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Mortality Prediction with Machine Learning in COVID-19 Patients in Intensive Care Units: A Retrospective and Prospective Longitudinal Study

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Abstract

Aim: Predicting mortality is important for intensivists, yet conventional disease severity scores may not consistently predict mortality in patients with Coronavirus Disease 2019 (COVID-19). We aimed to develop a machine learning-based mortality prediction model for COVID-19 patients admitted to the intensive care unit (ICU).

Study Design: This study employs a retrospective and prospective longitudinal design. We retrospectively screened a total of 436 COVID-19 patients admitted to the ICU between March 15, 2020, and December 31, 2021. The worst laboratory results and vital signs within the first 24 hours of ICU admission were recorded. We selected 29 inputs to develop a model using machine learning (ML), employing an artificial neural network (ANN) as the decision model. For model testing, we prospectively followed 108 patients from January 1, 2022, to March 31, 2022.

Results: Our model predicted mortality with an 88% sensitivity and specificity. Conventional disease severity scores predicted mortality with lower sensitivity and specificity than our model did: 71% sensitivity and 70% specificity for the Acute Physiology and Chronic Health Evaluation II (APACHE-2), and 75% sensitivity and 75% specificity for both the Simplified Acute Physiology Score II (SAPS-2) and APACHE-4. Our model demonstrated greater discriminative power for mortality with an area under the curve (AUC) of 0.93 (95% confidence interval [CI], 0.87-0.98) compared to conventional disease severity scores. Respiratory support within the first 24 hours of ICU admission was identified as the most important factor affecting mortality.

Conclusions: In scenarios such as epidemics, where conventional disease scores fall short in predicting mortality, machine learning models can be developed to reliably forecast disease outcomes.

Keywords: COVID-19; intensive care unit; machine learning; mortality.

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Introduction

Coronavirus Disease 2019 (COVID-19) has persisted as a global outbreak affecting the world for over two years. During this period, more than 600 million people have been infected, and over 6 million have died.[1]

Initially, the case fatality rate (CRF) in China was reported as 2.3%. This rate increases with age, reaching up to 47% in critical cases.[2] Meta-analyses have indicated a CRF of 1% in the general population, 13% in hospitalized patients, and 37% in intensive care unit (ICU) patients.[3] Mortality rates for ICU patients worldwide have varied from 13% to 78%.[4–6] Factors such as advanced age, the presence of comorbidities, the need for invasive mechanical ventilation, and elevated levels of certain laboratory markers like ferritin and D-Dimer are associated with increased mortality. Nonetheless, mortality rates in ICUs can differ significantly across different centers and geographic regions.[6–10] Using conventional disease severity scores, such as the Acute Physiology And Chronic Health Evaluation II (APACHE-2) and the Simplified Acute Physiology Score II (SAPS-2), for mortality prediction often fails to consistently forecast COVID-19 mortality. Despite their demonstrated discriminative power for mortality, these scores may underestimate the actual mortality risk in COVID-19 cases.[11]

Beyond mortality prediction, disease severity scores serve crucial roles in ICUs for assessing care quality and guiding treatment decisions. However, conventional disease severity scores may not suit COVID-19 patients effectively. Machine Learning (ML) and Artificial Intelligence (AI) technologies can be utilized to assess disease severity and predict mortality. Several studies have demonstrated that ML and AI techniques can rapidly and accurately predict mortality in COVID-19 patients.[12–17]

In this study, we aimed to develop an ML-based mortality prediction model for COVID-19 patients admitted to ICUs in Turkiye.

Materials and Methods

The study was conducted from March 15, 2020, to March 31, 2022, at Dr. Suat Seren Chest Disease and Surgery Training and Research Hospital. Patients with COVID-19, aged 18 years and older, who were followed in the ICU, were included in the study. The diagnosis of COVID-19 was confirmed by polymerase chain reaction (PCR).

This study received approval from the ethics committee of University of Health Sciences, İzmir School of Medicine, Dr. Suat Seren Chest Disease and Surgery Training and Research Hospital (IRB number: 2022/24-32) and was conducted in accordance with the Declaration of Helsinki 2013. Informed consent was obtained from each patient or their next of kin.

Data Collection

A total of 436 patients, who were followed from March 15, 2020, to December 31, 2021, were retrospectively screened. Demographic details, clinical characteristics, and laboratory results were extracted from the hospital's electronic health records. The most adverse laboratory results and vital signs within the first 24 hours of ICU admission were documented. This data served as the basis for developing the ML model. Additionally, 108 patients monitored from January 1, 2022, to March 31, 2022, were included, and their data were prospectively recorded. Data from these patients was utilized for testing the model. To manage missing data, we calculated the mean value for each biomarker from the training data and imputed these mean values into the missing entries in both the training and testing datasets.

Machine Learning

Data Preprocessing

Our dataset included data from 436 COVID-19 patients. We implemented a two-step pipeline for data processing: data normalization and architecture decisions, as detailed below.

Data Normalization

In our dataset, categorical data were processed using one-hot encoding, and numerical data inputs were normalized through min-max normalization, which is one of the most common ways to normalize data. This method involves subtracting the minimum possible value from each value and then dividing by the range (the difference between the maximum and minimum possible values), resulting in a decimal value between 0 and 1. After one-hot encoding and normalization, the dataset comprised 29 inputs for the model.

Artificial Neural Network (ANN) Architecture

ANN is a well-documented AI model inspired by the structure of biological neurons in humans. It has been successfully employed to predict outcomes in COVID-19 cases.[14,18] The architecture of the ANN was determined

by testing multiple ANNs, each with one input layer, one output layer with a single node (for binary classification), and varying numbers of hidden layers. The models underwent training using 10-fold cross-validation, utilizing Python version 3.0.8 and the scikit-learn machine-learning library version 1.1.3. A precision score was selected for evaluating the models due to the high cost associated with false positives. The selected model featured three fully connected hidden layers, each with 30 nodes (Figure 1). Rectified Linear Units were chosen as the activation functions, and the output layer utilized a sigmoid function, given the classification of patients into survivors and non-survivors. To gain a better understanding of the relationship between our input and output data, we employed scikit-learn's built-in permutation feature importance method. Permutation feature importance is defined as the decrease in model score resulting from the shuffling of a single feature's values. [19] This procedure shows the extent to which the model depends on features. The code has been made available on GitHub at https://github.com/suneclionur/Mortality-Prediction-with-ML.

Statistical Analysis

The normality of the data was assessed using the Kolmogorov-Smirnov test. Continuous data were summarized using the median and interquartile range (IQR), and comparisons were made using the Mann-Whitney U test. Categorical data were presented as n (%), and comparisons were made using the Chi-Square test. The discriminative ability of conventional disease severity scores (APACHE-2, SAPS-2, and APACHE-4) and our model for mortality was evaluated using receiver operating characteristic (ROC) analysis. The ROC analysis was conducted in the test group. A p-value of ≤ 0.05 was considered statistically significant.

Results

During the study period, 544 patients were monitored in the ICU, and the characteristic features and laboratory findings of 436 patients were utilized for model training and validation. The model's performance was assessed using data from 108 patients, which were recorded prospectively. The training and test groups exhibited similar characteristic features and disease severity scores, except that a higher number of patients in the training group received Non-Invasive Ventilation (NIV) or High Flow Nasal Oxygen (HFNO). With the exception of D-dimer and C-reactive protein levels, which were higher in the test group, the laboratory results of the two groups were comparable. The survival rates of the two groups were also similar (46.6% vs. 45.4%, p=0.82) (Table 1).

Our model predicted mortality with an 88% sensitivity and specificity. It outperformed conventional disease severity scores, achieving higher sensitivity and specificity (71% sensitivity and 70% specificity for APACHE-2;

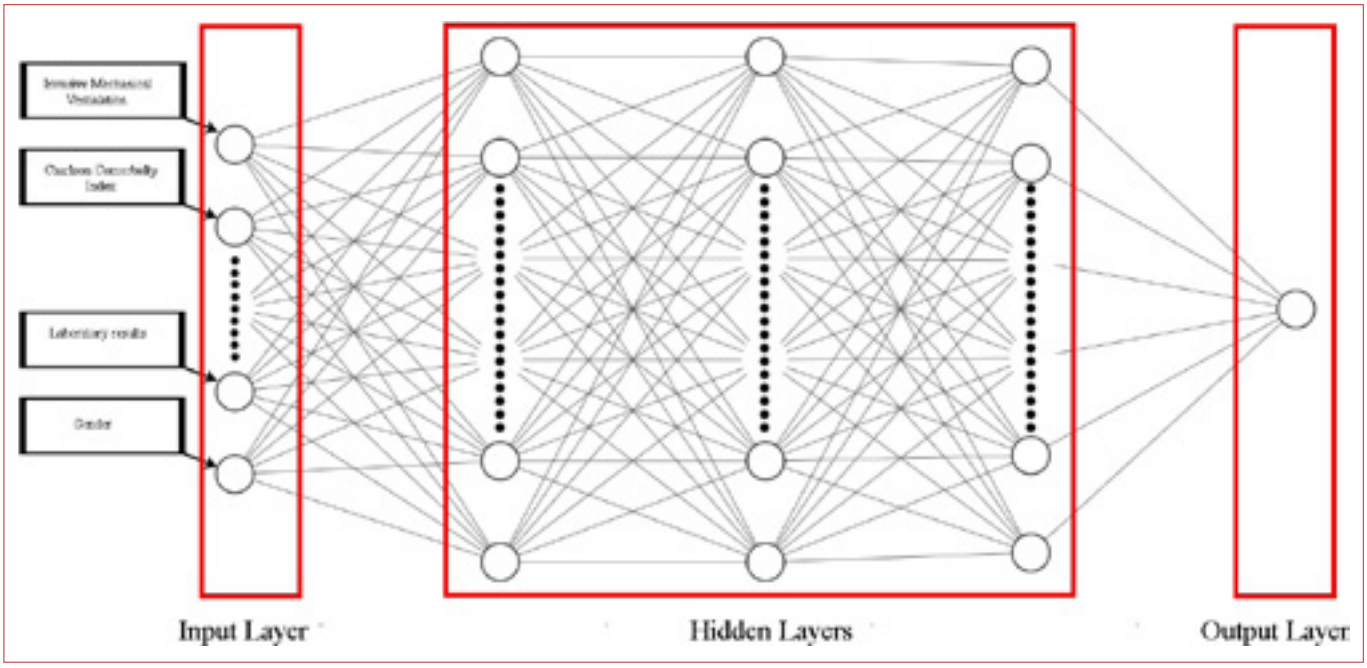

Figure 1. Architecture of neural network.

Table 1. Demographic features, clinical characteristics and laboratory results of training and test group.

	Training Group (n=436)	Test Group (n=108)	p
Age, years, median (IQR)	66 (56 – 75)	64 (57 – 63)	0.19
Gender, male, n (%)	294 (67.4)	72 (66.7)	0.88
Body mass index, kg/m^2, median (IQR)	26.0 (23.9 – 29.4)	26.7 (24.3 – 29.4)	0.25
Charlson comorbidity index, median (IQR)	3 (2 – 85)	3 (2 – 4)	0.19
APACHE-2, median (IQR)	14 (10 – 22)	14 (10 – 23)	0.84
SAPS-2, median (IQR)	38 (29 – 58)	38 (27 – 61)	0.93
APACHE-4, median (IQR)	72 (60 – 105)	71 (61 – 117)	0.92
Respiratory support on the first day in ICU, n (%)			
Only oxygen support	131 (30)	50 (46.3)	<0.001
NIV or HFNC	174 (40)	22 (20.4)	
IMV	131 (30)	36 (33.3)	
Blood Count, median (IQR)			
Leucocyte, $\times10^9$/L	11.4 (8.2 – 15.3)	9.7 (7.2 – 12.8)	0.002
Lymphocyte, $\times10^9$/L	0.5 (0.4 – 08)	0.6 (0.4 – 1.0)	0.11
Platelet, $\times10^9$/L	280 (211 – 371)	290 (218 – 346)	0.53
Hematocrit, %	36 (32 – 40)	35 (31 – 38)	0.035
Creatinine, mg/dL, median (IQR)	0.90 (0.72 – 1.29)	0.88 (0.69 – 1.41)	0.68
Ferritin, ng/dL, median (IQR)	720 (352 – 1388)	847 (326 – 1573)	0.41
D-Dimer, ng/dL, median (IQR)	1458 (843 – 3327)	1938 (1181 – 4357)	0.001
CRP, mg/dL, median (IQR)	99 (57 – 159)	168 (99 – 257)	<0.001
Procalcitonin, ng/dL, median (IQR)	0.22 (0.10 – 0.68)	0.32 (0.13 – 1.10)	0.70
Pro-BNP	786 (283 – 2911)	924 (217 – 2995)	0.43
Arterial blood gas, median (IQR)			
pH	7.43 (7.34 – 7.47)	7.43 (7.30 – 7.47)	0.91
PaO_2, mmHg	64 (58 – 75)	67 (60 – 82)	0.17
$PaCO_2$, mmHg	37 (32 – 46)	36 (32 – 47)	0.62
SaO_2, mmHg	92 (89 – 95)	93 (90 – 95)	0.06
FiO_2, mmHg	50 (40 – 50)	40 (40 – 50)	0.25
PaO_2/FiO_2	135 (114 – 160)	152 (135 – 170)	<0.001
Respiratory rate, breath per min, median (IQR)	27 (24 – 31)	26 (24 – 32)	0.51
Pulse, beat per min, median (IQR)	80 (64 – 104)	90 (72 – 110)	0.021
Fever, °C, median (IQR)	36.5 (36.4 – 36.7)	36.7 (36.5 – 36.9)	<0.001
Survivors, n (%)	203 (46.6)	49 (45.4)	0.82

APACHE: Acute Physiology And Chronic Health Evaluation; CRP: C-reactive protein; HFNC: High Flow Nasal Cannula; IMV: Invasive mechanical ventilation; NIV: Non-invasive mechanical ventilation; Pro-BNP: pro B-type natriuretic peptide; SAPS: simplified acute physiology score.

75% sensitivity and 75% specificity for both SAPS-2 and APACHE-4). Furthermore, our model demonstrated greater discriminative power for mortality, with an area under the curve (AUC) of 0.93 (95% confidence interval [CI], 0.87-0.98) compared to the conventional disease severity scores (AUC of 0.83 for APACHE-2, 95% CI, 0.75-0.90; 0.84 AUC for SAPS-2, 95% CI, 0.77-0.91; and 0.84 AUC for APACHE-4, 95% CI, 0.77-0.91) (Figure 2). In our model, seven patients (12%) were misclassified as false positives in mortality prediction. However, the rate of false positivity was found to be higher in conventional disease severity scores, at 25% for SAPS-2 and APACHE-4, and at 30% for APACHE-2. Factors such as respiratory support in the first 24 hours of ICU admission, the Charlson Comorbidity Index, systolic blood pressure, and ferritin levels were identified as the most significant in influencing mortality in our model (Figure 3).

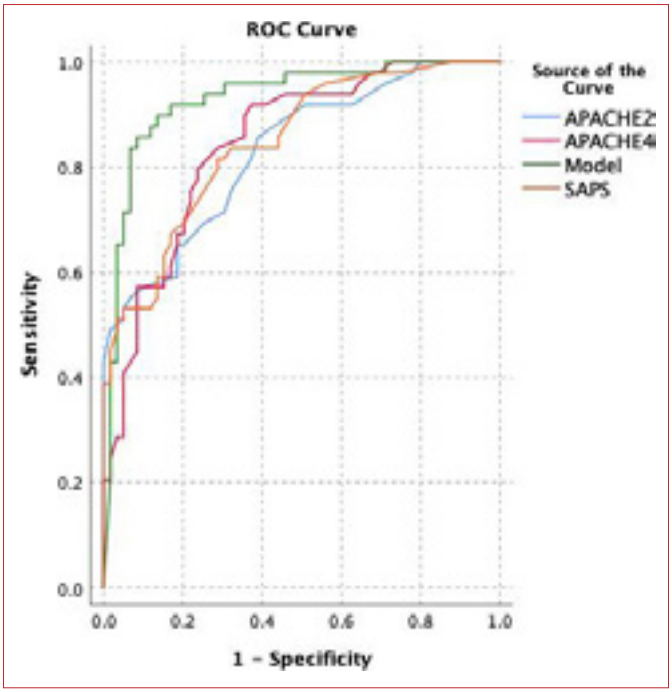

Figure 2. ROC analysis of conventional severity scores and machine learning model.
APACHE: Acute Physiology and Chronic Health Evaluation; ROC: Receiver Operating Characteristic; SAPS: Simplified Acute Physiology Score.

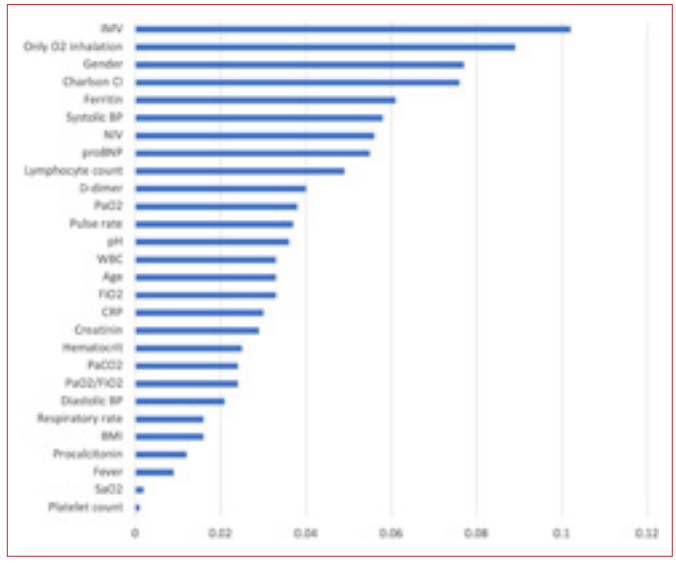

Figure 3. Feature of importance ranking in mortality prediction.
This ranking measure impacts of features on prediction for mortality in descending order. Respiratory status on the first day in intensive care unit, gender, Charlson comorbidty index, serum level of ferritin and systolic blood pressure were the most salient factor for mortality.
BMI: Body Mass Index; BP: Blood Pressure; Charlson CI: Charlson Comorbidity Index; IMV: Invasive Mechanical Ventilation; NIV: Non-Invasive Ventilation; WBC: White Blood Cell.

Discussion

In this study, we developed a novel ML-based method for predicting mortality. Our model demonstrates greater predictive accuracy than the three conventional disease severity scores in forecasting ICU mortality among COVID-19 patients.

Our model leveraged demographic features, laboratory results, and clinical characteristics of patients within the first 24 hours of ICU admission, demonstrating good discriminative power for ICU mortality. Several centers have developed mortality prediction models using ML or AI, with their discriminative power for mortality ranging from 0.72 to 0.93,[13,16,20,21] and some models achieving an AUC of up to 0.99.[22,23] Our model exhibited discriminative power comparable to these other models. The efficacy of a model varies based on the parameters included and the number of samples analyzed. Fang et al. created a severity score using an AI-based framework, utilizing only chest tomography images from 193 patients across two centers, achieving a discriminative power for mortality with an AUC of 0.72.[16] Li et al. developed a mortality prediction model using an ML method, incorporating 87 features from 3,057 COVID-19 patients, with their model's AUC for mortality reaching 0.91.[21] Our model includes four demographic variables, 10 clinical features, and 15 laboratory findings. In our analysis, respiratory status, gender, the Charlson Comorbidity Index, ferritin level, and systolic blood pressure emerged as the most significant predictors of mortality. Of all the variables, respiratory support within the first 24 hours was identified as the most critical factor for ICU mortality, with the need for invasive mechanical ventilation (IMV) emerging as the most crucial. This finding was anticipated, considering respiratory failure is the leading cause of ICU admission among COVID-19 patients. Meta-analysis revealed that the requirement for IMV is a major risk factor for mortality, with an odds ratio (OR) of 16.46 in COVID-19 patients.[24] Mortality rates for patients requiring IMV reached 78% and 80% in two multicenter studies conducted in Turkiye.[25,26] Furthermore, our model highlighted the Charlson Comorbidity Index as a key predictor of mortality. The presence of comorbid conditions and advanced age may exacerbate disease progression in COVID-19. Having comorbid diseases is an independent risk factor for mortality in COVID-19, and the risk of death escalates with an increase in the number of comorbid diseases.[8] Kim et al. reported that the age-adjusted Charlson Comorbidity Index (CCI) was the best predictor of mortality in COVID-19 patients.[27] Additionally, fer-

ritin level was identified as the most significant predictor of mortality among all laboratory results. Serum ferritin is a recognized biomarker of inflammation in COVID-19. The exact mechanism linking elevated ferritin levels to increased disease severity in COVID-19 is uncertain. Hypotheses include pro-inflammatory cytokine release, cellular damage, and acidosis as potential mechanisms driving the association between high ferritin levels and COVID-19 severity.[28] Elevated serum ferritin levels have been associated with poorer outcomes in COVID-19 patients, including increased rates of ICU admission, the necessity for IMV, and mortality.[29]

Our mortality prediction model demonstrated better discriminative power than conventional disease severity scores in predicting mortality. Conventional disease severity scores such as APACHE-2 and SAPS-2 have been utilized for decades in ICU mortality prediction. During the COVID-19 outbreak, these scores were frequently applied to assess the severity of ICU patients in Turkiye and other countries.[6,25,26,30–32] COVID-19 has impacted countries worldwide for two years. In prior research, the predictive value of conventional disease severity scores for COVID-19 varied widely, with AUCs ranging from 0.73 to 0.96.[33–35] Although conventional disease severity scores exhibit good discriminative power for mortality, they appear to underestimate it.[11] This underestimation may be due to COVID-19's unique clinical progression, the increased patient load in intensive care units, or the insufficient resources and trained personnel available in ICUs. In addition, the risk factors varying by country and intensive care unit may have led to inconsistent results from conventional disease severity scores. These scores are derived from patients' physiological symptoms and laboratory results. However, each intensive care unit may have different experiences and equipment, which can affect mortality rates. This variability is not accounted for in the scoring system. Mortality predictions can be generated using artificial intelligence or machine learning, allowing the determination of mortality risk for each intensive care unit. A study conducted before the COVID-19 outbreak demonstrated that a model created with artificial intelligence exhibited better discriminative power in predicting mortality compared to conventional disease severity scores.[18] Utilizing ML or AI, several models have been developed with enhanced discriminative power for predicting COVID-19 mortality.[13,21,22]

Our study has several limitations. First, it was conducted in a single center focusing on a unique disease and involved a relatively small sample size, which means our results may not be generalizable to other centers or diseases. Second, we did not include medical treatments in our model that could affect mortality rates. Third, we did not incorporate chest imaging severity scores in our model, despite their association with mortality.

Conclusion

Our model can accurately predict mortality in patients with COVID-19 with higher specificity and sensitivity. Conventional disease severity scores are useful for predicting mortality in ICUs, yet their specificity and sensitivity may diminish in overwhelming health crises like COVID-19.

Ethics Committee Approval: This study was approved by the ethics committee of University of Health Sciences, İzmir School of Medicine, Dr. Suat Seren Chest Disease and Surgery Training and Research Hospital (IRB number: 2022/24-32). (2022)

Informed Consent: Informed consent was obtained from each patient or their relatives.

Peer-review: Externally peer-reviewed.

Author Contribution: Concept: S.Y., O.S., C.K.; Design: S.Y., O.S., C.K.; Supervision: C.K.; Data Collection and/or Processing: S.Y., O.S.; Analysis and/or Interpretation: S.Y., O.S., C.K.; Literature Search: S.Y., O.S., C.K.; Writing: S.Y., O.S., C.K.; Critical Review: C.K.

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Conflict of Interest: The authors declare that they have no conflict of interest.

Financial Disclosure: The authors declare they have no financial interests.

References

1. WHO Coronavirus (COVID-19) Dashboard. WHO Coronavirus (COVID-19) Dashboard With Vaccination Data. Available at: https://covid19.who.int.
2. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. JAMA. 2020;323(13):1239—1242. [CrossRef]
3. Alimohamadi Y, Tola HH, Abbasi-Ghahramanloo A, Janani M, Sepandi M. Case fatality rate of COVID-19: a systematic review and meta-analysis. J Prev Med Hyg. 2021;62(2):E311—E320.
4. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395(10229):1054—1062. Erratum in: Lancet. 2020;395(10229):1038. Erratum in: Lancet. 2020;395(10229):1038.[CrossRef]

5. The Australian and New Zealand Intensive Care Society (ANZICS). ANZICS Centre for Outcome and Resources Evaluation: Report on COVID-19 admissions to Intensive Care in Australia. Available at: https://www.anzics.com.au/wp-content/uploads/2022/12/ANZICS-CORE-Covid-Report-Jan-2020_Sept-2022.pdf
6. Wendel Garcia PD, Fumeaux T, Guerci P, et al.; RISC-19-ICU Investigators. Prognostic factors associated with mortality risk and disease progression in 639 critically ill patients with COVID-19 in Europe: Initial report of the international RISC-19-ICU prospective observational cohort. EClinicalMedicine. 2020;25:100449. [CrossRef]
7. Li J, He X, Yuan Yuan, et al. Meta-analysis investigating the relationship between clinical features, outcomes, and severity of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pneumonia. Am J Infect Control. 2021;49(1):82—89. [CrossRef]
8. Ge E, Li Y, Wu S, et al. Association of pre-existing comorbidities with mortality and disease severity among 167,500 individuals with COVID-19 in Canada: A population-based cohort study. PLoS One. 2021;16(10):e0258154. [CrossRef]
9. Lino K, Guimarães GMC, Alves LS, et al. Serum ferritin at admission in hospitalized COVID-19 patients as a predictor of mortality. Braz J Infect Dis. 2021;25(2):101569. [CrossRef]
10. Poudel A, Poudel Y, Adhikari A, et al. D-dimer as a biomarker for assessment of COVID-19 prognosis: D-dimer levels on admission and its role in predicting disease outcome in hospitalized patients with COVID-19. PLoS One. 2021;16(8):e0256744. [CrossRef]
11. Yildirim S, Kirakli C. Accuracy of conventional disease severity scores in predicting COVID-19 ICU mortality: retrospective single-center study in Turkey. Ann Saudi Med. 2022;42(6):408—414. [CrossRef]
12. Bottino F, Tagliente E, Pasquini L, et al. COVID Mortality Prediction with Machine Learning Methods: A Systematic Review and Critical Appraisal. J Pers Med. 2021;11(9):893. [CrossRef]
13. Yu L, Halalau A, Dalal B, et al. Machine learning methods to predict mechanical ventilation and mortality in patients with COVID-19. PLoS One. 2021;16(4):e0249285. [CrossRef]
14. Abdulaal A, Patel A, Charani E, et al. Comparison of deep learning with regression analysis in creating predictive models for SARS-CoV-2 outcomes. BMC Med Inform Decis Mak. 2020;20(1):299.
15. Vaid A, Somani S, Russak AJ, et al. Machine Learning to Predict Mortality and Critical Events in a Cohort of Patients With COVID-19 in New York City: Model Development and Validation. J Med Internet Res. 2020;22(11):e24018. [CrossRef]
16. Fang X, Kruger U, Homayounieh F, et al. Association of AI quantified COVID-19 chest CT and patient outcome. Int J Comput Assist Radiol Surg. 2021;16(3):435—445. [CrossRef]
17. Bertsimas D, Lukin G, Mingardi L, et al.; Hellenic COVID-19 Study Group. COVID-19 mortality risk assessment: An international multi-center study. PLoS One. 2020;15(12):e0243262. [CrossRef]
18. Mirzakhani F, Sadoughi F, Hatami M, et al. Which model is superior in predicting ICU survival: artificial intelligence versus conventional approaches. BMC Med Inform Decis Mak. 2022;22(1):167.
19. Breiman L. Random forests. Machine Learning. 2001;45:5–32.
20. Booth AL, Abels E, McCaffrey P. Development of a prognostic model for mortality in COVID-19 infection using machine learning. Mod Pathol. 2021;34(3):522—531. [CrossRef]
21. Li S, Lin Y, Zhu T, et al. Development and external evaluation of predictions models for mortality of COVID-19 patients using machine learning method. Neural Comput Appl. 2023;35(18):13037—13046. [CrossRef]
22. Rahman T, Al-Ishaq FA, Al-Mohannadi FS, et al. Mortality Prediction Utilizing Blood Biomarkers to Predict the Severity of COVID-19 Using Machine Learning Technique. Diagnostics (Basel). 2021;11(9):1582. [CrossRef]
23. Guan X, Zhang B, Fu M, et al. Clinical and inflammatory features based machine learning model for fatal risk prediction of hospitalized COVID-19 patients: results from a retrospective cohort study. Ann Med. 2021;53(1):257—266. [CrossRef]
24. Chang R, Elhusseiny KM, Yeh YC, et al. COVID-19 ICU and mechanical ventilation patient characteristics and outcomes-A systematic review and meta-analysis. PLoS One. 2021;16(2):e0246318.
25. Gündoğan K, Akbudak İH, Hancı P, et al. Clinical Outcomes and Independent Risk Factors for 90-Day Mortality in Critically Ill Patients with Respiratory Failure Infected with SARS-CoV-2: A Multicenter Study in Turkish Intensive Care Units. Balkan Med J. 2021;38(5):296—303. Erratum in: Balkan Med J. 2021;38(6):397.
26. Sungurtekin H, Ozgen C, Arslan U, et al. Characteristics and outcomes of 974 COVID-19 patients in intensive care units in Turkey. Ann Saudi Med. 2021;41(6):318—326. [CrossRef]
27. Kim DH, Park HC, Cho A, et al. Age-adjusted Charlson comorbidity index score is the best predictor for severe clinical outcome in the hospitalized patients with COVID-19 infection. Medicine (Baltimore). 2021;100(18):e25900. [CrossRef]
28. Lin Z, Long F, Yang Y, et al. Serum ferritin as an independent risk factor for severity in COVID-19 patients. J Infect. 2020;81(4):647—679. [CrossRef]
29. Kaushal K, Kaur H, Sarma P, et al. Serum ferritin as a predictive biomarker in COVID-19. A systematic review, meta-analysis and meta-regression analysis. J Crit Care. 2022;67:172—181. [CrossRef]
30. Kocayiğit H, Özmen Süner K, Tomak Y, et al. Characteristics and outcomes of critically ill patients with covid-19 in Sakarya, Turkey: a single centre cohort study. Turk J Med Sci. 2021;51(2):440—447.
31. Plotnikow GA, Matesa A, Nadur JM, et al.; Grupo Argentino Telegram nCoV19. Characteristics and outcomes of patients infected with nCoV19 requiring invasive mechanical ventilation in Argentina. Rev Bras Ter Intensiva. 2020;32(3):348—353. [CrossRef]
32. Carbonell R, Urgelés S, Rodríguez A, et al.; COVID-19 SEMICYUC Working Group. Mortality comparison between the first and second/third waves among 3,795 critical COVID-19 patients with pneumonia admitted to the ICU: A multicentre retrospective cohort study. Lancet Reg Health Eur. 2021;11:100243. [CrossRef]
33. Zou X, Li S, Fang M, et al. Acute Physiology and Chronic Health Evaluation II Score as a Predictor of Hospital Mortality in Patients of Coronavirus Disease 2019. Crit Care Med. 2020;48(8):e657—e665.
34. Fernandes S, Sérvio R, Patrício P, et al. Validation of the Acute Physiology and Chronic Health Evaluation (APACHE) II Score in COVID-19 Patients Admitted to the Intensive Care Unit in Times of Resource Scarcity. Cureus. 2023;15(2):e34721. [CrossRef]
35. Beigmohammadi MT, Amoozadeh L, Rezaei Motlagh F, et al. Mortality Predictive Value of APACHE II and SOFA Scores in COVID-19 Patients in the Intensive Care Unit. Can Respir J. 2022;2022:5129314.