Submitted: 17 June, 2025 Accepted: 10 September, 2025 Published: 08 October, 2025 DOI:10.22514/sv.2025.150

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ORIGINAL RESEARCH

Construction of a multi-dimensional predictive model for sepsis-associated disseminated intravascular coagulation and its clinical utility

Hui Chen[1], Longhuan Zeng[1], Fu Tian[1], Kai Qiu[1], Yang Chen[1], Leifei Chen[1], Shihan Zhou[1], Zhicheng Huang[1], Nanyuan Gu[1,*]

[1]Intensive Care Unit, Hangzhou Geriatric Hospital, 310022 Hangzhou, Zhejiang, China

***Correspondence**
gunanyuan2022@163.com
(Nanyuan Gu)

Abstract

Background: This study aimed to analyze the independent risk factors for sepsis patients complicated by disseminated intravascular coagulation (DIC) using the Medical Information Mart for Intensive Care IV (MIMIC-IV) database and to construct and validate a dynamic predictive model, thereby providing a basis for early clinical intervention. **Methods**: A total of 3586 Intensive Care Unit (ICU) patients meeting the Sepsis-3 criteria from the MIMIC-IV database between 2008 and 2019 were included. Patients were categorized into a DIC group (1311 cases) and a non-DIC group (2275 cases) based on the International Society on Thrombosis and Haemostasis (ISTH) overt DIC scoring criteria. Predictive variables were screened using Least Absolute Shrinkage and Selection Operator (LASSO) regression, and a multivariate logistic regression model was constructed. The model's performance was evaluated using the receiver operating characteristic (ROC) curve. **Results**: The independent risk factors for sepsis complicated by DIC included the Sequential Organ Failure Assessment (SOFA) score, international normalized ratio (INR), total bilirubin, red blood cell distribution width (RDW), red blood cell count (RBC), absolute neutrophil count (Neutrophils Abs), age, chronic kidney disease (renal disease), mean corpuscular hemoglobin concentration (MCHC), and absolute monocyte count (Monocytes Abs). The predictive model achieved an area under the curve (AUC) of 0.781, with a sensitivity of 68.9% and a specificity of 75.3%, outperforming single indicators (*e.g.*, INR with an AUC of 0.761). **Conclusions**: The predictive model constructed in this study integrates multidimensional indicators encompassing inflammation, coagulation, and red blood cell parameters, demonstrating good clinical utility. It can assist in the early identification of high-risk critically ill patients and optimize personalized intervention strategies. This model is specifically applicable to critically ill patients admitted to the ICU.

Keywords

Sepsis; Disseminated intravascular coagulation; Risk factors; Predictive model; MIMIC-IV database; Logistic regression

1. Introduction

Sepsis is a systemic inflammatory response syndrome triggered by infection, with its global incidence steadily increasing and becoming one of the leading causes of mortality among patients in intensive care units (ICUs) [1, 2]. Studies indicate that there are over 49 million sepsis cases worldwide annually, with approximately 20% of these cases progressing to septic shock and mortality rates ranging from 30% to 50% [3]. The pathophysiological processes of sepsis are complex and often accompanied by multiple complications, among which disseminated intravascular coagulation (DIC) stands as a critical secondary condition significantly elevating the risk of multi-organ failure and death [4, 5]. Research has shown that approximately 30% to 80% of sepsis patients develop DIC, and the mortality rate among these patients is nearly doubled compared to those without DIC [6, 7]. While guidelines for DIC diagnosis, such as those proposed by the International Society on Thrombosis and Haemostasis (ISTH) and the Japanese Ministry of Health and Welfare (JMHW), exist, there is no unified consensus on diagnostic criteria specifically for sepsis-induced DIC due to its distinct characteristics [8, 9]. The sepsis-induced coagulopathy (SIC) scoring system, as a novel diagnostic tool, has demonstrated certain diagnostic value but exhibits considerable heterogeneity across different populations [10]. Therefore, early identification of risk factors associated with the progression of sepsis to DIC and the establishment of a reliable predictive model hold signifi-

cant importance for optimizing clinical decision-making and improving patient outcomes. The Medical Information Mart for Intensive Care IV (MIMIC-IV), recognized as one of the largest publicly accessible critical care databases globally, integrates detailed clinical data from tens of thousands of ICU patients across multiple medical centers. This comprehensive dataset encompasses demographic characteristics, vital signs, laboratory test results, medication records, and other multi-dimensional information, providing high-quality data support for exploring risk factors related to sepsis-associated complications and constructing predictive models [11]. Leveraging machine learning and statistical modeling approaches, this study aims to systematically analyze the independent risk factors for sepsis patients complicated by DIC using the MIMIC-IV database and to develop a dynamic risk assessment predictive model. The objective is to furnish evidence-based guidance for early clinical intervention, thereby reducing the incidence and mortality rates of sepsis-related DIC.

2. Materials and methods

2.1 Data source and study population

The data for this study were sourced from the publicly accessible critical care database MIMIC-IV (v2.2), which encompasses information on ICU patients admitted to Beth Israel Deaconess Medical Center in the United States between 2008 and 2019. Data extraction adhered to the MIMIC-IV usage protocols and was conducted through the PhysioNet platform (access link: https://physionet.org/content/mimiciv/2.2/). The study was reviewed and approved by the Ethics Committee of the Massachusetts Institute of Technology (Exemption Review Number: 66822508).

Inclusion Criteria: ① Patients aged 18 years or older; ② Patients meeting the Sepsis-3 criteria (infection combined with a Sequential Organ Failure Assessment (SOFA) score $\geq$2) [12]; ③ Patients admitted to the ICU for the first time with a hospital stay duration of $\geq$24 hours. Exclusion Criteria: ① Patients with a data missing rate $>$20%; ② Patients previously diagnosed with DIC or hematological disorders (such as leukemia, coagulation factor deficiencies), advanced liver cirrhosis, or receiving anticoagulant therapy prior to admission; ③ Pregnant patients or those in the terminal stages of malignant tumors; ④ Patients with missing data on platelet count, prothrombin time (PT), fibrinogen, or D-dimer levels.

2.2 Variable definitions and data extraction

All predictive variables were extracted from the first laboratory tests and clinical assessments performed within 24 hours after ICU admission to ensure consistency in data collection timing.

2.2.1 Outcome variable

To judge whether sepsis patients are complicated by DIC within 7 days after admission, DIC diagnosis was based on the International Society on Thrombosis and Haemostasis (ISTH) overt DIC scoring criteria ($\geq$5 points) [13]. The diagnostic criteria are outlined in Table 1.

2.2.2 Predictive variables

① Demographic characteristics: gender, age, ethnicity, weight, smoking status, alcohol consumption, hypertension, diabetes mellitus, chronic kidney disease, and chronic obstructive pulmonary disease. ② Vital signs indicators: Acute Physiology and Chronic Health Evaluation (APACHE) III score, SOFA score, Systemic Inflammatory Response Syndrome (SIRS) score, body temperature, heart rate, and respiratory rate. ③ Laboratory indicators: C reactive protein, white blood cell count, lymphocyte count, neutrophil count, monocyte percentage, neutrophil percentage, monocyte count, lymphocyte percentage, mean corpuscular hemoglobin concentration (MCHC), red blood cell distribution width (RDW), red blood cell count, creatinine, blood urea nitrogen (BUN), international normalized ratio (INR), alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin, and hemoglobin.

2.3 Statistical analysis

Data processing and analysis were conducted using SPSS (version 26.0, IBM Corp., Armonk, NY, USA) and R software. This observational study was conducted in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. Missing values for continuous variables were imputed using the median, while missing values for categorical variables were filled with the mode. Baseline characteristics were compared between the DIC and non-DIC groups using the *t*-test (for normally distributed data), Mann-Whitney U test (for non-normally distributed data), or chi-square test (for categorical variables). Least Absolute Shrinkage and Selection Operator (LASSO) regression was employed to extract key predictive features, and a multivariate logistic regression model was constructed. Model performance was evaluated using the area under the receiver operating characteristic curve (AUC), sensitivity, specificity, and calibration curves. A p-value of less than 0.05 was considered statistically significant.

3. Results

3.1 Comparison of clinical data between the two groups

After screening, a total of 3586 patients were included in the study. Among them, 1311 patients with sepsis complicated by DIC were included in the observation group, while the remaining 2275 patients were included in the control group. Patients in the observation group were younger, with a higher proportion of Caucasians, and a lower proportion of patients with hypertension, diabetes mellitus, renal disease, and chronic obstructive pulmonary disease compared to the control group. Additionally, the APACHE III and SOFA scores were higher in the observation group, and significant differences in serum biomarker levels were also observed ($p < 0.05$). The detailed comparisons are presented in Table 2.

TABLE 1. Diagnostic criteria for DIC.

Markers	ID-9 code	Scoring rules
Platelet count	51265	$\geq 100 \times 10^9$/L → 0 points; $<100 \times 10^9$/L → 1 point; $<50 \times 10^9$/L → 2 points
D-dimer	5090810	Normal → 0 points; moderately elevated → 1 point; significantly elevated → 2 points (to be combined with laboratory reference values)
PT	51237	Prolonged <10 seconds → 0 points; prolonged 10–16 seconds → 1 point; prolonged >6 seconds → 2 points
Fibrinogen	512143	≥1.0 g/L → 0 points; <1.0 g/L → 1 point

PT: prothrombin time.

TABLE 2. Comparison of clinical data between the two groups.

Mark	Observation group (n = 1311)	Control group (n = 2275)	$t/\chi^2/Z$	p
Gender (male, %)	758 (57.82)	1352 (59.43)	0.890	0.345
Age (yr, $\bar{x} \pm s$)	61.64 ± 16.53	64.23 ± 16.09	4.604	<0.001
Race (n, %)				
Asian	90 (6.86)	175 (7.69)	9.946	0.019
White	803 (61.25)	1288 (56.62)		
Black	249 (18.99)	444 (19.52)		
Unknown	169 (12.89)	368 (16.18)		
Weight (kg, $\bar{x} \pm s$)	83.60 ± 33.97	84.01 ± 25.57	0.411	0.681
Smoker (n, %)	55 (4.20)	108 (4.75)	0.584	0.445
Alcohol (n, %)	6 (0.46)	17 (0.75)	1.094	0.295
Hypertension (n, %)	383 (29.21)	777 (34.15)	9.273	0.002
Diabetes (n, %)	369 (28.15)	731 (32.13)	6.212	0.013
Renaldisease (n, %)	285 (21.74)	568 (24.97)	4.780	0.029
CPD (n, %)	265 (20.21)	533 (23.43)	4.969	0.026
APS III (M (P25, P75))	63 (48, 83)	55 (40, 73)	9.326	<0.001
SOFA (M (P25, P75))	10 (7, 14)	8 (5, 11)	13.780	<0.001
SIRS (n, %)				
0–1	47 (3.59)	114 (5.01)	6.529	0.163
2	258 (19.68)	441 (19.38)		
3	610 (46.53)	1003 (44.09)		
4	396 (30.21)	717 (31.52)		
Temperature (°C, $\bar{x} \pm s$)	36.75 ± 1.07	36.73 ± 1.04	0.790	0.430
HR (Times/min, $\bar{x} \pm s$)	97.78 ± 21.36	95.67 ± 22.80	2.785	0.005
Resp rate (Times/min, $\bar{x} \pm s$)	21.84 ± 6.74	21.26 ± 6.66	2.512	0.012
MBP (mmHg, $\bar{x} \pm s$)	79.74 ± 19.31	82.98 ± 21.33	4.658	<0.001
WBC ($\times 10^9$/L, M (P25, P75))	9.80 (5.10, 16.30)	12.70 (8.50, 18.80)	10.581	<0.001
Lymphocytes Abs ($\times 10^9$/L, M (P25, P75))	0.76 (0.36, 1.34)	1.04 (0.61, 1.74)	10.780	<0.001
Neutrophils Abs ($\times 10^9$/L, M (P25, P75))	7.79 (3.58, 13.68)	10.77 (6.72, 16.66)	12.100	<0.001
Monocytes (%, M (P25, P75))	5.30 (2.80, 9.00)	4.90 (3.00, 7.30)	3.722	<0.001
Neutrophils (%, M (P25, P75))	79.00 (66.10, 86.20)	81.30 (73.80, 87.20)	6.574	<0.001
Monocytes Abs ($\times 10^9$/L, M (P25, P75))	0.48 (0.18, 0.98)	0.62 (0.34, 1.04)	6.888	<0.001
Lymphocytes (%, M (P25, P75))	8.30 (4.50, 15.90)	8.50 (4.40, 14.20)	1.065	0.287
MCHC (g/dL, $\bar{x} \pm s$)	32.78 ± 1.85	32.43 ± 1.71	5.519	<0.001

TABLE 2. Continued.

Mark	Observation group (n = 1311)	Control group (n = 2275)	$t/\chi^2/Z$	p
RDW (%, $\bar{x} \pm s$)	17.01 ± 3.28	15.62 ± 2.74	12.894	<0.001
RBC ($\times 10^{12}$/L, $\bar{x} \pm s$)	3.05 ± 0.82	3.57 ± 0.89	17.476	<0.001
Creatinine (mg/dL, M (P25, P75))	1.40 (0.90, 2.30)	1.20 (0.80, 2.00)	2.988	0.003
BUN (mg/dL, M (P25, P75))	28.00 (17.00, 47.00)	24.00 (16.00, 42.00)	4.287	<0.001
INR, M (P25, P75)	1.80 (1.50, 2.40)	1.30 (1.20, 1.60)	26.201	<0.001
ALT (U/L, M (P25, P75))	39.00 (20.00, 127.00)	30.00 (17.00, 68.00)	7.305	<0.001
AST (U/L, M (P25, P75))	73.00 (35.00, 226.00)	48.00 (27.00, 110.00)	9.791	<0.001
Bilirubin (mg/dL, M (P25, P75))	1.70 (0.80, 4.60)	0.70 (0.40, 1.50)	19.711	<0.001
Hemoglobin (mg/dL, M (P25, P75))	9.10 (7.70, 11.00)	10.50 (8.70, 12.40)	14.394	<0.001

SOFA: Sequential Organ Failure Assessment; MCHC: mean corpuscular hemoglobin concentration; RDW: red blood cell distribution width; RBC: red blood cell count; BUN: blood urea nitrogen; INR: international normalized ratio; ALT: alanine aminotransferase; AST: aspartate aminotransferase; Neutrophils Abs: absolute neutrophil count; Monocytes Abs: absolute monocyte count; Lymphocytes Abs: Absolute Lymphocyte Count; SIRS: Systemic Inflammatory Response Syndrome; HR: Heart Rate; MBP: Mean Blood Pressure; WBC: White Blood Cell Count; CPD: Chronic Pulmonary Disease; APS: Acute Physiology Score.

3.2 Feature selection for the predictive model

LASSO regression was employed to screen the main factors contributing to the predictive model for the occurrence of DIC in sepsis patients. As illustrated in Fig. 1, when the model included 10 variables, it achieved a balance between simplicity and high accuracy. Through LASSO regression, the following predictive variables were selected for the model: "renaldisease" (chronic kidney disease), "SOFA" (Sequential Organ Failure Assessment score), "neutrophilsAbs" (absolute neutrophil count), "neutrophils" (neutrophil percentage), "MCHC" (mean corpuscular hemoglobin concentration), "RDW" (red blood cell distribution width), "RBC" (red blood cell count), "INR" (international normalized ratio), "bilirubin" (total bilirubin), and "age". Feature importance was further evaluated using SHapley Additive exPlanations (SHAP) values, which ranked SOFA score (SHAP mean |value| = 0.28), INR (0.25), and RDW (0.21) as the top three contributors to model prediction. Model performance under different variable combinations (*e.g.*, with/without red blood cell parameters) showed the integrated model had the highest AUC (0.781 *vs.* 0.752 without RDW/RBC).

3.3 Construction of the logistic regression model for predicting DIC in sepsis patients

"Renaldisease" (chronic kidney disease), "SOFA" (Sequential Organ Failure Assessment score), "neutrophilsAbs" (absolute neutrophil count), "neutrophils" (neutrophil percentage), "MCHC" (mean corpuscular hemoglobin concentration), "RDW" (red blood cell distribution width), "RBC" (red blood cell count), "INR" (international normalized ratio), "bilirubin" (total bilirubin), and "age" were identified as independent predictive factors for the occurrence of DIC in sepsis patients. The specific multivariate logistic regression model for predicting DIC in sepsis patients is presented in Table 3. Below is a nomogram as shown in Fig. 2.

3.4 ROC curve analysis of the predictive model

The AUC of the prediction model is 0.781, and the sensitivity and specificity are 68.9% and 75.3%, respectively. The prediction effect of the model is good and the consistency is good, and it has a good diagnostic efficiency for DIC in sepsis patients. See Table 4, Figs. 3,4 for details.

4. Discussion

Disseminated intravascular coagulation (DIC) is a common and potentially life-threatening complication observed in infectious diseases. In this study, a total of 3586 patients were included, among whom 1311 patients had sepsis complicated by DIC, accounting for 35.56% of the cohort. This proportion is consistent with findings from previous studies, which have reported rates ranging from 30% to 50% [14]. Coagulation activation and inflammatory responses are fundamental reactions of the host in combating infection during septic shock and also underlie the pathogenesis of DIC, albeit with detrimental effects on the host. Through multivariate logistic regression analysis, this study identified 10 independent risk factors for DIC in sepsis patients, including the Sequential Organ Failure Assessment (SOFA) score, international normalized ratio (INR), bilirubin, red blood cell distribution width (RDW), red blood cell count (RBC), absolute neutrophil count (Neutrophils Abs), age, chronic kidney disease (Renal disease), mean corpuscular hemoglobin concentration (MCHC), and absolute monocyte count (Monocytes Abs).

The findings of this study indicate that the SOFA score, INR, and total bilirubin are independent predictive factors for the risk of DIC in sepsis patients. Consistent with our results, Iba *et al.*'s [15] study also demonstrated a significant correlation between the SOFA score and DIC resolution, suggesting that

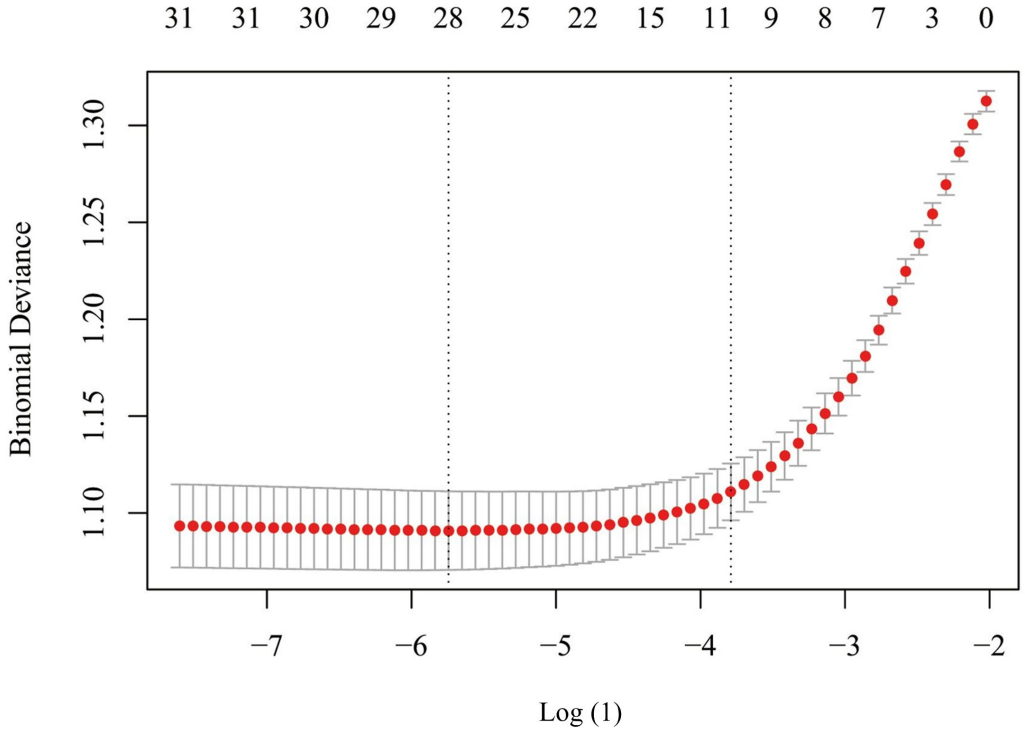

FIGURE 1. Relationship between Log(λ) and binomial deviance in LASSO regression.

TABLE 3. Multivariate logistic regression model for predicting DIC in sepsis patients.

Predictor variable	β	SE	Wald χ^2	p	OR	95% CI
Renaldisease	−0.286	0.097	8.707	0.003	0.751	0.621–0.908
SOFA	0.103	0.010	111.393	<0.001	1.109	1.088–1.130
Neutrophils Abs	−0.038	0.005	49.345	<0.001	0.963	0.953–0.973
Neutrophils	−0.010	0.002	19.31	<0.001	0.990	0.985–0.994
MCHC	0.140	0.024	32.627	<0.001	1.150	1.096–1.206
RDW	0.093	0.015	37.006	<0.001	1.098	1.065–1.131
RBC	−0.532	0.049	115.801	<0.001	0.587	0.533–0.647
INR	0.301	0.034	78.739	<0.001	1.351	1.264–1.444
Bilirubin	0.024	0.010	6.346	0.012	1.024	1.005–1.044
Age	−0.006	0.003	5.158	0.023	0.994	0.989–0.999
Constant	−4.853	0.991	23.975	<0.001	0.008	-

SOFA: Sequential Organ Failure Assessment; MCHC: mean corpuscular hemoglobin concentration; RDW: red blood cell distribution width; RBC: red blood cell count; INR: international normalized ratio; SE: standard error; OR: odds ratio; CI: Confidence Interval.

organ dysfunction and coagulation disorders are the primary mechanisms underlying the development of DIC in sepsis patients. The SOFA score, recognized as the gold standard for assessing the degree of organ dysfunction in sepsis patients, exhibits a strong correlation with the risk of DIC, rooted in the core pathophysiological mechanisms of sepsis: systemic inflammatory responses leading to endothelial cell injury, microthrombus formation, and fibrinolysis inhibition, thereby triggering an imbalance in the coagulation-anticoagulation system [16]. Studies have shown that for every one-point increase in the SOFA score, the risk of DIC rises by approximately 11%, indicating that the cumulative effect of organ failure may directly activate the coagulation cascade through the release of tissue factors and pro-inflammatory cytokines [17]. Additionally, patients with high SOFA scores often exhibit concomitant hepatic and renal dysfunction, further impairing the synthesis of anticoagulant proteins and exacerbating DIC progression. An elevated INR reflects abnormalities in the extrinsic coagulation pathway and serves as a critical indicator for DIC diagnosis [18]. In sepsis, endotoxins and inflammatory mediators upregulate tissue factor (TF) expression, promoting the formation of prothrombinase complexes and accelerating thrombin burst, leading to the consumption of coagulation factors and prolonged prothrombin time (PT) [19].

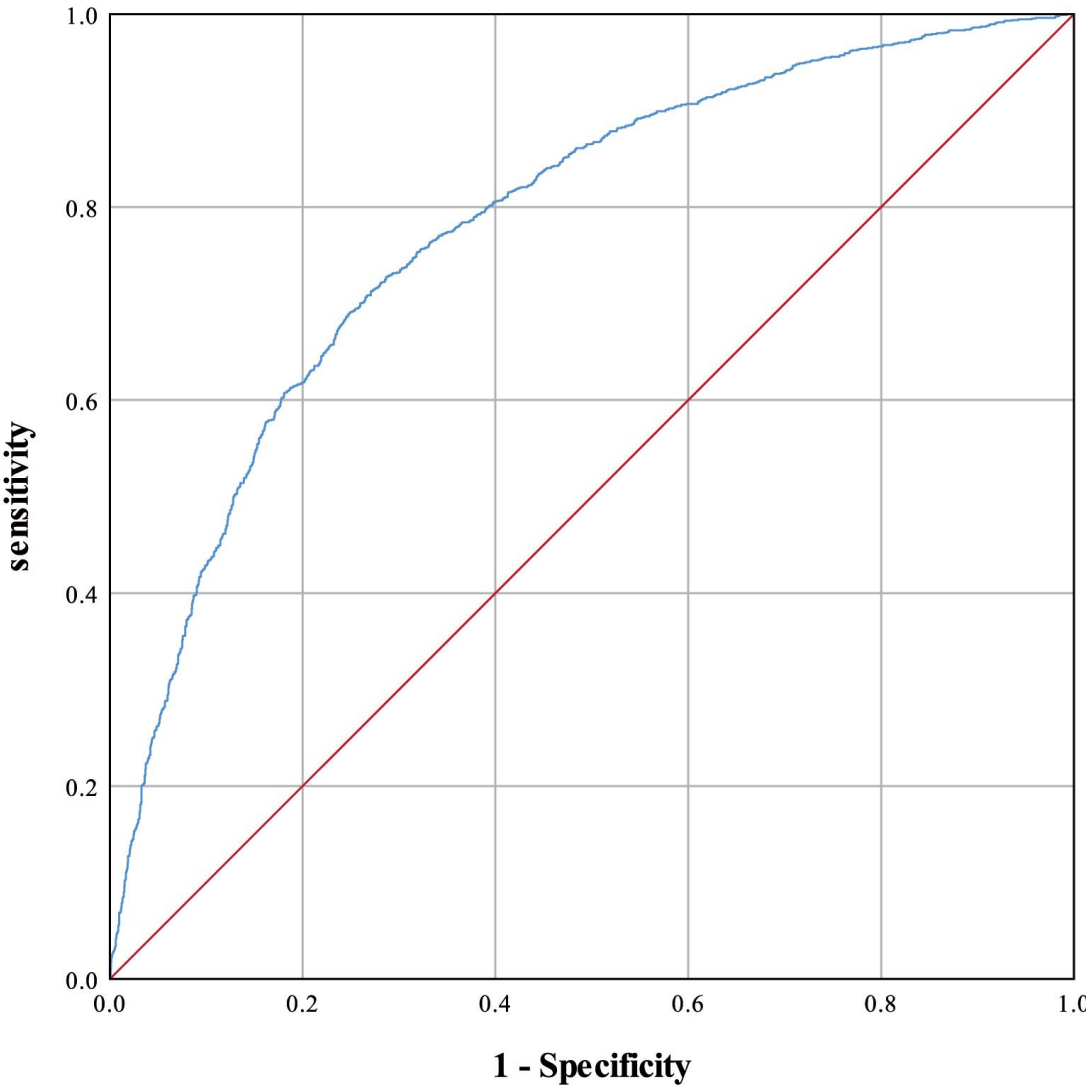

FIGURE 2. Nomogram.

TABLE 4. Diagnostic value analysis of the predictive model for identifying DIC in sepsis patients.

Predictor variable	Cut-off	AUC	Standard error	*p*	95% CI	Sensitivity (%)	Specificity (%)
Age	60.500	0.548	0.010	<0.001	0.528–0.567	43.6	64.2
Renaldisease	-	0.516	0.010	0.107	0.497–0.536	78.3	25.0
SOFA	9.500	0.638	0.009	<0.001	0.619–0.656	56.1	62.0
Neutrophils Abs	6.325	0.621	0.010	<0.001	0.602–0.641	42.6	78.2
Neutrophils	71.350	0.566	0.010	<0.001	0.546–0.586	33.3	79.5
MCHC	33.150	0.556	0.010	<0.001	0.536–0.576	44.0	65.6
RDW	15.750	0.638	0.010	<0.001	0.620–0.657	56.8	63.4
RBC	2.975	0.670	0.009	<0.001	0.652–0.688	53.1	72.7
INR	1.450	0.761	0.008	<0.001	0.745–0.778	81.2	66.7
Bilirubin	1.250	0.697	0.009	<0.001	0.679–0.715	59.2	70.6
Predictive_Model	0.366	0.781	0.008	<0.001	0.766–0.797	68.9	75.3

SOFA: Sequential Organ Failure Assessment; MCHC: mean corpuscular hemoglobin concentration; RDW: red blood cell distribution width; RBC: red blood cell count; INR: international normalized ratio; AUC: area under the curve; CI: Confidence Interval.

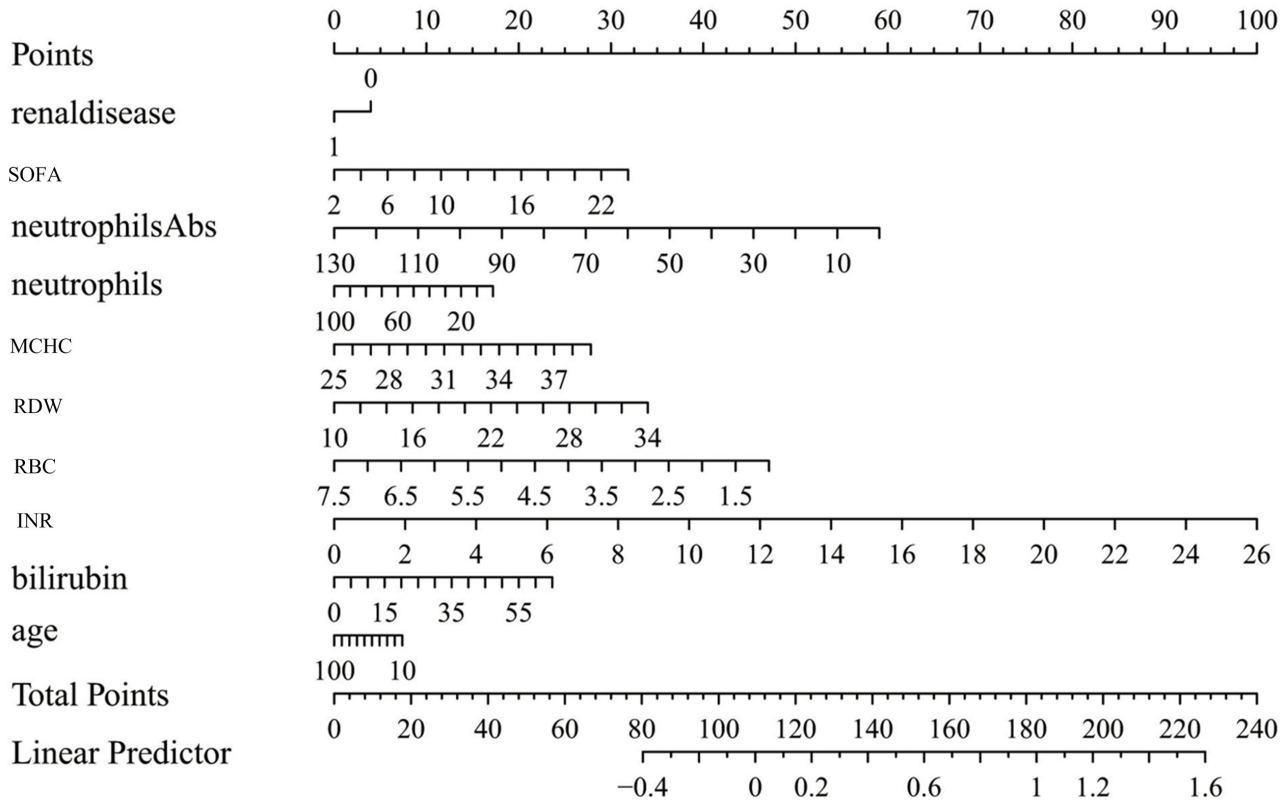

FIGURE 3. ROC curve of the predictive model for identifying DIC in sepsis patients. SOFA: Sequential Organ Failure Assessment; MCHC: mean corpuscular hemoglobin concentration; RDW: red blood cell distribution width; RBC: red blood cell count; INR: international normalized ratio; neutrophilsAbs: absolute neutrophil count.

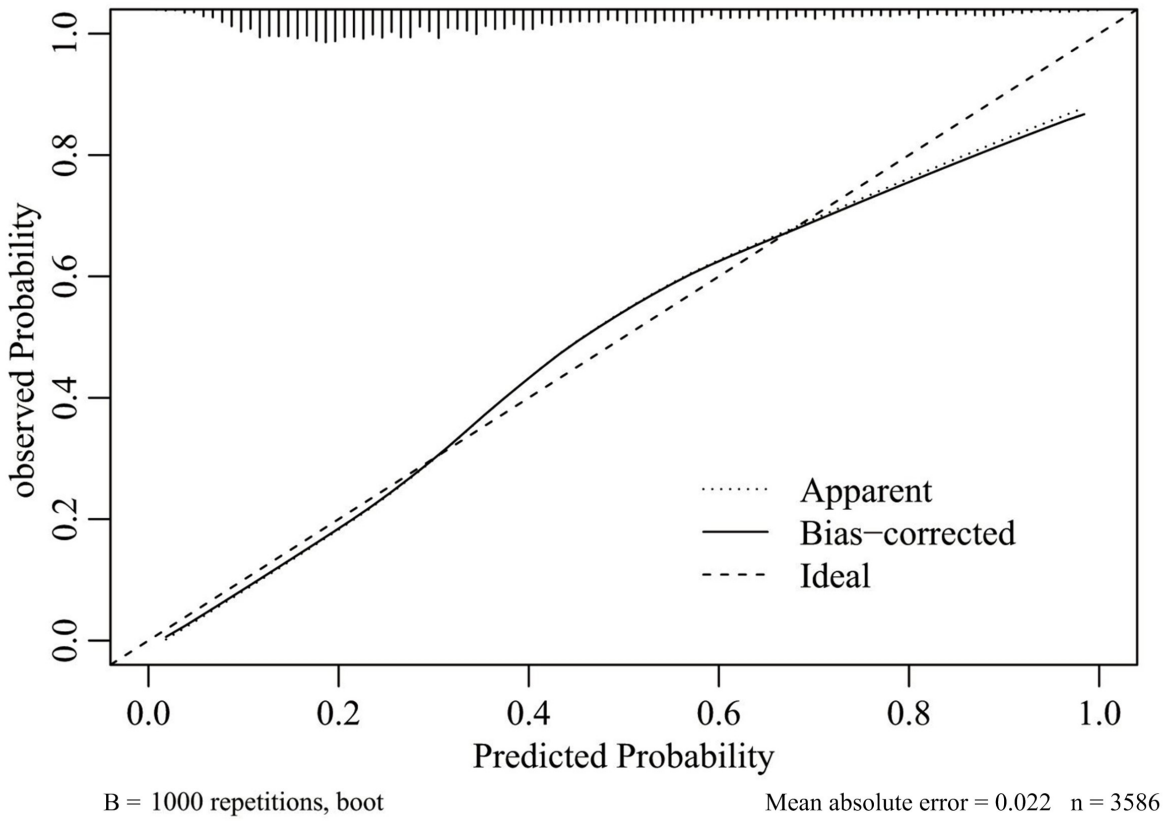

FIGURE 4. Calibration curve.

For every 0.1-unit increase in INR, the risk of DIC increases by 35%, underscoring the importance of dynamic INR monitoring for early identification of coagulation disorders [20]. The association between decreased absolute monocyte count and DIC risk aligns with Wang *et al*. [21], who found monocyte-derived TF expression correlates with coagulation activation. Notably, when INR exceeds 1.5, the risks of both bleeding and thrombotic events in patients rise concurrently, necessitating a comprehensive assessment incorporating platelet counts and fibrinogen levels [22]. Our study further revealed that when bilirubin levels exceed 1.25 mg/dL, the risk of DIC significantly increases, suggesting that bilirubin may serve as an early warning marker for hepatogenic coagulation abnormalities. Impaired liver function leads to reduced synthesis of coagulation factors (such as fibrinogen and prothrombin), exacerbating coagulation disorders. Bilirubin, through oxidative stress, damages vascular endothelial cells and promotes microthrombus formation. Hemolysis (*e.g.*, microangiopathic hemolysis) releases free hemoglobin, further depleting haptoglobin and activating the coagulation system [23].

The findings of this study demonstrate a significant association between RDW, RBC, MCHC, and the risk of DIC in sepsis patients, suggesting that erythrocyte abnormalities and microcirculatory disturbances play crucial roles in the progression of DIC. An elevated RDW reflects increased heterogeneity in RBC volume. Chronic inflammatory states suppress erythropoietin responsiveness, leading to ineffective erythropoiesis and impaired RBC maturation. Microvascular thrombosis triggers mechanical hemolysis, releasing procoagulant substances (such as Adenosine Diphosphate and phospholipids), while oxidative stress damages the stability of the RBC membrane [24]. In this study, patients with an RDW $\geq$15.75% exhibited a nearly 10% increase in the risk of DIC, implying that RDW may serve as an indirect marker of the crosstalk between inflammation and coagulation. A decreased RBC count was negatively correlated with the risk of DIC, which may be attributed to direct causes such as coagulation-related consumption or bleeding events leading to anemia [25]. When the RBC count was $<2.975 \times 10^{12}$/L, the risk of DIC decreased by approximately 41%. This reduction might be associated with earlier interventions, such as blood transfusions or erythropoiesis-stimulating agents, in patients with severe anemia, necessitating further validation incorporating treatment factors. An elevated MCHC reflects hemoglobin concentration within erythrocytes, often due to dehydration or hyperosmolar states causing RBC shrinkage, which increases blood viscosity and microcirculatory resistance. MCHC serves as a diagnostic indicator for DIC through its impact on abnormal blood flow variations [26].

This study demonstrates that Neutrophils Abs and Monocytes Abs are closely associated with DIC in septic patients. A decline in Neutrophil Abs suggests immunosuppression or bone marrow reserve depletion. In sepsis, neutrophils contribute to microthrombus formation through neutrophil extracellular trap formation (NETosis), and their excessive consumption may lead to impaired pathogen clearance capacity, exacerbating secondary infections and coagulation disorders [27]. When Neutrophil Abs fall below 6.325×10^{9}/L, the risk of DIC increases by 3.7%. Monitoring dynamic changes in these counts holds significant value for assessing the infection-coagulation vicious cycle. Similarly, reduced Monocyte abs are correlated with increased DIC risk. Monocytes activate the extrinsic coagulation pathway by expressing TF, while their apoptosis or immune depletion weakens pathogen clearance capacity. Dysregulated monocyte-endothelial cell interactions further exacerbate endothelial damage. Dynamic monitoring of monocyte counts has potential value for predicting coagulation-immune imbalance [28].

The study also revealed that advanced age and chronic kidney disease (CKD) are inversely associated with DIC risk, contradicting previous assumptions. The primary reasons include: elderly patients often die from underlying diseases before progressing to DIC, immune senescence mitigates inflammatory responses and coagulation activation, and earlier initiation of restrictive treatment in clinical practice reduces iatrogenic coagulation disorders. For CKD patients, earlier receipt of renal replacement therapy (RRT) clears inflammatory mediators and uremic toxins, while the accompanying platelet dysfunction counteracts hypercoagulability. Combined with adjusted anticoagulant dosing, this reduces bleeding risks [29, 30]. These findings suggest that DIC risk assessment models need to be optimized by incorporating age stratification.

This study constructed a concise and highly interpretable predictive model by combining LASSO regression with logistic modeling. In comparison to existing models, our study is the first to incorporate "red blood cell distribution width (RDW)" into the predictive framework. As an indirect marker of inflammation and oxidative stress, an elevated RDW may contribute to the progression of DIC by promoting endothelial dysfunction, providing a new direction for mechanistic research. Our model, based on multidimensional data from the MIMIC-IV database (including demographics, laboratory results, and treatment measures), is the first to integrate erythrocyte parameters (such as RDW and RBC) and absolute neutrophil count, thereby addressing the limitations of traditional studies that focused solely on coagulation function. The model achieved an area under the curve (AUC) of 0.781, which outperformed previous single-indicator models (*e.g.*, INR with an AUC of 0.761) or small-scale cohort studies (AUC = 0.740) [31]. The model demonstrated a good balance between sensitivity (68.9%) and specificity (75.3%), surpassing the Japanese Association for Acute Medicine DIC criteria [32, 33], making it suitable for early clinical screening. Indicators such as the SOFA score and INR can be dynamically monitored in the ICU, enabling real-time risk prediction through data updates and supporting personalized interventions.

However, this study also has certain limitations. Firstly, it is based on retrospective data, which may introduce selection bias (*e.g.*, exclusion of patients with >20% missing data). Secondly, therapeutic measures such as glucocorticoids and fluid resuscitation may influence the risk of DIC, but due to the complexity of confounding factors, they were not included in the model, necessitating further stratified analysis. Lastly, the ratio of the control group to the observation group was approximately 2:1, which may introduce data imbalance. Although logistic regression was used in this study, models insensitive to imbalance (*e.g.*, random forests, gradient boosting trees such as eXtreme Gradient Boosting or Light Gradient

Boosting Machine) generally perform better in such scenarios and could be considered in future studies to optimize predictive performance. Future research should focus on: (1) multicenter prospective validation; (2) head-to-head comparison with existing scoring systems (*e.g.*, SIC score); and (3) exploring model performance in specific subgroups (*e.g.*, elderly or CKD patients).

5. Conclusions

The ten risk factors identified in this study encompass multidimensional pathological processes, including inflammatory responses, coagulation disorders, organ dysfunction, and hematological abnormalities, aligning closely with the "dual-pathway mechanism" of sepsis-induced DIC (where inflammation drives coagulation, and coagulation exacerbates inflammation). Notably, the combined application of traditional coagulation indicators (such as INR and platelet count) with novel markers (such as RDW and MCHC) can enhance the sensitivity and specificity of early DIC diagnosis. This model provides ICU physicians with a quantitative tool for early identification of high-risk patients and initiation of targeted interventions (such as anticoagulation therapy and organ support). Future multicenter prospective studies are needed to validate the independent contributions and interactions of these factors and to explore targeted intervention targets.

AVAILABILITY OF DATA AND MATERIALS

According to the information on the web page, this paper obtained the consent of the original data collection.

AUTHOR CONTRIBUTIONS

HC, LHZ, FT and NYG—designed the study and carried them out. HC, LHZ, FT, KQ, YC, LFC, SHZ and ZCH—prepared the manuscript for publication and reviewed the draft of the manuscript; supervised the data collection; analyzed the data, interpreted the data. All authors have read and approved the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was reviewed and approved by the Ethics Committee of the Massachusetts Institute of Technology (Exemption Review Number: 66822508). The study was based on publicly available databases, and no patient informed consent was required.

ACKNOWLEDGMENT

Not applicable.

FUNDING

This work was supported by Zhejiang Province Medical and Health Science and Technology Program (Grant: 2020KY773).

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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How to cite this article: Hui Chen, Longhuan Zeng, Fu Tian, Kai Qiu, Yang Chen, Leifei Chen, *et al*. Construction of a multi-dimensional predictive model for sepsis-associated disseminated intravascular coagulation and its clinical utility. Signa Vitae. 2025; 21(10): 129-138. doi: 10.22514/sv.2025.150.