. Centers were contacted regularly to obtain missing data.

The participant's vaccination status was categorized as unvaccinated (those who had not received any COVID-19 vaccine), incompletely vaccinated (those who had received two doses of a vaccine and had contracted SARS-CoV-2 within 14 days after receiving the second dose), and fully vaccinated (those who had received two doses of a vaccine within the last six months).

#### Phase 2

The first day of ICU admission of each patient screened in phase 1 was identified. The patients were followed up for 28 days from the day of ICU admission and the mortality rate was estimated.

### Statistical analysis

The data were analyzed using SPSS (version 25.0; IBM Corp., Armonk, NY, USA). Normal distribution of the variables was evaluated using the Kolmogorov-Smirnov test. Continuous variables are presented as means and standard deviations or medians and interquartile ranges. Categorical variables are presented as frequencies (n) and percentages (%). The independent samples t-test was used to compare the continuous variables of two groups. When the assumption of normality was not met, the Mann-Whitney U test was used. The chi-square and Fisher's exact tests were used to compare categorical variables.

Only participants who were unvaccinated and who had received  $\geq 2$  doses of the CoronaVac vaccine were compared (n = 817). The variables associated with 28-day mortality were analyzed



using univariate and multivariate analyses. All the variables with a  $p$ -value  $< 0.10$  in the univariate analysis and those considered to be clinically important were included in the logistic regression analysis (backward stepwise method). The strength of associations are presented with odds ratios (ORs) and 95% confidence interval (CI). A  $p$ -value  $< 0.05$  was considered statistically significant.

### Ethical approval

The study protocol was approved by the clinical research ethics board of the Marmara University School of Medicine (no: 09.2021.955; date of approval: August 8, 2021). The study was conducted in accordance with the principles of the Declaration of Helsinki.

## RESULTS

### Participant's characteristics

The mean age of the patients was  $65.42 \pm 16.74$  years, and 48.6% ( $n = 448$ ) of them were female. The mean BMI of the patients was  $27.74 \pm 5.78$  kg/m<sup>2</sup>, and 26.2% ( $n = 241$ ) of them were obese. At least one comorbid disease was detected in 75.6% ( $n = 696$ ) of the patients, with hypertension ( $n = 448$ , 48.6%) being the most common comorbidity. Approximately 46.1% of the patients required invasive mechanical ventilation on the first day of ICU admission. The median APACHE II score and SOFA score of the patients was 16 (12-23) and 5 (4-8), respectively, on the first day of ICU admission (Table 1).

Among the included participants, 52.6% ( $n = 484$ ) of them were unvaccinated, 7.7% ( $n = 71$ ) were incompletely vaccinated, and 39.8% ( $n = 366$ ) were fully vaccinated. The fully vaccinated participants had received the following vaccination schedules: two doses of the CoronaVac vaccine ( $n = 333$ , 36.2%), three doses of the CoronaVac vaccine ( $n = 18$ , 2%), two doses of mRNA vaccine ( $n = 5$ , 0.5%), or two doses of CoronaVac vaccine with one dose of the mRNA vaccine ( $n = 10$ , 1.1%). Among the patients who were incompletely vaccinated, 50 (5.4%) had received only a single dose of the CoronaVac vaccine and 21 (2.3%) had received only a single dose of mRNA vaccine (Figure 1).

Information regarding the causative SARS-CoV-2 variant of 342 patients was available. Delta was the most common strain of COVID-19 virus ( $n = 221$ ; 64.6%) detected (Figure 2).

The overall 28-day mortality rate was 56.6% ( $n = 521$ , 95% CI: 53.3-59.8). The 28-day mortality rate among the unvaccinated patients and those who had received two doses of the CoronaVac vaccine was 56.8% ( $n = 275$ ) and 57.4% ( $n = 191$ ), respectively (Table 2). Seven of the 21 patients who had received one dose of the mRNA vaccine and two of the five patients who had received both doses of the mRNA vaccine died.

### Comparison of the unvaccinated and fully vaccinated ( $\geq 2$ doses of CoronaVac) groups

A total of 817 patients who were unvaccinated ( $n = 484$ ) or had received two doses of the CoronaVac vaccine ( $n = 333$ ) were included in this analysis. There was no significant difference in

**TABLE 1.** Demographic and Clinical Characteristics of the Patients.

<b>Age, years (mean <math>\pm</math> SD)</b>	65.42 $\pm$ 16.74
< 65, n (%)	382 (41.5)
65-74, n (%)	219 (23.8)
75-84, n (%)	225 (24.4)
$\geq 85$ , n (%)	95 (10.3)
<b>Gender</b>	
Female, n (%)	448 (48.6)
Male, n (%)	473 (51.4)
<b>Body mass index, kg/m<sup>2</sup> (mean <math>\pm</math> SD)</b>	27.74 $\pm$ 5.78
<b>Obesity, n (%)</b>	241 (26.2)
<b>Smoking*, n (%)</b>	222 (29.8)
<b>Comorbidity</b>	
No comorbidity, n (%)	225 (24.4)
1 comorbidity, n (%)	256 (27.8)
2 comorbidity, n (%)	253 (27.5)
$\geq 3$ comorbidity, n (%)	187 (20.3)
<b>Comorbid diseases</b>	
Hypertension, n (%)	448 (48.6)
Diabetes mellitus, n (%)	268 (29.1)
Coronary artery disease, n (%)	138 (15.0)
COPD, n (%)	96 (10.4)
Congestive heart failure, n (%)	71 (7.7)
Malignancy, n (%)	67 (7.3)
Cerebrovascular disease, n (%)	50 (5.4)
Chronic renal failure, n (%)	47 (5.1)
Dementia, n (%)	44 (4.8)
<b>CO-RADS score **</b>	
CO-RADS 1, n (%)	12 (1.5)
CO-RADS 2, n (%)	74 (9.1)
CO-RADS 3, n (%)	145 (17.8)
CO-RADS 4, n (%)	190 (23.3)
CO-RADS 5, n (%)	393 (48.3)
<b>APACHE II, median (IQR)</b>	16 (12-23)
<b>SOFA, median (IQR)</b>	5 (4-8)
<b>Type of respiratory support</b>	
IMV, n (%)	425 (46.1)
CPAP, n (%)	166 (18.0)
HFNC, n (%)	177 (19.2)
Mask with reservoir, n (%)	153 (16.6)

\*: Evaluated in 745 patients.

\*\*: Evaluated in 814 patients.

COPD, Chronic obstructive pulmonary disease; CO-RADS, Coronavirus Disease 2019 Reporting and Data System (CO-RADS); APACHE II, acute physiology and chronic health evaluation II; SOFA, sequential organ failure assessment score; IMV, invasive mechanical ventilation; CPAP, continuous positive airway pressure HFNC, high flow nasal cannula; SD, standard deviation; IQR, interquartile range

sex between the two groups (Table 2). Patients in the unvaccinated group were younger than those in the two-dose CoronaVac group ( $58.94 \pm 18.04$  years vs.  $73.47 \pm 10.65$  years,  $p < 0.001$ ).

The frequency of comorbidities was higher in the two-dose CoronaVac group than in the unvaccinated group. Approximately 62.4% ( $n = 302$ ) of the patients in the unvaccinated group had at least one comorbid condition; this rate was 90.4% ( $n = 301$ ) in the two-dose CoronaVac group ( $p < 0.001$ ). Hypertension was the most frequently encountered comorbidity in both the groups. The prevalence of hypertension was higher in the two-dose CoronaVac group ( $n = 196$ ; 58.9%) than in the unvaccinated group ( $n = 184$ ; 38.0%) ( $p < 0.001$ ).

The mortality rate in the unvaccinated group ( $n = 275$ ; 56.8%) was similar to that in the two-dose CoronaVac group ( $n = 191$ ; 57.4%) ( $p = 0.878$ ). When the patients were categorized according to their age, there was no significant difference in the 28-day mortality in patients aged  $< 65$  years than in those aged 65-74 years. However, among patients aged  $> 75$  years, the 28-day mortality was higher in among the unvaccinated patients ( $n = 88$ ; 80.0%) than among those who received two doses of the CoronaVac vaccine ( $n = 94$ ; 59.1%) ( $p < 0.001$ ) (Figure 3).

The Delta variant was the most common SARS-CoV-2 type in both the groups. The variant virus rates did not differ significantly between the groups ( $p = 0.975$ ). The rate of use of a mask with reservoir, CPAP, and HFNC as respiratory support was similar in

both groups. Approximately 45.7% ( $n = 221$ ) of the unvaccinated group and 49.8% ( $n = 166$ ) of the two-dose CoronaVac group required invasive mechanical ventilation ( $p = 0.239$ ). The median APACHE II (18 [14-24] vs. 15 [10-21];  $p < 0.001$ ) and SOFA (5 [4-8] vs. 5[3-8];  $p = 0.024$ ) scores were higher in the two-dose CoronaVac group than in the unvaccinated group (Table 2).

### 28-Day Mortality

The 28-day mortality rate was associated with age, hypertension, number of comorbid diseases, type of respiratory support, APACHE II score, and SOFA score ( $p < 0.05$ ) (Supplemental Table 1).

The following variables were included in the multivariate analysis: age, sex, number of comorbid conditions, vaccination status, APACHE II and SOFA scores, and respiratory support. With the non-vaccinated group as the reference category, the OR for the 28-day mortality for those who had received two doses of the CoronaVac vaccine was 0.591 (95% CI: 0.413-0.848). Each unit increase in the SOFA score resulted in a 1.1 times increased mortality risk (OR: 1.111; 95% CI: 1.048-1.177). With reservoir mask usage as the reference category, HFNC use was not associated with an increase in mortality. However, the need for CPAP and invasive mechanical ventilation was associated with a 2.2-fold (OR: 2.196; 95% CI: 1.311-3.679) and 3.6-fold (OR: 3.593; 95% CI: 2.237-5.771) increase in mortality, respectively. Patients with one comorbid disease (OR: 1.733; 95% CI: 1.112-2.699) or two comorbid diseases (OR: 1.723; 95% CI: 1.086-2.733) had a greater risk of mortality than those without any comorbidities. In patients with three or more comorbidities, there was an approximately 2-fold increase in the risk of mortality (OR: 1.930; 95% CI: 1.152-3.233). Mortality was also associated with the patient's age. With patients aged 18-65 years as the reference category, the risk of mortality was 1.6 times (OR: 1.671; 95% CI: 1.099-2.541) and 2.2 times (OR: 2.215; 95% CI: 1.402-3.499) in those aged 65-74 years and 75-84 years, respectively. In patients aged  $\geq 85$  years, there was a 2.5 times (OR: 2.422; 95% CI: 1.324-4.432) increase in mortality (Table 3).

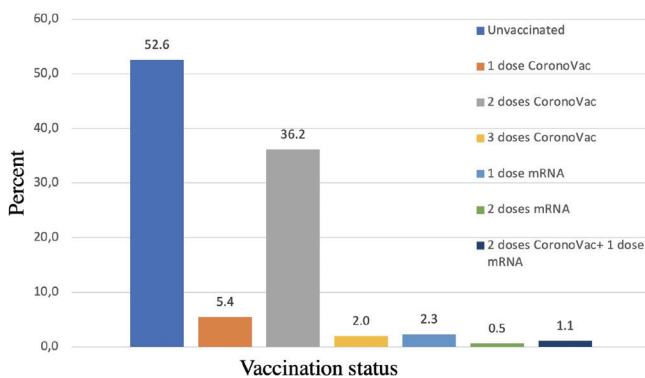


FIG. 1. Vaccination status of the patients ( $n = 921$ ).

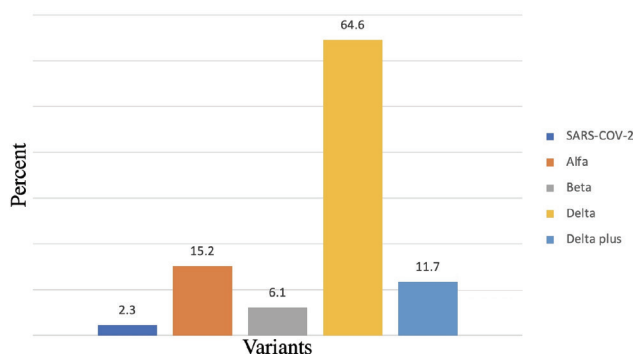


FIG. 2. Prevalence of the SARS-CoV-2 variants ( $n = 342$ ).  
SARS-CoV-2, severe acute respiratory infection-coronavirus-2

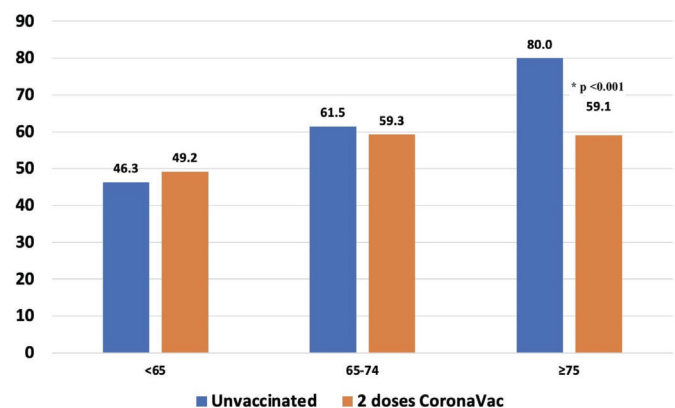


FIG. 3. Mortality rates according to age groups in unvaccinated and vaccinated patients.

## DISCUSSION

In the present study, we evaluated the vaccination status and 28-day mortality rate of critically ill patients with COVID-19 who had been admitted to ICUs in Türkiye. Our analysis showed that more than half of the patients with COVID-19 in the ICUs were unvaccinated, and the majority of the rest had received the CoronaVac vaccine. The 28-day mortality rate was associated with age, the number of comorbid diseases, type of respiratory support, and high APACHE II and SOFA scores. Additionally, vaccination with at least two doses of the CoronaVac vaccine within six months decreased the mortality rate when compared to being unvaccinated.

Vaccines are essential for preventing symptomatic diseases and reducing the morbidity and mortality associated with COVID-19. During the pandemic, multiple companies were involved in the rapid development of different types of vaccines.<sup>12</sup> The inactivated SARS-CoV-2 vaccine CoronaVac (Sinovac) was administered in several countries, including Türkiye.<sup>15,18</sup> The CoronaVac vaccine effectively prevented the development of a symptomatic disease in placebo-controlled phase 3 clinical trials (50.65-83.50%). Additionally, it effectively prevented the need for hospitalization and mortality.<sup>11,19</sup> However, the previous studies were limited to relatively young study populations with a low prevalence of chronic diseases. The efficacy of the vaccine in preventing mortality in patients admitted to the ICU who are older and have multiple chronic comorbidities has not been adequately evaluated. Additionally, the median observation period in the previous studies has been as short as two months; thus, the long-term protective effects of CoronaVac remain unknown.<sup>11,15</sup>

The efficacy of the CoronaVac vaccine in preventing COVID-19, hospitalization, ICU admission, and COVID-19-related mortality were evaluated in a prospective observational clinical study that covered approximately 80% of the Chilean population.<sup>19</sup> In that study, patients who had completed 14 days from the second vaccine dose were considered fully immunized.<sup>19</sup> They concluded that the CoronaVac vaccine had an efficacy of 65.9%, 87.5%, 90.3%, and 86.3% in preventing the disease, hospitalizations, ICU admissions, and COVID-19-related mortality, respectively, among fully vaccinated patients. Furthermore, a subgroup analysis demonstrated that the CoronaVac vaccine had an efficacy of 66.6%, 85.3%, 89.2%, and 86.5% in preventing the disease, hospitalization, ICU admission, and COVID-19-related mortality, respectively, in patients aged  $\geq 60$  years. However, the long-term effects of the vaccine for preventing mortality were not evaluated.<sup>19</sup>

Another study demonstrated that 47.8% of the hospitalized patients with COVID-19 were unvaccinated, while 53.1% of those admitted to the ICU were unvaccinated.<sup>20</sup> A recently published study demonstrated that 22.6% of patients with COVID-19 requiring intensive care were individuals who were fully vaccinated. Additionally, unvaccinated patients were more likely to require invasive mechanical ventilation, vasopressors, and extracorporeal membrane oxygenation than vaccinated patients.<sup>21</sup> Furthermore, critically ill vaccinated patients were older, had more comorbidities, and had higher APACHE II and SOFA scores than critically ill unvaccinated patients.<sup>21-24</sup> Consistent with the findings of previous

studies, the present study demonstrated that 52.6% of patients with COVID-19 admitted to the ICU were unvaccinated. Furthermore, the unvaccinated patients were older, had more comorbidities, and had higher APACHE II scores than the vaccinated patients. However, contrary to the findings of previous studies, the rate of need for invasive mechanical ventilation was similar between the vaccinated and unvaccinated patients in the present study.

The hospitalization rate was lower among patients who had received two doses of the CoronaVac vaccine and a booster dose with the mRNA-based COVID-19 vaccine than patients who had received three doses of the CoronaVac vaccine. However, the impact of the COVID-19 vaccines on mortality was not evaluated in this clinical study.<sup>20</sup>

Another real-life study investigating the effectiveness of CoronaVac among healthcare workers during the period where the Alpha variant was prevalent revealed a 65% effectiveness in preventing the development of the disease. The effectiveness in this study was lower than that in the previous phase III clinical trial in Türkiye.<sup>25</sup>

Adults aged  $\geq 65$  years are at a higher risk for developing adverse outcomes such as mortality and morbidity due to COVID-19 than those aged  $< 65$  years. Even though the risk of hospitalization and mortality is higher in older adults and patients having comorbidities, COVID-19 can cause severe illness and death in individuals of any age group.<sup>26-29</sup> Therefore, effective and prompt vaccination of high-risk groups, including older adults, is critical in reducing the development of severe COVID-19. Clinical studies and real-world data have demonstrated the importance of vaccinating the older high-risk population. Data from the USA demonstrate that receiving the complete Pfizer-BioTech vaccination schedule prevents COVID-19-related hospitalizations by 96% and 91% in adults aged 65-74 years and  $\geq 75$  years, respectively.<sup>10,30</sup> However, only a few studies have evaluated the efficacy of CoronaVac in adults aged  $\geq 60$  years.<sup>31</sup> Ozdemir et al. demonstrated that the CoronaVac vaccine improved survival rates in hospitalized patients with COVID-19 aged  $\geq 65$  years.<sup>32</sup> Another clinical study aiming to assess the effectiveness of a two-dose regimen of CoronaVac in adults aged  $\geq 70$  years determined that CoronaVac administration decreased the incidence of symptomatic diseases, hospital admissions, and deaths.<sup>33</sup> In the present study, there was no significant difference in the 28-day mortality between fully vaccinated (CoronaVac) patients aged  $< 65$  years and those aged 65-74 years. However, in patients aged  $\geq 75$  years, the 28-day mortality was higher among unvaccinated patients than among those who had received two doses of CoronaVac.

The mRNA-based COVID-19 vaccines contain the mRNA of the spike protein, which is the antibody-forming antigenic structure of SARS-CoV-2. In phase 3 clinical studies, mRNA-based COVID-19 vaccines demonstrated a 94-95% protection rate against COVID-19 and provided approximately 100% protection against severe COVID-19.<sup>12,14</sup> Real-life data demonstrated that although mRNA-based COVID-19 vaccines significantly reduced COVID-19-related hospitalizations and disease progression (risk of ICU admission, mechanical ventilation requirement, and mortality) in

adults, this effect was significantly reduced in immunosuppressed adults.<sup>34-36</sup> Another recently published clinical study demonstrated that complete immunization with the mRNA-based COVID-19 vaccine was associated with lower mortality rates among critically ill patients who require invasive mechanical ventilation.<sup>37</sup> Moreover, these protective effects reportedly last up to 24 weeks.<sup>38</sup> In a clinical study among adults aged  $\geq 50$  years, completion of the mRNA vaccine regimen (14 days after the second dose) was highly effective against SARS-CoV-2 infection that required emergency room admission, hospitalization, or intensive care admission.<sup>39</sup> Similarly, after the vaccination campaigns, there was a significant decrease in the number of SARS-CoV-2 infections in patients aged  $\geq 65$  years. The rate of COVID-19-related emergency service admissions and the number of hospitalizations also decreased after the vaccine campaigns.<sup>40</sup> In our study, only a few patients

had received the mRNA vaccine. Thus, we could not evaluate its effectiveness.

Our study had the following limitations: (i) Although the study included a large cohort, we could not evaluate the effectiveness of mRNA-based vaccines because there were only a few patients in this group. (ii) We could not evaluate the difference in vaccine effectiveness according to the SARS-CoV-2 lineage. A larger sample size would be ideal to confer a more robust generalization of our results. (iii) We could not evaluate the impact of laboratory parameters and SARS-CoV-2 viral load on mortality. (iv) We could not determine if patients had been previously diagnosed with COVID-19. (v) This study included patients who had been vaccinated within the last six months; the long-term impact of CoronaVac on mortality was not assessed.

**TABLE 2.** General Characteristics of the Unvaccinated and Two-doses CoronaVac Vaccine Groups.

	Unvaccinated (n = 484)	2 doses CoronaVac (n = 333)	P value
<b>Age, year (mean <math>\pm</math> SD)</b>	58.94 $\pm$ 18.04	73.47 $\pm$ 10.65	< 0.001
< 65, n (%)	283 (58.5)	61 (18.3)	
65-74, n (%)	91 (18.8)	113 (33.9)	
75-84, n (%)	73 (15.1)	112 (33.6)	< 0.001
$\geq 85$ , n (%)	37 (7.6)	47 (14.1)	
<b>Gender</b>			
Female, n (%)	238 (49.2)	161 (48.3)	
Male, n (%)	246 (50.8)	172 (51.7)	0.817
<b>Body mass index, kg/m<sup>2</sup> (mean <math>\pm</math> SD)</b>	26.74 (24.0-29.95)	27.10 (24.20-30.80)	0.396
<b>Obesity, n (%)</b>	123 (25.4)	90 (27.0)	0.606
<b>Smoking*, n (%)</b>	119 (31.1)	76 (27.8)	0.372
<b>Comorbid diseases</b>			
Hypertension, n (%)	184 (38.0)	196 (58.9)	<0.001
Diabetes mellitus, n (%)	114 (23.6)	121 (36.3)	<0.001
Coronary artery disease, n (%)	51 (10.5)	69 (20.7)	<0.001
Congestive heart failure, n (%)	24 (5.0)	42 (12.6)	<0.001
COPD, n (%)	36 (7.4)	42 (12.6)	0.013
Cerebrovascular disease, n (%)	26 (5.4)	21 (6.3)	0.573
Chronic renal failure, n (%)	15 (3.1)	21 (6.3)	0.028
Malignancy, n (%)	28 (5.8)	28 (8.4)	0.145
Dementia, n (%)	18 (3.7)	20 (6.0)	0.127
<b>Comorbidity frequency, n (%)</b>	302 (62.4)	301 (90.4)	< 0.001
<b>Number of comorbidities, median (IQR)</b>	1 (0-2)	2 (1-3)	<0.001
No comorbidity, n (%)	182 (37.6)	32 (9.6)	
1 comorbidity, n (%)	131 (27.1)	99 (29.7)	
2 comorbidity, n (%)	103 (21.3)	109 (32.7)	< 0.001
$\geq 3$ comorbidity, n (%)	68 (14.0)	93 (28.0)	
<b>APACHE II, median (IQR)</b>	15 (10-21)	18 (14-24)	< 0.001
<b>SOFA, median (IQR)</b>	5 (3-8)	5 (4-8)	0.024
<b>Type of respiratory support</b>			
IMV, n (%)	221 (45.7)	166 (49.8)	
CPAP, n (%)	93 (19.2)	53 (15.9)	
HFNC, n (%)	94 (19.4)	54 (16.2)	
Mask with reservoir, n (%)	76 (15.7)	60 (18.0)	0.297

\*: Evaluated in 656 patients.

COPD, Chronic obstructive pulmonary disease; APACHE II, acute physiology and chronic health evaluation II; SOFA, sequential organ failure assessment score; IMV, invasive mechanical ventilation; CPAP, continuous positive airway pressure; HFNC, high flow nasal cannula; SD, standard deviation; IQR: interquartile range.



**TABLE 3.** Factors Associated with 28-day Mortality, Multivariate Analysis.

	OR	CI 95%	P value
<b>Age, year</b>			
18-65	Reference		
65-74	1.671	1.099-2.541	0.016
75-84	2.215	1.402-3.499	< 0.001
≥ 85	2.422	1.324-4.432	0.004
<b>Vaccination status</b>			
Unvaccinated	Reference		
2 doses CoronaVac	0.591	0.413-0.848	0.004
<b>Number of comorbidities</b>			
No comorbidity	Reference		
1 comorbidity	1.733	1.112-2.699	0.015
2 comorbidity	1.723	1.086-2.733	0.021
≥ 3 comorbidity	1.930	1.152-3.233	0.012
<b>SOFA</b>	1.111	1.048-1.177	< 0.001
<b>Type of respiratory support</b>			
Mask with reservoir	Reference		
HFNC	1.475	0.884-2.461	0.137
CPAP	2.2196	1.311-3.679	0.003
IMV	3.593	2.237-5.771	< 0.001

SOFA: Sequential organ failure assessment score; HFNC, high flow nasal cannula; CPAP, continuous positive airway pressure; IMV, invasive mechanical ventilation; OR: odds ratio; CI: confidence interval.

To the best of our knowledge, this is the first study to evaluate the effectiveness of CoronaVac in patients with SARS-CoV-2 variants requiring ICU admission due to severe COVID-19. During the period when the Delta variant was dominant, unvaccinated patients constituted more than half of the patients in the ICU's of Türkiye. Mortality was associated with older age, presence of comorbidities, high SOFA scores, not having received both doses of CoronaVac within the last six months, and the need for invasive mechanical ventilation and CPAP support. CoronaVac significantly reduced mortality among patients aged ≥ 75 years.

**Ethics Committee Approval:** This study protocol was approved by the clinical research ethics board of the Marmara University School of Medicine (no:09.2021.955, date of approval: August 8, 2021).

**Informed Consent:** Informed consents were obtained from all patients at admission.

**Data Sharing Statement:** Not applicable.

**Authorship Contributions:** Concept- F.G., I.C.; Data Collection and Processing F.G., I.C., U.S.K., P.A.; Analysis or Interpretation- F.G.; Literature Search- F.G., U.S.K.; Writing- F.G., U.S.K., I.C.; Final Manuscript- All authors.

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

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