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ORIGINAL RESEARCH

A Nomogram for Predicting Survival in Patients with SARS-CoV-2 Omicron Variant Pneumonia Based on Admission Data

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Purpose: Patients with severe SARS-CoV-2 omicron variant pneumonia pose a serious challenge. This study aimed to develop a nomogram for predicting survival using chest computed tomography (CT) imaging features and laboratory test results based on admission data.

Patients and Methods: A total of 436 patients with SARS-CoV-2 pneumonia (323 and 113 in the training and validation groups, respectively) were enrolled. Pneumonitis volume, assessed on chest CT scans at admission, was used to identify low- and high-risk groups. Risk analysis was performed using clinical symptoms, laboratory findings, and chest CT imaging features. A predictive algorithm was developed using Cox multivariate analysis.

Results: The high-risk group had a shorter survival duration than the low-risk group. Significant differences in mortality rate, neutrophil and lymphocyte counts, C-reactive protein (CRP) concentration, and urea nitrogen level were observed between the two groups. In the training group, age, pneumonia volume, total bilirubin, and blood urea nitrogen were independent prognostic factors. In the validation group, age, pneumonia volume, neutrophil count, and CRP were independent prognostic factors. A personalized prediction model for survival outcomes was developed using independent predictors.

Conclusion: A personalized prediction model was created to forecast the 5-, 10-, 15-, 20-, and 30-day survival rates of patients with COVID-19 omicron variant pneumonia based on admission data, and can be used to determine the survival rate and early treatment of severe patients.

Keywords: predictive nomogram, prognosis, COVID-19, pneumonia, omicron

Introduction

Coronaviruses are single-positive-stranded RNA viruses.[1] By 2019, seven coronaviruses that could infect humans were identified, including SARS-CoV-2 which was isolated from the lower respiratory tract of patients with pneumonia.[2] The virus has been detected in various tissues, including lung, liver, kidney, and endothelial cells.[3] SARS-CoV-2 infection is characterized by rapid onset and progression, and a relatively short course of illness.[4] Clinical presentations can vary from asymptomatic or mild symptoms such as fever, dry cough, and fatigue to severe symptoms such as hypoxemia, dyspnea, acute respiratory distress syndrome, and multiple organ failure.[5] Patients with severe COVID-19 are at a high risk of multiple organ complications and potential fatalities.[6] Early identification of patients with possible poor outcomes and timely interventions such as admission to the intensive care unit and the use of ventilators may be necessary to improve outcomes.

Severe cases exhibit significant inflammatory infiltration of the lungs.[7] Physicians dedicate considerable time to monitoring the condition of patients with severe pneumonia and delivering personalized treatments.[8] This poses

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significant challenges for both doctors and patients. Chest CT is an important tool to monitor the progress of Omicron variant COVID-19, which is helpful to evaluate the progress of COVID-19 in the lungs. To timely and accurately identify severe COVID-19 cases and predict survival outcomes based on clinical features, chest computed tomography (CT) imaging findings, and preliminary laboratory results at admission. Early intervention and treatment based on severe patients is an urgent problem to be solved.[9]

Although a plethora of overall survival (OS) and progression-free survival (PFS) prediction models have been established for patients with cancer, the occurrence of SARS-CoV-2 infection has posed challenges in the creation of high-precision prediction models.[10] In December 2022, China revised its COVID-19 response policy. Changzheng Hospital admitted a substantial number of patients with COVID-19 and shared clinical information, laboratory data, and CT findings related to patients with SARS-CoV-2 Omicron variant pneumonia.[11] These resources have laid a solid foundation for developing a high-precision prediction model for patients with COVID-19.[12,13]

This study aimed to analyze the chest CT imaging features and laboratory findings of patients with severe COVID-19 and to develop a prognostic model that combines pneumonia manifestations with clinical risk factors. This model aimed to precisely forecast survival rates at various intervals, offering the opportunity to tailor treatment for patients with COVID-19.[14,15]

Materials and Methods

Data Source

All individuals diagnosed with Omicron infection, confirmed by SARS-CoV-2 reverse transcription polymerase chain reaction (RT-PCR) tests, in our hospital between December 15, 2022, and January 15, 2023, were enrolled (Figure 1). RT-PCR assays were conducted using a commercial kit from China® (New Coronavirus nucleic acid 2019-nCoV nucleic acid detection kit, Bioustar, Hangzhou, China). Patients were excluded if they met any of the following criteria: (1) current uncontrolled infection (aside from Omicron variant) within the past four weeks, (2) end-stage tumors (referring to the

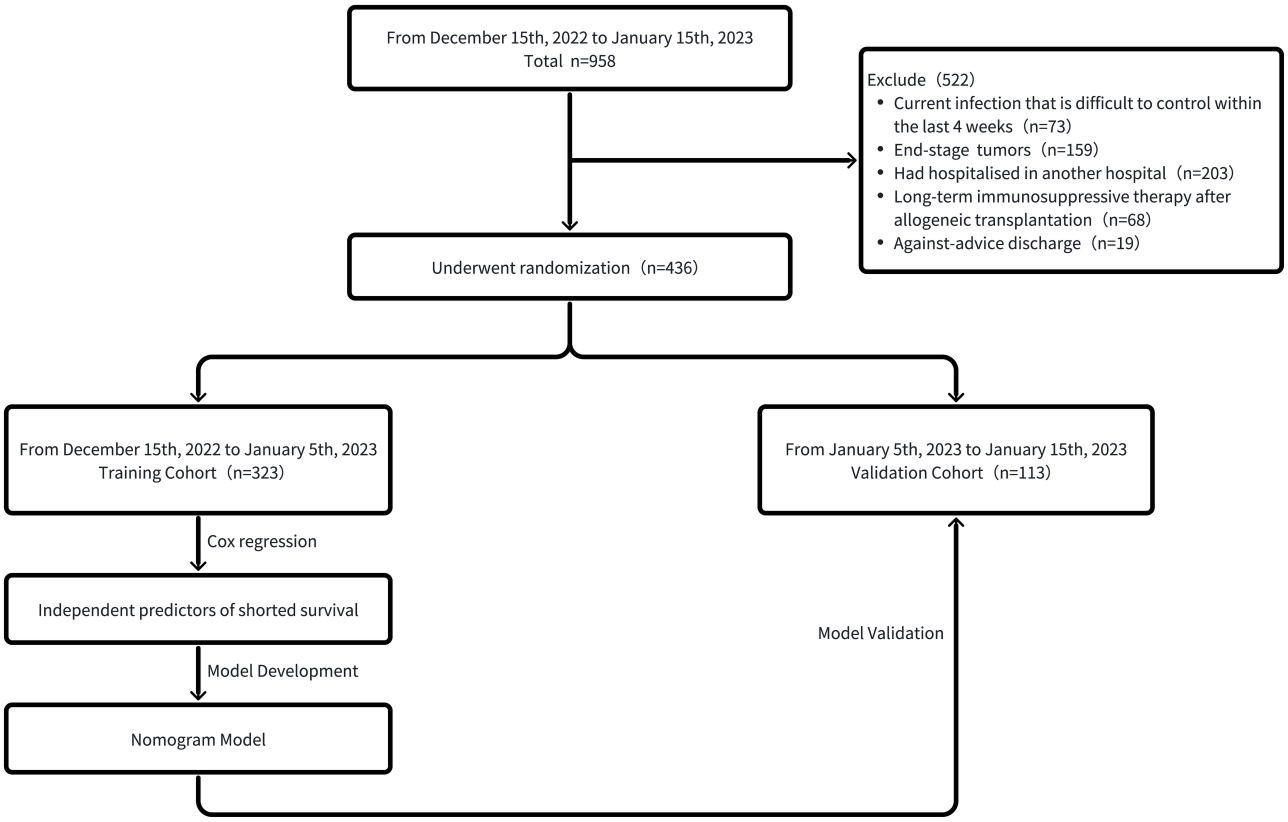

Figure 1 Flowchart of participant inclusion and exclusion.

advanced stage of malignant tumor, characterized by rapid tumor growth and widespread diffusion, possibly involving organs and nerves in other parts of the body), (3) prior hospitalization at another facility, (4) prolonged immunosuppressive therapy after allogeneic transplantation, and (5) discharge against medical advice.

The study was reviewed and approved by the ethical committees of the Changzheng Hospital. A total of 436 patients with Omicron variant pneumonia were enrolled. According to admission time, 323 patients were assigned to the training group (From December 15th, 2022 to January 5th, 2023), and 113 patients were included in the validation group (From January 5th,2023 to January 15th,2023). The training group was used for Nomogram construction, and the validation group was used for external validation of the Nomogram. Mortality was the primary endpoint of the study.

Written informed consent for participation was not provided by the participants' legal guardians because the requirement for written informed consent was waived since no additional interventions and potential harm were posed to these patients.

On admission, all patients underwent medical history review, chest CT, and laboratory tests. Using InferRead CT Pneumonia® (Infervision Medical Technology Co., Ltd. Beijing, China), an artificial intelligence program that uses combined imaging, lesions in both lungs were automatically identified and delineated. The software quantitatively analyzed the volume of pneumonia lesions and the extent of lung involvement due to pneumonia.[16] The interpretation of CT images mainly focused on the lesion features, such as ground glass opacity, consolidation, patchy or nodular lesions, reticular changes, and interlobular septal thickening. At the same time, attention should be paid to the distribution and extent of the lesion: the lesion was located in the upper, middle or lower lobe of the right lung or the upper or lower lobe of the left lung. Subpleural or central distribution. Pneumonia volume Method: Each lung lobe was scored according to the percentage of infection: 0, no involvement; 1, < 50%; 2 points, > 50%. The CT score was derived from the sum of the individual lobar scores, so that the CT score for each CT scan ranged from 0 to 10. To ensure accuracy, three pneumonia treatment experts independently reviewed and made corrections without access to the patient information. The patients were stratified into high- and low-risk groups based on their pneumonia volumes.

Statistical Analysis

Kaplan–Meier survival analysis was conducted to assess potential differences in outcome indicators between the two risk groups. Statistical analyses were performed using R software (version 4.2.3, https://www.r-project.org/), IBM SPSS Statistics (version 24.0, Chicago, IL, USA), and GraphPad Prism (version 8.0, La Jolla, CA, USA). The significance level for all statistical tests was set at $P < 0.05$.

R Studio, as the integrated development environment (IDE) for the R programming language, is widely used in clinical prediction models (eg, nomogram development) due to its open-source ecosystem and scalability, supporting over 6000 extension packages (eg, ggplot2, survival).[17] IBM SPSS Statistics is renowned for its user-friendly interface and standardized workflows, providing various statistical operations through built-in statistical templates.[18] GraphPad Prism features publication-grade charting tools and is particularly suited for visualization tasks such as logistic regression and survival analysis.[19]

Nomogram Construction

Univariate and multivariate Cox analysis were used to evaluate the prognostic value of the indicators. The regression modelling Strategies (RMS) package in R was used to develop a nomogram analysis for the training group. The nomogram consists of a scoring system in the first part, and a prediction system in the second part. The 5-day, 10-day, 15-day, 20-day, and 30-day survival rates of patients with severe COVID-19 were forecasted based on the individual scores assigned to each factor and the overall score. Predictive accuracy was confirmed using data from patients in the validation group. Calibration curves and concordance index (C-index) values were used to demonstrate the precision of survival predictions.

Results

Characteristics of Participants

In this study, 958 individuals were diagnosed with COVID-19 pneumonia attributed to the Omicron variant. Among them, 436 were eligible for analysis. A flowchart depicting the patient selection process is shown in Figure 1. The

Table 1 Demographic and Clinical Features of Patients in the Training and Validation Group

	Training Set	Validation Set
Number of patients, n	323	113
Age, years	72.12 ± 13.5	67.59 ± 15.56
Sex		
Male	193(59.75%)	71(62.83%)
Female	130(40.25%)	42(37.17%)
Leucocyte, E+09/L	7.15 ± 3.79	6.32 ± 2.68
Lymphocytes, E+09/L	1.09 ± 0.7	1.11 ± 0.55
Neutrophil, E+09/L	5.47 ± 3.72	4.59 ± 2.55
CRP, mg/L	57.87 ± 69.56	66.59 ± 66.25
PCT, ng/mL	1.31 ± 6.81	0.97 ± 3.65
IL-6,pg/mL	35.3 ± 96.82	57.09 ± 178.62
D-dimer unit, ug/mL	1.81 ± 2.75	1.11 ± 1.05
ESR, mm/h	46.3 ± 31.71	44.98 ± 28.08
Ferritin,ug/L	706.09 ± 504.7	683.36 ± 387.75
C1q, mg/L	192.24 ± 45.8	188.29 ± 48.46
ALT, U/L	33.36 ± 25.58	35.08 ± 31.57
AST, U/L	36.13 ± 21.71	49.09 ± 57.5
LDH, U/L	238.35 ± 99	246.77 ± 139.37
TBIL, umol/L	12.73 ± 6	12.27 ± 7.62
DBIL, umol/L	1.59 ± 2.2	1.12 ± 3.57
IBIL, umol/L	11.21 ± 5.35	11.14 ± 5.5
BUN, mmol/L	8.84 ± 7.2	7.28 ± 6.37
Glu, mmol/L	8.19 ± 4.66	7.66 ± 2.86
BNP, pg/mL	1479.18 ± 4099.82	1681.91 ± 4320.5
Length of stay, days	12.39 ± 7.3	12.22 ± 7.98
Death		
Yes	38(11.76%)	18(15.93%)
No	285(88.24%)	95(84.07%)

Notes: Results are expressed as number (%) for categorical variables and as mean (± standard deviation) for quantitative variables.

patients were categorized into a training group comprising 323 cases (from December 15, 2022, to January 5, 2023) and a validation group consisting of 113 cases (from January 6 to January 15, 2023), based on their admission dates.

The baseline clinical characteristics of the enrolled patients were examined (Table 1). The average age of patients in the training group was 72.12 ± 13.5 years, with 193 (59.75%) males and 130 (40.25%) females. The average length of hospital stay was 12.39 ± 7.3 days. Thirty-eight (11.76%) patients experienced adverse outcomes. The average age of patients in the validation group was 67.59 ± 15.56 years, with 71 (62.83%) males and 42 (37.17%) females. The average length of hospital stay was 12.22 ± 7.98 days. In total, 18 (15.93%) patients in this group experienced adverse outcomes. Laboratory examinations revealed elevated leukocyte and neutrophil counts, and decreased lymphocyte counts in both patient groups. Additionally, C-reactive protein (CRP), interleukin-6 (IL-6), procalcitonin (PCT), D-dimer, glucose (GLU), alanine aminotransferase (ALT), aspartate aminotransferase (AST), and blood urea nitrogen (BUN) levels were above the normal range in both groups.

Risk Stratification Based on COVID-19 Pneumonia Volume

The patients were stratified into high- and low-risk groups based on their pneumonia volumes. The volume of pneumonia < 50% was defined as the low-risk group, and the volume > 50% was defined as the high-risk group. An analysis of the clinical characteristics and laboratory results for patients in each risk category (Figure 2) revealed significant differences in mortality rates, neutrophil and lymphocyte levels, and CRP and BUN concentrations between the high- and low-risk groups ($P < 0.05$).

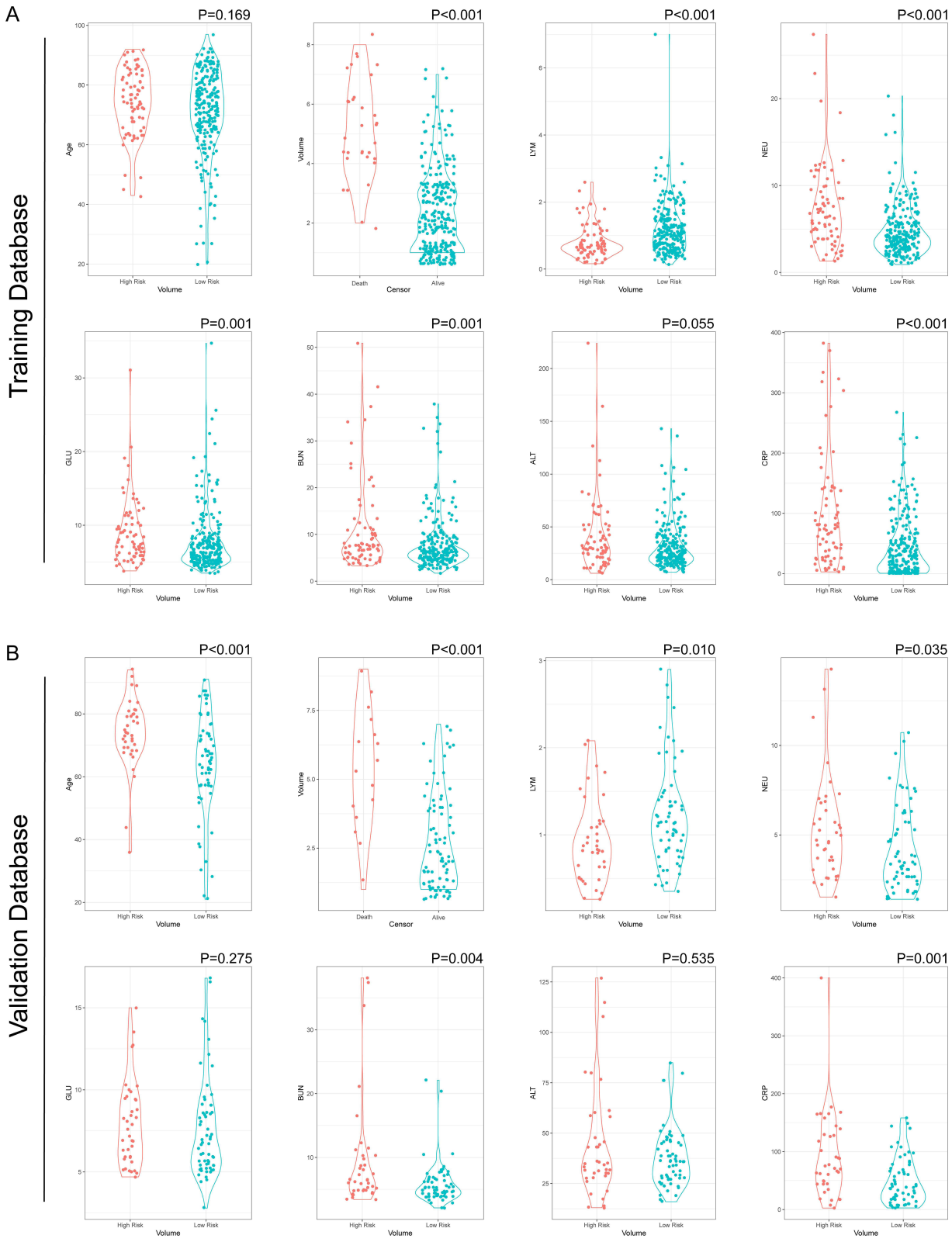

Figure 2 The relationship between pneumonia volume and clinical characteristics of COVID-19. (**A** and **B**) Violin charts showed the distribution of clinical characteristics between different pneumonia volume of COVID-19 in training and validation groups. The significance of the difference between the two groups was verified by Mann Whitney test.

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Development of a Predictive Nomogram for the Patients with SARS-CoV-2 Omicron Variant Pneumonia

The individualized prognostic model demonstrated a robust predictive precision. Physiological parameters significantly influenced disease outcomes. Laboratory data were used to elucidate the host immune response to viral pathogens. In addition to chest CT imaging showing predictive efficacy for severe COVID-19, both physical status and laboratory findings are critical determinants for assessing the prognosis of individuals with COVID-19. These three elements collectively contribute to disease trajectory. Consequently, a prognostic model based on these factors was deemed applicable for forecasting the clinical course of patients with COVID-19.

Specific biomarkers identified through univariate Cox regression analysis were correlated with an adverse prognosis in hospitalized patients with COVID-19. These biomarkers included age, extent of pneumonia, lymphocyte and neutrophil counts, CRP, D-dimer, ALT, total bilirubin (TBIL), BUN, and GLU levels. Within the training cohort, multivariate Cox regression analysis identified age, extent of pneumonia, and TBIL and BUN levels as independent prognostic indicators (Table 2). In the validation cohort, age, extent of pneumonia, neutrophil count, and CRP levels were independent prognostic factors (Table 3). Regardless of the training group or the validation group, the volume of pneumonia was within the independent risk factors.

Patients in different risk groups showed different survival days. Pneumonia volume showed good predictive value for survival days in both the training and validation databases (Figure 3). A personalized prediction model was

Table 2 Selection of Variables Independently Associated with OS by Univariate and Multivariate Cox Proportional Hazards Analysis in the Training Database

Variable	Univariate Cox			Multivariate Cox		
	HR	95% CI for HR	P	HR	95% CI for HR	P
Age	1.064	1.025–1.105	0.001	1.099	1.038–1.165	0.001
Pneumonia volume	1.834	1.518–2.214	0.000	1.640	1.267–2.123	0.000
Lymphocytes	0.375	0.173–0.816	0.013	0.804	0.286–2.261	0.679
Neutrophil	1.134	1.085–1.185	0.000	1.024	0.951–1.102	0.535
CRP	1.006	1.002–1.009	0.001	1.003	0.998–1.007	0.286
D-dimer unit	1.103	1.038–1.173	0.002	1.039	0.943–1.143	0.440
ALT	1.010	1.002–1.019	0.018	1.006	0.993–1.019	0.393
TBIL	1.079	1.036–1.125	0.000	1.064	0.999–1.132	0.053
BUN	1.077	1.048–1.107	0.000	1.042	1.004–1.082	0.031
Glu	1.097	1.05–1.146	0.000	1.056	0.974–1.145	0.184

Abbreviation: CI, confidence interval.

Table 3 Selection of Variables Independently Associated with OS by Univariate and Multivariate Cox Proportional Hazards Analysis in the Validation Database

Variable	Univariate Cox			Multivariate Cox		
	HR	95% CI for HR	P	HR	95% CI for HR	P
Age	1.031	0.986–1.079	0.183	1.112	1–1.238	0.050
Pneumonia volume	1.474	1.116–1.947	0.006	1.477	1.074–2.032	0.017
Lymphocytes	0.849	0.314–2.294	0.747	0.142	0.017–1.158	0.068
Neutrophil	1.109	0.951–1.293	0.186	1.439	1.103–1.879	0.007
CRP	1.004	0.997–1.01	0.263	0.972	0.956–0.99	0.002
D-dimer unit	1.066	0.744–1.527	0.729	0.743	0.389–1.418	0.367
ALT	0.998	0.983–1.012	0.741	1.014	0.974–1.056	0.490
TBIL	0.996	0.948–1.046	0.867	1.106	0.973–1.256	0.123
BUN	1.039	0.994–1.085	0.088	1.000	0.925–1.081	0.998
Glu	1.105	0.981–1.244	0.099	1.149	0.931–1.419	0.195

Abbreviation: CI, confidence interval.

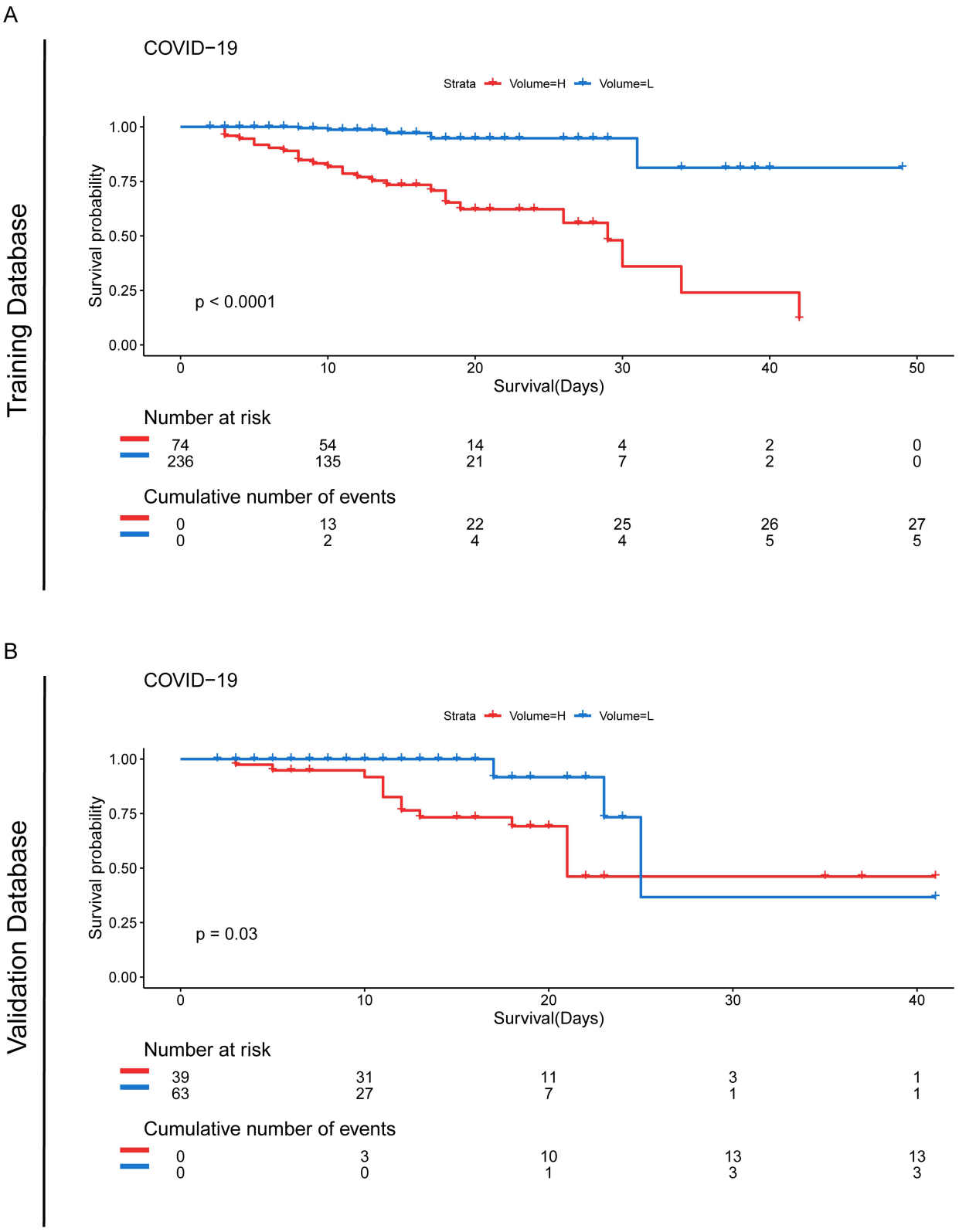

Figure 3 The signature was found to well predict the survival information. (**A**) Pneumonia volume replied to survival information in the training database (P < 0.0001). (**B**) Pneumonia volume replied to survival information in the validation database (P =0.03).

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developed to enhance the clinical utility of the prognostic model. Utilizing independent prognostic predictors, including the extent of pneumonia, age, TBIL, GLU, and BUN, this model was designed to forecast the survival probabilities of patients with COVID-19. Correlations between independent variables have been calculated and uploaded as supplementary data. As depicted in Figure 4A, the individualized model accurately predicted the survival

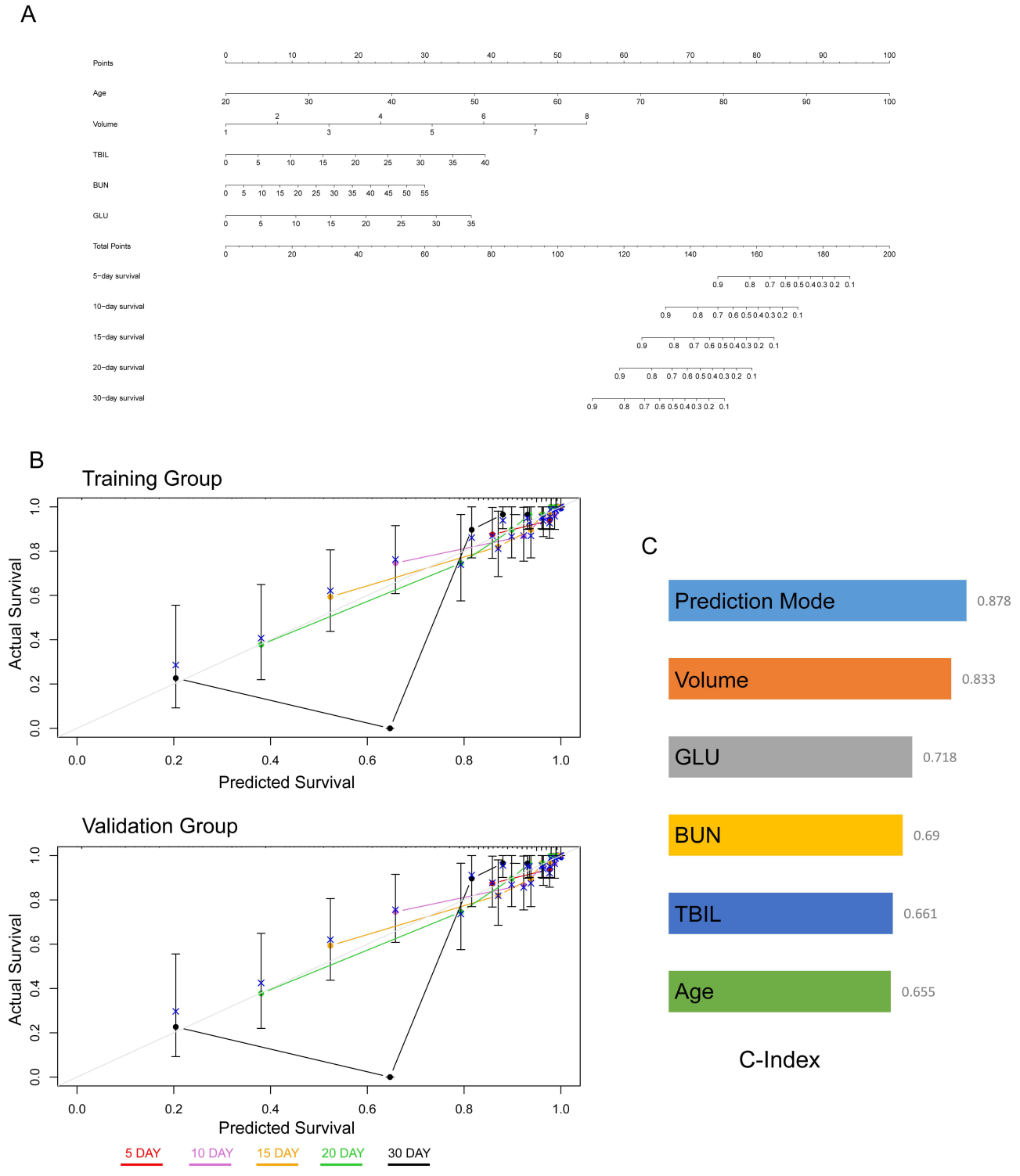

Figure 4 The individualized prediction models for survival in COVID-19. (**A**) The 5, 10, 15, 20, and 30-day survival of COVID-19 patients could exactly be predicted by the nomogram. (**B**) The Calibration plots showed the comparison of survival for 5, 10, 15, 20, and 30-day survival probabilities in training and validation groups. (**C**) The predictive effect of the individualized prediction model, pneumonia volume and clinical prognostic factors of COVID-19 patients on survival was evaluated by C-Index.

rates at 5, 10, 15, 20, and 30 days post-onset for patients with COVID-19. The calibration curves, which juxtapose the predicted modal values with the actual observed data, revealed substantial alignment in both the training and validation cohorts, thereby underscoring the model's predictive fidelity (Figure 4B). The C-index of the model, at a value of 0.878, surpassed that of the existing prognostic models, as illustrated in Figure 4C, thereby affirming its robust predictive accuracy.

Discussion

Monitoring pneumonia volume and laboratory indicators such as leukocyte, neutrophil counts, lymphocyte counts, CRP, IL-6, PCT, GLU, ALT, AST, and BUN in patients with COVID-19, especially those with severe COVID-19, is of great clinical significance.[20] Although some retrospective studies have been conducted on the novel coronavirus, the virus is prone to mutations, and long-term follow-up samples are insufficient.[21] Few studies have been able to accurately predict the survival of patients with severe COVID-19.[22] If the patient's pneumonia volume and laboratory indicators are used to construct a prognostic Nomogram, the personalized prediction model can accurately predict the severity of COVID-19 in patients, which will make better clinical decisions and improve the prognosis of patients.

As shown in Table 2 and Table 3, the volume of pneumonia was an independent risk factor for prognosis in both the training group and the validation group. This is also confirmed in Figure 3. The KM survival curve shows that there are differences in the prognosis of different pneumonia volumes. Chest CT imaging can effectively reflect the signs of chest infection caused by the Omicron variant.[23] In the early stages of COVID-19, diffuse alveolar injury, swelling of the alveolar wall, and exudation into the alveolar cavity occur, appearing as single or multiple ground-glass density shadows and small nodules.[24] The lesions are mostly distributed in the peripheral lung band and subpleura, accumulating in the lower lobes and dorsal segments of both lungs.[25] In the advanced stages, the range of lesions increases rapidly. The lesions progress from the peripheral zone to the central region along the bronchial vascular bundle, increasing in density and becoming uneven. There may be a thickening or traction shift near the pleura at the affected site, and a bright linear shadow may appear below the pleura.[26] As the disease progresses, the fibrous exudation of the alveolar cavity and capillary congestion of the alveolar wall disappear. Most lesions partially or completely dissipate, with some pulmonary signs progressing to pulmonary fibrosis and consolidation. As an imaging marker of severe COVID-19, consolidation manifests as increased lung tissue density over a large area and unclear lesion tissue boundaries. The main characteristic of consolidation was air bronchial signs, with a few patients showing white lung signs.[27]

In addition to lung damage, COVID-19 can damage various tissues, including the liver and kidneys.[28] Liver function indices revealed elevated aminotransferase and bilirubin levels. Renal function indices showed changes in urea nitrogen and creatinine levels. COVID-19 infection also promotes insulin resistance and beta cell dysfunction, leading to elevated blood sugar levels.[29]

A typical feature of SARS-CoV-2 infection in routine blood tests is a significant reduction in the lymphocyte count.[30] Patients with severe COVID-19 are highly susceptible to bacterial, fungal, and viral coinfections, including ventilator-associated pneumonia and blood infections.[31] Infection may increase neutrophil counts and inflammatory markers such as CRP, IL-6, and PCT.[32] In the present study, the univariate and multivariate Cox results in Table 2 and Table 3 also further confirm the above discussion. Inflammatory markers were not included in predictive models in this study. This is because most patients take oral or intravenous antibiotics in the early stages of the disease, which causes serious interference with such indicators.[33]

We constructed a nomogram based on pneumonia volume to predict the survival of patients with COVID-19 patients.[34] Combining nomograms of pneumonia volume, age, and bilirubin, glucose, and urea nitrogen levels, early-stage high-risk patients were successfully identified. The nomogram provided better prediction accuracy than models based on clinical and blood factors or chest CT features alone, demonstrating the value of the nomogram for the prognosis of patients with COVID-19.[35] The C-index of the model was 0.878, which also exceeded the existing prediction models. In addition, our nomogram is convenient and can be used as a rapid and effective tool for personalized prognostic cues and treatment guidance for patients with COVID-19.[36]

As a tool for clinical application, our nomogram includes data from the routine clinical screening of patients with COVID-19. The correction shows numerical agreement between the predicted probabilities and actual results. Although imperfect, this result represents an encouraging level of prediction accuracy.

Unlike earlier models constrained by singular data streams, our multidimensional nomogram integrates radiographic quantification of lung involvement via standardized CT scoring with hematological and biochemical indicators.[14,37–39] This synthesis optimizes severity prediction in hospitalized Omicron-variant COVID-19 patients, achieving superior accuracy for survival outcomes. Notably, the easily accessible factors and user-friendly operation methods of this predictive model render it widely applicable.

This study has several limitations. The limited sample size may have affected the model training. The limited sample size may also have led to a bias in the relationship between prognostic predictions and actual clinical outcomes. To achieve a higher prediction accuracy, the parameters and predictors of the model must be updated to cope with SARS-CoV-2 variants. Another limitation is that we only assessed patients' symptoms, laboratory results, and chest CT findings at admission and did not have data on changes in biomarker levels throughout the disease. This information is important for predicting the clinical course of COVID-19.

In future studies, we will adjust the model parameters and predictors according to the evolving COVID-19 variants. Combined with the whole course data of hospitalized patients, a model that can be predicted from time to time during hospitalization was constructed.

Conclusion

In summary, based on the chest CT imaging of the patient at admission, we evaluated the area of the patient's lung inflammation, combined with the blood test results and history data of the patient at admission. The KM survival curve was constructed by grouping the patients according to the volume of pneumonia. Single- and multi-factor Cox analyses were used to select the most representative prognostic indicators to evaluate disease severity in patients.[40] Individualized prediction models were established to predict the 5-, 10-, 15-, 20-, and 30-day survival rates of patients with COVID-19, which can be used to judge and intervene early in severe patients.

Data Sharing Statement

The raw data supporting the conclusions of this article will be made available by the corresponding authors, without undue reservation. Please contact hangxfdoc@smmu.edu.cn.

Ethics Approval and Consent to Participate

The studies involving human participants were reviewed and approved by the Medical Ethical Committees of Shanghai Changzheng Hospital. Written informed consent for participation was not provided by the participants' legal guardians because the requirement for written informed consent was waived since no additional interventions and potential harm were posed to these patients. The waiver of need for informed consent was approved by the above Medical Ethical Committees. All methods of the study were carried out in accordance with relevant guidelines and regulations. All research studies on humans (individuals, samples or data) have been performed in accordance with the principles stated in the Declaration of Helsinki.

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Disclosure

The authors declared no potential conflicts of interest with respect to the research, authorship, and publication of this article.

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