

# Serum lactate and the mortality of critically ill patients in the emergency department: A retrospective study

XIAOYU MA<sup>1</sup>, JIANING LI<sup>1</sup>, QIYANG ZHOU<sup>2</sup> and JUEJIN WANG<sup>3</sup>

<sup>1</sup>The Second Clinical Medical School, Nanjing Medical University, Nanjing, Jiangsu 210011;

<sup>2</sup>The First Clinical Medical School, Nanjing Medical University, Nanjing, Jiangsu 210006;

<sup>3</sup>Department of Physiology, Nanjing Medical University, Nanjing, Jiangsu 210000, P.R. China

Received November 23, 2022; Accepted May 5, 2023

DOI: 10.3892/etm.2023.12070

**Abstract.** Serum lactate levels have been widely studied as a prognostic marker in critically ill patients, particularly those in the intensive care unit. However, it remains unknown whether the serum lactate levels affect the mortality rate of critically ill patients admitted to hospital. To investigate this hypothesis, the vital signs and blood gas analysis data of 1,393 critically ill patients who visited the Emergency Department of Affiliated Kunshan Hospital of Jiangsu University (Kunshan, China) between January and December 2021 were collected. Patients were divided into two groups, 30-day survival group and a 30-day death group, and logistic regression analysis was used to investigate the association between vital signs, laboratory results and mortality rates of critically ill patients. A total of 1,393 critically ill patients was enrolled in the present study, with a male-to-female ratio of 1.17:1.00, a mean age of 67.72±19.29 years and a mortality rate of 11.6%. The multivariate logistic regression analysis revealed that increased serum lactate levels were an independent risk factor for mortality rate of critically ill patients [Odds ratio (OR)=1.50, 95% confidence interval (95% CI): 1.40-1.62]. The critical cut-off value for the serum lactate levels was identified as 2.35 mmol/l. In addition, OR values of age, heart rate, systolic blood pressure, transcutaneous oxygen saturation (SpO<sub>2</sub>) and hemoglobin were 1.02, 1.01, 0.99, 0.96 and 0.99, respectively (95% CI: 1.01-1.04, 1.00-1.02, 0.98-0.99, 0.94-0.98 and 0.98-1.00, respectively). The logistic regression model was found to be of value in terms of identifying the mortality rate of patients and the area under the receiver operating characteristic curve was 0.894 (95% CI: 0.863-0.925; P<0.001). In conclusion, the present study showed that high serum lactate levels in critically ill

patients upon admission to hospital are associated with higher 30-day mortality rate.

## Introduction

Critically ill patients are those who have unstable vital signs, rapid disease progression, instability or failure of more than two organ systems and a high risk of mortality due to their condition (1). The emergency department serves a crucial role during the process of diagnosing and treating certain critically ill patients. The physiological parameters and laboratory blood gas analysis results measured at the time of first admission to the emergency department may serve as auxiliary parameters for physicians to determine whether hospitalization is necessary and their likely risk of mortality (2). Among these parameters, serum lactate is a product of the metabolic reaction in cases of acute disease, and it is easily measured in the laboratory (3-6). Serum lactate measurements have been shown to be strongly associated with prognosis of sepsis, gastrointestinal bleeding, pulmonary embolism and other disease (7-9).

Previous studies have used lactate levels to stratify risk in patients with sepsis (7,10,11). Lactate levels <2 mmol/l are considered low and lactate >4 mmol/l is considered high; high levels of serum lactate are considered to be an independent predictor of mortality (12). However, to the best of our knowledge, whether serum lactate levels can be used as a predictor of mortality rate in critically ill patients admitted to emergency departments remains unknown (12,13). In addition, the role of other physiological and laboratory parameters in predicting patient mortality remains unclear.

The aim of the present study was to identify parameters and their cutoff values that were independently associated with mortality in critically ill patients who presented to the Emergency Department in the Affiliated Kunshan Hospital of Jiangsu University (Kunshan, China). Furthermore, a prediction model was constructed to assess the mortality of patients to aid diagnosis and treatment.

## Patients and methods

**Study design and setting.** This was a single center, retrospective cohort study. Cases attending the Emergency Department of Affiliated Kunshan Hospital of Jiangsu University between

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*Correspondence to:* Professor Juejin Wang, Department of Physiology, Nanjing Medical University, 818 Tianyuan East Road, Nanjing, Jiangsu 210000, P.R. China  
E-mail: juejinwang@njmu.edu.cn

**Key words:** lactate, critically ill patient, mortality, logistic regression, emergency department

January and December 2021 were collected. Cases under the age of 16 years and those transferred to the hospital after admission or discharged against medical advice were excluded. Finally, a total of 1,393 cases was included in the present study. These critically ill patients were divided into 30-day survival ( $n=1,231$ ) and a 30-day death group ( $n=162$ ).

Demographic parameters (age and sex), patient classification (disease type), vital signs [systolic blood pressure (SBP), diastolic blood pressure (DBP), heart and respiratory rate, temperature and transcutaneous oxygen saturation ( $SpO_2$ )] and laboratory results [serum lactate levels, white blood cell (WBC) count, hemoglobin levels, platelet count, prothrombin time, creatinine and total bilirubin levels and base excess (BE)] of cases were analyzed. Blood samples (0.5-1.0 ml) were collected for blood gas analysis within 30 min of arrival at the emergency department. The laboratory results were measured using an ABL90FLEX blood gas analyzer (Radiometer Medical).

The present study was approved by the Ethics Review Committee of The Affiliated Kunshan Hospital of Jiangsu University (grant no. 2021-03-015-H01). The requirement for consent to participate was waived due to the retrospective nature of the study.

**Statistical analysis.** IBM SPSS version 26 software was used for statistical analysis (IBM Corp.). Descriptive statistical parameters (mean, standard deviation, median, minimum, maximum and frequency) were used to evaluate data. First, whether the quantitative data conformed to the normal distribution was tested using quantile-quantile and probability-probability plots and the Shapiro-Wilk test. An unpaired Student's t-test was used to compare the quantitative variables with normal distribution between survival group and death group. The Mann-Whitney U test was used to compare the quantitative variables without normal distribution. Pearson's  $\chi^2$  test was used to compare qualitative data between the two groups. Binary logistic regression analysis was used to construct the prognosis model. Sensitivity, specificity and the area under receiver operating characteristic (AUROC) curve analysis were used to determine the diagnostic critical value for the parameters.  $P<0.05$  was considered to indicate a statistically significant difference.

## Results

**Demographics and outcomes.** A total of 1,393 cases was included in the present study, of which 63.1% ( $n=879$ ) were male and 36.9% ( $n=514$ ) were female. The ages of the cases were between 16 and 104 years and the mean age was  $67.72\pm 19.29$  years. Patients were primarily diagnosed with the following seven categories of disease: Respiratory (38.3%), cardiovascular (17.1%), nervous system (13.2%), digestive system (10.8%) and endocrine system (7.8%), poisoning (4.5%) and urinary system diseases (4.0%); a residual population (4.1%) were classified as 'other diseases'. Serum lactate measurements ranged between 0.20 and 26.00 mmol/l, with a mean value of  $2.64\pm 3.15$  mmol/l. Blood glucose measurements ranged between 0.90 and 73.30 mmol/l, with a mean value of  $11.13\pm 7.80$  mmol/l. Vital signs and laboratory results of the cases are shown in Table I. Of total cases, 1,042 hospitalizations (74.8%) and 162 deaths (11.6%) were observed. The

number of days of hospitalization was 0-90, with a mean value of  $9.55\pm 9.15$  days (Table I).

**Association between serum lactate levels and clinical outcomes in critically ill patients.** Among the demographic parameters, ages of the cases in the mortality group were significantly higher compared with the survival group ( $P=0.003$ ), whereas the mortality rates did not differ significantly between males and females ( $P=0.936$ ; Table II). Among the vital signs, heart rate ( $P=0.001$ ), SBP ( $P<0.001$ ), DBP ( $P<0.001$ ) and  $SpO_2$  ( $P<0.001$ ) in the mortality group were significantly higher compared with those in the survival group, although no significant differences were observed with respiratory rate ( $P=0.492$ ) or temperature ( $P=0.443$ ; Table II). Among the laboratory results, the serum lactate ( $P<0.001$ ), BE ( $P<0.001$ ) and hemoglobin levels ( $P<0.001$ ), platelet ( $P=0.049$ ) and WBC count ( $P<0.001$ ), creatinine levels ( $P<0.001$ ) and prothrombin time ( $P<0.001$ ) in the mortality group were significantly higher compared with those in the survival group, whereas glucose and total bilirubin measurements were not found to be associated with mortality ( $P=0.085$ ; Table II).

**Risk factors for mortality of critically ill patients.** The univariate logistic regression showed that age, heart and respiratory rate, SBP, DBP,  $SpO_2$ , serum lactate and BE levels, WBC count, creatinine, hemoglobin and total bilirubin levels and prothrombin time were risk factors for mortality of critically ill patients (all  $P<0.05$ ; Table III). The multivariate logistic regression analysis showed that age (OR=1.02;  $P=0.003$ ), heart rate (OR=1.01;  $P=0.012$ ), SBP (OR=0.99;  $P<0.001$ ),  $SpO_2$  (OR=0.96;  $P<0.001$ ) and serum lactate (OR=1.50,  $P<0.001$ ) and hemoglobin levels (OR=0.99;  $P=0.004$ ) were significantly associated with the mortality of critically ill patients, whereas DBP, BE, creatinine, prothrombin time and WBC and platelet count were not associated with mortality (Table III). The prediction model was constructed as follows:

$$\text{logit}(p)=0.021*\text{age}+0.010*\text{heart rate}+(-0.013)*\text{systolic blood pressure}+(-0.041)*\text{SpO}_2+0.407*\text{serum lactate}+(-0.012)*\text{hemoglobin}+0.869$$

The prediction model was found to be of good value with respect to identifying the mortality rate of patients [sensitivity=44.4% (72/162) and specificity=98.5% (1,213/1,231)]. AUROC curve was 0.894 [95% confidence interval (95% CI): 0.863-0.925;  $P<0.001$ ; Fig. 1]. The estimated probability was 0.095; values  $>0.095$  were classified as a case of poor prognosis.

AUROC value of the model of serum lactic acid levels and predicted mortality was 0.891 (95% CI: 0.864-0.919;  $P<0.001$ ; Fig. 2). The sensitivity and specificity values were 87.7 and 75.8%, respectively. The cut-off value obtained for the serum lactate levels was identified as  $\geq 2.35$  mmol/l. The OR values of the other parameters were close to 1 and their AUROC values were too small to accurately predict the mortality of patients.

## Discussion

The present study identified the vital signs and laboratory parameters associated with mortality in patients admitted to the emergency department and constructed a predictive

Table I. Descriptive characteristics and distribution of demographic parameters, vital signs and laboratory results.

Characteristic	Median (range)	Mean $\pm$ SD or number (%)	Mortality rate, n (%)
Age, years	73 (16-104)	67.72 $\pm$ 19.29	
Sex			
Male		879 (63.1)	102 (11.6)
Female		514 (36.9)	60 (11.7)
Disease			
Respiratory		533 (38.3)	50 (9.4)
Urinary system		56 (4.0)	6 (10.7)
Endocrine system		109 (7.8)	2 (1.8)
Nervous system		184 (13.2)	37 (20.1)
Digestive system		152 (10.8)	15 (9.9)
Cardiovascular		240 (17.1)	30 (12.5)
Poisoning		62 (4.5)	5 (8.1)
Other		57 (4.1)	17 (29.8)
Total mortality rate			162 (11.6)
SBP, mmHg	140.0 (43.0-265.0)	141.28 $\pm$ 32.44	
DBP, mmHg	83.0 (23.0-167.0)	83.02 $\pm$ 20.63	
Temperature, °C	37.0 (33.6-40.5)	37.21 $\pm$ 0.88	
Heart rate, bpm	99.0 (10.0-212.0)	100.15 $\pm$ 25.27	
Respiratory rate, breaths/min	22.0 (0-49.0)	23.40 $\pm$ 5.59	
pH	7.4 (6.8-7.7)	7.36 $\pm$ 0.13	
SpO <sub>2</sub> , %	95.0 (39.0-100.0)	90.97 $\pm$ 10.23	
Serum lactate, mmol/l	1.6 (0.2-26.0)	2.64 $\pm$ 3.15	
Prothrombin time, sec	11.9 (1.2-104.2)	12.76 $\pm$ 4.64	
Hemoglobin, g/l	133.0 (34.0-225.0)	131.42 $\pm$ 27.78	
Platelet count, $\times 10^9$ /l	196.0 (6.0-725.0)	203.16 $\pm$ 86.30	
WBC count, $\times 10^9$ /l	9.8 (0.58-151.9)	11.16 $\pm$ 7.33	
Creatinine, mg/dl	80 (21-1465)	117.80 $\pm$ 144.14	
Total bilirubin, mg/dl	14.7 (2.4-172.2)	19.62 $\pm$ 16.88	
BE, mmol/l	-0.4 (-29.5-27.0)	-1.21 $\pm$ 8.17	
Glucose, mmol/l	8.6 (0.9-73.3)	11.13 $\pm$ 7.80	
Hospitalization length, days	9 (0-90)	9.55 $\pm$ 9.15	

SBP, systolic blood pressure; DBP, diastolic blood pressure; SpO<sub>2</sub>, transcutaneous oxygen saturation; WBC, white blood cell; BE, base excess.

model for patient mortality. There were significant differences between the mortality and survival group with respect to the age, heart rate, SBP, DBP, SpO<sub>2</sub>, serum lactate, BE, hemoglobin, platelet and WBC count, creatinine and prothrombin time. However, in the multivariate model, only age, heart rate, SBP, SpO<sub>2</sub>, serum lactate and hemoglobin were significantly associated with the mortality of patients. Among these, serum lactate was the most useful independent predictor, with a critical cut-off value of 2.35 mmol/l.

For patients in the intensive care unit (ICU), elevated lactate levels provide an indicator of critical clinical condition, and are a marker of poor prognosis (14). Respiratory or circulatory failure in critically ill patients due to shock and other reasons leads to a lack of oxygen in tissues and organs (15-17). Therefore, when oxygenation is poor, cells utilize glucose through anerobic glycolysis, resulting in an increase in the serum lactate levels, leading to hyperlactemia (16). Several studies have investigated the association between serum lactate

and a variety of diseases, such as sepsis, cardiac arrest, hypoxia or heart failure, in hospitalized patients and identified serum lactate as an independent predictor of mortality (15,18-25). Liu *et al* (26) included 3,713 patients with sepsis from the MIMIC III database and found that lactate was an independent predictor of sepsis prognosis and its AUROC (0.664; 95% CI: 0.639-0.689) was significantly higher compared with the AUROC of the quick Sequential Organization Failure Assessment (0.547; 95% CI: 0.521-0.574) recommended by the Third International Consumption Definitions for Sepsis and Sepsis Shock (Sepsis-3) (27). Nichol *et al* (28) evaluated the lactic acid levels at the admission of 7,155 patients in the ICU of four Australian university hospitals and found that a higher time-weighted lactic acid concentration was independently associated with an increase in in-hospital mortality (OR=3.7, 95% CI: 1.9-7.00; P<0.0001). Another study of a German population showed that lactate, pH and BE were all predictors of mortality for patients in the ICU, although

Table II. Vital signs and laboratory tests at admission to hospital.

Characteristic	Survival group (n=1,231)	Mortality group (n=162)	P-value
	Mean $\pm$ SD or n (%)	Mean $\pm$ SD or n (%)	
Age, years	67.21 $\pm$ 19.42	71.52 $\pm$ 17.90	0.003
Sex			0.936
Male	777 (88.40)	102 (11.60)	
Female	454 (88.33)	60 (11.67)	
Temperature, °C	37.22 $\pm$ 0.92	37.19 $\pm$ 1.03	0.443
Heart rate, bpm	99.47 $\pm$ 23.87	105.34 $\pm$ 33.75	0.001
Respiratory rate, breaths/min	23.60 $\pm$ 4.99	21.86 $\pm$ 8.76	0.492
SBP, mmHg	144.16 $\pm$ 30.24	119.38 $\pm$ 39.57	<0.001
DBP, mmHg	84.57 $\pm$ 19.46	71.26 $\pm$ 25.12	<0.001
pH	7.38 $\pm$ 0.11	7.26 $\pm$ 0.19	<0.001
SpO <sub>2</sub> , %	91.94 $\pm$ 9.25	83.59 $\pm$ 13.76	<0.001
Serum lactate, mmol/l	1.99 $\pm$ 1.88	7.56 $\pm$ 5.59	<0.001
<2.35	933 (97.9)	20 (2.1)	0.001
$\geq$ 2.35	298 (67.7)	142 (32.3)	
BE, mmol/l	-0.31 $\pm$ 7.64	-8.05 $\pm$ 8.83	<0.001
Glucose, mmol/l	11.09 $\pm$ 7.88	11.50 $\pm$ 7.15	0.067
Hemoglobin, g/l	132.69 $\pm$ 27.03	121.77 $\pm$ 31.37	<0.001
Platelet count, $\times 10^9/l$	204.68 $\pm$ 84.28	191.57 $\pm$ 99.90	0.049
WBC count, $\times 10^9/l$	10.80 $\pm$ 6.14	13.83 $\pm$ 13.01	<0.001
Creatinine, mg/dl	112.46 $\pm$ 138.51	158.38 $\pm$ 176.61	<0.001
Prothrombin time, sec	12.42 $\pm$ 4.35	15.36 $\pm$ 5.83	<0.001
Total bilirubin, mg/dl	19.26 $\pm$ 16.61	22.33 $\pm$ 18.60	0.085

SBP, systolic blood pressure; DBP, diastolic blood pressure; SpO<sub>2</sub>, transcutaneous oxygen saturation; WBC, white blood cell; BE, base excess.

Table III. Association between serum lactate levels and mortality of critically ill patients using logistic regression analysis.

Characteristic	Univariate			Multivariate		
	$\beta$ -value	P-value	OR (95% CI)	$\beta$ -value	P-value	OR (95% CI)
Sex	0.007	0.969	1.01 (0.72-1.41)			
Age	0.013	0.008	1.01 (1.00-1.02)	0.021	0.003	1.02 (1.01-1.04)
Temperature	-0.036	0.688	0.96 (0.81-1.15)			
Heart rate	0.009	0.005	1.01 (1.00-1.02)	0.010	0.012	1.01 (1.00-1.02)
Respiratory rate	-0.060	<0.001	0.94 (0.91-0.97)			
SBP	-0.026	<0.001	0.97 (0.97-0.98)	-0.013	<0.001	0.99 (0.98-0.99)
DBP	-0.035	<0.001	0.97 (0.96-0.97)			
SpO <sub>2</sub>	-0.60	<0.001	0.94 (0.93-0.95)	-0.041	<0.001	0.96 (0.94-0.98)
Serum lactate	0.456	<0.001	1.58 (1.48-1.69)	0.407	<0.001	1.50 (1.40-1.62)
BE	-0.103	<0.001	0.90 (0.89-0.92)			
WBC count	0.044	<0.001	1.05 (1.02-1.07)			
Platelet count	-0.002	0.069	1.00 (1.00-1.00)			
Glucose	0.006	0.529	1.01 (0.99-1.03)			
Creatinine	0.001	<0.001	1.00 (1.00-1.00)			
Hemoglobin	-0.014	<0.001	0.99 (0.98-0.99)	-0.012	0.004	0.99 (0.98-1.00)
Total bilirubin	0.009	0.033	1.01 (1.00-1.02)			
Prothrombin time	0.113	<0.001	1.12 (1.08-1.16)			

SBP, systolic blood pressure; DBP, diastolic blood pressure; SpO<sub>2</sub>, transcutaneous oxygen saturation; WBC, white blood cell; BE, base excess.

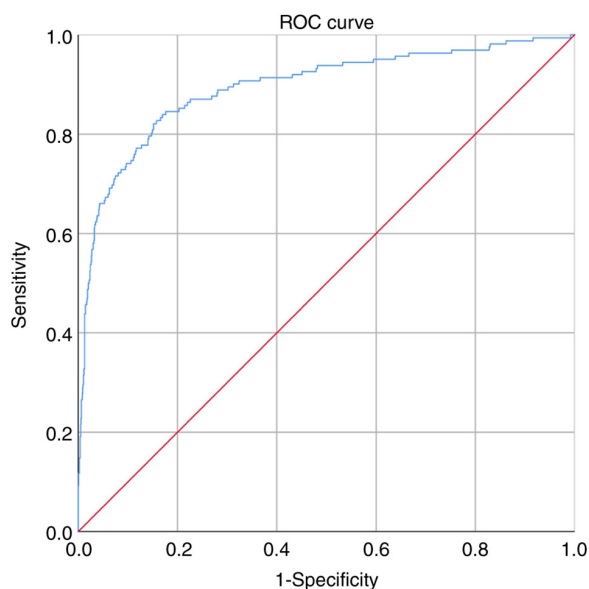


Figure 1. Performance of the logistics model of predicting the mortality of critically ill patients. ROC, receiver operating characteristic.

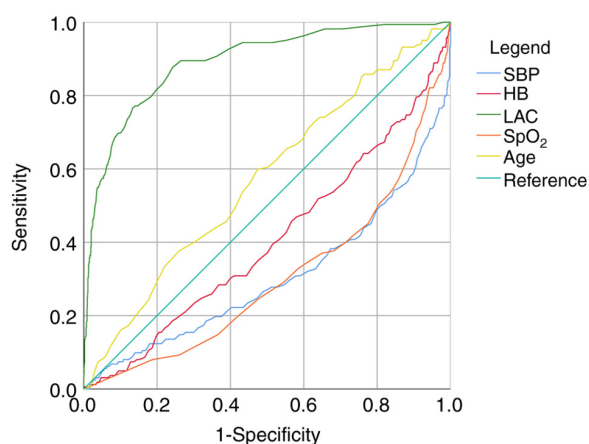


Figure 2. Receiver operating characteristic curve for predicting the mortality of critically ill patients. HB, hemoglobin; LAC, serum lactate; SBP, systolic blood pressure; SpO<sub>2</sub>, transcutaneous oxygen saturation.

lactate was the best predictor [AUROC, 0.74; cut-off value, 2.7 mmol/l; hazard ratio (HR), 3.20] (29). Here, serum lactate levels of patients admitted to the emergency department with non-traumatic conditions were significantly associated with mortality. Therefore, collectively, these results suggested that higher serum lactate levels may be associated with increased risk of mortality in the population, regardless of whether patients are infected or not.

In the present study, AUROC curve exhibited a cut-off value of 2.35 mmol/l for the serum lactate prediction of mortality in non-traumatic disease. Aduen *et al* (30) found that lactate concentration >4 mmol/l has 96% specificity in terms of predicting mortality in non-hypotensive patients. Nichol *et al* (28) found that when the weighted lactate concentration is >0.75 mmol/l, the lactate concentration was significantly associated with an increase in the in-hospital mortality rate of patients. The cut-off value of serum lactate may be 2.7 or 3.6 mmol/l (2,29). Different studies may report

different cut-off values for mortality in critically ill patients for several reasons, including heterogeneity of patient populations, variability in study designs and diversity of statistical analysis methods. In addition to serum lactate, other parameters may also predict the mortality of critically ill patients in the emergency department. Univariate analysis has shown that age is a key factor in the prognosis of patients: Seker *et al* (2) investigated 1,382 patients in the emergency department of a hospital in Turkey, and found that the mortality of patients >65 years of age is significantly higher compared with that of patients <65 years old. Chebl *et al* (12) also demonstrated that age is an independent risk factor for mortality.

The present study showed that heart rate was an independent risk factor for mortality. Ley *et al* (31) investigated the admission heart rate of 103,799 patients with trauma in Los Angeles (USA); mortality rate (2.0%) of patients with moderate and severe injury with a heart rate of 80-89 was lower compared with that of all other heart rate ranges, whereas the mortality rate of patients with a heart rate <60 or ≥100 was significantly higher. To the best of our knowledge, however, at present, studies on the cut-off value of heart rate, together with randomized controlled trials based on heart rate, are lacking. The present study revealed that higher SBP was a predictive factor for mortality. Kristensen *et al* (32) suggested that the SBP threshold for predicting mortality is 100-110 mmHg. However, the mean SBP of patients in the present mortality group was 119.38±39.57 mmHg. Meanwhile, it was difficult to determine the cut-off value of SBP at time of admission due to its poor performance in predicting mortality.

The present study had certain limitations. This was a single-center, retrospective study and there was a large difference between patient numbers in the mortality and survival groups, which could have interfered with the predictive performance of logistic regression model.

In conclusion, the present study demonstrated that serum lactate serves as an independent predictor of mortality in critically ill patients. The logistic regression model composed of age, heart rate, SBP, SpO<sub>2</sub> and serum lactate and hemoglobin levels may be effective in predicting the mortality of patients.

## Acknowledgements

The study was performed XM, JL and QZ during their internship at the Affiliated Kunshan Hospital of Jiangsu University (Kunshan, China), which is the teaching practice hospital of Nanjing Medical University (Nanjing, China).

## Funding

No funding was received.

## Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Authors' contributions

XM, JL and QZ collected and analyzed the data. XM and JW confirm the authenticity of all the raw data. XM and JW



designed the study. All authors have read and approved the final manuscript.

### Ethics approval and consent to participate

The study was approved by the Ethics Review Committee of The Affiliated Kunshan Hospital of Jiangsu University (No. 2021-03-015-H01). The requirement for patient consent was waived as the present study was a retrospective study.

### Patient consent for publication

Not applicable.

### Competing interests

The authors declare that they have no competing interests.

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