

Impact of COVID-19 Vaccination Status on Intensive Care Unit Mortality in Patients with COVID-19 Pneumonia: A Retrospective Observational Study

COVID-19 Pnömonisi Tanısıyla Yoğun Bakım Ünitesinde Yatan Hastalarda Aşılama Durumunun Mortalite Üzerine Etkisi: Retrospektif Gözlemsel Çalışma

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Abstract

Objective: The aim of this study is to evaluate the effects of age, gender, clinical scores [sequential organ failure assessment (SOFA), acute physiology and chronic health evaluation (APACHE) II], radiological involvement, vaccination status, need for intubation, presence of comorbidities, waiting times at home and in the hospital ward, and the general clinical condition at the time of intensive care unit (ICU) admission on mortality in patients who were followed up in the intensive care unit due to coronavirus disease-2019 (COVID-19).

Method: Data from 806 patients with confirmed COVID-19 pneumonia admitted to the ICU of the University of Health Sciences Turkey, İstanbul Bağcılar Training and Research Hospital (March 2020-September 2021) were retrospectively analyzed. Demographic, clinical, and radiological data—including vaccination status (BioNTech or Sinovac), number of doses, and intubation status—were recorded. Independent predictors of mortality were identified using multivariate logistic regression analysis.

Öz

Amaç: Bu çalışmanın amacı, koronavirüs hastalığı-2019 (COVID-19) nedeniyle yoğun bakımda takip edilen hastalarda yaş, cinsiyet, klinik skorlar [ardışık organ yetmezliği değerlendirme (SOFA), akut fizyoloji ve kronik sağlık değerlendirme (APACHE) II], radyolojik tutulum, aşılama durumu, entübasyon gereksinimi, komorbidite varlığı, evde ve serviste bekleme süreleri ile yoğun bakım ünitesi (YBÜ) kabul anındaki genel durumun mortalite üzerindeki etkilerini değerlendirmektir.

Yöntem: Mart 2020-Eylül 2021 tarihleri arasında Sağlık Bilimleri Üniversitesi, İstanbul Bağcılar Eğitim ve Araştırma Hastanesi YBÜ'de COVID-19 pnömonisi tanısıyla izlenen 806 hastanın verileri retrospektif olarak incelendi. Hastaların demografik, klinik ve radyolojik bulguları; aşılama durumu ve tipi (BioNTech, Sinovac), doz sayısı, entübasyon gereksinimi, SOFA ve APACHE II skorları kaydedildi. Mortaliteyi etkileyen faktörler çok değişkenli lojistik regresyon analizi ile değerlendirildi.

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Abstract

Results: Of 806 patients, 58.6% were male, and the mean age was 63.9±15.3 years. The overall mortality rate was 67.5%. Mortality was significantly associated with older age, higher SOFA and APACHE II scores, need for intubation, poor general condition, comorbidities, and severe computed tomography (CT) involvement ($p<0.05$). Mortality was 70.7% among unvaccinated and 48.3% among vaccinated patients. Patients vaccinated with BioNTech (BNT162b2) had a significantly lower mortality rate than those who received CoronaVac (Sinovac) (41.2% vs. 55.6%, $p=0.038$). In multivariate analysis, age, APACHE II score, intubation, poor general condition, comorbidities, and severe CT findings were independent risk factors for mortality, whereas vaccination was a protective factor (odds ratio=0.46; 95% confidence interval: 0.29-0.73; $p=0.001$).

Conclusion: Mortality in ICU patients with COVID-19 was independently associated with advanced age, comorbidities, poor clinical condition, higher APACHE II scores, intubation, and severe radiological involvement. Vaccination—particularly with the mRNA-based BioNTech vaccine—significantly reduced mortality, underscoring the importance of early diagnosis, timely critical care, and widespread immunization in reducing ICU deaths.

Keywords: BioNTech, comorbidity, COVID-19, intensive care, intubation, mortality, Sinovac, vaccination

Öz

Bulgular: Hastaların %58,6'sı erkek, yaş ortalaması 63,9±15,3 yılı idi. Genel mortalite oranı %67,5 bulundu. Mortalite ileri yaş, yüksek APACHE II skoru, entübasyon gereksinimi, kötü genel durum, komorbidite ve ağır bilgisayarlı tomografi (BT) tutulumuyla anlamlı şekilde ilişkiliydi ($p<0,05$). Aşısız hastalarda mortalite oranı %70,7 iken, aşıllarda %48,3 olarak saptandı. BioNTech (BNT162b2) aşısı yapılanlarda mortalite oranı, CoronaVac (Sinovac) grubuna göre belirgin olarak daha düşüktü (41,2% vs. 55,6%, $p=0,038$). Lojistik regresyon analizine göre yaş, APACHE II skoru, entübasyon gereksinimi, kötü genel durum, komorbidite varlığı ve ağır BT tutulumu mortaliteyi artıran bağımsız değişkenler; aşılanma ise koruyucu faktördü (olasılık oranı=0,46; %95 güven aralığı: 0,29-0,73; $p=0,001$).

Sonuç: COVID-19 hastalarında mortaliteyi belirleyen başlıca faktörler ileri yaş, komorbidite, kötü klinik durum, yüksek APACHE II skoru, entübasyon ve ağır radyolojik tutulumdur. Aşılanma, özellikle mRNA temelli BioNTech aşısı, YBÜ mortalitesini anlamlı düzeyde azaltmaktadır. Erken başvuru, hızlı klinik değerlendirme ve yaygın aşılanma, mortaliteyi azaltmada kilit öneme sahiptir.

Anahtar kelimeler: Aşı, BioNTech, COVID-19, entübasyon, komorbidite, mortalite, Sinovac, yoğun bakım

Introduction

Since its emergence in Wuhan, China, in late 2019, coronavirus disease-2019 (COVID-19) has evolved into a major global public health crisis and has been declared a pandemic by the World Health Organization on March 11, 2020 (1). The disease presents with a wide clinical spectrum ranging from asymptomatic infection to severe pneumonia, acute respiratory distress syndrome, and multiorgan failure requiring intensive care support.

Advanced age, male sex, obesity, hypertension, diabetes mellitus, cardiovascular disease, and chronic kidney failure have been consistently identified as major risk factors for severe disease and mortality (2-4).

Despite advances in supportive care, mortality among intensive care unit (ICU) patients—particularly those requiring mechanical ventilation—remains high, ranging from 30% to 70% worldwide (4,5). Disease severity scores, comorbidity burden, radiological lung involvement, and timing of treatment initiation are key determinants of outcome (6-10).

Delayed access to healthcare, reflected by prolonged home and ward waiting times, has been associated with worsening hypoxemia, cytokine storm, and increased ICU mortality (11). Therefore, early diagnosis, timely referral, and prompt treatment initiation remain essential strategies to improve survival (10-12).

Vaccination has been the most effective intervention for reducing severe disease, hospitalization, and mortality (13-17). In Turkey, vaccination began with CoronaVac in January 2021, expanded to include BioNTech in April 2021, and booster recommendations were issued in July 2021. However, variations in vaccination coverage and hesitancy have influenced overall effectiveness.

Although international studies clearly show higher ICU admission and mortality rates among unvaccinated individuals (13-17), data focusing on critically ill COVID-19 patients in Turkey remain limited. Therefore, evaluating the impact of vaccination status on ICU mortality is essential to better define its protective role in this high-risk population.

Materials and Methods

This retrospective, observational cohort study was conducted in the ICU of the University of Health Sciences Turkey, İstanbul Bağcılar Training and Research Hospital, between March 11, 2020, and September 30, 2021. Ethical approval was obtained from the Clinical Research Ethics Committee of University of Health Sciences Turkey, Prof. Dr. Cemil Taşcıoğlu City Hospital (approval no: E-48670771-514.99, date: 08.11.2021).

All patients admitted to the ICU during the study period with a confirmed diagnosis of COVID-19 pneumonia were included. Patient data were retrospectively obtained from the hospital's electronic medical record system.

COVID-19 pneumonia was diagnosed based on the presence of at least one respiratory symptom (fever, cough, or dyspnea) together with either a positive SARS-CoV-2 real time-polymerase chain reaction (RT-PCR) test or typical thoracic computed tomography (CT) findings.

Patients with negative RT-PCR results but thoracic CT findings compatible with COVID-19, such as bilateral peripheral ground-glass opacities, consolidations, and interstitial involvement, were also considered to have COVID-19 pneumonia. The diagnosis was confirmed through multidisciplinary clinical evaluation by infectious disease and intensive care specialists.

Demographic and clinical variables extracted from the electronic records included age, sex, comorbidities, degree of thoracic CT involvement, general clinical condition at ICU admission, time spent waiting at home, ward length of stay prior to ICU admission, ICU length of stay, need for endotracheal intubation, and clinical outcome (survival or death).

Thoracic CT involvement was graded by the attending radiologist according to the estimated percentage of lung parenchymal involvement as:

- Mild: $\leq 25\%$
- Moderate: 26-50%
- Severe: $>50\%$.

General clinical condition at ICU admission was classified by the attending intensivist based on vital signs, oxygen requirement, level of consciousness, and hemodynamic stability into three categories:

- Good: Patients breathing spontaneously with low-flow oxygen support and hemodynamically stable.
- Moderate: Patients requiring high-flow oxygen therapy or non-invasive ventilation without vasopressor support.
- Poor: Patients requiring invasive mechanical ventilation and/or presenting with severe hypoxemia or hemodynamic instability.

Home waiting time was defined as the interval between the onset of the first COVID-19-related symptoms and the date of the first hospital admission, expressed in days. Symptom onset was recorded based on reports from the patient or family, as documented in the medical records. Ward waiting time was defined as the duration between hospital admission and ICU transfer.

Vaccination status and vaccination dates were verified using the Turkish Ministry of Health National Vaccination Tracking System. During the national vaccination program, two vaccines were available: the inactivated CoronaVac (Sinovac) and the mRNA-based BNT162b2 (BioNTech).

Patients were categorized into eight predefined groups according to vaccine type, number of doses, and immune maturation interval:

- 0 = Unvaccinated
- 1 = One dose of Sinovac
- 2 = Two doses of Sinovac
- 3 = Three doses of Sinovac
- 4 = Two doses of Sinovac + one dose of BioNTech
- 5 = One dose of BioNTech
- 6 = Two doses of BioNTech
- 7 = Vaccinated but <14 days since the last dose (immune response not yet developed).

A total of 997 patients were screened for eligibility. Of these, 191 were excluded because of missing data regarding vaccination status, thoracic CT findings, general clinical condition, or clinical outcome. The final analysis included 806 patients.

As the study encompassed all eligible ICU admissions during the specified period, no prior sample size calculation was performed. Continuous variables were checked for plausibility, and clearly erroneous values were treated as missing data. Only complete cases were included in regression analyses. Missingness patterns were summarized. When the proportion of missing data for any key variable exceeded 10%, indicator-variable methods were applied in sensitivity analyses.

Statistical Analysis

All analyses were conducted using IBM SPSS Statistics version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were tested for normality using the Shapiro-Wilk test. Normally distributed variables were expressed as mean \pm standard deviation, and non-normally distributed variables as median [interquartile range, (IQR)]. Categorical variables were summarized as numbers (percentages). Comparisons between survivors and non-survivors were made using the Student's t-test or Mann-Whitney U test for continuous data and the chi-square or Fisher's exact test for categorical data. To identify independent predictors of mortality, univariate logistic regression analyses were first performed; variables with $p < 0.10$ were subsequently entered into a multivariate logistic regression model using backward stepwise selection. Adjusted odds ratios and 95%

confidence intervals were reported. A two-tailed $p < 0.05$ was considered statistically significant.

Results

Demographic and Baseline Characteristics

A total of 806 patients with COVID-19 pneumonia were included in the final analysis. The cohort consisted of 472 males (58.6%) and 334 females (41.4%), with a mean age of 63.9 ± 15.3 years (range: 16-102). The overall ICU mortality rate was 67.5% ($n=544$). Baseline demographic and clinical characteristics of the study population are summarized in Table 1.

The mean age of non-survivors was significantly higher than that of survivors (66.7 ± 14.9 vs. 58.2 ± 15.8 years, $p < 0.001$). At ICU admission, 596 patients (73.9%) were classified as having poor general condition, 195 (24.2%) as moderate, and 15 (1.9%) as good. Mortality rates were 81.5%, 23.6%, and 12.5%, respectively ($p < 0.001$).

Clinical and Radiological Findings

Comorbidities were present in 85.7% of non-survivors compared with 61.2% of survivors ($p < 0.001$). Comparisons of major clinical variables between survivors and non-survivors are shown in Table 2.

The mean sequential organ failure assessment (SOFA) score was slightly higher in non-survivors (13.7 ± 3.8 vs. 13.4 ± 3.2 , $p = 0.047$), while the acute physiology and chronic health evaluation (APACHE) II score was significantly higher (27.8 ± 6.9 vs. 25.1 ± 5.7 , $p < 0.001$). The median ICU length of stay was also longer among non-survivors [11.2 (IQR 6-18) vs. 9.4 (IQR 5-16) days, $p = 0.032$].

Thoracic CT involvement was classified as mild in 132 patients (16.4%), moderate in 272 (33.8%), and severe in 402 (49.8%). Mortality increased significantly with increasing CT severity ($p < 0.001$) (Table 3).

Vaccination Status and Outcomes

Among all patients, 632 (78.4%) were unvaccinated, whereas 174 (21.6%) had received at least one dose of a COVID-19 vaccine. Vaccination status and associated mortality rates are presented in Table 4.

The mortality rate was significantly higher in unvaccinated patients than in vaccinated patients (70.7% vs. 48.3%, $p < 0.001$). Among vaccinated patients, those who received BioNTech exhibited significantly lower mortality than those vaccinated with CoronaVac (41.2% vs. 55.6%, $p = 0.038$).

Predictors of Mortality

Multivariate logistic regression analysis identified several independent predictors of ICU mortality (Table 5).

Vaccination was identified as an independent protective factor against ICU mortality.

Summary of Key Findings

Mortality was significantly associated with advanced age, poor general clinical condition, comorbidities, high APACHE II scores, severe thoracic CT involvement, and need for intubation. Vaccination, particularly with the mRNA-based BioNTech vaccine, significantly reduced mortality risk. Longer waiting times at home and on the ward were also associated with increased mortality, indicating the impact of delayed access to healthcare.

Table 1. Demographic and baseline clinical characteristics of ICU patients with COVID-19

Variable	Total (n=806)
Age, mean \pm SD (years)	63.9 \pm 15.3
Male, n (%)	472 (58.6)
Female, n (%)	334 (41.4)
Poor general condition, n (%)	596 (73.9)
Moderate general condition, n (%)	195 (24.2)
Good general condition, n (%)	15 (1.9)
Intubation requirement, n (%)	559 (69.4)
ICU mortality, n (%)	544 (67.5)

SD: Standard deviation, ICU: Intensive care unit, COVID-19: Coronavirus disease-2019

Table 2. Clinical characteristics according to survival status

Variable	Survivors	Non-survivors	p-value
Age (years), mean \pm SD	58.2 \pm 15.8	66.7 \pm 14.9	<0.001
Comorbidity \geq 1, %	61.2	85.7	<0.001
SOFA score, mean \pm SD	13.4 \pm 3.2	13.7 \pm 3.8	0.047
APACHE II score, mean \pm SD	25.1 \pm 5.7	27.8 \pm 6.9	<0.001
ICU-LOS, median (IQR)	9.4 (5-16)	11.2 (6-18)	0.032

SD: Standard deviation, ICU: Intensive care unit, IQR: Interquartile range, SOFA: Sequential organ failure assessment, LOS: Length of stay, APACHE: Acute physiology and chronic health evaluation

Discussion

In this retrospective cohort of 806 critically ill patients with COVID-19, we comprehensively evaluated the factors influencing ICU mortality. Our findings demonstrated that advanced age, the presence of comorbidities, poor general clinical condition at ICU admission, higher APACHE II scores, the requirement for endotracheal intubation, and severe thoracic involvement on CT were independently associated with increased mortality. Conversely, vaccination—particularly with the mRNA-based BNT162b2 (BioNTech) vaccine—was significantly associated with reduced risk of death. These results are consistent with previous multicenter ICU studies conducted worldwide (5).

Age, Comorbidities, and Disease Severity

Since the onset of the pandemic, older age and comorbidities have consistently been identified as major risk factors for severe COVID-19 and mortality (6-8). In the landmark study by Zhou et al. (4), age, hypertension, and diabetes were found to be independent predictors of poor outcomes, a finding later supported by Petrilli et al. (6) and Jordan et al. (7). In our cohort, non-survivors were significantly older and exhibited a markedly higher prevalence of chronic diseases (85.7%).

Table 3. Thoracic CT involvement and mortality

CT involvement	n (%)	Mortality (%)
Mild ($\leq 25\%$)	132 (16.4)	31.0
Moderate (26-50%)	272 (33.8)	54.8
Severe ($>50\%$)	402 (49.8)	82.4

CT: Computed tomography

Table 4. Vaccination status and mortality

Vaccination status	n (%)	Mortality, n (%)
Unvaccinated	632 (78.4)	447 (70.7)
Vaccinated (any dose)	174 (21.6)	84 (48.3)
CoronaVac only	117 (14.5)	65 (55.6)
BioNTech (any dose)	57 (7.1)	24 (41.2)

Table 5. Multivariate logistic regression analysis for ICU mortality

Variable	Adjusted OR	95% CI	p-value
Age (per year)	1.04	1.02-1.06	<0.001
Poor general condition	3.89	2.12-7.13	<0.001
Severe CT involvement	2.77	1.46-5.26	0.002
≥ 1 comorbidity	2.23	1.41-3.56	<0.001
Intubation requirement	4.62	2.87-7.44	<0.001
APACHE II score	1.08	1.04-1.12	<0.001
Vaccinated (any dose)	0.46	0.29-0.73	0.001

OR: Odds ratio, CI: Confidence interval, ICU: Intensive care unit, APACHE: Acute physiology and chronic health evaluation, CT: Computed tomography

Each one-year increase in age raised the risk of death by 4%, underscoring the impact of immunosenescence and reduced physiological reserve in elderly patients. Poor general condition at ICU admission was associated with an 81.5% mortality rate, suggesting that delayed presentation and pre-ICU clinical deterioration play critical roles in disease progression.

Both APACHE II and SOFA scores have been validated as objective predictors of disease severity in critically ill COVID-19 patients. In the present study, higher APACHE II scores remained independently associated with mortality, supporting previous reports linking multiorgan dysfunction and systemic inflammation to fatal outcomes (4,12). Similarly, patients requiring mechanical ventilation had a more than fourfold increased mortality risk, consistent with other ICU cohorts (10).

Prognostic Value of Thoracic CT Involvement

Radiological assessment of pulmonary involvement is an essential component of COVID-19 severity evaluation. We observed a strong stepwise relationship between CT involvement and mortality, with 31% in mild disease, 54.8% in moderate disease, and 82.4% in severe disease. These findings align with those of Wu et al. (11) and Francone et al. (9), who demonstrated that higher CT scores correlated with worsening oxygenation and increased ventilatory support requirements. Extensive radiological involvement likely reflects diffuse alveolar damage and a heightened inflammatory burden, leading to severe hypoxemia and a poor prognosis. Accordingly, CT severity scoring may serve as a valuable complementary prognostic tool alongside clinical severity indices in early risk stratification.

Impact of Vaccination on Mortality

The protective effect of vaccination against severe COVID-19 and death has been clearly demonstrated worldwide. In the present study, mortality was 70.7% among unvaccinated patients compared with 48.3% among

vaccinated individuals ($p < 0.001$). Among vaccinated patients, mortality was significantly lower in those who received BioNTech (mRNA) than in those who received CoronaVac (41.2% vs. 55.6%).

This observation is consistent with the findings of Haas et al. (13), who reported a marked reduction in COVID-19-related mortality following widespread BioNTech vaccination in Israel. Tanriover et al. (14) demonstrated that CoronaVac reduced severe disease but elicited a shorter-lived immune response. Recent meta-analyses further confirm that mRNA vaccines induce stronger humoral and cellular immunity, and that booster doses significantly improve survival, particularly among older adults and individuals with comorbidities (15-17).

Our results reinforce the importance of sustained vaccination strategies and booster administration to mitigate ICU mortality in high-risk groups.

Timing of Care and Delayed Admission

Patients with prolonged home and ward waiting times exhibited higher mortality, highlighting the adverse effect of delayed medical attention. Similar to the observations of Li et al. (12), delayed presentation permits progression of hypoxemia and cytokine storm, thereby reducing the opportunity for effective intervention. Therefore, Early diagnosis, timely hospital admission, and prompt initiation of respiratory support remain crucial determinants of survival in severe COVID-19.

Study Limitations

The strengths of this study include its large sample size, reliable vaccination data verified through the National Vaccination Tracking System, and standardized classification of thoracic CT involvement. However, several limitations should be acknowledged.

The retrospective design and heterogeneity of treatment protocols may introduce residual confounding. In addition, viral variant differences and the absence of certain inflammatory biomarkers (such as IL-6, D-dimer, and ferritin) limit external generalizability. Despite these limitations, the study provides robust real-world evidence regarding mortality determinants in vaccinated and unvaccinated ICU patients with COVID-19.

Clinical Implications

Our findings emphasize the multifactorial nature of COVID-19 mortality and the necessity for integrated management strategies. Patients presenting with advanced

age, comorbidities, high APACHE II scores, or severe CT involvement require early intensive monitoring and aggressive supportive care. Moreover, maintaining high vaccination and booster coverage remains a critical, cost-effective approach to reducing ICU admissions and mortality.

Conclusion

In conclusion, advanced age, comorbidities, poor general condition at ICU admission, high APACHE II scores, requirement for intubation, and severe thoracic CT involvement were identified as strong independent predictors of ICU mortality in patients with COVID-19.

Conversely, vaccination—particularly with the mRNA-based BioNTech (BNT162b2) vaccine—was significantly associated with reduced mortality, underscoring its crucial protective role in high-risk individuals. Delayed hospital admission and prolonged pre-ICU waiting times were also linked to worse outcomes, highlighting the importance of early recognition, timely referral, and rapid initiation of critical care.

These findings demonstrate that a comprehensive strategy combining early intervention, optimized intensive care management, and sustained vaccination coverage is essential for improving survival in patients with severe COVID-19.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Clinical Research Ethics Committee of University of Health Sciences Turkey, Prof. Dr. Cemil Taşcıoğlu City Hospital (approval no: E-48670771-514.99, date: 08.11.2021).

Informed Consent: All patients admitted to the ICU during the study period with a confirmed diagnosis of COVID-19 pneumonia were included. Patient data were retrospectively obtained from the hospital's electronic medical record system.

Footnotes

Authorship Contributions

Surgical and Medical Practices: S.K.S., C.G., B.A., M.S.S., Concept: S.K.S., S.D., R.O.K., A.S., Design: S.K.S., S.D., R.O.K., A.S., Data Collection or Processing: S.K.S., C.G., B.A., A.S., Analysis or Interpretation: S.K.S., C.G., B.A., S.D., R.O.K., Literature Search: S.K.S., C.G., B.A., S.D., R.O.K., Writing: S.K.S., B.A., S.D., C.G., R.O.K.

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