

(c) (i)

Original Article

Predictors of Intensive Care Unit Admissions in Patients Presenting with Coronavirus Disease 2019

Lahib Douda¹ Heraa Hasnat¹ Jennifer Schwank² Sarien Nassar² Nancy M. Jackson¹ Jeffrey C. Flynn¹ Joseph Gardiner³ Dawn P. Misra³ Abdulghani Sankari^{1,2,4}

Avicenna J Med

Address for correspondence Abdulghani Sankari, MD, PhD, Department of Medical Education, Ascension Providence Hospital, Wayne State University School of Medicine, Michigan State University College of Human Medicine, 16001 West Nine Mile Rd, Southfield, MI 48075, United States (e-mail: abdulghani.sankari@ascension.org).

Abstract

positive patients admitted to intensive care units (ICUs) highlight a compelling need to establish predictive criteria for ICU admissions. The aim of our study was to identify criteria for recognizing patients with COVID-19 at elevated risk for ICU admission. Methods We identified patients who tested positive for COVID-19 and were hospitalized between March and May 2020. Patients' data were manually abstracted through review of electronic medical records. An ICU admission prediction model was derived from a random sample of half the patients using multivariable logistic regression. The

model was validated with the remaining half of the patients using c-statistic.

Background Increased mortality rates among coronavirus disease 2019 (COVID-19)

Results We identified 1,094 patients; 204 (18.6%) were admitted to the ICU. Correlates of ICU admission were age, body mass index (BMI), quick Sequential Organ Failure Assessment (qSOFA) score, arterial oxygen saturation to fraction of inspired oxygen ratio, platelet count, and white blood cell count. The c-statistic in the derivation subset (0.798, 95% confidence interval [CI]: 0.748, 0.848) and the validation subset (0.764, 95% CI: 0.706, 0.822) showed excellent comparability. At 22% predicted probability for ICU admission, the derivation subset estimated sensitivity was 0.721, (95% CI: 0.637, 0.804) and specificity was 0.763, (95% CI: 0.722, 0.804). Our pilot predictive model identified the combination of age, BMI, qSOFA score, and oxygenation status as significant predictors for ICU admission.

Conclusion ICU admission among patients with COVID-19 can be predicted by age, BMI, level of hypoxia, and severity of illness.

Keywords

- coronavirus disease 2019
- intensive care units
- mortality
- risk factors
- prediction model

DOI https://doi.org/ 10.1055/s-0043-1778068. ISSN 2231-0770.

© 2024. The Author(s).

¹ Department of Medical Education, Ascension Providence Hospital/Michigan State University College of Human Medicine, Southfield, Michigan, United States

²Department of Medicine, Michigan State University College of Human Medicine, East Lansing, Michigan, United States

³ Department of Epidemiology and Biostatistics, Michigan State University College of Human Medicine, East Lansing, Michigan, United States

⁴Department of Medicine, Wayne State University, Detroit, Michigan, **United States**

Introduction

The first wave of coronavirus disease 2019 (COVID-19) occurred from March to May 2020 with the number of cases peaking in April of 2020. Patients who contracted COVID-19 during this time and were hospitalized had an all-cause mortality rate between 16 and 21%. A higher all-cause mortality rate (between 35 and 42%) was reported in COVID-19 positive patients if they were admitted to intensive care units (ICUs) during this first wave of the pandemic. Coronaviruses have a high mortality rate in critically ill patients as was seen in previous severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus. Despite advanced ICU supports, the mortality rate is greater than what has been reported with previous viral pneumonitis pandemics, such as the 2009 H1N1 influenza pandemic mortality rates (35–42 vs. 5–14%). 6–8,12,13

The delay in ICU admission not only affects hospital resources but can impact patient outcomes both before and during the COVID-19 pandemic.¹⁴ Conversely, an unwarranted admission to ICU can increase demand on hospital resources and lead to an insufficient availability of beds which has been linked to increased mortality from COVID-19.¹⁵ This stark increase in mortality rates among those admitted to the ICU versus those admitted to the general floors highlights a compelling need to establish an accurate and predictive criterion for ICU admissions among COVID-19 positive patients. Current literature has already identified several clinical features associated with the severity of COVID-19 infection, and calculators have also been developed such as confusion/urea/respiratory rate/blood pressure/age>65 (CURB-65), Quick COVID-19 Severity Index (qCSI), and Brescia-COVID Respiratory Severity Scale (BCRSS) to provide a uniform analysis for ICU admission, but a simple scoring system specific to COVID-19 is lacking. 16-20

In this study, we aimed to identify predictors of admission to the ICU among patients admitted to the hospital with COVID-19 and develop a predictive tool for admission to ICU among these patients. We hypothesized that one or more factors relating to the severity of illness can predict which patients with COVID-19 are admitted to the ICU. In doing so, we hope to decrease ICU admission and therefore mortality in patients with COVID-19.²¹

Methods

Participants

We conducted a retrospective observational study of patients who tested positive for COVID-19 and presented to our hospital from March 9, 2020, through May 16, 2020. Patients eligible for this study were between 18 and 99 years of age, presented to either the Southfield or Novi, Michigan campus with a diagnosis of COVID-19 determined by a nasopharyngeal swab with RT-PCR test. The study was approved by the hospital's Institutional Review Board (#1590494) prior to patient identification and data collection; a waiver of informed consent was granted due to the minimal risk nature of the study (chart review).

Patients and Public Involvement

This was a retrospective study, and no patients were involved in the study design or in setting the research questions or reported outcomes. No patients were asked for advice on interpretation or in reporting the results.

Data Collection

Patients' demographics, symptomatology, clinical data, laboratory results, and radiographic images were manually abstracted through review of electronic medical records by project team members. For each patient, the Charlson Comorbidity Index (CCI) was calculated by summing assigned weights to 17 comorbid conditions.²² The quick Sequential Organ Failure Assessment (qSOFA) score was calculated from the Glasgow Coma Scale, respiratory rate, and systolic blood pressure.²³ The compiled data were de-identified and shared with a biostatistician for analysis. Data quality was ensured by random sample review by the co-investigators, continuous communication with project principal investigator and the data collection team, and by manual review of entered data by the biostatistician. Where found missing, duplicate, and discordant inputs were identified and communicated with the data collection team. They were subsequently adjusted and confirmed as appropriate. Deaths were identified by either death at discharge or death following discharge to hospice care. All discharges to hospice care during the review period were confirmed to result in death of the patient. To be conservative, we included all deaths, whether at discharge or following hospice.

Statistical Analyses

Derivation and Validation Subsets

To derive a predictive model for ICU admission, we randomly split the patient cohort of N=1,094 into two subsets. The first, called the derivation (or training) subset, was used to develop the predictive model from the potential correlates of ICU admission. The holdout subset, called the validation subset (also called the "test" dataset in the literature), was used solely to test the performance of the predictive model with metrics such as the c-statistic, Brier score, Hosmer–Lemeshow χ^2 statistic, true positive fraction, and false positive fraction. These metrics were calculated (not estimated) in the validation subset using estimated parameters from the derivation model.

It is difficult to give a general rule for the fractions of the patient cohort assigned to training and validation. Therefore, we followed a previously suggested method to split the sample at 50%.²⁴ The derivation subset was used to develop the prediction model for ICU admission based on demographic characteristics, vital signs, clinical and laboratory findings that were available within 24 hours of hospital admission.

Characteristics of patients were summarized as frequencies and proportions for categorical variables and by means, standard deviations for continuous variables. Comparisons between derivation and validation subsets were assessed using χ^2 tests for categorical variables and by Wilcoxon tests

for continuous variables. Statistical significance was declared for a p-value <0.05.

Development of the Prediction Model

Multivariable logistic regression was used to construct a model for predicting the binary outcome, ICU admission, based on the variables in **Table 1**. The derivation subset

alone was used for this purpose. An appropriate form for continuous predictors was discerned by examining the strength of their association with outcome under different transformations. We viewed their distributions before considering the following transformations: (i) logarithm and square root, (ii) polynomial and restricted cubic spline, and (iii) categorization of the predictor to two or more levels.

Table 1 Characteristics of patients in full cohort, and derivation and validation subsets

| Characteristics | All N = count (%) | Derivation N = count (%) | Validation N = count (%) | <i>p</i> -Value ^a |
|--|-------------------|--------------------------|--------------------------|------------------------------|
| ICU admission | • | | • | 0.16 ^b |
| Yes | 204 (18.6) | 111 (20.3) | 93 (17.0) | |
| No | 890 (81.4) | 436 (79.7) | 454 (83.0) | |
| Age, years | | | | |
| < 50 | 210 (19.2) | 92 (16.8) | 118 (21.6) | |
| 50 to <60 | 167 (15.3) | 91 (16.6) | 76 (13.9) | |
| 60 to <70 | 245 (22.4) | 135 (24.7) | 110 (20.1) | |
| 70 to <80 | 231 (21.1) | 121 (22.1) | 110 (20.1) | |
| ≥80 | 241 (22.0) | 108 (19.7) | 133 (24.3) | |
| Age, mean (SD) | 65.0 (17.5) | 65.1 (16.5) | 65.0 (18.5) | 0.70 ^c |
| Gender | • | • | • | 0.23 ^b |
| Female | 558 (51.0) | 269 (49.2) | 289 (52.8) | |
| Male | 536 (49.0) | 278 (50.8) | 258 (47.2) | |
| Race | • | ' | ' | 0.52 ^b |
| Caucasian | 278 (25.4) | 131 (24.0) | 147 (26.9) | |
| African American | 785 (71.8) | 404 (73.9) | 381 (69.7) | |
| Hispanic | 3 (0.3) | 1 (0.18) | 2 (0.37) | |
| Asian | 15 (1.4) | 6 (1.10) | 9 (1.65) | |
| Other | 13 (1.2) | 5 (0.91) | 8 (1.46) | |
| Body mass index (BMI), kg/m ² | | | | |
| < 25 | 272 (24.9) | 126 (23.0) | 146 (26.7) | |
| 25 to <30 | 301 (27.5) | 166 (30.4) | 135 (24.7) | |
| 30 to <35 | 226 (20.7) | 124 (22.7) | 102 (18.7) | |
| ≥35 | 295 (27.0) | 131 (24.0) | 164 (30.0) | |
| BMI, mean (SD) | 31.0 (8.4) | 30.5 (7.4) | 31.5 (9.2) | 0.40 ^c |
| Charlson Comorbidity Index (CCI) | • | • | • | 0.36 ^b |
| < 4 | 473 (43.2) | 244 (44.6) | 229 (41.9) | |
| ≥4 | 621 (56.8) | 303 (55.4) | 318 (58.1) | |
| CCI, mean (SD) | 4.3 (3.1) | 4.4 (3.2) | 4.2 (3.0) | 0.47 ^c |
| Systolic blood pressure, mm Hg | 129.6 (20.8) | 130.2 (21.2) | 129.1 (20.3) | 0.42 ^c |
| Missing, count | 2 | 2 | 0 | - |
| Diastolic blood pressure, mm Hg | 71.9 (14.0) | 71.6 (14.2) | 72.1 (13.8) | 0.36 ^c |
| Missing, count | 2 | 2 | 0 | - |
| Heart rate, beats/minute | 87.4 (17.5) | 87.4 (17.9) | 87.3 (17.1) | 0.70 ^c |
| Missing, count | 1 | 1 | 0 | - |
| Respiratory rate, breaths/minute | 20.2 (5.2) | 20.3 (5.9) | 20.1 (4.3) | 0.85 ^c |
| Missing, count | 1 | 1 | 0 | - |

(Continued)

Table 1 (Continued)

| Characteristics | All N = count (%) | Derivation N = count (%) | Validation N = count (%) | <i>p</i> -Value ^a |
|--|-------------------|--------------------------|--------------------------|------------------------------|
| Temperature (°C) | 37.1 (0.7) | 37.2 (0.7) 37.1 (0.7) | | 0.19 ^c |
| Missing, count | 2 | 1 1 | | - |
| White blood cell count, 10 ⁹ /L | 7.85 (4.33) | 7.98 (4.36) | 7.72 (4.30) | 0.18 ^c |
| Missing, count | 77 | 31 | 46 | - |
| Hemoglobin, g/dL | 12.46 (2.15) | 12.41 (2.19) | 12.52 (2.10) | 0.41 ^c |
| Missing, count | 78 | 31 | 47 | - |
| Blood urea nitrogen, mg/dL | 30.41 (26.70) | 31.51 (28.46) | 29.27 (24.73) | 0.43 ^c |
| Missing, count | 80 | 32 | 48 | - |
| Platelets count, 10 ⁹ /L | 216.23 (86.81) | 213.78 (83.26) | 218.77 (90.34) | 0.62 ^c |
| Missing, count | 79 | 31 | 48 | T - |
| SaO ₂ /FiO ₂ | | | | 0.33 ^b |
| < 2 | 101 (9.2) | 54 (9.9) | 47 (8.6) | |
| 2 to <4 | 321 (29.3) | 169 (30.9) | 152 (27.8) | 1 |
| ≥4 | 672 (61.4) | 324 (59.2) | 348 (63.6) |] |
| qSOFA | | | | 0.32 ^b |
| 0 | 551 (50.4) | 276 (50.5) | 275 (50.3) | |
| 1 | 394 (36.0) | 204 (37.3) | 190 (34.7) |] |
| 2 | 132 (12.1) | 57 (10.4) | 75 (13.7) |] |
| 3 | 17 (1.6) | 10 (1.8) | 7 (1.3) | 7 |
| qSOFA, mean (SD) | 0.65 (0.75) | 0.64 (0.74) | 0.66 (0.76) | 0.66 ^c |

Abbreviations: qSOFA, Quick Sequential Organ Failure Assessment; SaO₂/FiO₂, arterial oxygen saturation to fraction of inspired oxygen ratio; SD, standard deviation.

Data presented as N (%) or mean (SD).

For example, the age at admission had a wide range, from 17 to 102 years. Its effect cannot be modeled by a single linear term because it would imply a constant risk for ICU admission at any given age. Distributions that were highly skewed required categorization. Although in some instances a more elaborate transformation such as the restricted cubic spline was more compelling, the selected form was tempered by ease of interpretability and parsimony.

Log transformation was applied to white blood cell count, hemoglobin, blood urea nitrogen and platelets, whereas categories were used for age, body mass index (BMI), CCI, oxygen saturation captured by the arterial oxygen saturation to fraction of inspired oxygen (SaO₂/FiO₂) ratio. Among the constellation of potential predictors, forward selection was applied with a liberal 15% *p*-value for variable entry. Hierarchy was required for multicategory variables. Results from the final model are presented as adjusted odds ratios (ORs) with associated 95% confidence intervals (CIs).

The CCI is a summary measure of several comorbid conditions associated with risk of mortality in hospitalized patients. Since its introduction, the CCI, and various modifications, has been used as a risk factor for outcomes other

than mortality. Depending on the setting and application, one or more threshold points of the CCI have been used.²⁵ For our study we explored modeling the CCI (i) in its original continuous scale, (ii) as a spline function with knot placement at percentiles, and (iii) categorized at two or more thresholds as was done previously.²⁶

The final model was subjected to rigorous evaluation for detecting potential outliers, influential observations and was assessed for overall goodness-of-fit and predictive power. A model's predictive ability was assessed by the c-statistic, and goodness-of-fit by the Hosmer–Lemeshow χ^2 test, Spiegelhalter calibration test based on the Brier score (average squared error). 27,28

Receiver Operating Characteristic Curve

From the prediction model we obtained the patient-specific predicted probability π of ICU admission. The model's discriminative power is measured by the c-statistic. For a pair of patients, one who was admitted to ICU (case) and the other who was not admitted to ICU (control), the c-statistic is the probability that the model estimates a higher probability in the case than in the control. The c-statistic is equivalent to the

^ap-Value for comparison between derivation and validation subsets on nonmissing data.

 $^{^{}b}p$ -Value from χ^{2} test.

^cp-Value from Wilcoxon test.

area under the receiver operating characteristic (ROC) curve. For a cutoff α , the true positive fraction (sensitivity) is the proportion among cases where $\pi \geq \alpha$, and the false positive fraction (1-specificity) is the proportion among controls where $\pi \geq \alpha$. The ROC plots the points (sensitivity, 1-specificity) as the cut-point a varies between 0 and 1. A c-statistic above 0.75 is considered excellent. Submodels with fewer covariates may be compared with respect to their c-statistics. The true positive fraction and false positive fraction were calculated at a cutoff $\alpha=0.22$, which was near the highest point on the ROC relative to the point (0,1) of perfect discrimination.

Scoring Algorithm

A total score was calculated for each patient by summation of weights assigned to the predictor variables in the final derivation model. Only the derivation subset was used for this purpose. The risk of ICU admission was assessed using the total score as a single predictor in a logistic model. Details for scoring and evaluation of the total score as a predictor are supplied in **Supplementary Materials** (available in the online version only).

Use of Validation Subset

The performance of the prediction model was validated in a dataset that had no role in model construction. Several statistics were calculated in the validation subset, including, c-statistic, Brier score, Hosmer–Lemeshow χ^2 statistic, true positive fraction, and false positive fraction at the same cutoff $\alpha = 0.22$ used in the prediction model.²⁹ All statistical analyses were performed in SAS Software, version 9.4, Analytics 15.1 (SAS Institute Inc, Cary, NC).

Results

We identified 1,094 unique patients who tested positive for COVID-19 and were admitted to our hospital between March 9, 2020 and May 16, 2020. In this cohort, 18.6% (204/1094) were admitted to the ICU.

Demographic Characteristics

In this cohort, when Hispanic, Asian and other race are excluded, 74% (785/1,063) identified as African American (AA) and 26% (278/1063) identified as non-Hispanic White (WH). The AA group was younger on average than the WH group (mean age 64.4 ± 16.7 vs. 68.1 ± 19.1 years, p=0.005), and had a higher proportion of female patients compared with the WH group (53.6 vs. 45.0%, p=0.013). Mean BMI was significantly greater in AA compared with WH (31.6 \pm 8.6 vs. 29.5 ± 7.8 , p<0.0002), with a significantly lower proportion of AA having a BMI < 25 compared with WH (22.6 vs. 32.4%, p=0.001).

Correlates of Intensive Care Unit Admission

Patient characteristics were balanced between the derivation and validation subsets (**Table 1**). Using the derivation subset, potential correlates of ICU admission were age, BMI,

qSOFA, CCI, SaO₂/FiO₂, and on the log transformed scale platelets, white blood cell count, and blood urea nitrogen. The final multivariable model derived by forward selection contained the variables in ightharpoonup Table 2. The SaO₂/FiO₂ ratio was a strong predictor of ICU admission driven by the values <2 versus 2 to <4 (OR = 5.60, 95% CI: 2.64, 11.90). Higher qSOFA was associated with higher odds of ICU admission (OR = 2.33, 95% CI: 1.67, 3.26). A two-fold increase in platelet count was associated with an OR = 0.369 (95% CI: 0.227, 0.598). A twofold increase in white blood cell count was associated with an OR = 1.479 (95% CI: 0.994, 2.199). Fig. 1A shows that the model predicted an average probability of 28.0% for ICU admission in the 70 to <80 age group, whereas the <50 and ≥80 age groups had lower average ICU admission probabilities at 13.3 and 15.2%, respectively. There was a gradual increase in predicted probability of ICU admission, with increasing BMI (►Fig. 1B).

Performance Metrics

The prediction model exhibited excellent discrimination: the c-statistic, which is the area under the ROC curve, was 0.798 (95% CI: 0.748, 0.848). The Hosmer–Lemeshow test did not indicate lack of fit (p = 0.549, χ^2 test, 8 DF), and the Spiegelhalter calibration test based on the Brier score was also not significant (p = 0.927, χ^2 test, 1 DF). In the validation subset, the c-statistic was 0.764 (95% CI: 0.706, 0.822) showing excellent comparability with the derivation model's c-statistic (\sim Fig. 2).

A cut-point of 0.22 in the predicted probability $\pi(\mathbf{x})$ for ICU admission was suggested by the ROC curve. Patients were classified as having the event if $\pi(\mathbf{x}) \geq 0.22$, or not having the event if $\pi(\mathbf{x}) < 0.22$. As shown in **Table 3** for the derivation subset, sensitivity was 0.721 (95% CI: 0.637, 0.804) and specificity was 0.763 (95% CI: 0.722, 0.804). In the validation subset, sensitivity was 0.648 (95% CI: 0.550, 0.747) and specificity was 0.762 (95% CI: 0.721, 0.804).

Scoring Algorithm

A simple scoring rule was obtained from the log-ORs of the six predictors in **Table 2**. For each patient the "Total ICU-19" score is the weighted sum of points of values of these predictors. Details are provided in **Supplementary Materials** (available in the online version only). The constructed Total ICU-19 score as a single predictor of ICU admission risk had excellent performance characteristics. In the derivation subset the c-statistic was 0.771 (95% CI: 0.716, 0.825), and in the validation subset the c-statistic was 0.735 (95% CI: 0.674, 0.796).

Discussion

The major findings of this study were that patients positive for COVID-19 with the following risk factors had an increased likelihood to be admitted to the ICU: (1) hypoxia (an SaO_2/FiO_2 of <2), (2) 50 to 80 years of age, (3) morbid obesity (BMI \geq 35), and (4) a qSOFA score \geq 1. Thus, oxygenation status, age, BMI and qSOFA score are significant predictors for ICU

Table 2 Multivariable logistic regression model for intensive care unit admission: odds ratios and 95% confidence intervals

| Effect | Adjusted odds ratio | 95% Confide | ence limits | <i>p</i> -Value | Overall p-Value |
|------------------------------------|---------------------|-------------|-------------|-----------------|-----------------|
| Age, years | | | | | |
| 50 to <60 versus <50 | 1.636 | 0.659 | 4.059 | 0.288 | 0.006 |
| 60 to <70 versus <50 | 1.061 | 0.444 | 2.531 | 0.895 | |
| 70 to <80 versus <50 | 1.514 | 0.628 | 3.647 | 0.355 | |
| ≥ 80 versus < 50 | 0.366 | 0.132 | 1.015 | 0.053 | |
| BMI, kg/m ² | | | | | |
| 25 to <30 versus <25 | 1.565 | 0.760 | 3.223 | 0.224 | 0.155 |
| 30 to <35 versus <25 | 2.108 | 0.981 | 4.530 | 0.056 | |
| ≥35 versus <25 | 2.243 | 1.061 | 4.743 | 0.034 | |
| qSOFA score ^a | 2.330 | 1.666 | 3.260 | <0.0001 | <0.0001 |
| SaO ₂ /FiO ₂ | | | | | |
| < 2 versus 2 to <4 | 5.602 | 2.638 | 11.897 | <0.0001 | < 0.0001 |
| ≥4 versus 2 to <4 | 0.737 | 0.428 | 1.269 | 0.271 | - |
| log_platelets ^b | 0.237 | 0.118 | 0.477 | < 0.0001 | < 0.0001 |
| log_WBC ^b | 1.758 | 0.991 | 3.118 | 0.054 | 0.054 |

Abbreviations: BMI, body mass index; qSOFA, Quick Sequential Organ Failure Assessment; SaO₂/FiO₂, arterial oxygen saturation to fraction of inspired oxygen ratio; WBC, white blood cell count.

^aUnit increase.

^bUnit increase on log scale.

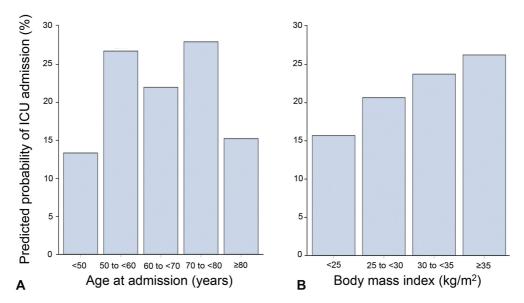


Fig. 1 Predicted probability of ICU admission by age (A) and body mass index (B) at admission. ICU, intensive care unit.

admission and contribute significantly to this predictive model and scoring algorithm.

Overall, 18.6% of patients who tested positive for COVID-19 were admitted to the ICU. This is lower than the reported 32% of patients being admitted to the ICU in a large systematic review of nearly 25,000 patients.³⁰ The time-frame of the study and country are important as the rate of admission to ICU differed between the first and subsequent

waves of the COVID-19 pandemic in 2020. Our sample was selected from the first wave of the COVID-19 pandemic for the period between March and May 2020. The latter report included studies from different countries such as China and the Middle East, and many of these reported studies did not provide data on comorbidities and risk factors for ICU admission.³¹ The rate of admission to ICU in our study did not show significant differences between the derivative and

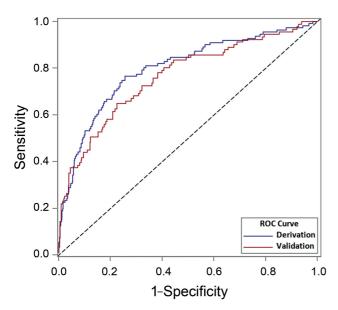


Fig. 2 Receiver operating characteristic (ROC) curves. Derivation curve: c-statistic = 0.798, 95% confidence interval, 0.748 to 0.848. Validation curve: c-statistic = 0.764, 95% confidence interval, 0.706 to 0.822. Diagonal: Reference line.

validation samples. In one report from Germany, the proportion of hospitalized patients requiring ICU treatment decreased by half (from 30% early in 2020 to 14%) by the end of 2020.³² The significant drop in admission to ICU was thought to be due to improvement in the management of patients with COVID-19 prior to requiring ICU transfer.³³

We found hypoxia indicators (SaO₂/FiO₂) to be strongest predictors for admission to ICU, which corroborates with other studies.³⁴ We also found that older age (50 to <80 years) contributed to the increased risk for ICU admission; however, more than 80 years were less likely to be admitted to ICU. This finding is similar to other studies which showed that older patients were less likely to be admitted to ICU.³⁴ The exact cause of inverse relationship between those aged more than 80 years and ICU admission is not fully understood. It is thought to be due to an earlier presentation in older patients and changes to their code status to refuse resuscitation in-line with these patients' end-of-life goals and preferences.

Increased BMI (>35 kg/m²) was an independent predictor of ICU admission in this study. This finding is consistent with earlier reports from Centers for Disease Control and Prevention (CDC) showing that obesity is a risk factor for hospitalization and death, particularly in younger patients (<65 years

old). ³⁵ Obesity was found also to be associated with increasing length of stay in the ICU and higher mortality. ³⁶ However, the risk of mortality was found to be higher than those with mild to moderate obesity (BMI from 29 to 39 kg/m²) compared with morbid obesity (BMI \geq 40 kg/m²) which emphasizes the importance of BMI as predictor ICU admission in the proposed model. ²¹

We observed that the combination of age, BMI, oxygenation, and severity of illness (i.e., qSOFA score) yielded excellent predictive performance and provided a simple and reliable diagnostic tool for predicting ICU admission among patients with COVID-19. The accuracy of the predictive model was comparable when assessed in two independent samples with high levels of concordance of statistics. Recent studies found that physiologic variables (such as heart rate, pulse oximetry, respiratory rate, and systolic blood pressure) and symptoms predicted admission to ICU.37 Likewise, we and others found that a limited number of characteristics (age, BMI, and comorbidities) were sufficient to predict ICU admission in patients with COVID-19 and metrics of comorbidities such low oxygenation and qSOFA were the strongest predictors.³⁸ As reported by other studies, patients with lower oxygen saturation were more likely to be admitted to ICU as an indication of developing acute respiratory distress syndrome from COVID-19 pneumonia.³⁸ In contrast to earlier studies, we decided to use the ratio SaO₂/FiO₂ which accurately assesses hypoxia by accounting for the level of oxygen saturation adjusted to the level of oxygen supplementation.

Our study has some limitations such as the number of patients included in this study, which was limited to one hospital system. Additionally, we focused on the first wave to avoid confounding those who received and did not receive the COVID-19 vaccination for which additional patient data could change these results; however, given the number of therapeutic options and vaccines currently available, the presence of herd immunity, different SARS-CoV-2 variants, etc., the generalizability of the results with the current state of COVID-19 may be diminished. A larger and multinational sample would be needed to address the generalizability of our findings. We have performed the study on the first surge sample during the peak of the pandemic; however, due to the limited ICU capacity and number of beds available this may have affected the threshold for ICU admission and hence the predictive model. However, validating the data internally by separate samples with similar demographics helps in ensuring the accuracy of the model. Furthermore, the changing

Table 3 Sensitivity and specificity: derivation and validation^a

| | Derivation | | Validation | |
|---------------------------|------------|-----------------------|------------|-----------------------|
| Statistic | Estimate | 95% Confidence limits | Estimate | 95% Confidence limits |
| Sensitivity | 0.7207 | 0.6373 to 0.8042 | 0.6484 | 0.5502 to 0.7465 |
| Specificity | 0.7630 | 0.7215 to 0.8044 | 0.7623 | 0.7209 to 0.8036 |
| Positive predictive value | 0.4545 | 0.3810 to 0.5281 | 0.3782 | 0.3021 to 0.4543 |
| Negative predictive value | 0.9088 | 0.8782 to 0.9394 | 0.9067 | 0.8759 to 0.9375 |

^aCalculations on a predicted probability of 22% for intensive care unit admission.

criteria for SARS-CoV-2 testing associated with the course of the pandemic likely also affects the results.

Conclusion

In patients with COVID-19 the combination of the dataset on age, BMI, oxygenation, and severity of illness can predict admission to ICU. The role of this model, using simple demographic and physiological data from patients recorded upon admission, in predicting clinician decision-making and patients outcomes merit additional investigation and validation.

Conflict of Interest

None declared.

References

- 1 Hoogenboom WS, Pham A, Anand H, et al. Clinical characteristics of the first and second COVID-19 waves in the Bronx, New York: a retrospective cohort study. Lancet Reg Health Am 2021;3:100041
- 2 Mulhem E, Oleszkowicz A, Lick D. 3219 hospitalised patients with COVID-19 in Southeast Michigan: a retrospective case cohort study. BMJ Open 2021;11(04):e042042
- 3 Ughi N, Bernasconi DP, Del Gaudio F, et al; Niguarda COVID Working Group. Trends in all-cause mortality of hospitalized patients due to SARS-CoV-2 infection from a monocentric cohort in Milan (Lombardy, Italy). J Public Health (Berl) 2022;30(08): 1985–1993
- 4 Zakaria A, Piper M, Douda L, et al. Corrigendum to "Determinants of all-cause in-hospital mortality among patients who presented with COVID-19 to a community teaching hospital in Michigan" [Heliyon 7 (12) (December 2021), Article e08566]. Heliyon 2022;8 (02):e08760
- 5 Rodriguez-Morales AJ, Cardona-Ospina JA, Gutiérrez-Ocampo E, et al; Latin American Network of Coronavirus Disease 2019-COVID-19 Research (LANCOVID-19). Electronic address: https://www.lancovid.orgClinical, laboratory and imaging features of COVID-19: a systematic review and meta-analysis. Travel Med Infect Dis 2020;34:101623
- 6 Armstrong RA, Kane AD, Kursumovic E, Oglesby FC, Cook TM. Mortality in patients admitted to intensive care with COVID-19: an updated systematic review and meta-analysis of observational studies. Anaesthesia 2021;76(04):537–548
- 7 Richards-Belle A, Orzechowska I, Gould DW, et al; ICNARC COVID-19 Team. COVID-19 in critical care: epidemiology of the first epidemic wave across England, Wales and Northern Ireland. Intensive Care Med 2020;46(11):2035–2047
- 8 Zeiser FA, Donida B, da Costa CA, et al. First and second COVID-19 waves in Brazil: a cross-sectional study of patients' characteristics related to hospitalization and in-hospital mortality. Lancet Reg Health Am 2022;6:100107
- 9 Bravata DM, Perkins AJ, Myers LJ, et al. Association of intensive care unit patient load and demand with mortality rates in US Department of Veterans Affairs Hospitals during the covid-19 pandemic. JAMA Netw Open 2021;4(01):e2034266
- 10 Tan E, Song J, Deane AM, Plummer MP. Global impact of coronavirus disease 2019 infection requiring admission to the ICU: a systematic review and meta-analysis. Chest 2021;159(02):524–536
- 11 Abdelghany TM, Ganash M, Bakri MM, Qanash H, Al-Rajhi AMH, Elhussieny NI. SARS-CoV-2, the other face to SARS-CoV and MERS-CoV: future predictions. Biomed J 2021;44(01):86–93
- 12 Webb SA, Pettilä V, Seppelt I, et al; ANZIC Influenza Investigators. Critical care services and 2009 H1N1 influenza in Australia and New Zealand. N Engl J Med 2009;361(20):1925–1934
- 13 Nguyen-Van-Tam JS, Openshaw PJ, Hashim A, et al; Influenza Clinical Information Network (FLU-CIN) Risk factors for hospitalisation and

- poor outcome with pandemic A/H1N1 influenza: United Kingdom first wave (May-September 2009). Thorax 2010;65(07):645-651
- 14 Chalfin DB, Trzeciak S, Likourezos A, Baumann BM, Dellinger RPDELAY-ED study group. Impact of delayed transfer of critically ill patients from the emergency department to the intensive care unit. Crit Care Med 2007;35(06):1477–1483
- 15 Olivas-Martínez A, Cárdenas-Fragoso JL, Jiménez JV, et al. Inhospital mortality from severe COVID-19 in a tertiary care center in Mexico City; causes of death, risk factors and the impact of hospital saturation. PLoS One 2021;16(02):e0245772
- 16 Gude-Sampedro F, Fernández-Merino C, Ferreiro L, et al. Development and validation of a prognostic model based on comorbidities to predict COVID-19 severity: a population-based study. Int J Epidemiol 2021;50(01):64–74
- 17 Guo J, Zhou B, Zhu M, et al. CURB-65 may serve as a useful prognostic marker in COVID-19 patients within Wuhan, China: a retrospective cohort study. Epidemiol Infect 2020;148:e241
- 18 Haimovich AD, Ravindra NG, Stoytchev S, et al. Development and validation of the quick COVID-19 Severity Index: a prognostic tool for early clinical decompensation. Ann Emerg Med 2020;76(04): 442–453
- 19 Rodriguez-Nava G, Yanez-Bello MA, Trelles-Garcia DP, et al. Clinical characteristics and risk factors for death of hospitalized patients with COVID-19 in a community hospital: a retrospective cohort study. Mayo Clin Proc Innov Qual Outcomes 2021;5(01): 1–10
- 20 Rodriguez-Nava G, Yanez-Bello MA, Trelles-Garcia DP, Chung CW, Friedman HJ, Hines DW. Performance of the quick COVID-19 severity index and the Brescia-COVID respiratory severity scale in hospitalized patients with COVID-19 in a community hospital setting. Int J Infect Dis 2021;102:571–576
- 21 Kooistra EJ, Brinkman S, van der Voort PHJ, et al. Body mass index and mortality in coronavirus disease 2019 and other diseases: a cohort study in 35,506 ICU patients. Crit Care Med 2022;50(01): e1–e10
- 22 Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40(05):373–383
- 23 Seymour CW, Liu VX, Iwashyna TJ, et al. Assessment of Clinical Criteria for Sepsis: For the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 2016;315 (08):762-774
- 24 Hastie TJ, Tibshirani RJ, Friedman JH. The Elements of Statistical Learning: Data Mining, Inference, and Prediction. New York, NY: Springer-Verlag;; 2001
- 25 Christensen DM, Strange JE, Gislason G, et al. Charlson Comorbidity Index Score and risk of severe outcome and death in Danish COVID-19 patients. J Gen Intern Med 2020;35(09):2801–2803
- 26 Gardiner JC, Reed PL, Bonner JD, Haggerty DK, Hale DG. Incidence of hospital-acquired pressure ulcers - a population-based cohort study. Int Wound J 2016;13(05):809–820
- 27 Hosmer DW, Hosmer T, Le Cessie S, Lemeshow S. A comparison of goodness-of-fit tests for the logistic regression model. Stat Med 1997;16(09):965–980
- 28 Spiegelhalter DJ. Probabilistic prediction in patient management and clinical trials. Stat Med 1986;5(05):421–433
- 29 Steyerberg EW, Nieboer D, Debray TPA, van Houwelingen HC. Assessment of heterogeneity in an individual participant data meta-analysis of prediction models: an overview and illustration. Stat Med 2019;38(22):4290–4309
- 30 Abate SM, Ahmed Ali S, Mantfardo B, Basu B. Rate of Intensive Care Unit admission and outcomes among patients with coronavirus: a systematic review and meta-analysis. PLoS ONE 2020;15(07): e0235653
- 31 Zhang M, Hu P, Xu X, et al. A look back at the first wave of COVID-19 in China: a systematic review and meta-analysis of mortality and health care resource use among severe or critical patients. PLoS ONE 2022;17(03):e0265117

- 32 Karagiannidis C, Windisch W, McAuley DF, Welte T, Busse R. Major differences in ICU admissions during the first and second COVID-19 wave in Germany. Lancet Respir Med 2021;9(05):e47–e48
- 33 Doidge JC, Gould DW, Ferrando-Vivas P, et al. Trends in intensive care for patients with COVID-19 in England, Wales, and Northern Ireland. Am J Respir Crit Care Med 2021;203(05):565–574
- 34 Vanhems P, Gustin MP, Elias C, et al; COVID-Outcomes-HCL Consortium. Factors associated with admission to intensive care units in COVID-19 patients in Lyon-France. PLoS One 2021; 16(01):e0243709
- 35 Kompaniyets L, Goodman AB, Belay B, et al. Body mass index and risk for COVID-19-related hospitalization, intensive care unit admission, invasive mechanical ventilation, and death United

- States, March-December 2020. MMWR Morb Mortal Wkly Rep 2021;70(10):355–361
- 36 Sjögren L, Stenberg E, Thuccani M, et al. Impact of obesity on intensive care outcomes in patients with COVID-19 in Sweden-a cohort study. PLoS ONE 2021;16(10):e0257891
- 37 Fernandes M, Mendes R, Vieira SM, et al. Predicting intensive care unit admission among patients presenting to the emergency department using machine learning and natural language processing. PLoS ONE 2020;15(03):e0229331
- 38 Jimenez-Solem E, Petersen TS, Hansen C, et al. Developing and validating COVID-19 adverse outcome risk prediction models from a bi-national European cohort of 5594 patients. Sci Rep 2021;11(01):3246