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ORIGINAL RESEARCH

A Clinical Risk Score Based on Albumin and Electrolyte Levels for Predicting Death Risk in Hospitalized Elderly COVID-19 Patients

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Background: The Omicron subvariants of SARS-CoV-2 spread rapidly since 2021. Following China's relaxation of containment measures in December 2022, a surge in COVID-19 cases poses a public health threat. Early identification of elderly COVID-19 patients at death risk is crucial for optimizing treatment and resource use.

Objective: To develop a clinical score for predicting death risk in elderly COVID-19 patients at hospital admission, based on a cohort from the Second Hospital of Shandong University.

Methods: We established a retrospective cohort of hospitalized COVID-19 patients from November 1, 2022, to March 31, 2023. Cox regression identified prognostic factors, leading to the development of a nomogram-based prediction model and a clinical risk score. Patients were classified into low- and high-risk groups using optimal segmentation thresholds, with survival curves generated by the Kaplan–Meier method. An online risk calculator was developed to facilitate real-time risk assessment in clinical settings.

Results: The cohort included 1413 hospitalized COVID-19 patients. Elderly patients (≥60 years, N = 971) had a high mortality rate of 18.13%. Four independent predictors of mortality were identified: age (HR = 1.07), serum albumin (HR = 0.88), serum potassium (HR = 0.35), and serum sodium (HR = 0.91). The developed risk score demonstrated strong predictive performance and effectively stratified patients into risk categories.

Conclusion: We developed a validated clinical risk score integrating age, serum albumin, potassium, and sodium levels to predict mortality in hospitalized elderly COVID-19 patients. This scoring system enables early risk stratification, assisting clinicians in decision-making and optimizing patient management.

Keywords: hospitalized elder patients with COVID-19, clinical risk score, death risk, albumin, electrolyte levels

Introduction

Coronavirus disease 2019 (COVID-19), was a form of respiratory and systemic zoonosis discovered in December 2019 in Wuhan, China. Since then, it was spreading rapidly around the world, thus turning into a pandemic emergency. As of on May 3, 2023, there were 765,222,932 confirmed global cases of COVID-19, with 6,921,614 deaths, reported to the WHO.[1]

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In response to the COVID-19 pandemic, China has taken the most stringent and proactive public health measures, as exemplified by the "zero COVID" strategy[2] in the first 2 years of the pandemic. But, this is just an initial approach to buy time for assessment and preparation, not a sustainable strategy.[3] As the latest Omicron subvariants of SARS-CoV-2 spread rapidly worldwide in 2022 winter, China's containment strategy faces serious challenges. Just after China abruptly relaxed containment measures on 7 December 2022, a surge in COVID-19 infections, and more severe cases than hospitals can accommodate, pose a major public health threat.[4]

As previously reported from huge studies, the clinical spectrum of COVID-19 pneumonia ranges from mild to critically ill cases. Most of the COVID-19 infections have a milder clinical course, ranging from no symptoms to mild flu-like symptoms such as fever or cough. Whereas some patients may develop severe pneumonia and associated multiple organ failure with high mortality rate in a few days, requiring comprehensive care in ICU.[5] Clinical research has found that, age significantly determined the clinical features and prognosis of COVID-19,[6] and was clearly identified as a significant independent risk factor in COVID-19 critical cases or deaths.[7,8] A WHO worldwide report regarding COVID-19 Mortality and Progress Toward Vaccinating Older Adults, 2020–2022, described that, persons aged ≥60 years accounted for >80% of the overall COVID-19 mortality across all income groups.[9] The COVID-19 pandemic has highlighted the complex interplay between immune aging and viral infection, which can potentially accelerate neuroimmune aging and contribute to, leading to increased risks of neurodegenerative processes and impaired immune function. Key factors include oxidative stress, chronic immune dysregulation, neuroinflammation, and the disruption of cellular processes, which may be related to the high death risk of COVID-19 elderlies.[10] Therefore, more critical illness and a higher death risk in COVID-19 patients aged 60 years or older than the young, clinicians would pay more attention to elder patients requiring hospitalization.

One important lesson from previous epidemiological events is that, when healthcare resources are under severe pressure, early detection of COVID-19 patients who are likely to develop critical illness or death is of great importance, aiding in delivering proper care and optimizing use of limited resources.[4,11] Here, it is important to know which laboratory features of COVID-19 could be used in the initial assessment of death risk in hospitalized patients at admission. To the best of our knowledge, previous research mostly focused on representative abnormal inflammation biomarkers associated with the COVID-19 infection, such as CRP, LDH, IL-10 and D-dimer.[7,8,12] Serum albumin and electrolytes, acting as very crucial basic components guaranteeing immunity in the hospitalized elder patients with COVID-19, were despised. Until now, their influence on adverse outcomes in hospitalized patients with COVID-19 is still lacking.

In the study, we conducted a retrospective cohort study among hospitalized COVID-19 patients admitted in the Second Hospital of Shandong University. Despite the growing body of research on COVID-19, there remains a significant gap in understanding the role of serum albumin and electrolyte levels, which are often overlooked, in predicting mortality among elderly COVID-19 patients. Our hypothesis is that age, these serum albumin and electrolyte levels at admission are key predictors of mortality in hospitalized elderly COVID-19 patients. This study clarifies the critical role of these serum albumin and electrolyte levels serving as critical early indicators of death risk in hospitalized elderly COVID-19 patients. By identifying these key and easily accessible biomarkers at admission, our researchers developed a rapid and practical risk prediction score among hospitalized COVID-19 patients aged 60 years or older. This score would help clinicians identify at-risk patients upon admission, allowing for better risk stratification and more targeted interventions.

Materials and Methods

Design, Subjects, and Procedure

A retrospective cohort study was performed in the Second Hospital of Shandong University, Shandong, China. One thousand four hundred and thirteen adult (age ≥ 18 years) COVID-19 hospitalized patients from November 1, 2022, to March 31, 2023, were included, with clinical and/or radiologic indications of COVID-19 infection, and SARS-CoV-2 confirmed by detection of viral RNA on nasopharyngeal material, using a real-time reverse transcription polymerase chain reaction method (RT-PCR; 2019-nCoV nucleic acid detection kit, Maccura Biotechnology Co., Ltd., GN7111116;

fully automated fluorescence PCR analyzer, Roche Molecular Systems, cobas z480), which is considered the gold standard for COVID-19 diagnosis due to its high sensitivity, specificity, and ability to detect even low viral loads.[13] The exclusion criteria were those <18 years old (n = 276) or with incomplete data (n = 58). Demographic, clinical, and laboratory characteristics of patients were collected. The study was approved by the Research Ethics Committee of the Second Hospital of Shandong University (KYLL-2023LW039) and was conducted in compliance with the World Medical Association Declaration of Helsinki. Informed consent was obtained, and the privacy rights of human subjects were observed.

Data Collection

Data including patient age, gender, hospitalization time, disease outcome, comorbidities, serum albumin (ALB), serum potassium (K), serum sodium (Na), serum chlorine (Cl), serum calcium (Ca), serum magnesium (Mg) and serum phosphorus (P) were extracted from the hospital information systems. All the hematological indicators were measured using the enzyme-linked immunosorbent assays (ELISA) method in the Department of Clinical Laboratory the Second Hospital of Shandong University. Adult reference intervals (all derived from previously performed ad hoc local studies) are: ALB, 35–50 g/L; K, 3.5–5.3 mmol/L; Na, 137–147 mmol/L; Cl, 99–110 mmol/L; Ca, 2.11–2.52 mmol/L; Mg, 0.75–1.02 mmol/L; P, 0.85–1.51 mmol/L. Hypoalbuminemia, hypokalemia, and hyponatremia are defined as ALB < 35 g/L, K < 3.5 mmol/L, and Na < 137 mmol/L, respectively.

Statistical Analysis

Continuous data were expressed as means and Standard Deviations (SD) or median and Interquartile Range (IQR), and Mann–Whitney tests were used for continuous variables. Categorical data were expressed as counts (percentage, %), and Chi-square tests were used for categorical variables. The COVID-19 patients aged 18–59 years old were classified as the young group, and those aged ≥60 years old were classified as the elderly group.

Correlations of COVID-19 death and various characteristics were evaluated using multivariate cox regression analyses. COVID-19 death was used as a dependent variable, while independent variables were: age, gender, comorbidities (including hypertension, cardiovascular disease, chronic pulmonary disease, diabetes mellitus), serum albumin (ALB), serum electrolytes (including serum K, Na, Cl, Ca, Mg and P). To evaluate the associations of COVID-19 death with age, serum ALB, serum K, and serum Na, three models were used. Model 1 was unadjusted. Model 2 was adjusted for gender and comorbidities. Model 3 additionally adjusted for gender, comorbidities, serum Cl, Ca, Mg and P.

The nomogram prediction model was formulated based on the independent prognostic factors, including age, serum ALB, serum K, and serum Na. In the construction of prediction model, the primary endpoint was overall survival (OS), which was defined as the time from diagnosis of COVID-19 infection to all causes of death. Model performance was evaluated by discrimination and calibration. The discriminative ability of the model was evaluated with receiver operating characteristic (ROC) curve analysis and Harrell's concordance index (C-index). A higher C-index value and a larger area under the curve (AUC) in the ROC curve indicated better discrimination ability. Calibration curves were used to evaluate the calibration ability, which was the consistency of predicted and actual survival rates.

Internal validation was performed to evaluate the prediction model in both the training and internal validation sets in the ratio of 7:3, employing the bootstrap resampling method. Calibration and discrimination were assessed to ensure the reliability and generalizability of the model. Additionally, the AUC scores, calculated using multivariable Cox regression models, were separately evaluated in these two sets.

The risk scores of hospitalized elder patients with COVID-19 were calculated using the nomogram. Hypothesis testing was performed to record the hazard ratios (HR) and *P*-values of the Log rank test. The optimal segmentation threshold was determined when the minimum *P*-value was obtained. Patients whose risk scores were higher than the optimal segmentation threshold were assigned to the high-risk group, and the rest were assigned to the low-risk group. The survival curves of the two groups were produced with the Kaplan–Meier method.

All hypotheses were tested at a significance level of 0.05. Data analyses were performed with the statistical software packages R (http://www.R-project.org, The R Foundation) and Free Statistics software version 1.7.1.

Results

A total of 1,413 adult COVID-19 hospitalized patients (≥18 years old) from the Second Hospital of Shandong University were enrolled and analyzed in this clinical study, with 764 males (54.07%) and 649 females (45.93%), suffering from hypertension (588,41.61%), cardiovascular disease (484, 34.25%), chronic pulmonary disease (308, 21.80%) and diabetes mellitus (478, 33.83%).

Sociodemographic characteristics of the elderly group aged ≥60 years old (N = 971) vs the young group aged 18–59 years old (N = 442) are summarized in Table 1. Compared with the young COVID-19 patients, elderly patients showed more comorbidities ($P < 0.001$), longer hospitalization time ($P<0.001$), and more death outcome ($P < 0.001$). While the mortality in young group was only 3.62%, which in elderly group was as high as 18.13%. Regarding the serum albumin and electrolyte levels, the elderly COVID-19 patients had lower serum albumin (ALB) ($P < 0.001$), serum potassium (K) ($P < 0.001$), sodium (Na) ($P < 0.001$), and chlorine (Cl) ($P = 0.014$) than the young patients. No statistically significant difference existed between the two groups in serum calcium (Ca), magnesium (Mg), and phosphorus (K).

A focused analysis was conducted on survival and death outcomes among hospitalized elderly patients with COVID-19. Supplementary Table 1 presents a comprehensive overview of the characteristics of these patients. Significant differences were observed between survival and death groups across various parameters. Survivors of elderly patients exhibited lower level of age ($P < 0.001$), and higher levels of serum ALB ($P < 0.001$), K ($P < 0.001$) and Na ($P < 0.001$) compared to non-survivors. The differences in serum Ca, Mg and P levels were not statistically significant between the two groups.

Multivariate cox regression for death risk in the hospitalized elderly patients with COVID-19, adjusted for gender, comorbidities, serum Cl, Ca, Mg and P, revealed that age (HR = 1.07; 95% CI 1.05–1.08; $P<0.001$) was independent risk factors for death outcome, while serum albumin (HR = 0.88; 95% CI 0.85–0.91; $P < 0.001$), serum K (HR = 0.35; 95% CI 0.25–0.47; $P < 0.001$), and serum Na (HR = 0.91; 95% CI 0.88–0.93; $P < 0.001$) were protective factors (Table 2).

Based on the results of multivariate cox regression analyses, we constructed the prediction model for COVID-19 outcomes in hospitalized people aged ≥60 years old (N = 971). Figure 1 showed the nomogram of the prediction model. Individual patient's value is located on each variable axis, and a line is drawn upward to determine the number of points

Table 1 Characteristics of Hospitalized Patients with COVID-19 (N=1413)

Characteristics	Total (n=1413)	Young (n=442)	Elderly (n=971)	*P*-value
Gender, n (%)				<0.001
Male	764 (54.07)	200 (45.25)	564 (58.08)	
Female	649 (45.93)	242 (54.75)	407 (41.72)	
Hospitalization time, Median (IQR)	11 (6~18)	8 (4~15)	12 (7~19)	<0.001
Outcome, n (%)				<0.001
Survival, n (%)	1221 (86.41)	426 (96.38)	795 (81.87)	
Death, n (%)	192 (13.59)	16 (3.62)	176 (18.13)	
Comorbidities, n (%)				
Hypertension	588 (41.61)	102 (23.08)	486 (50.05)	<0.001
Cardiovascular disease	484 (34.25)	86 (19.46)	398 (40.99)	<0.001
Chronic pulmonary disease	308 (21.80)	50 (11.31)	258 (26.57)	<0.001
Diabetes mellitus	478 (33.83)	83 (18.78)	395 (40.68)	<0.001
Serum albumin (ALB), Mean±SD	36.27±6.44	39.92±5.64	34.61±6.09	<0.001
Serum electrolytes, Mean±SD				
Potassium (K)	3.99±0.45	4.07±0.47	3.75±0.52	<0.001
Sodium (Na)	137.20±4.51	137.52±4.31	134.29±4.93	<0.001
Chlorine (Cl)	103.00±5.33	103.30±5.31	102.09±5.33	0.014
Calcium (Ca)	2.15±0.17	2.16±0.18	2.14±0.17	0.172
Magnesium (Mg)	0.86±0.15	0.86±0.14	0.86±0.15	0.917
Phosphorus (P)	1.12±0.47	1.14±0.36	1.12±0.47	0.397

Notes: Values are presented as means ± SD,Median (IQR) or percents (n). For categorical variables, *P*-values were calculated using $\chi 2$ tests; for continuous variables, *P*-values were calculated using Mann–Whitney tests.
Abbreviations: IQR, Inter-Quartile Range; COVID-19, the coronavirus disease 2019.

Table 2 Multivariate Regression Analysis of Death Outcome in Hospitalized Elder Patients with COVID-19 (N=971)

Variable	Model 1		Model 2		Model 3	
	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
Age	1.06 (1.05~1.08)	<0.001	1.07 (1.05~1.09)	<0.001	1.07 (1.05~1.08)	<0.001
Gender	1.23 (0.91~1.66)	0.175	-	-	-	-
Comorbidities						
Hypertension	0.81 (0.6, 1.11)	0.189	-	-	-	-
Cardiovascular disease	0.81 (0.59, 1.13)	0.218	-	-	-	-
Chronic pulmonary disease	0.99 (0.69, 1.42)	0.970	-	-	-	-
Diabetes mellitus	1.07 (0.79, 1.46)	0.648	-	-	-	-
Serum ALB	0.88 (0.85~0.9)	<0.001	0.88 (0.85~0.9)	<0.001	0.88 (0.85~0.91)	<0.001
Serum electrolytes						
K	0.34 (0.25~0.46)	<0.001	0.34 (0.25~0.46)	<0.001	0.35 (0.25~0.47)	<0.001
Na	0.91 (0.89~0.93)	<0.001	0.91 (0.89~0.93)	<0.001	0.91 (0.88~0.93)	<0.001
Cl	0.98 (0.95~1.01)	0.066	0.98 (0.95~1.01)	0.081	-	-
Ca	0.85 (0.36~2.02)	0.717	0.95 (0.4~2.24)	0.904	-	-
Mg	1.47 (0.55~3.94)	0.444	1.46 (0.54~3.93)	0.452	-	-
P	0.85 (0.6~1.2)	0.364	0.84 (0.59~1.19)	0.335	-	-

Notes: Multivariate cox regression analyses were used. Model 1: unadjusted. Model 2: additionally adjusted for comorbidities and gender. Model 3: additionally adjusted for comorbidities, gender, serum Cl, Ca, Mg and P.
Abbreviations: HR, hazard ratio; CI, confidence interval.COVID-19, the coronavirus disease 2019.

received for each variable value. The sum of these numbers is located on the Total Points axis. Then, risk scores were calculated from the Risk Score axis corresponding each total point of the nomogram, and downward to the survival axes to determine the likelihood of 7-, 14- and 28-day survival probability.

Here, we explored the performance of the prediction model in Figure 2. The ROC curves (Figure 2A) and C-index (Figure 2B) were used to assess the discrimination of the model. The 7-day AUC was 0.74 (95% CI 0.68–0.80), the 14-day AUC was 0.82 (95% CI 0.76–0.87), and the 28-day AUC was 0.78 (95% CI 0.71–0.85). The C-index for the prediction was 0.78 (95% CI 0.83–0.73). All the above indicate good discrimination of the prediction model. For the calibration of the model, as shown in Figure 2C, the calibration curve revealed good concordance between the predicted and observed probabilities, respectively, at 7-, 14- or 28-day.

We integrated the performance metrics derived from internal validation in Supplementary Table 2 and Supplementary Figure 1. The characteristics of the training and testing cohorts are outlined in Supplementary Table 2. In the training set, the 7-day AUC was 0.75, the 14-day AUC was 0.81, and the 28-day AUC was 0.89 (Supplementary Figure 1A). Meanwhile, in the internal validation set, the 7-day AUC was 0.73, the 14-day AUC was 0.80, and the 28-day AUC was 0.79 (Supplementary Figure 1B). These findings further underscore the robustness and reliability of our prediction model across different datasets, reaffirming its efficacy in forecasting COVID-19 outcomes among hospitalized elderly patients.

Next, we got the risk scores of each hospitalized elder patient with COVID-19 based on the nomogram. The different risk scores were correlated with the corresponding log-rank *P*-values, and the optimal segmentation threshold was determined to be 1.03 (Figure 3A). Then, patients were divided into high-risk and low-risk groups according to the optimal segmentation threshold (Figure 3B). This risk stratification is also represented in the nomogram as a band divided into green (low-risk) and red (high-risk) as showed in Figure 2. Finally, Kaplan–Meier curves were drawn for both high-risk and low-risk groups (Figure 3C), showing significant differences in OS between the two subgroups ($P < 0.001$).

Furthermore, an online calculator based on prediction model was developed regarding the hospitalized elderly patients with COVID-19 (Figure 4). Clinicians were allowed to enter each patient's values of the 4 variables of age, serum ALB, K and Na at admission, and the total point and probability of COVID-19 death risk can be calculated automatically, individual patient was assigned to high-risk or low-risk group.

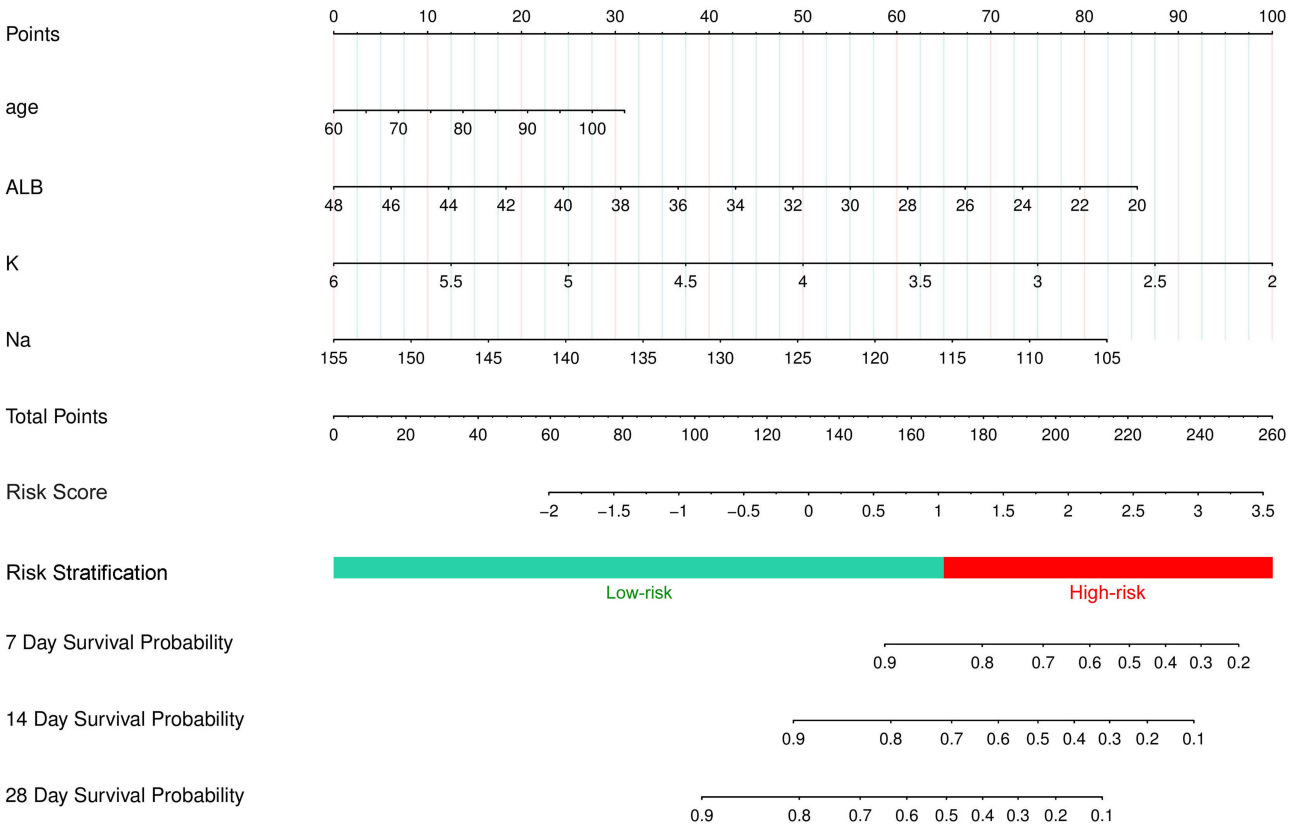

Figure 1 Nomogram for COVID-19 prediction model. The four variable points are allocated for age, ALB, K and Na axis, and the top line points are the value for each variables. The sum of the corresponding points for the variables is the total points. The risk scores calculated by the nomogram correspond to the risk stratification, and 7-, 14-, 28-day survivals are visualized.

Discussion

In our study, the retrospective cohort study conducted in the COVID-19 patients hospitalized in the Second Hospital of Shandong University demonstrated that, four features, including age, albumin levels, sodium and potassium levels at admission were significant predictors of death risk in hospitalized COVID-19 elder patients aged ≥60 years. The 14-day survival prediction model for elder COVID-19 patients constructed with these four features revealed satisfactory performance with the AUC accuracy of 0.82. Based on this model, we developed a clinical risk score to predict the fatal risk among hospitalized elder patients with COVID-19, and patients were categorized into low- and high-risk groups. Given the probability for COVID-19 death risk of up to 67.33% in the high-risk group, we recommend active use of this clinical risk score for risk stratification in elder COVID-19 patients at admission, ensuring that critically ill patients receive appropriate treatment and care support. To our knowledge, this study is the first to establish this predictive model and clinical mortality risk score for hospitalized elder patients with COVID-19 regarding this Omicron wave, since November 2022, China.

China adjusted the zero-COVID strategy in early December 2022, triggering an unprecedentedly large Omicron wave.[14,15] A surge in cases of COVID-19 poses a major public health threat this winter, leading to a sharp increase in fatalities.[4,14] However, there are few reports about hospital mortality of COVID-19 patients during this widespread wave. Based on the retrospective cohort from the Second Hospital of Shandong University, our study reported 18.13% fatality rate of the hospitalized elder COVID-19 patients aged ≥60 years, which is significantly higher than fatality rate of 3.6% among younger patients. It is worth noting that, hospitalized patients aged ≥60 years accounted for 91.7% of the overall COVID-19 mortality, which was consistent with the previous data (>80%) from a report regarding COVID-19 Mortality Older Adults – World Health Organization, Worldwide, 2020–2022.[9] In our study, further multiple cox regression analysis demonstrated that age was an independent predictor of fatal risk in COVID-19 patients, which was supported

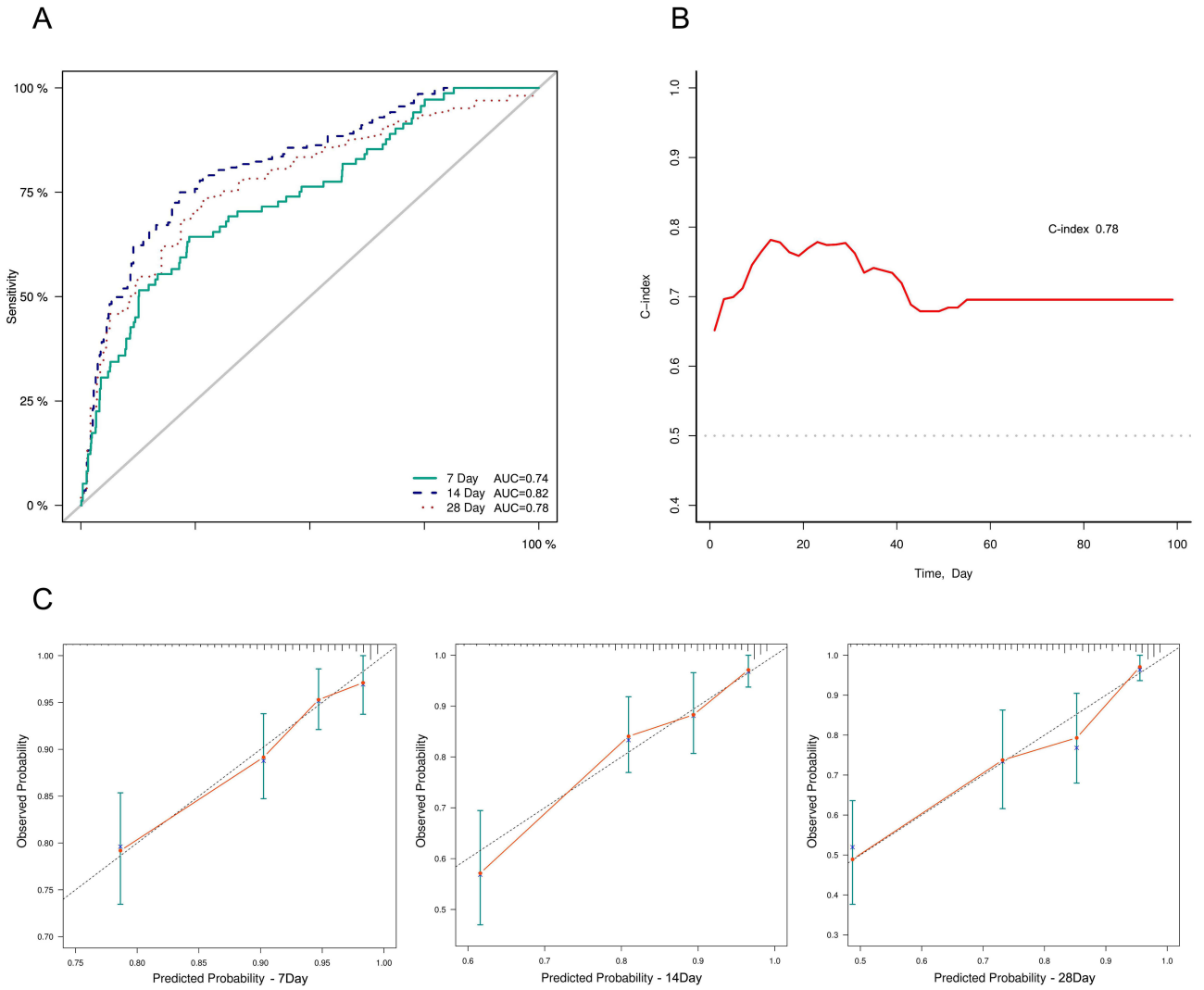

Figure 2 Model performance of nomogram. (**A**) The receiver operating characteristic (ROC) curves of the nomogram at 7 days, 14 days and 28 days. (**B**) Harrell's concordance index (C-index) of the nomogram. (**C**) Calibration curves for predicting patient survival at 7 days, 14 days and 28 days.

by lots of previous research evidence.[16,17] Here, we emphasized that hospitalized elder patients with COVID-19 should be paid much attention to take appropriate treatment to further reduce their death risk.

Using laboratory biomarkers to construct prediction models is an efficient method for identifying fatal risk of COVID-19 patients.[14] In our study, according to the results of multiple regression analysis, three biomarkers, albumin, sodium and potassium levels at admission, were selected as risk factors for death prediction among hospitalized elder COVID-19 patients aged ≥60 years. Admission serum albumin levels have been previously identified as a crucial biomarker in COVID-19 studies, with lower albumin levels being associated with worse clinical outcomes. A study analyzing elderly COVID-19 patients demonstrated that hypoalbuminemia was significantly associated with disease severity, prolonged hospital stays, and increased mortality.[18] In a study conducted in two community hospitals, hypoalbuminemia was significantly correlated with adverse outcomes, including ARDS, venous thromboembolism (VTE), ICU admissions, and 90-day readmissions.[19] This may be due to a diminished immunological response in patients with hypoalbuminemia, reducing their ability to scavenge oxygen radicals during sepsis, thereby increasing their susceptibility to complications such as ARDS, VTE, and mortality.[20,21]

Electrolyte imbalances, particularly sodium and potassium abnormalities, have also been linked to COVID-19 severity. A study by Nicholas Wong Wai Cheong et al found that hypokalemia was associated with gastrointestinal

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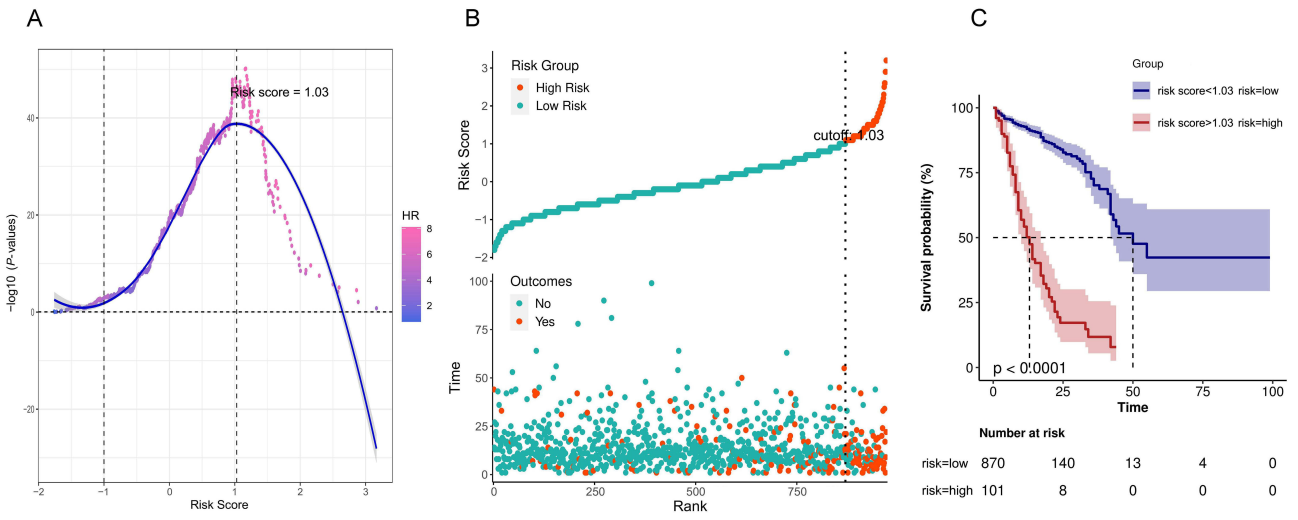

Figure 3 Determine the optimal segmentation threshold of risk score and risk stratification from COVID-19 prediction model. (**A**) Determine the optimal segmentation threshold of risk score by the corresponding log-rank *P*-values of COVID-19 patients. (**B**) Risk factor association chart. The graph above shows the predicted risk scores for each patient ranked in descending order. Two groups are differentiated by the optimal segmentation threshold cutoff value: low-risk (green) and high-risk (red). The graph below presents the relationship between the predicted value-at-risk ranked patients and the survival time. The green dots represent the living patients, and the red dots represent the dead patients. (**C**) Kaplan–Meier curves for overall survival of high-risk and low-risk patients based on the optimal segmentation threshold.

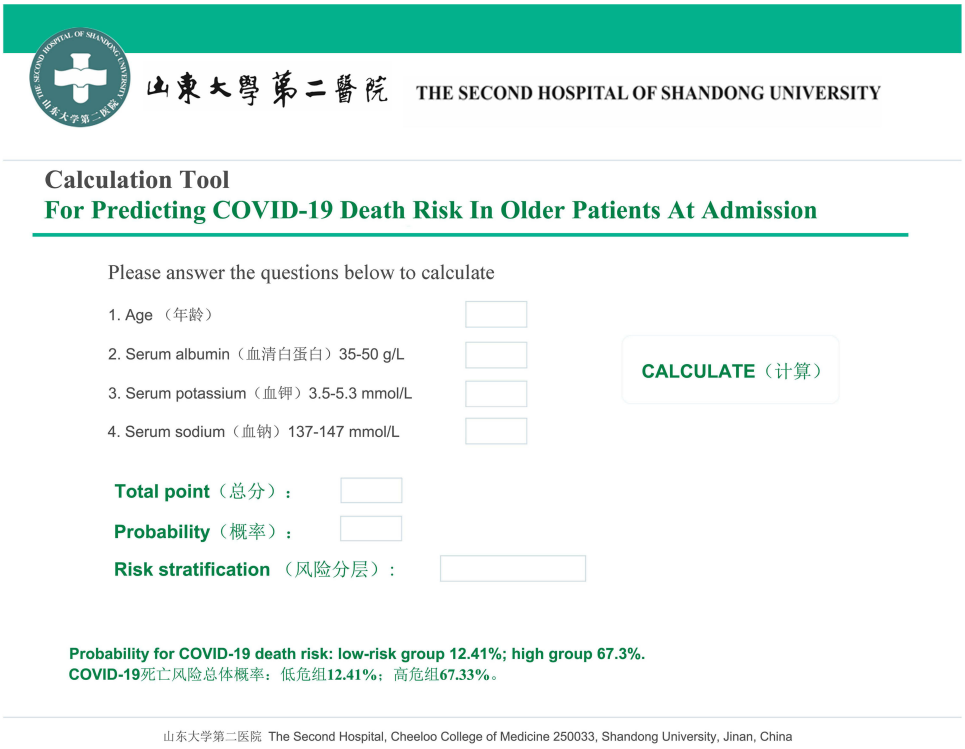

Figure 4 The online calculator for predicting the outcome of elder patients with COVID-19.

symptoms and poorer outcomes in COVID-19 patients treated in public hospitals in Singapore.[22] Similarly, a case series of 306 Mediterranean COVID-19 patients demonstrated that hypokalemia was highly prevalent and served as an independent predictor of invasive mechanical ventilation, making it a sensitive biomarker for disease severity.[23] Moreover, Fatemeh Yasari et al reported that electrolyte imbalances such as hyponatremia and hypocalcemia were predictive of severe disease outcomes.[24] A systematic review also confirmed that hyponatremia was significantly

associated with increased mortality risk, ICU admission, mechanical ventilation requirement, and prolonged LOS.[25] In our study, albumin, potassium, and sodium were analyzed as continuous variables, meaning their protective effects were observed even if they did not cross standard cutoff values. This approach aligns with previous findings that lower levels are associated with worse outcomes. These findings reinforce the importance of monitoring albumin and electrolyte levels upon hospital admission to identify high-risk COVID-19 patients.

Furthermore, electrolyte imbalances have been recognized as key factors in severe COVID-19 cases across different strains of the virus. Lippi G, South A.M., and Henry BM reported that severe COVID-19 patients often presented with significant disturbances in sodium, potassium, and calcium levels, which were linked to increased disease severity and mortality risk.[26] This study, conducted during the early stages of the pandemic, highlights the persistent role of electrolyte imbalances in COVID-19 progression. By comparing our findings with these earlier reports, we provide further evidence that monitoring electrolyte levels remains crucial, regardless of the variant, in predicting patient outcomes and guiding early clinical interventions.

In this study, based on the upper prediction model, we developed a clinical risk score to predict the fatal risk among hospitalized elder patients with COVID-19. The performance of this risk score was satisfactory and can be used by clinicians to estimate an individual elder COVID-19 patient's risk of developing death at admission. The 4 variables required for calculation of the fatal risk are generally readily available at hospital admission, and the clinical risk score is easy to use. We categorized risk into low- and high-risk groups, as we believe that clinicians can stratify COVID-19 elder patients by calculating the fatal risk for each individual, then provide better appropriate treatment approaches and reduce deaths. For example, if the patient's estimated risk for death is low, the clinician may choose to monitor in a general ward, whereas high-risk estimates might support admission to the ICU and more aggressive treatment. Given probability ofCOVID-19 death risk of up to 67.33% in the high-risk group of our study, in areas with high case volume or limited resources, this clinic risk score could help optimize patient outcomes by providing more aggressive care and maximized availability of ICU beds and ventilators for high-risk patients.

Furthermore, our study aligns with findings from prior research on COVID-19 mortality risk among elderly individuals. A study by Chen et al emphasized that advanced age, along with comorbidities, was a major determinant of COVID-19 severity and mortality.[27] Similarly, a large-scale population study by Ioannidis et al demonstrated that the mortality risk of COVID-19 was significantly lower in non-elderly individuals, particularly those without underlying diseases.[28] These studies reinforce the urgent need for effective risk stratification tools, such as our clinical risk score, to improve early identification and management of high-risk elderly COVID-19 patients.

Limitations

Potential limitations of this study include the data for score development and validation are entirely from the Second Hospital of Shandong Province, which could potentially limit the generalizability of this risk score in other areas. External validation using independent cohorts from different geographic areas and healthcare settings is necessary to confirm the robustness and applicability of our findings. Additionally, potential confounding factors, such as pre-existing comorbidities affecting albumin and electrolyte levels, were not fully accounted for due to data limitations, which should be addressed in future research. Furthermore, this study did not include path analysis or structural equation modeling (SEM) to examine causal and non-causal relationships among variables within a hypothesized framework. While the sample size was sufficient for model development and internal validation, it remains relatively small. Combined with the moderate AUC values, this indicates that further refinement and external validation in larger and more diverse cohorts are essential for broader clinical application. Moreover, the model was based on only four variables, which may limit its comprehensiveness, although it allows for a quick and straightforward risk assessment in clinical practice. Future studies could incorporate more advanced analytical techniques to better understand the mechanisms underlying mortality risk in elderly COVID-19 patients.

Conclusions

In this study, we identified four key predictors of mortality in hospitalized elderly COVID-19 patients: age, serum albumin, sodium, and potassium levels at admission. Utilizing these variables, we developed a simple, practical survival prediction

model and a clinical risk score. This risk score enables quick and efficient early identification of high-risk patients, facilitating timely clinical interventions and optimized allocation of medical resources. Our findings highlight the importance of routine assessment of these biomarkers at hospital admission to improve risk stratification and patient outcomes.

Abbreviations

ALB, Albumin; ARDS, Acute Respiratory Distress Syndrome; AUC, Area Under the Curve; CI, Confidence Interval; COVID-19, Coronavirus Disease 2019; CRP, C-Reactive Protein; HR, Hazard Ratio; ICU, Intensive Care Unit; IL-10, Interleukin 10; IQR, Interquartile Range; LDH, Lactate Dehydrogenase; LOS, Length of Stay; Mg, Magnesium; Na, Sodium; P, Phosphorus; ROC, Receiver Operating Characteristic; RT-PCR, Real-time Reverse Transcription Polymerase Chain Reaction; SARS-CoV-2, Severe Acute Respiratory Syndrome Coronavirus 2; SD, Standard Deviation; VTE, Venous Thromboembolism; WHO, World Health Organization.

Data Sharing Statement

The original contributions presented in this study are included in the article/supplementary materials, further inquiries can be directed to the corresponding author/s.

Ethics Approval and Consent to Participate

The study was approved by the Research Ethics Committee of the Second Hospital of Shandong University (KYLL-2023LW039) and was conducted in compliance with the World Medical Association Declaration of Helsinki. Informed consent was obtained for experimentation with human subjects, and the privacy rights of human subjects must always be observed.

Consent for Publication

All authors have read and approved the final manuscript and consent to its publication.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors have no competing Interest to declare in this work.

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