Original Article

# Development and validation of a survival prediction model for patients received mechanical ventilation in the intensive care unit: a large sample size cohort from the MIMIC database

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**Background:** Mechanical ventilation remains one of the primary management measures for critically ill patients in intensive care units (ICUs). However, previous studies on the prognosis prediction of ICU patients received mechanical ventilation were limited. This study was to develop and validate a nomogram for predicting short- and long-term survival among patients who received mechanical ventilation in the ICU.

**Methods:** This was a retrospective cohort study with a 3-year follow-up. Demographic, laboratory, clinical data of 16,775 participants aged ≥18 years who received mechanical ventilation in the ICU were extracted from the Medical Information Mart for Intensive Care III (MIMIC-III) database. The outcomes of this study were 1-month, 3-month, 1-year, and 3-year survival. All eligible patients were randomly classified into the training and testing groups with a ratio of 7:3. A multivariate Cox regression in the training group was used to explore the predictors and develop the predictive nomogram. Internal and subgroup validations were performed, and the C-index was calculated to estimate the predictive performance of the nomogram. The time-dependent receiver operating characteristic curves were drawn, and corresponding areas under the curve (AUC) were calculated.

**Results:** Totally 6,291 patients died during the follow-up duration. Age, gender, ethnicity, ICU type, comorbidity, days of mechanical ventilation, white blood cell count, blood urea nitrogen, the fraction of inspiration $O_2$, Sequential Organ Failure Assessment scores, and the Glasgow coma score were predictors of the survival of ICU patients who received mechanical ventilation ($P<0.05$). The C-index of the nomogram was 0.819 and was validated in the testing group at 0.816. The AUCs for the prognostic nomogram for 1-month, 3-month, 1-year, and 3-year survival were 0.889, 0.892, 0.882, and 0.866, respectively.

**Conclusions:** This nomogram showed good predictive performance for short- and long-term survival in ICU patients treated with mechanical ventilation, which may be a useful tool for clinicians to assess the prognosis of patients and to adjust treatment strategies in time.

**Keywords:** Mechanical ventilation; MIMIC-III database; survival; intensive care unit (ICU); nomogram

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## Introduction

Mechanical ventilation remains one of the primary management measures for many critically ill patients in intensive care units (ICUs), from scheduled surgical operations to acute organ failure (1). It has been reported that the rate of mechanical ventilation for ICU patients varies from 32.9% to 70% (2-4). However, mechanical ventilation has been associated with high short- and long-term mortality and decreased quality of life for patients (5-7). Therefore, it is important for physicians to identify patients requiring mechanical ventilation who have poor prognoses to improve their quality of life.

Many factors have been identified that affect the prognosis of patients receiving mechanical ventilation. Age and sepsis have been shown to be independently associated with increased mortality in patients needing mechanical ventilation in ICU (8-10). Lee *et al.* evaluated a cohort of 311 patients who received prolonged acute mechanical ventilation. Their results indicated that a body mass index ≤21 kg/m$^2$ was an independent predictor of decreased survival (11). Several studies have focused on single factors influencing the prognosis of patients who have received mechanical ventilation, and various predictive models have been built to assess patient survival. A nomogram is a graphical tool integrating multiple factors that could be adopted to predict death risk for patients. It is a more intuitive and convenient way to explain this risk to patients or family members in doctor-patient communications (8). It has been increasingly used in clinical research to predict prognosis in various diseases, such as acute pancreatitis and colorectal cancer (12,13). A previous study based on 736 participants proposed a model to predict mortality in patients receiving mechanical ventilation and incorporated age, platelet count, the requirement for vasopressors and hemodialysis, and non-trauma admission (14). However, the authors only assessed mortality within 1 year based on small sample and lack of validity evidence, and did not investigate the performance of the prediction model validated in different subgroups based on the reasons for mechanical ventilation, which may have weakened the evidence from the study. An improved prediction model for these patients should be developed.

Herein, we conducted a nomogram to predict short- and long-term survival (1-month, 3-month, 1-year, and 3-year survival) in patients receiving mechanical ventilation using 16,775 participants from the Medical Information Mart for Intensive Care III (MIMIC-III) database. Furthermore, we conducted the internal and subgroup validations based on the reasons for mechanical ventilation (shock, sepsis, trauma, and other causes) to estimate the predictive performance of the nomogram. We present the following article in accordance with the TRIPOD reporting checklist (available at https://apm.amegroups.com/article/view/10.21037/apm-22-646/rc).

## Methods

### *Study design and population*

We conducted the development and validation of a prognosis predicting model using patients from the MIMIC-III, an openly available clinical database (15). The MIMIC-III database contains comprehensive and high-quality data of well-defined and characterized patients admitted to ICUs at the Beth Israel Deaconess Medical Center between 2001 and 2012. Patients aged ≥18 years old who received mechanical ventilation were included in this study. We analyzed only the last ICU stay for patients admitted to the ICU more than once. In total, 16,775 eligible patients were included in the study. The patients were randomly divided into training (n=11,742) and testing (n=5,033) groups according to a 7:3 ratio using a completely random sampling method. An ethics committee or institutional review board approval was exempted because the data were accessed from the MIMIC, a publicly available database. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

### *Data extraction*

The patient information was collected within 24 h of admission to the ICU. The demographic data of the studied population included age, gender, and ethnicity. Clinical characteristics included ICU type [intensive care unit (ICU), coronary care unit (CCU), cardiac surgery recovery unit (CSRU), medical intensive care unit (MICU), surgical intensive care unit (SICU), and trauma surgical intensive care unit (TSICU)], days of mechanical ventilation, ventilator-associated pneumonia, chronic pulmonary disease (CPD), heart failure (HF), hypertension, sepsis, shock, trauma, atrial fibrillation, liver cirrhosis, diabetes mellitus (DM), respiratory failure, malignant tumor, renal failure, and coronary heart disease (CHD). Laboratory indicators included white blood cell (WBC) count, blood urea nitrogen (BUN), and the fraction of inspiration $O_2$ ($FIO_2$). Indexes of disease severity were estimated by the Sequential Organ Failure Assessment (SOFA) and Glasgow Coma

 

Scale (GCS) scores. The causes of mechanical ventilation were recorded, including sepsis, shock, trauma, and others.

### *Outcome variables*

The primary outcomes of this study were 1-month, 3-month, 1-year, and 3-year survival. The follow-up duration of this study was 3 years. The survival status of patients was recorded at 1-month, 3-month, 1-year, and 3-year after ICU withdrawal. The follow-up was terminated when death occurred during the follow-up period.

### *Missing values and outliers*

There were 47 (0.27%) missing values in WBC, 272 (1.62%) in $FIO_2$, 113 (0.67%) in GCS score, and 4 (0.02%) in SOFA score. The missing values were imputed by multiple imputations. For the outliers in this study, multiple imputations were also applied. There were 493 (2.94%) outliers in WBC, imputed by the median ± 3* interquartile range (9.4±3*5.1). BUN had 740 (4.41%) outliers, filled into the median ± 3* interquartile range (19±3*18). Additionally, a sensitivity analysis was performed on the data set before and after imputation. The results of the sensitivity analysis are presented in Table S1.

### *Statistical analysis*

The statistical analyses were performed using R programmer v.4.0.3 (Institute for Statistics and Mathematics, Vienna, Austria). Measurement data are represented by the mean ± standard deviation (mean ± SD) or median with interquartile spacing [M (Q1, Q3)], and the independent samples *t*-test or Mann-Whitney U test was used for intergroup comparisons. Count data are described by the number of cases or constituent ratio [N (%)], and the $\chi^2$ test or Fisher's exact test was adopted for intergroup comparisons.

Univariate and multivariate Cox regression analyses were used to explore the predictors of survival and develop the predictive model for patients' survival using mechanical ventilation therapy. The hazard ratio (HR) was calculated, represented by a 95% confidence interval (CI). The time-dependent receiver operating characteristic (ROC) curves and C-index were adopted to assess the predictive capacity of the nomogram. The areas under the ROC curve (AUC), sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated by MedCalc software (MedCalc Software Ltd). The threshold value of AUC was over 0.8, indicating the nomogram had well performance. To further verify the stability and performance of the nomogram, we divided patients into different subgroups based on the reasons for mechanical ventilation, including shock, sepsis, trauma, and other causes. Two-sided P<0.05 was considered statistically significant for all analyses.

## Results

### *Subject characteristics*

A total of 16,775 participants were initially obtained from the MIMIC database, divided into training (n=11,742) and testing (n=5,033) sets (*Figure 1*). In the training set, the average age was 64.04 (47.22, 80.86) years, with 4,785 (40.75%) females and 6,927 (59.25%) males. There were 2,493 (21.23%) patients with specific reasons for mechanical ventilation and 9,749 (78.77%) individuals with other causes. Further detailed analyses of other specific causes for mechanical ventilation found that the main reasons were sepsis (579, 4.07%), shock (616, 4.33%), trauma (240, 1.69%), sepsis + shock (989, 6.95%), sepsis + trauma (17, 0.12%), shock + trauma (41, 0.29%), and sepsis + shock + trauma (11, 0.08%) (*Figure 2*). Of the 11,742 patients, 7340 (62.51%) survived, and 4402 (37.49%) died, with a median survival time of 1,095.00 (52.00, 1,095.00) days. In the testing set, the average age was 64.38 (47.75, 81.01) years, with 2,023 (40.19%) females and 3,010 (59.81%) males. Among the 5,033 patients, 3,144 (62.47%) survived and 1,889 (37.53%) died. There were no differences between the two sets in age, gender, ethnicity, ICU type, median days of mechanical ventilation, comorbidity, reasons for mechanical ventilation, SOFA score, GCS score, and laboratory values (*Table 1*).

### *Predictor selection and nomogram construction*

Age, gender, ethnicity, ICU type, comorbidity (HF, sepsis, CPD, hypertension, liver cirrhosis, DM, respiratory failure, malignant tumor, renal failure, and CHD), days of mechanical ventilation, WBC, BUN, $FIO_2$, SOFA score, and GCS score were identified as significant predictors in the univariate Cox regression analysis for the training set (P<0.05) (*Table 2*). Furthermore, in the multivariate Cox stepwise regression, age, gender, ICU type, comorbidity (sepsis, CPD, hypertension, liver cirrhosis, respiratory

 

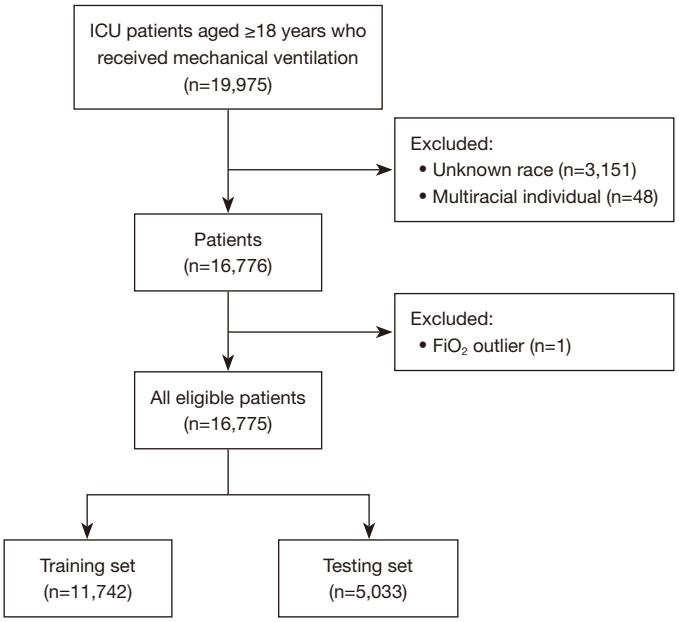


**Figure 1** Data filtering flowchart for patients who received mechanical ventilation. ICU, intensive care unit; $FIO_2$, fraction of inspiration $O_2$.

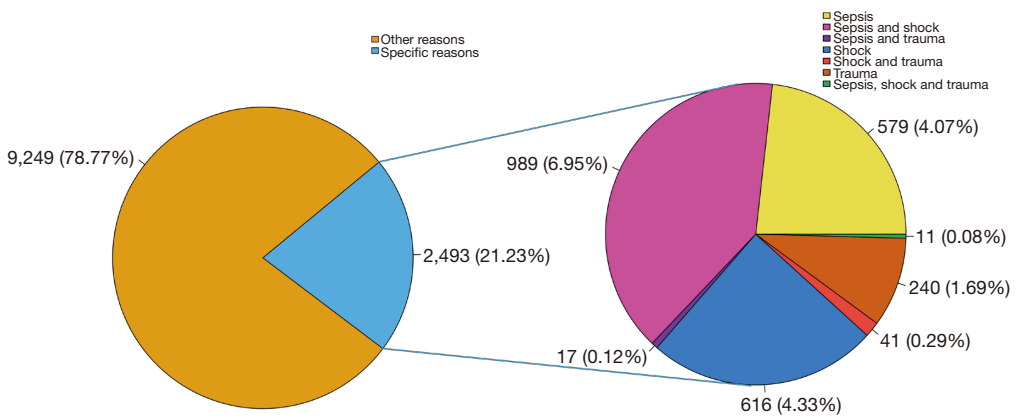


**Figure 2** Pie chart of reasons for mechanical ventilation in the training set.

failure, malignant tumor, and CHD), days of mechanical ventilation, WBC, BUN, $FIO_2$, SOFA score, and GCS score were identified as significantly associated with the survival of ICU patients who received mechanical ventilation ($P<0.05$) (*Table 3*). Based on the predictors, the nomogram for predicting individuals' short- and long-term survival was established (*Figure 3*).

### *Predictive performance of the nomogram*

In the training set, the AUCs of the nomogram for 1-month, 3-month, 1-year, and 3-year survival prediction were 0.889 (95% CI: 0.882–0.896), 0.892 (95% CI: 0.886–0.898), 0.882 (95% CI: 0.876–0.888), and 0.866 (95% CI: 0.859–0.872), respectively. In the testing set, the AUCs of the nomogram for 1-month, 3-month, 1-year, and 3-year survival prediction were 0.885 (95% CI: 0.875–0.896), 0.885 (95% CI: 0.875–0.895), 0.878 (95% CI: 0.868–0.888), and 0.866 (95% CI: 0.844–0.864), respectively. The nomogram had a good predictive ability, with a C-index of 0.819 (95% CI: 0.813–0.825) and was validated in the testing set by a C-index of 0.816 (95% CI: 0.808–0.824) (*Table 4* and *Figure 4*).

**Table 1** Characteristics of studied patients who received mechanical ventilation

| Variables | Total (n=16,775) | Training (n=11,742) | Testing (n=5,033) | Statistics | P |
|---|---|---|---|---|---|
| Age (years), mean ± SD | 64.14±16.76 | 64.04±16.82 | 64.38±16.63 | T=1.18[a] | 0.237 |
| Gender, n (%) | | | | $\chi^2$=0.452[b] | 0.501 |
| Female | 6,808 (40.58) | 4,785 (40.75) | 2,023 (40.19) | | |
| Male | 9,967 (59.42) | 6,957 (59.25) | 3,010 (59.81) | | |
| Ethnicity, n (%) | | | | $\chi^2$=1.039[b] | 0.904 |
| Asian | 443 (2.64) | 304 (2.59) | 139 (2.76) | | |
| Black | 1,227 (7.31) | 855 (7.28) | 372 (7.39) | | |
| Hispanic or Latino | 596 (3.55) | 415 (3.53) | 181 (3.60) | | |
| Other | 501 (2.99) | 344 (2.93) | 157 (3.12) | | |
| White | 14,008 (83.51) | 9,824 (83.67) | 4,184 (83.13) | | |
| ICU type, n (%) | | | | $\chi^2$=1.181[b] | 0.881 |
| CCU | 1,504 (8.97) | 1,070 (9.11) | 434 (8.62) | | |
| CSRU | 5,276 (31.45) | 3,679 (31.33) | 1,597 (31.73) | | |
| MICU | 4,918 (29.32) | 3,438 (29.28) | 1,480 (29.41) | | |
| SICU | 2,753 (16.41) | 1,931 (16.45) | 822 (16.33) | | |
| TSICU | 2,324 (13.85) | 1,624 (13.83) | 700 (13.91) | | |
| Days of mechanical ventilation | 2.00 (1.00, 5.00) | 2.00 (1.00, 5.00) | 2.00 (1.00, 5.00) | Z=1.201[c] | 0.230 |
| $FIO_2$ (%), M (Q1, Q3) | 50.00 (40.00, 50.00) | 50.00 (40.00, 50.00) | 50.00 (40.00, 50.00) | Z=1.038[c] | 0.299 |
| HF, n (%) | | | | $\chi^2$=0.003[b] | 0.957 |
| No | 11,997 (71.52) | 8,399 (71.53) | 3,598 (71.49) | | |
| Yes | 4,778 (28.48) | 3,343 (28.47) | 1,435 (28.51) | | |
| CPD, n (%) | | | | $\chi^2$=0.573[b] | 0.449 |
| No | 14,338 (85.47) | 10,052 (85.61) | 4,286 (85.16) | | |
| Yes | 2,437 (14.53) | 1,690 (14.39) | 747 (14.84) | | |
| Sepsis, n (%) | | | | $\chi^2$=0.141[b] | 0.708 |
| No | 14,494 (86.40) | 10,153 (86.47) | 4,341 (86.25) | | |
| Yes | 2,281 (13.60) | 1,589 (13.53) | 692 (13.75) | | |
| Hypertension, n (%) | | | | $\chi^2$=0.020[b] | 0.886 |
| No | 9,195 (54.81) | 6,432 (54.78) | 2,763 (54.90) | | |
| Yes | 7,580 (45.19) | 5,310 (45.22) | 2,270 (45.10) | | |
| Shock, n (%) | | | | $\chi^2$=0.013[b] | 0.908 |
| No | 14,424 (85.99) | 10,094 (85.96) | 4,330 (86.03) | | |
| Yes | 2,351 (14.01) | 1,648 (14.04) | 703 (13.97) | | |

**Table 1** *(continued)*

**Table 1** *(continued)*

| Variables | Total (n=16,775) | Training (n=11,742) | Testing (n=5,033) | Statistics | P |
|---|---|---|---|---|---|
| Trauma, n (%) | | | | $\chi^2$=0.194[b] | 0.66 |
| No | 16,348 (97.45) | 11,439 (97.42) | 4,909 (97.54) | | |
| Yes | 427 (2.55) | 303 (2.58) | 124 (2.46) | | |
| Atrial fibrillation, n (%) | | | | $\chi^2$=0.130[b] | 0.719 |
| No | 11,808 (70.39) | 8,275 (70.47) | 3,533 (70.20) | | |
| Yes | 4,967 (29.61) | 3,467 (29.53) | 1,500 (29.80) | | |
| Liver cirrhosis, n (%) | | | | $\chi^2$=1.749[b] | 0.186 |
| No | 15,945 (95.05) | 11,144 (94.91) | 4,801 (95.39) | | |
| Yes | 830 (4.95) | 598 (5.09) | 232 (4.61) | | |
| DM, n (%) | | | | $\chi^2$=0.078[b] | 0.781 |
| No | 13,301 (79.29) | 9,317 (79.35) | 3,984 (79.16) | | |
| Yes | 3,474 (20.71) | 2,425 (20.65) | 1,049 (20.84) | | |
| Respiratory failure, n (%) | | | | $\chi^2$=0.032[b] | 0.858 |
| No | 11,765 (70.13) | 8,240 (70.18) | 3,525 (70.04) | | |
| Yes | 5,010 (29.87) | 3,502 (29.82) | 1,508 (29.96) | | |
| Malignant tumor, n (%) | | | | $\chi^2$=0.001[b] | 0.977 |
| No | 13,383 (79.78) | 9,367 (79.77) | 4,016 (79.79) | | |
| Yes | 3,392 (20.22) | 2,375 (20.23) | 1,017 (20.21) | | |
| Renal failure, n (%) | | | | $\chi^2$=0.084[b] | 0.772 |
| No | 12,928 (77.07) | 9,042 (77.01) | 3,886 (77.21) | | |
| Yes | 3,847 (22.93) | 2,700 (22.99) | 1,147 (22.79) | | |
| CHD, n (%) | | | | $\chi^2$=0.000[b] | 0.998 |
| No | 10,972 (65.41) | 7,680 (65.41) | 3,292 (65.41) | | |
| Yes | 5,803 (34.59) | 4,062 (34.59) | 1,741 (34.59) | | |
| WBC (k/mL), M (Q1, Q3) | 9.40 (7.20, 12.30) | 9.40 (7.20, 12.30) | 9.40 (7.30, 12.30) | Z=−0.012[c] | 0.990 |
| BUN (mg/dL), M (Q1, Q3) | 19.00 (13.00, 31.00) | 20.00 (13.00, 31.00) | 19.00 (13.00, 30.00) | Z=−0.720[c] | 0.472 |
| SOFA score, M (Q1, Q3) | 6.00 (4.00, 8.00) | 6.00 (4.00, 8.00) | 6.00 (4.00, 8.00) | Z=−0.228[c] | 0.819 |
| GCS score, M (Q1, Q3) | 9.00 (5.00, 14.00) | 9.00 (5.00, 14.00) | 9.00 (5.00, 14.00) | Z=0.880[c] | 0.379 |
| Survival time (days), M (Q1, Q3) | 1,095.00 (53.00, 1095.00) | 1,095.00 (52.00, 1095.00) | 1,095.00 (56.00, 1095.00) | Z=−0.063[c] | 0.950 |
| Survival status, n (%) | | | | $\chi^2$=0.003[b] | 0.958 |
| Survival | 10,484 (62.50) | 7,340 (62.51) | 3,144 (62.47) | | |
| Death | 6291 (37.50) | 4,402 (37.49) | 1,889 (37.53) | | |

[a], using *t*-test; [b], using Chi-square; [c], using Mann-Whitney. ICU, intensive care unit; CCU, coronary care unit; CSRU, cardiac surgery recovery unit; MICU, medical intensive care unit; SICU, surgical intensive care unit; TSICU, trauma surgical intensive care unit; $FIO_2$, fraction of inspiration $O_2$; HF, heart failure; CPD, chronic pulmonary disease; DM, diabetes mellitus; CHD, coronary heart disease; WBC, white blood cell; BUN, blood urea nitrogen; GCS, Glasgow Coma Scale; SOFA, Sequential Organ Failure Assessment.

**Table 2** Results of univariate Cox regression analysis

| Variables | HR (95% CI) | P |
|---|---|---|
| Age | 1.035 (1.033–1.037) | <0.001 |
| Gender | | |
| Female | Ref | |
| Male | 0.787 (0.741–0.835) | <0.001 |
| Ethnicity | | |
| Asian | Ref | |
| Black | 1.107 (0.894–1.369) | 0.351 |
| Hispanic/Latino | 0.634 (0.486–0.826) | <0.001 |
| Other | 0.721 (0.550–0.946) | 0.018 |
| White | 1.013 (0.839–1.222) | 0.894 |
| ICU type | | |
| MICU | Ref | |
| CSRU | 0.146 (0.132–0.162) | <0.001 |
| CCU | 0.850 (0.773–0.933) | <0.001 |
| SICU | 0.705 (0.651–0.763) | <0.001 |
| TSICU | 0.456 (0.414–0.502) | <0.001 |
| Days of mechanical ventilation | 1.030 (1.027–1.033) | <0.001 |
| HF | | |
| No | Ref | |
| Yes | 1.929 (1.816–2.048) | <0.001 |
| CPD | | |
| No | Ref | |
| Yes | 1.571 (1.458–1.693) | <0.001 |
| Hypertension | | |
| No | Ref | |
| Yes | 0.682 (0.642–0.725) | <0.001 |
| Sepsis | | |
| No | Ref | |
| Yes | 2.873(2.681–3.078) | <0.001 |
| Atrial fibrillation | | |
| No | Ref | |
| Yes | 1.341 (1.260–1.427) | <0.001 |
| Liver cirrhosis | | |
| No | Ref | |
| Yes | 1.898 (1.700–2.120) | <0.001 |
| DM | | |
| No | Ref | |
| Yes | 1.033 (0.961–1.111) | 0.374 |
| Respiratory failure | | |
| No | Ref | |
| Yes | 3.017 (2.843–3.202) | <0.001 |
| Malignant tumor | | |
| No | Ref | |
| Yes | 1.793 (1.680–1.914) | <0.001 |
| Renal failure | | |
| No | Ref | |
| Yes | 2.676 (2.517–2.844) | <0.001 |
| CHD | | |
| No | Ref | |
| Yes | 0.614 (0.574–0.657) | <0.001 |
| Laboratory indicators | | |
| $FIO_2$ (%) | 1.017 (1.016–1.019) | <0.001 |
| WBC (k/μL) | 1.125 (1.118–1.131) | <0.001 |
| BUN (mg/dL) | 1.036 (1.035–1.038) | <0.001 |
| GCS score | 0.973 (0.967–0.979) | <0.001 |
| SOFA score | 1.144 (1.134–1.154) | <0.001 |

HR, hazard ratio; CI, confidence interval; ICU, intensive care unit; CCU, coronary care unit; CSRU, cardiac surgery recovery unit; MICU, medical intensive care unit; SICU, surgical intensive care unit; TSICU, trauma surgical intensive care unit; HF, heart failure; CPD, chronic pulmonary disease; DM, diabetes mellitus; CHD, coronary heart disease; $FIO_2$, fraction of inspiration $O_2$; WBC, white blood cell; BUN, blood urea nitrogen; GCS, Glasgow Coma Scale; SOFA, sequential organ failure assessment.

### *Validation of the predictive performance of the nomogram in different subgroups based on reasons for mechanical ventilation*

For the subgroup of patients who received mechanical ventilation due to shock, the AUCs of the nomogram for 1-month, 3-month, 1-year, and 3-year survival prediction were 0.844 (95% CI: 0.829–0.860), 0.852 (95% CI: 0.837–0.868), 0.848 (95% CI: 0.832–0.863), and 0.844 (95% CI: 0.828–0.860), respectively. For the subgroup

**Table 3** Results of multivariate Cox regression analysis

| Variables | HR (95% CI) | P |
|---|---|---|
| Age | 1.029 (1.027–1.031) | <0.001 |
| Gender | | |
| Female | Ref | |
| Male | 0.928(0.872–0.986) | <0.001 |
| Ethnicity | | |
| Asian | Ref | |
| Black | 1.032 (0.833–1.279) | 0.771 |
| Hispanic/Latino | 0.901 (0.689–1.177) | 0.443 |
| Other | 0.953 (0.726–1.251) | 0.728 |
| White | 1.158 (0.959–1.398) | 0.129 |
| ICU type | | |
| MICU | Ref | |
| CSRU | 0.187 (0.166–0.211) | <0.001 |
| CCU | 0.812 (0.735–0.897) | <0.001 |
| SICU | 0.897 (0.823–0.978) | <0.001 |
| TSICU | 0.774 (0.697–0.858) | <0.001 |
| Days of mechanical ventilation | 0.990 (0.986–0.995) | <0.001 |
| CPD | | |
| No | Ref | |
| Yes | 1.571 (1.458–1.693) | <0.001 |
| Hypertension | | |
| No | Ref | |
| Yes | 0.682 (0.642–0.725) | <0.001 |
| Sepsis | | |
| No | Ref | |
| Yes | 2.873 (2.681–3.078) | <0.001 |
| Liver cirrhosis | | |
| No | Ref | |
| Yes | 1.898 (1.700–2.120) | <0.001 |
| Respiratory failure | | |
| No | Ref | |
| Yes | 3.017 (2.843–3.202) | <0.001 |
| Malignant tumor | | |
| No | Ref | |
| Yes | 1.793 (1.680–1.914) | <0.001 |
| Renal failure | | |
| No | Ref | |
| Yes | 2.676 (2.517–2.844) | <0.001 |
| CHD | | |
| No | Ref | |
| Yes | 0.614 (0.574–0.657) | <0.001 |
| $FIO_2$ (%) | 1.017 (1.016–1.019) | <0.001 |
| WBC (k/μL) | 1.125 (1.118–1.131) | <0.001 |
| BUN (mg/dL) | 1.036 (1.035–1.038) | <0.001 |
| GCS score | 0.973 (0.967–0.979) | <0.001 |
| SOFA score | 1.144 (1.134–1.154) | <0.001 |

HR, hazard ratio; CI, confidence interval; ICU, intensive care unit; CCU, coronary care unit; CSRU, cardiac surgery recovery unit; MICU, medical intensive care unit; SICU, surgical intensive care unit; TSICU, trauma surgical intensive care unit; CPD, chronic pulmonary disease; CHD, coronary heart disease; $FIO_2$, fraction of inspiration $O_2$; WBC, white blood cell; BUN, blood urea nitrogen; GCS, Glasgow Coma Scale; SOFA, sequential organ failure assessment.

of patients who received mechanical ventilation due to sepsis, the AUCs of the nomogram for 1-month, 3-month, 1-year, and 3-year survival prediction were 0.829 (95% CI: 0.812–0.846), 0.834 (95% CI: 0.818–0.851), 0.830 (95% CI: 0.813–0.847), and 0.820 (95% CI: 0.803–0.838). For the subgroup of patients who received mechanical ventilation due to trauma, the AUCs of the nomogram for 1-month, 3-month, 1-year, and 3-year survival prediction were 0.865 (95% CI: 0.819–0.912), 0.882 (95% CI: 0.840–0.924), 0.873 (95% CI: 0.831–0.914), and 0.867 (95% CI: 0.824–0.909). For the subgroup of patients who received mechanical ventilation due to other causes, the AUCs of the nomogram for 1-month, 3-month, 1-year, and 3-year survival prediction were 0.883 (95% CI: 0.875–0.890), 0.881 (95% CI: 0.874–0.887), 0.870 (95% CI: 0.863–0.877), and 0.854 (95% CI: 0.847–0.860) (*Table 5*). The results of the subgroup validation indicated that our nomogram demonstrated good predictive performance for patients who received mechanical ventilation due to multiple causes, such as shock, sepsis, trauma, and other causes.

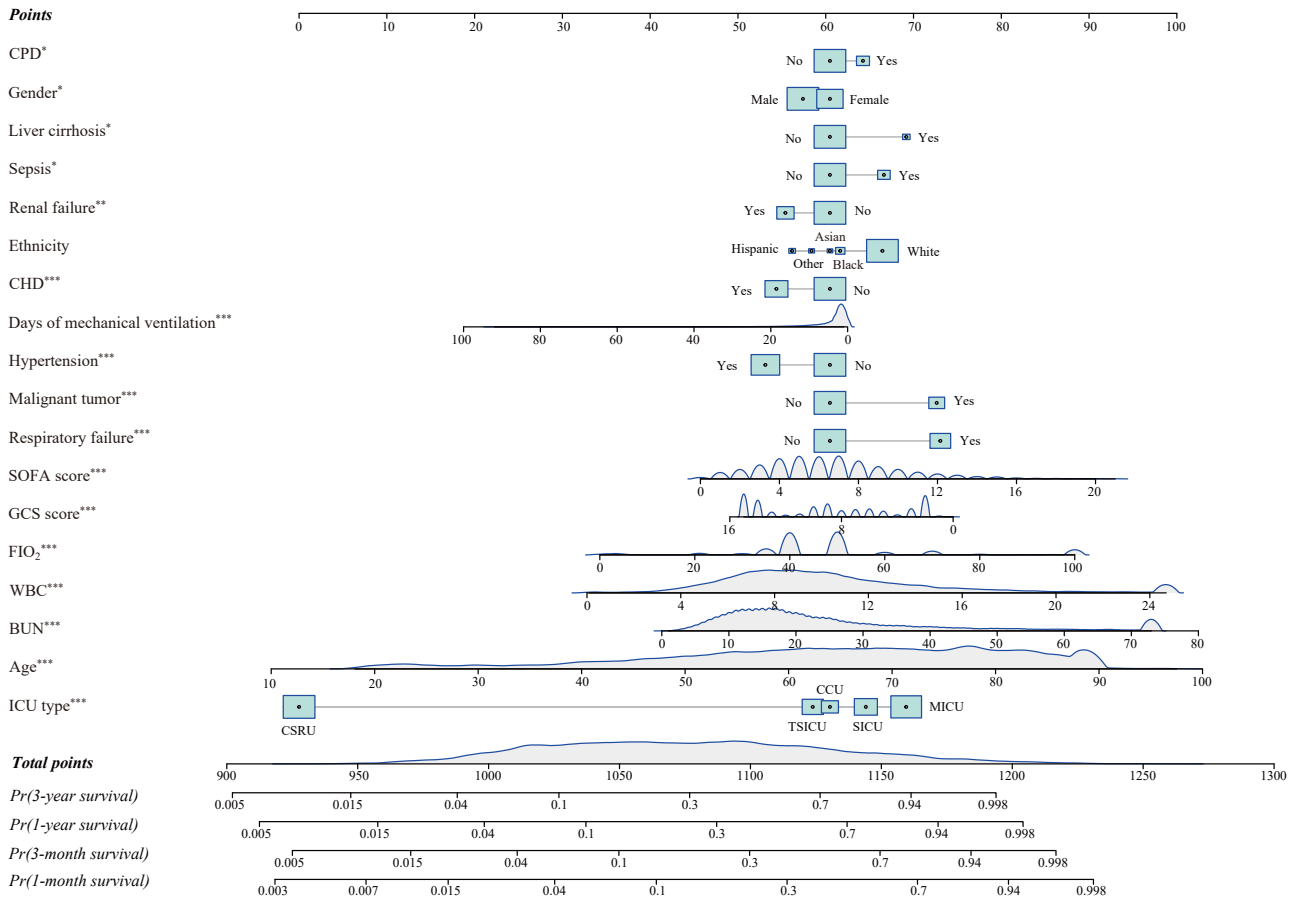


**Figure 3** Nomogram for predicting the survival of patients receiving mechanical ventilation. *P<0.05; **P<0.01; ***P<0.001. CPD, chronic pulmonary disease; CHD, coronary heart disease; SOFA, Sequential Organ Failure Assessment; GCS, Glasgow Coma Scale; $FIO_2$, fraction of inspiration $O_2$; WBC, white blood cell; BUN, blood urea nitrogen; ICU, intensive care unit; CSRU, cardiac surgery recovery unit; TSICU, trauma surgical intensive care unit; CCU, coronary care unit; SICU, surgical intensive care unit; MICU, medical intensive care unit.

**Table 4** AUC values at 1-month, 3-month, 1-year, and 3-year survival on the training and testing sets

| | AUC (95% CI) | | | |
|---|---|---|---|---|
| | 1-month survival | 3-month survival | 1-year survival | 3-year survival |
| Training set | 0.889 (0.882–0.896) | 0.892 (0.886–0.898) | 0.882 (0.876–0.889) | 0.866 (0.859–0.873) |
| Testing set | 0.884 (0.873–0.895) | 0.884 (0.874–0.894) | 0.877 (0.867–0.887) | 0.866 (0.855–0.876) |

AUC, area under the curve; CI, confidence interval.

### *Example of the nomogram application*

A 22.95-year-old male admitted to TSICU without sepsis, CPD, or hypertension had a white blood cell count of $11.1\times10^9$/μL, a SOFA score of 7, a GCS score of 9, $FIO_2$ of 40%, and BUN of 18 mg/dL. According to our nomogram, the patient's total score was 1030, and the predicted risk of death within 1 month, 3 months, 1 year, and 3 years was 0.0476, 0.0669, 0.0818, and 0.114, respectively. The patient's actual situation was 'survival,' with a survival time ≥1,095 days, which indicated that the prediction from the nomogram was correct (*Figure 5*).

 

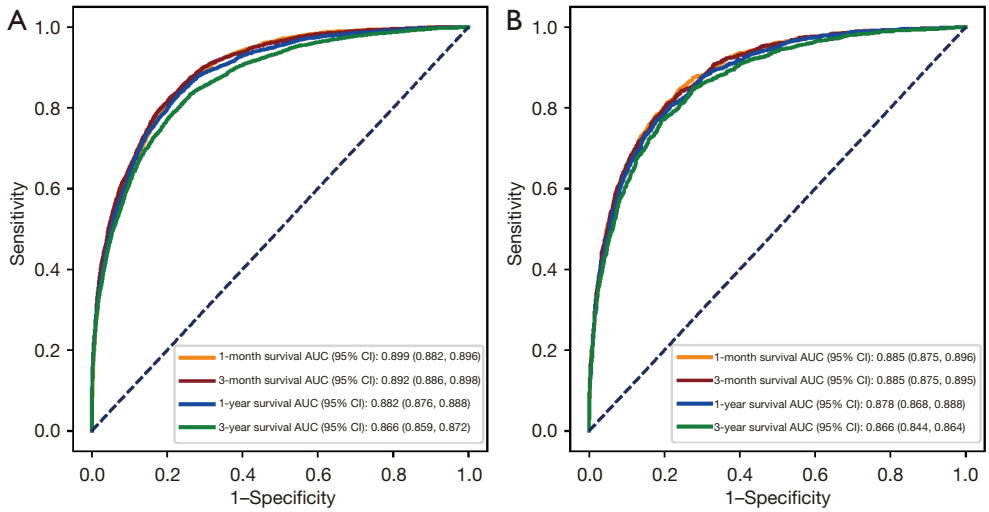


**Figure 4** ROC curves of the training set (A) and the testing set (B). ROC, receiver operating characteristic; AUC, area under the curve; CI, confidence interval.

**Table 5** Predictive performance of the nomogram for the 1-month, 3-month, 1-year, and 3-year survival in shock, sepsis, trauma, and other subgroups

| Models | AUC (95% CI) | Sensitivity (95% CI) | Specificity (95% CI) | PPV (95% CI) | NPV (95% CI) |
|---|---|---|---|---|---|
| Shock | | | | | |
| 1-month survival | 0.844 (0.829–0.860) | 0.756 (0.731–0.781) | 0.772 (0.749–0.796) | 0.765 (0.741–0.789) | 0.764 (0.739–0.789) |
| 3-month survival | 0.852 (0.837–0.868) | 0.755 (0.732–0.778) | 0.793 (0.768–0.819) | 0.835 (0.814–0.855) | 0.701 (0.674–0.728) |
| 1-year survival | 0.848 (0.832–0.863) | 0.718 (0.695–0.741) | 0.813 (0.787–0.839) | 0.868 (0.849–0.887) | 0.627 (0.598–0.655) |
| 3-year survival | 0.844 (0.828–0.860) | 0.829 (0.802–0.856) | 0.695 (0.672–0.717) | 0.893 (0.875–0.910) | 0.570 (0.541–0.599) |
| Sepsis | | | | | |
| 1-month survival | 0.829 (0.812–0.846) | 0.713 (0.686–0.740) | 0.799 (0.777–0.822) | 0.758 (0.732–0.785) | 0.759 (0.736–0.783) |
| 3-month survival | 0.834 (0.818–0.851) | 0.722 (0.698–0.746) | 0.794 (0.769–0.820) | 0.831 (0.810–0.853) | 0.670 (0.642–0.697) |
| 1-year survival | 0.830 (0.813–0.847) | 0.723 (0.700–0.746) | 0.779 (0.751–0.808) | 0.856 (0.836–0.875) | 0.608 (0.579–0.638) |
| 3-year survival | 0.820 (0.803–0.838) | 0.700 (0.677–0.723) | 0.793 (0.763–0.823) | 0.880 (0.862–0.898) | 0.550 (0.519–0.580) |
| Trauma | | | | | |
| 1-month survival | 0.865 (0.819–0.912) | 0.845 (0.768–0.923) | 0.752 (0.706–0.798) | 0.455 (0.377–0.533) | 0.952 (0.927–0.977) |
| 3-month survival | 0.882 (0.840–0.924) | 0.860 (0.790–0.931) | 0.772 (0.727–0.817) | 0.513 (0.434–0.591) | 0.952 (0.927–0.977) |
| 1-year survival | 0.873 (0.831–0.914) | 0.830 (0.756–0.904) | 0.777 (0.732–0.822) | 0.532 (0.454–0.610) | 0.937 (0.908–0.966) |
| 3-year survival | 0.867 (0.824–0.909) | 0.813 (0.739–0.887) | 0.784 (0.739–0.829) | 0.558 (0.480–0.636) | 0.926 (0.895–0.957) |
| Others | | | | | |
| 1-month survival | 0.883 (0.875–0.890) | 0.857 (0.842–0.872) | 0.749 (0.740–0.757) | 0.397 (0.383–0.412) | 0.964 (0.961–0.968) |
| 3-month survival | 0.881 (0.874–0.887) | 0.828 (0.814–0.843) | 0.774 (0.766–0.782) | 0.487 (0.473–0.501) | 0.946 (0.941–0.951) |
| 1-year survival | 0.870 (0.863–0.877) | 0.836 (0.823–0.848) | 0.752 (0.743–0.760) | 0.540 (0.526–0.553) | 0.929 (0.924–0.935) |
| 3-year survival | 0.854 (0.847–0.860) | 0.784 (0.771–0.797) | 0.772 (0.763–0.781) | 0.607 (0.594–0.620) | 0.888 (0.882–0.895) |

AUC, area under the curve; CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value.

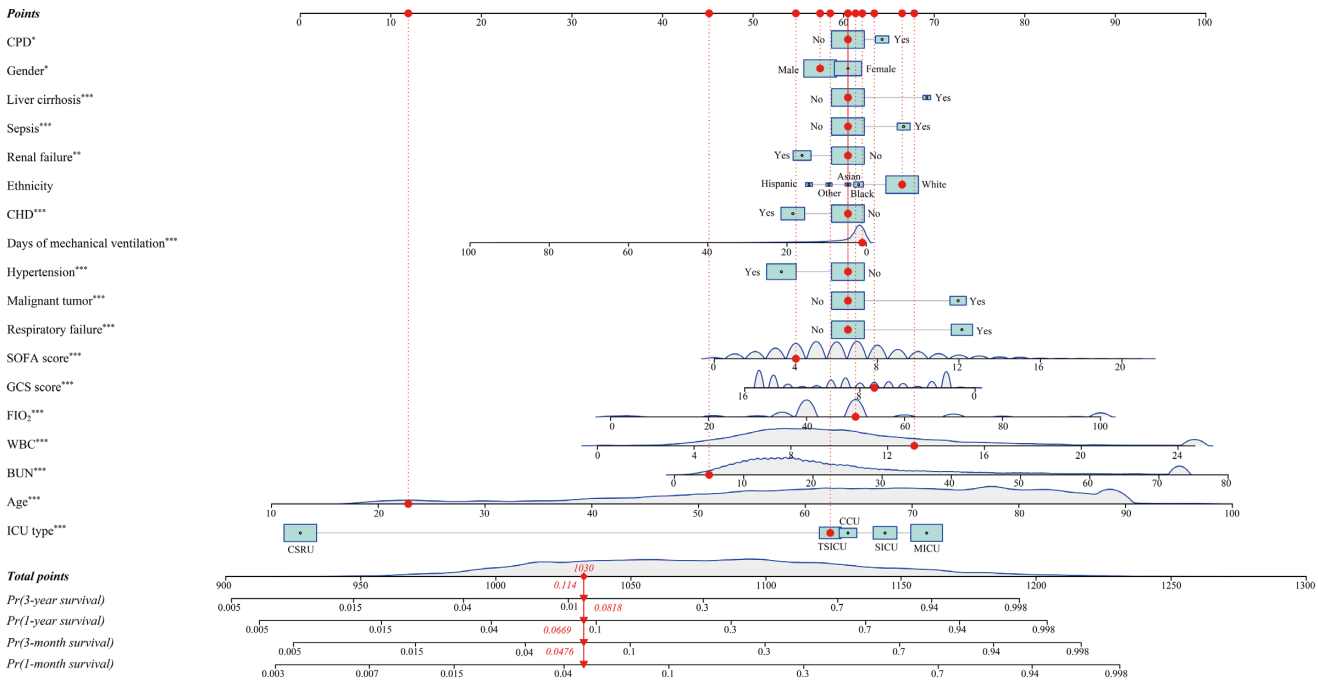


**Figure 5** Predicted nomogram results of the patient selected randomly from the training set. *P<0.05; **P<0.01; ***P<0.001. CPD, chronic pulmonary disease; CHD, coronary heart disease; SOFA, Sequential Organ Failure Assessment; GCS, Glasgow Coma Scale; $FIO_2$, fraction of inspiration $O_2$; WBC, white blood cell; BUN, blood urea nitrogen; ICU, intensive care unit; CSRU, cardiac surgery recovery unit; TSICU, trauma surgical intensive care unit; CCU, coronary care unit; SICU, surgical intensive care unit; MICU, medical intensive care unit.

## Discussion

In this study, we developed and validated a novel prediction tool for the survival of ICU patients who receive mechanical ventilation. The selected predictive factors included age, gender, ICU type, comorbidity (sepsis, CPD, hypertension, liver cirrhosis, respiratory failure, malignant tumor, and CHD), days of mechanical ventilation, WBC, BUN, $FIO_2$, SOFA score, and GCS score. Based on those predictors, a predictive nomogram for survival in ICU patients receiving mechanical ventilation was established, with a C-index of 0.819, validated in the testing set by an index of 0.816. The AUCs of the nomogram for 1-month, 3-month, 1-year, and 3-year survival prediction were 0.889, 0.892, 0.882, and 0.866, respectively, and were validated in the testing set by indexes of 0.884, 0.884, 0.877, and 0.866, respectively. Additionally, subgroup validations based on the reasons for mechanical ventilation also showed good predictive performance of the nomogram for both short- and long-term survival.

The evidence is inconclusive regarding the association between age and survival in patients receiving mechanical ventilation. A previous study indicated that, despite the association between age and an increased weaning failure rate, age was not a significant predictor of prognosis in patients who received mechanical ventilation (16). Additionally, it was reported that patients with superior respiratory function and less comorbidity who received mechanical ventilation were more likely to experience a better prognosis, regardless of age (17). However, other studies have demonstrated a significant association between age and survival in patients who received mechanical ventilation. A multicenter cohort study conducted by Blot *et al.* found that older age was a risk factor for higher mortality in patients receiving mechanical ventilation (18). A Spanish study showed that older patients aged ≥75 years had increased ICU mortality compared with younger patients, with no difference in mechanical ventilation duration (19). Additionally, age was shown to be a predictor of mortality in patients who received mechanical ventilation in research conducted in Brazil, the USA, and China (20-22). Our results found that as age increased, the patient's prognosis became worse, consistent with these

 

studies (20-22). With increased age, organ reserve and compensatory function reduce, and the incidence of chronic disease increases, which might adversely impact survival. More attention should be paid to the safety of using mechanical ventilation in elderly ICU patients.

In the current research, higher GCS and lower SOFA scores were associated with a better prognosis in ICU patients who received mechanical ventilation. The GCS has good validity and reliability, and GCS scores have been shown to be correlated with mortality in ICU patients (23,24). SOFA scores have also been used to assess the prognosis of ICU patients (25). Previous research is consistent with our results and suggests that doctors should attempt to increase the GCS score and reduce the SOFA score in the ICU patient as much as possible before starting mechanical ventilation therapy. Future studies could investigate the best cutoff values for GCS and SOFA scores to optimize the management of ICU patients treated with mechanical ventilation.

Our results found that the existence of sepsis increased the risk of death in ICU patients who received mechanical ventilation. Sepsis, caused by a dysregulated host response to an infection, can result in life-threatening tissue damage and organ dysfunction (26,27). It can progress into septic shock, which involves circulatory dysfunction and abnormal cell metabolism, leading to substantially increased mortality (28), which might explain our result. Another study also suggested that sepsis might be a vital risk factor for mortality in elderly ICU patients who received mechanical ventilation (29). Those results indicated that ICU patients with sepsis who were treated with mechanical ventilation had a poor prognosis, and more effective adjuvant therapy should be investigated to improve their prognosis in future studies.

The present research showed that a higher serum creatinine level, an indicator of kidney function, was an independent predictor of decreased survival in ICU patients who received mechanical ventilation (30). Acute kidney injury has been associated with poor outcomes after discharge in patients admitted to the ICU (31). A previous study compared survival in patients with and without kidney damage who received mechanical ventilation and found that all patients who received renal replacement therapy died within 1 year (32). A meta-analysis demonstrated that renal dysfunction (both acute and chronic, regardless of the need for dialysis) was associated with 1-year mortality (33). Early assessment of the patient's renal function and related treatment might improve the prognosis of ICU patients who receive mechanical ventilation. Additionally, we found that an increased number of WBCs was an independent predictor of survival in ICU patients who received mechanical ventilation. It has been reported that hospital-acquired infections are more likely to occur in ICU patients (34), and ICU-acquired infections have been shown to be independently associated with hospital mortality (35,36). The main reason for an increased WBC count is infection. Hence, reducing the risk of nosocomial infection might be an effective measure to improve the prognosis of ICU patients who receive mechanical ventilation.

Several models have been built to estimate survival in ICU patients who receive mechanical ventilation. Carson *et al.* developed a scoring model for predicting 1-year mortality in ICU patients requiring prolonged mechanical ventilation (37). In this model, points were assigned to age ≥65 years, age 50–64 years, platelets $\leq 150\times10^9$/L, vasopressors, and hemodialysis. However, long-term survival was not assessed, which is an essential element allowing clinicians and family members to conduct a comprehensive evaluation of patients. Our nomogram for predicting short- and long-term survival (1-month, 3-month, 1-year, and 3-year) in ICU patients who received mechanical ventilation was based on a large sample size, thereby providing a good foundation for the reliability of the prediction model. In addition, subgroup validations based on the reasons for mechanical ventilation (including shock, sepsis, trauma, and other causes) were conducted to reduce heterogeneity, and we found that the predictive performance of the nomogram was satisfactory in those four types of subgroups.

The nomogram developed in this study was based on a relatively large sample and had a moderate predictive ability. However, there are several limitations to this research. Firstly, one limitation of this study is the retrospective nature of the design. Secondly, the lack of external validation is another limitation of our study. Thirdly, more accurate indicators for mechanical ventilation could not be collected. Fourthly, since the data were extracted from a database, this may have limited the reasons for mechanical ventilation in this study. Our subgroup analysis based on shock, sepsis, trauma, and other causes may not be able to determine the nomogram's predictive performance based on different mechanical ventilation causes. Further prospective multicenter studies are needed to validate the present model. In addition, many predictors were included in the current predicting model, future studies may attempt to use machine learning to simplify the model and make it more convenient for clinicians to apply it better.

 

## Conclusions

Several predictors have been associated with the survival of ICU patients treated with mechanical ventilation, including age, gender, ICU type, comorbidity (sepsis, CPD, and hypertension), days of mechanical ventilation, WBC, BUN, $FIO_2$, SOFA score, and GCS score. Based on those factors, a nomogram with good predictive performance for short- and long-term survival (1-month, 3-month, 1-year, and 3-year) in ICU patients treated with mechanical ventilation was developed and validated among 16,775 individuals from the MIMIC III database. We believe that the nomogram might provide a reference for physicians in clinical work to optimize the management of ICU patients who require mechanical ventilation based on individual short- and long-term survival.

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## Footnote

*Reporting Checklist:* The authors have completed the TRIPOD reporting checklist. Available at https://apm.amegroups.com/article/view/10.21037/apm-22-646/rc

*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at https://apm.amegroups.com/article/view/10.21037/apm-22-646/coif). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).



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## Supplementary

**Table S1** Sensitivity analysis results before and after imputations

| Variables | Sensitivity | | Z | P |
|---|---|---|---|---|
| | Before (n=16,775) | After (n=16,775) | | |
| WBC (k/μL), M ($Q_1$, $Q_3$) | 9.40 (7.20, 12.30) | 9.40 (7.20, 12.30) | 0.095 | 0.925 |
| BUN (mg/dL), M ($Q_1$, $Q_3$) | 19.00 (13.00, 31.00) | 19.00 (13.00, 31.00) | 0.342 | 0.732 |
| $FIO_2$, M ($Q_1$, $Q_3$) | 50.00 (40.00, 50.00) | 50.00 (40.00, 50.00) | 0.155 | 0.877 |
| SOFA score, M ($Q_1$, $Q_3$) | 6.00 (4.00, 8.00) | 6.00 (4.00, 8.00) | –0.002 | 0.998 |
| GCS score, M ($Q_1$, $Q_3$) | 9.00 (5.00, 14.00) | 9.00 (5.00, 14.00) | –0.359 | 0.720 |

WBC, white blood cell; BUN, blood urea nitrogen; $FIO_2$, fraction of inspiration $O_2$; SOFA, sequential organ failure assessment; GCS, Glasgow Coma Scale.


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