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Original Article

Analysis of in-hospital mortality and associated risk factors in hospitalized elderly patients with an Omicron infection

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Abstract

Introduction: The aim of this study was to evaluate the in-hospital mortality rate and associated risk factors in elderly patients hospitalized with an Omicron coronavirus disease 2019 (COVID-19) infection.

Methodology: This retrospective cohort study included 137 elderly patients with Omicron infection. The cases were divided into survival and mortality groups based on the discharge outcomes. The basic data were collected. A logistic regression model was used to analyze the risk factors for mortality.

Results: The in-hospital mortality rate was 25.54% (102 survivors, 35 non-survivors). The mean age was higher in the mortality group. Shock and dyspnea were more common in the mortality group ($p = 0.041$). Multivariable logistic regression analysis concluded that advanced age (odds ratio, (OR) = 2.158, 95% confidence interval (CI): 1.183–3.368), shock (OR = 2.876, 95% CI: 1.538–8.304), high neutrophil-to-lymphocyte ratio (NLR; OR = 1.872, 95% CI: 1.060–2.424), radiographic pleural effusion (OR = 1.756, 95% CI: 1.592–3.662), and elevated fasting glucose (OR = 1.785, 95% CI: 1.263–3.821) were independent predictors of in-hospital mortality. The Hosmer–Lemeshow test showed that the proposed model had a good fit with observed values ($\chi^2 = 4.681$, $p = 0.341$). The receiver operating characteristic curve indicated that the proposed model had an area under the curve of 0.791 for predicting mortality, with a sensitivity of 83.9% and specificity of 61.5%.

Conclusions: The in-hospital mortality rates were high in elderly patients with Omicron infection. Advanced age, glucose level, shock, NLR, and pleural effusion were identified as risk factors.

Key words: Omicron; elderly patients; mortality; risk factors; prediction model.

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Introduction

Since the coronavirus disease-2019 (COVID-19) outbreak in December 2019, the number of confirmed cases and deaths from COVID-19 has increased steadily, worldwide. As the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus spread, it mutated from the original ancestor strain to Alpha, Beta, Delta, and finally to Omicron variants. Omicron was detected for the first time at the end of 2021 [1–2]. The Omicron spike protein has accumulated 32 mutations, twice as many as the Delta variant with up to 10 mutations occurring in the receptor binding domain where the virus first contacts human cells, and 5 times more than the Delta variant [1]. The Omicron variant has extremely high infectiousness, faster spread, and increased reinfection rate (especially higher immune system evasion potential); and has replaced the Delta variant as the predominant strain in China and the world. The Omicron subvariants currently infecting the Chinese population are mainly BA.5 and its sub-lineages BA.5.2 and BF.7, all of which spread rapidly after infection. Infection by these variants can swiftly progress to severe and critical illness, or even death, in elderly patients with weakened immunity and physiological function [3].

Omicron infections pose a major challenge to healthcare systems worldwide. A prospective, multicenter cohort study in Switzerland found that while COVID-2019 mortality decreased from an initial 12.8% to 7%, the in-hospital mortality rate for patients hospitalized with an Omicron infection remained 50% higher than for patients hospitalized with influenza [4]. Unlike prior variants, Omicron evades immunity more readily. While the 1-year Delta reinfection rate was just 1.2%, the probability of Omicron reinfection within 1 year of initial infection is around 13% [5]. Research has demonstrated that individuals experiencing reinfection are at a heightened risk of mortality, hospitalization, and development of various chronic conditions compared to those with primary infections [6]. Therefore, in order to improve survival in elderly patients hospitalized with Omicron, early identification of the risk factors for in-hospital mortality is crucial in clinical practice. Existing studies associate old age,

male gender, and comorbidities with a poorer prognosis; however, the results are somewhat inconsistent and definitive conclusions on some potential risks are lacking [7–9]. COVID-2019 management (including lowering mortality) will encounter new challenges globally as a result of relaxing pandemic restrictions.

This study evaluated the clinical data on Omicron cases in elderly patients hospitalized during the peak of the pandemic in China (November 2022 to February 2023), with the aim to investigate in-hospital mortality and the influencing factors in this population, to inform clinical prevention and management of Omicron variant infections.

Methodology

Study subjects

This study was a retrospective analysis of 137 cases of elderly patients with Omicron infection who were hospitalized at The First Hospital of Shanxi Medical University between December 2022 and February 2023. The inclusion criteria were: (1) diagnosed with an Omicron infection as per the diagnostic and clinical classification criteria stated in the Diagnosis and Treatment Protocol for COVID-19 (Trial Version 10) [10]; (2) age ≥ 60 years; and (3) hospitalized patients. The exclusion criteria were (1) patients with incomplete or missing medical records; and (2) patients who died within 24 hours of admission. This study was approved by the Ethics Committee of The First Hospital of Shanxi Medical University.

Research methods

The study subjects were divided into two groups: survival and mortality, based on the discharge outcomes. The clinical data, laboratory test results, and chest imaging findings of the two groups were compared. The risk factors for mortality in elderly patients hospitalized with an Omicron infection were analyzed using the discharge outcome as the dependent variable; and the clinical data, laboratory test results and chest imaging results as independent variables. A prediction model for such mortality was established, and its predictive performance was evaluated.

Data collected

The clinical information, laboratory results, and chest imaging findings of the study subjects were retrospectively collected; the latter two obtained within 48 hours of hospitalization.

The clinical information included gender, age, medical history (hypertension, diabetes, coronary artery disease, and chronic obstructive pulmonary disease), and symptoms (shock, altered mental status, fever, dyspnea, cough, sputum production, fatigue, chest tightness, chest pain, and diarrhea).

The chest imaging data included computed tomography (CT) findings of pneumonia or pleural effusion.

The laboratory test data included: (i) blood routine parameters such as white blood cells ($\times 10^9$/L), hemoglobin (g/L), platelets ($\times 10^9$/L), neutrophils ($\times 10^9$/L), lymphocyte percentage (%), neutrophil-to-lymphocyte ratio (NLR), lymphocytes ($\times 10^9$/L), aspartate aminotransferase (U/L), and alanine aminotransferase (U/L); (ii) inflammatory markers such as albumin (g/L), total bilirubin (umol/L), creatinine (umol/L), creatine kinase isoenzymes (ng/mL), C-reactive protein (mg/L), and procalcitonin (ng/ml); (iii) coagulation function parameters such as prothrombin time (PT, s), PT%, activated partial thromboplastin time (s), D-dimer (mg/L), and fibrinogen (g/L); (iv) blood biochemical parameters such as the potential of hydrogen (pH), partial pressure of carbon dioxide (PCO_2, mmHg), partial pressure of oxygen (mmHg), base excess (BE, mmol/L), bicarbonate (mmol/L), blood oxygen saturation (%), fraction of inspired oxygen, oxygen partial pressure (mmHg), fasting blood glucose (FBG, mmol/L), and lactic acid (Lac, mmol/L).

In addition, data on antiviral therapy; i.e. whether the patients received azithromycin, nirmatrelvir, ritonavir, etc. during hospitalization; was recorded.

Statistical analysis

We used Excel 2016 for data collation and verification, and SPSS 26.0 (IBM Corp, Armonk, NY, USA) for statistical description and analysis. Normally distributed quantitative data were expressed as mean ± standard deviation ($x \pm s$) and compared between groups using the t-test. Non-normally distributed quantitative data were expressed as median and interquartile range (P25, P75), and compared between groups using the Z-test. Qualitative data were expressed as frequency or percentage (%) and compared between groups using the Chi-squared test. Multivariable logistic regression analysis was conducted using in-hospital deaths to identify risk factors for mortality in patients with an Omicron infection. The Hosmer–Lemeshow test and receiver operating curve (ROC) were used to evaluate the predictive performance of the logistic regression model, and $p < 0.05$ was considered statistically significant.

Results

Characteristics of elderly patients hospitalized with Omicron infection

The in-hospital mortality rate was 25.55% among the 137 elderly patients hospitalized with Omicron infection (102 in the survival group and 35 in the mortality group). The mean age was higher in the mortality group (74.50 ± 14.16 years) compared to the survival group (t = 2.450, p = 0.016). The male-to-female ratio was 2.09:1 in the survival group and 1.92:1 in the mortality group, indicating no statistically significant difference. The main symptoms in both groups included fever, cough, sputum production, and fatigue; while shock and dyspnea were more common in the mortality group. Imaging findings showed a higher proportion of pleural effusion in the mortality group compared to the survival group (29.41 vs 60.00, χ^2 = 4.103, p = 0.043). There was no significant difference in the use of antiviral medications between the groups. The details are summarized in Table 1.

Comparison of laboratory test results in the two patient groups

There were statistically significant differences (p < 0.05) in routine blood parameters between the survival group and the mortality group in terms of white blood cell count (9.8 ± 5.33 vs 12.4 ± 5.41), neutrophil count (8.42 ± 5.08 vs 11.05 ± 5.43), lymphocyte percentage (8.7 ± 7.68 vs 4.64 ± 3.43), and NLR [2.08 (0.71, 3.47) vs 18.67 (9.82, 47.32)]. In addition, there were statistically significant differences (p < 0.05) in inflammatory markers between the groups in terms of albumin levels (30.92 ± 3.93 vs 29.06 ± 3.86). There were statistically significant differences (p < 0.05) in the biochemical indicators between the groups in terms of BE ((– 0.78 ± 8.03) vs (– 4.78 ± 7.84), FBG (9.6 ± 4.04 vs 16.35 ± 17.69), and Lac (2.26 ± 1.21 vs 3.63 ± 4.04). None of the coagulation indicators showed statistically significant differences between the survival and mortality groups (p > 0.05). The details are summarized in Table 2.

Multivariable logistic regression analysis of risk factors associated with mortality in Omicron infections

Our multivariable logistic regression model used discharge outcomes as the dependent variable and incorporated independent variables identified via univariate analysis as statistically significant and clinically meaningful. After directly inputting continuous variables into the model, the regression results indicated that advanced age (odds ratio (OR) = 2.158, 95%, confidence interval (CI): 1.183–3.368), presence of shock (OR = 2.876, 95% CI: 1.538–8.304), high NLR (OR = 1.872, 95% CI: 1.060–2.424), radiographic pleural effusion (OR = 1.756, 95% CI: 1.592–3.662), and elevated FBG (OR = 1.785, 95% CI: 1.263–3.821), were independent predictors of in-hospital mortality among hospitalized elderly patients with Omicron infection. The details are summarized in Table 3.

Performance evaluation of the prediction model

Based on the preceding analysis, five parameters—age, presence of shock, NLR, pleural effusion, and blood glucose level—were utilized to construct a logistic prediction model for in-hospital mortality in

Table 1. Comparison of baseline characteristics between the two groups.

	Survival group (n=102)	Mortality group (n=35)	t/χ^2	p
Age (years)	67.51 ± 14.49	74.50 ± 14.16	2.450	0.016
Gender (male/female)	69/33	23/12	0.119	0.732
Symptoms (N/%)			14.631	0.041
Shock	2 (1.96)	7 (20.00)		
Disturbance of consciousness	56 (54.90)	21 (60.00)		
Fever	84 (82.35)	28 (80.00)		
Difficulty breathing	52 (50.98)	31 (88.57)		
Cough, expectoration	79 (77.45)	28 (80.00)		
Fatigue	89 (87.25)	31 (88.57)		
Chest tightness, chest pain	8 (7.84)	2 (5.71)		
Diarrhea	8 (7.84)	2 (5.71)		
Basic diseases (N/%)				
Diabetes	26 (25.49)	11 (31.43)	0.466	0.495
Hypertension	21 (20.59)	13 (37.14)	3.827	0.046
Coronary heart disease	24 (23.53)	6 (17.14)	0.621	0.431
COPD	13 (12.75)	4 (11.43)	0.042	0.838
Chest imaging (N/%)				
Pneumonia	80 (78.43)	35 (100.00)	-	-
Pleural effusion in pneumonia	30 (29.41)	21 (60.00)	4.103	0.043
Used antivirals			0.873	0.350
Yes	80	30		
No	22	5		

COPD: chronic obstructive pulmonary disease.

Table 2. Comparison of laboratory test results between the groups.

Laboratory items	Survival group (n = 102)	Mortality group (n = 35)	*t/Z*	*p*
Blood routine				
White blood cells (*10^9)	**9.8 ± 5.33**	**12.4 ± 5.41**	**2.248**	**0.026**
Hemoglobin (g/L)	107.56 ± 29.29	94.73 ± 34.51	– 1.935	0.055
Platelets (*10^9)	171.49 ± 87.89	142.43 ± 71.76	– 1.590	0.115
Neutrophils (*10^9)	**8.42 ± 5.08**	**11.05 ± 5.43**	**2.353**	**0.020**
Lymphocyte percentage (%)	**8.7 ± 7.68**	**4.64 ± 3.43**	**– 2.704**	**0.008**
Lymphocytes (*10^9)	3.87 (1.85, 9.37)	0.49 (0.12, 4.07)	– 0.671	0.090
NLR	**2.08 (0.71, 3.47)**	**18.67 (9.82, 47.32)**	**97.340**	**< 0.001**
AST (U/L)	89.83 (42.37, 106.81)	55.54 (32.28, 96.21)	– 0.881	0.380
ALT (U/L)	78.71 (32.78, 136.14)	32.54 (12.84, 166.28)	– 1.107	0.271
Inflammatory factors				
Albumin (g/L)	**30.92 ± 3.93**	**29.06 ± 3.86**	**– 2.196**	**0.030**
Total bilirubin (umol/L)	17.7 ± 11.97	13.4 ± 7.63	– 1.783	0.077
Creatinine (umol/L)	153.16 (78.62, 201.39)	151.11 946.28, 271.13)	– 0.036	0.971
CK-MB (ng/mL)	8.52 ± 12.03	7.14 ± 10.9	– 0.302	0.764
C-reactive protein (mg/L)	99.51 ± 92.81	114.39 ± 53.39	0.485	0.630
Procalcitonin (ng/ml)	8.64 ± 27.54	8.33 ± 14.27	– 0.052	0.959
Coagulation				
PT (s)	14.27 ± 2.56	14.79 ± 2.51	0.942	0.348
APTT (s)	37.4 ± 18.37	42.09 ± 14.22	1.238	0.218
D-dimer (mg/L)	10.47 ± 18.02	13.68 ± 15.23	0.740	0.461
Fibrinogen (g/L)	4.24 ± 1.59	3.89 ± 1.71	– 0.996	0.321
Blood chemistry				
PH	7.32 ± 0.75	7.32 ± 0.14	– 0.033	0.973
PCO_2 (mmHg)	37.82 ± 12.51	42.65 ± 15.1	1.720	0.088
PO_2 (mmHg)	90.93 ± 44.41	76.18 ± 31.23	– 1.660	0.100
BE (mmol/L)	**– 0.78 ± 8.03**	**– 4.78 ± 7.84**	**– 2.353**	**0.020**
HCO_3 (mmol/L)	20.99 ± 6.82	– 0.78 ± 8.03	– 1.162	0.248
SpO_2 (%)	92.98 ± 8.95	89.56 ± 18.01	– 1.333	0.185
FIO_2	0.57 ± 0.23	0.52 ± 0.27	– 0.667	0.508
PO_2 (A-a) (mmHg)	157.86 ± 145.24	154.88 ± 199.14	– 0.059	0.953
FBG (mmol/L)	**9.6 ± 4.04**	**16.35 ± 17.69**	**3.152**	**0.002**
Lac (mmol/L)	**2.26 ± 1.21**	**3.63 ± 4.04**	**2.673**	**0.009**

NLR: neutrophil to lymphocyte ratio; AST: aspartate aminotransferase; ALT: glutamic-pyruvic transaminase; CK-MB: creatine kinase isoenzymes; PT: prothrombin time; APTT: activated partial thromboplastin time; PH: potential of hydrogen; PCO_2: partial pressure of carbon dioxide; PO_2: partial pressure of oxygen; BE: base excess; HCO_3: carbonic acid hydrogen radical; SpO_2: blood oxygen saturation, FIO_2: fraction of inspiration O_2; PO_2: oxygen partial pressure; FBG: fasting blood glucose; Lac: lactic acid. Bold font indicates significant differences between the two groups.

elderly patients hospitalized with Omicron infection. The Hosmer–Lemeshow test demonstrated an acceptable model fit with the observed outcomes (χ^2 = 4.681, p = 0.341). Additionally, the ROC curve showed that the model had an area under the curve of 0.791 for predicting in-hospital deaths in these hospitalized patients, with 83.9% sensitivity and 61.5% specificity (Figure 1).

Discussion

This study conducted a retrospective analysis of 137 patients hospitalized with Omicron infection. The findings indicate that advanced age, shock, high NLR ratio, radiographic evidence of pleural effusion, and elevated fasting blood glucose were independent risk factors for in-hospital mortality in elderly patients with Omicron. In the early stages of the pandemic, COVID-2019 patients with severe illness experienced rapid deterioration, with some developing various complications or multi-organ failure leading to death [11]. Therefore, it is especially important to identify high-risk patients more accurately, and to reduce mortality rates in critically ill patients. The SARS-CoV-2 has undergone multiple rounds of mutation, from the Alpha variant known for high transmissibility, to the immune-evading Beta and Gamma variants capable of

Table 3. Multivariable logistic regression analysis of mortality in Omicron patients.

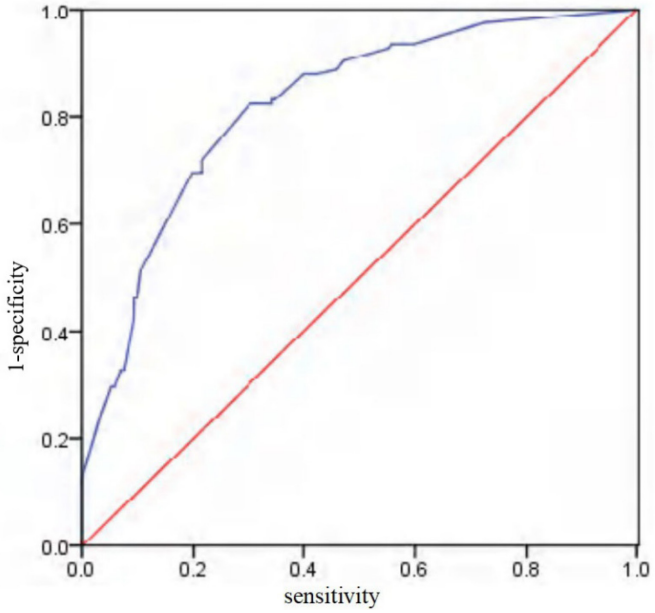
	β	SE	Wals	*p*	OR	95% CI
Age	0.444	0.075	4.531	0.033	2.158	1.183–3.368
Shock	0.513	0.068	5.256	0.022	2.876	1.538–8.304
NLR	0.271	0.083	6.512	0.023	1.872	1.060–2.424
FBG	0.126	0.061	4.195	0.041	1.785	1.263–3.821
Shock	0.513	0.068	5.256	0.022	2.876	1.538–8.304
Pleural effusion in pneumonia	0.365	0.077	4.321	0.038	1.756	1.592–3.662

NLR: neutrophil-to-lymphocyte ratio; FBG: fasting blood glucose; SE: standard error; OR: odds ratio; CI: confidence interval.

reinfecting recovered individuals [12]. The latest Omicron variant is characterized by high transmissibility, low virulence, reduced severity, and mortality. However, it is still responsible for considerable mortality in patients hospitalized with severe disease. For instance, Qin *et al*. reported a 5.7% mortality rate in hospitalized Omicron cases [13]. In particular, elderly individuals with multiple underlying conditions are extremely prone to developing fatal injuries, such as diffuse alveolar damage, acute respiratory distress syndrome, and multiple organ failure after infection [14]. Carvalho *et al*. reported 46.1% mortality in patients hospitalized with COVID-19 [15]. Moreover, Omicron's high transmissibility can overwhelm baseline healthcare resources with surges of infections. When there are large patient volumes and shortages of relevant medications, many critically ill patients may not receive effective treatment, which can contribute to high in-hospital mortality, as found in this study.

In this study, the clinical data, laboratory tests, imaging findings, and treatment outcomes of 137 hospitalized Omicron patients were retrospectively analyzed. The key findings were that the in-hospital mortality rate was 25.54% (35/137); and multivariable logistic regression identified advanced age, presence of shock, high NLR, imaging evidence of pleural effusion, and elevated fasting blood glucose as independent risk factors for in-hospital mortality. Previous studies suggest that the significantly higher in-hospital mortality in elderly patients compared to younger patients may relate to poorer physiological status, more comorbidities, lower immunity, and lower willingness or accessibility to diagnosis and treatment [16–18]. Some studies have also found that male patients with Omicron are more likely to die in the hospital compared to females. For example, in the study by Yang *et al*., among the 52 critically ill patients, 32 were non-survivors, of whom 21 were male and 11 were female [19]. Male patients with Omicron are more likely to die in the hospital primarily because they have more risk factors, such as a history of smoking and obesity. These factors contribute to more severe outcomes through multiple mechanisms, including impaired immune function (such as weaker immune responses and hormonal influences), exacerbated inflammatory responses (such as chronic inflammation and lung damage), cardiovascular damage (such as hypertension, heart disease, and vascular injury), and social and behavioral factors (such as lower health awareness and unhealthy lifestyle habits). These mechanisms collectively lead to more severe disease progression and

Figure 1. Receiver operating characteristic (ROC) curve of the logistic regression model.



a higher risk of death in male patients infected with Omicron. Other studies have identified smoking and obesity as risk factors for mortality [20]. However, in the present study, there were no significant gender differences in mortality, which may be attributable to the study population consisting of older adults. Regarding the clinical symptoms, shock at admission was identified as a mortality risk factor in elderly patients, consistent with previous reports [21]. Some patients with underlying conditions such as diabetes, hypertension, and renal impairment experienced rapidly deteriorating conditions, which led to acute respiratory distress syndrome, septic shock or refractory metabolic acidosis, and coagulopathy after infection; and eventually death by multiple organ failure [22]. However, this study did not identify these complications as risk factors, possibly due to the small sample size. Nevertheless, consistent with some previous studies [23], elevated fasting blood glucose was identified as a risk factor in this study. Hyperglycemia can increase the risk of mortality in older adults with Omicron infection through multiple mechanisms, including impaired immune function, exacerbated inflammatory responses, vascular damage, metabolic disorders, and multi-organ dysfunction. These mechanisms interact synergistically, collectively leading to disease progression and an increased risk of death. Additionally, it was found that cytokine storm syndrome in severe COVID-19 cases can cause uncontrolled inflammation, shock, and organ damage and failure [24]. Viral invasion activates the immune

system, leading to the release of a large number of cytokines (such as IL-1β, IL-6, and TNF-α), which form a positive feedback loop and trigger a systemic inflammatory response. The cytokine storm increases vascular permeability, causing edema and hypotension, and leads to microcirculatory disturbances and tissue hypoxia. Additionally, it causes damage to vital organs such as the lungs, heart, kidneys, and liver; potentially progressing to multiple organ dysfunction syndrome.

This study identified pleural effusion as a risk factor for in-hospital mortality. Pleural involvement likely only occurs with more severe disease progression, and associated chest pain and dyspnea may further exacerbate lung injury and inflammatory mediator release. Ionescu *et al.* also reported an association between pleuritis and other complications with increased in-hospital mortality in patients with COVID-19 [25].

This study demonstrated good predictive ability of the proposed model by developing a multivariate regression model encompassing multiple risk parameters, quantifying the risks, and evaluating model performance via multicollinearity testing and ROC analysis. This can aid the clinical evaluation of hospitalized elderly as a high-risk group and guide the selection of more targeted preventive strategies and clinical practices.

This study has several limitations. First, there may be biases in extrapolating the results due to the short study period and small sample size. To address this, large-scale multicenter cohort studies should be conducted to validate the risk factors for mortality after an Omicron infection. Second, this study did not consider the effects of other sociological factors (such as economic status, marital status, and smoking and alcohol consumption) on mortality in patients with an Omicron infection. Finally, since this was a cross-sectional study, the effects of risk factors on mortality were explored based only on clinical data collected at admission, without considering changes in these parameters during hospitalization. As such, future studies should incorporate follow-up to capture fluctuations in parameters during hospitalization to elucidate further how different factors influence mortality.

Conclusions

The in-hospital mortality rate for patients with Omicron infection remains high. Logistic regression analysis identified advanced age, glucose levels, shock, NLR, and pleural effusion as significant risk factors. Therefore, in the future management of Omicron cases, special attention should be paid to older patients, to vigilantly track glucose aberrations to gauge shock potential, and promptly implement interventions such as goal-directed therapy, when appropriate.

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Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of The First Hospital of Shanxi Medical University (No. KYLL-2023-230). Written informed consent was obtained from all participants/local guardians.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Authors' contributions

YL, study conception and design; JL and Y-NW, data collection and analysis; Y-TZ, JZ, and JC, manuscript draft and revision. All authors read and approved the final manuscript.

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Conflict of interest

No conflict of interest is declared.

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