Clin. Lab. 2026;72:XXX-XXX

ORIGINAL ARTICLE

Clinical Application of Combined CEACAM1_A and CEACAM1_B in Early Warning and Diagnosis of Sepsis

Lijuan Zhou [1, 2, *], Chuchu Xu [1, *], Huijuan Zhou [3], Xi Wang [1], Xiaona Yin [1], Dong mei Su [1], Chen Zhang [1], Jiling Wang [1], Xiaoqiong Wang [1]

[1] *Bengbu Medical University, Bengbu, Anhui, China*
[2] *Department of Respiratory and Critical Care Medicine, The Second People's Hospital of Hefei, Hefei Hospital Affiliated to Anhui Medical University, Hefei, Anhui, China*
[3] *School of Pharmacy, Henan University, Jinming Campus, Kaifeng City, Henan Province, China*

ABSTRACT

Background: **This retrospective observational study aimed to evaluate the predictive value of CEACAM1_A, CEACAM1_B, and their combined model in the early warning diagnosis of sepsis. Based on previously identified CEACAM1_A and CEACAM1_B, this study evaluated their potential in the early diagnosis of sepsis and explored the construction of predictive models that combine genetic markers with clinical indicators.**
Methods: **A total of 144 acutely infected patients admitted to Hefei Second People's Hospital between July 2023 and February 2025 were enrolled in this retrospective observational study. The patients were divided into sepsis and non-sepsis groups according to the Sepsis-3 standard. The sepsis group included 96 patients, and the non-sepsis group consisted of 48 patients. Baseline characteristics, biochemical parameters, and expression levels of the CEACAM1_A and CEACAM1_B genes were collected from both groups. Statistical analyses were performed via SPSS version 27.0 and the R programming language. For data distribution, intergroup comparisons were conducted via appropriate parametric and nonparametric tests. Univariate and multivariate logistic regression analyses were employed to identify independent predictors, and receiver operating characteristic (ROC) curve analysis was used to evaluate model performance.**
Results: **The study revealed significantly greater expression levels of CEACAM1_A and CEACAM1_B in the sepsis group than in the non-sepsis group ($p < 0.001$), with positive correlations with disease severity (correlation coefficients of 1 and 0.992, respectively). Multivariate analysis revealed that CEACAM1_A (odds ratio [OR] = 1.001, 95% confidence interval [CI]: 1.001 - 1.006, $p < 0.001$), CEACAM1_B (OR = 1.001, 95% CI: 1.000 - 1.002, $p < 0.001$), lactate (OR = 4.154, 95% CI: 2.207 - 7.819, $p < 0.001$), and C-reactive protein (OR = 1.012, 95% CI: 1.004 - 1.020, $p = 0.002$) were independent risk factors for sepsis. The area under the curve (AUC) for the combined predictive model of CEACAM1_A and CEACAM1_B was 0.914, outperforming the other indicators.**
Conclusions: **The combined application of these two biomarkers significantly improved the accuracy of early sepsis detection, potentially facilitating optimal resource allocation and improving patient outcomes.**
(Clin. Lab. 2026;72:xx-xx. DOI: 10.7754/Clin.Lab.2025.250818)

Correspondence:
Xiaoqiong Wang and Jiling Wang
Department of The Second People's Hospital of Hefei
Hefei Hospital Affiliated to Anhui Medical University Hefei
Anhui
China
Phone: + 86 15357920527
+ 86 15395192782
E-mail: xiaoqiongwang1220@163.com
lyli0719@163.com

KEYWORDS

CEACAM1_A, CEACAM1_B, sepsis, early warning, diagnostic efficacy

Manuscript accepted September 18, 2025

INTRODUCTION

Sepsis is recognized as a severe public health challenge, contributing to significant mortality and long-term disability worldwide. An estimated 50 million sepsis cases are documented annually worldwide, accompanied by 11 million sepsis-associated fatalities, yielding a mortality rate exceeding 20% 1. Consequently, rapid and accurate sepsis prediction is critical in clinical management. The Sepsis-3 criteria remain the primary reference in clinical practice. In 2021, the European Society of Intensive Care Medicine (ESICM) published the International Guidelines for Management of Sepsis and Septic Shock 2021 2 providing partial revisions and supplements to Sepsis-3. These criteria incorporate multiorgan scoring systems, microbiological assays, and biochemical indices, necessitating comprehensive assessments of systemic organ function. However, their reliance on complex multiorgan evaluations limits rapid specificity and simplicity in emergency triage.

Recent advancements in molecular technologies have enabled the elucidation of complex scientific questions through proteomic and genomic approaches. Sepsis is characterized by immune dysregulation in response to infection, creating a paradoxical situation for the immune system, which must simultaneously combat pathogens while preventing self-mediated tissue and organ damage. Significant alterations in the expression profiles of immune-regulatory mRNAs are observed during the pathological process 3. Consequently, the differential expression patterns of these key gene transcripts play critical roles in sepsis prediction and risk stratification 4. In our preliminary research, we conducted a systematic screening and comprehensive analysis of sepsis-related transcriptomic data from the NCBI GEO public database. Combined with evidence from previous literature and historical data, we performed in-depth comparison and validation of potential early warning mRNA biomarkers. Through this multidimensional analytical process, we identified CEACAM1_A and CEACAM1_B as being significantly dysregulated in patients with sepsis and closely associated with early disease warning. Therefore, these genes were selected as the core candidates of the present study to further evaluate their clinical utility.

On the basis of previously established findings, the diagnostic efficacy of CEACAM1_A and CEACAM-1_B in sepsis patients was evaluated through clinical validation via blood samples obtained from sepsis patients and non-sepsis patients. CEACAM1, a member of the immunoglobulin superfamily widely expressed in epithelial cells, endothelial cells, and immune cells, plays significant roles in immune regulation, cell adhesion, and signal transduction 5. CEACAM1_A and CEACAM1_B represent the two primary subtypes and exhibit distinct structural and functional characteristics 7. The present study was designed to investigate their correlation with disease severity and prognosis, assess their potential utility as early warning biomarkers, and develop prediction models incorporating conventional clinical parameters, thereby providing novel approaches for the early diagnosis and risk stratification of sepsis.

MATERIALS AND METHODS

Study design and patients

A retrospective analysis of the clinical data of 144 patients admitted to the Department of Respiratory Medicine at Hefei Second People's Hospital between July 2023 and February 2025 was conducted. The study protocol received ethical approval from the Institutional Review Board of Hefei Second People's Hospital (Number: 2024-Scientific Research-064). In the preliminary stage, we conducted a systematic search of the NCBI GEO public database and integrated evidence from literature and historical data to identify candidate mRNAs related to early warning of sepsis. CEACAM1_A and CEACAM1_B were ultimately selected as the biomarkers for this study.

The patients were divided into sepsis and non-sepsis groups according to the Sepsis-3 standard. The non-sepsis group included 48 patients, and the sepsis group included 96 patients (15 of whom ultimately died). Diagnostic criteria for sepsis: a) Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection, characterized by self-inflicted tissue and organ damage during systemic disease. Patients meeting the criteria for confirmed or suspected infection were classified as septic if they demonstrated a ≥ 2-point increase in the Sequential Organ Failure Assessment (SOFA) score from baseline 9. b) Diagnostic components: Clinical manifestations, laboratory findings, and imaging evidence were systematically evaluated.

The inclusion criteria were 1) ≥ 18 years of age; 2) confirmed or high suspicion of infection with apparent clinical symptoms. Patients who were highly suspected of having an infection with apparent clinical symptoms were also required to meet at least two of the following four diagnostic criteria for systemic inflammatory response syndrome 8: 1) body temperature of > 38°C or < 36°C; 2) heart rate of > 90 beats/min; 3) respiratory rate of > 20 breaths/min, or partial pressure of carbon dioxide of < 32 mmHg; 4) peripheral white blood cell count of > 12,000/mm^3 or < 4,000/mm^3; 5) ability to provide blood samples for mRNA detection, and complete clinical data.

The exclusion criteria were as follows: 1) unclear clinical diagnosis: cases with indistinguishable sepsis and non-sepsis states or coexisting conditions potentially confounding diagnostic accuracy; 2) significant comorbidities (malignancies, autoimmune disorders) potentially influencing mRNA expression profiles; 3) inadequate blood sample volume or specimens failing quality control standards for mRNA analysis; 4) pregnancy or lactation status; 5) history of immunosuppressive therapy within 3 months preceding enrollment.

All patients with infection (or high suspicion of infection) were divided into sepsis and non-sepsis (control) groups according to the Sepsis-3 standard. Patients who did not meet the sepsis criteria at admission but developed sepsis during hospitalization were grouped into the sepsis group.

Laboratory examination

We retrospectively analyzed the baseline characteristics of patients in the sepsis and non-sepsis groups, tracked 28-day clinical outcomes, and evaluated disease severity via the Sequential Organ Failure Assessment (SOFA) score and biochemical indicators. Peripheral blood samples (approximately 2 mL) were collected in anticoagulant-containing tubes within 24 hours of hospital admission, immediately stored at -80°C, and subsequently transferred to Shanghai Thalys Medical Laboratory for functional enrichment analysis of differentially expressed genes. Through this process, we identified potential early warning biomarkers for sepsis, including the CEACAM1_A and CEACAM1_B genes.

Data collection

Patient clinical data, including age, gender, body mass index (BMI), comorbidities, etiological examination results, number of patients transferred to the intensive care unit (ICU) within 7 days, number of deaths within 28 days, and Sequential Organ Failure Assessment (SOFA) scores, were recorded. The neutrophil/lymphocyte ratio (NLR) and Glasgow Coma Scale (GCS) score were also calculated. The study protocol received ethical approval from the Hefei Second People's Hospital's Institutional Review Board (2023-Scientific Research-084).

Statistical analysis

Statistical analysis was performed via SPSS 27.0 software and the R language. Categorical data are presented as n (%) and were compared via the chi-squared test. A normality test was conducted for all continuous variables. Data that met the criteria for a normal distribution are presented as means ± standard deviations (SDs) and were compared via the independent samples *t* test. Continuous data that failed to meet the criteria for normality are presented as medians (interquartile ranges) and were compared via the Mann-Whitney U test. Univariate logistic regression was used to screen for high-risk factors, which were then included in multivariate logistic regression analysis to identify independent predictors for patients with sepsis. Receiver operating characteristic (ROC) curves were constructed, and the area under the curve (AUC) was calculated. A combined prediction model was built on the basis of the multivariate logistic regression model to obtain the predicted probability (*logit P1*), which was used as an independent variable for ROC curve analysis. A two-tailed $p < 0.05$ was considered statistically significant.

RESULTS

Basic characteristics

A total of 144 patients were enrolled in this study, comprising 96 males and 48 females (male-to-female ratio of 2:1). Among these patients, 129 survived and 15 died within 28 days, resulting in a mortality rate of 10.4%. In the sepsis group, 35% of patients were transferred to the intensive care unit (ICU) within 7 days. The proportions of patients with cardiovascular disease and bacterial infection were 44.4% and 47.9%, respectively. The Sequential Organ Failure Assessment (SOFA) score was significantly greater in the sepsis group than in the non-sepsis group ($p < 0.05$). However, there were no statistically significant differences between the two groups in terms of body mass index (BMI), hypertension, diabetes, or other indicators ($p > 0.05$) (Table 1).

Univariate analysis

Univariate analysis revealed that the serum CEACAM1_A and CEACAM1_B levels were significantly greater in the sepsis group than in the non-sepsis group ($p < 0.001$). With respect to biochemical parameters, patients in the sepsis group had substantially greater white blood cell (WBC) counts, eosinophil absolute counts (EOSs), mean corpuscular volume (MCV), red cell distribution width (RDW), serum creatinine (Scr), blood urea nitrogen (BUN), total protein (TP), albumin (ALB), total bilirubin (TBIL), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT), lactate dehydrogenase (LDH), prothrombin time (PT), D-dimer (DD), lactate (Lac), C-reactive protein (CRP), procalcitonin (PCT), and neutrophil-lymphocyte ratio (NLR) counts and significantly lower Glasgow Coma Scale (GCS) scores than did those in the non-sepsis group, with statistically significant differences ($p < 0.05$). However, there were no statistically significant differences between the two groups in terms of the neutrophil absolute count (NEU), hematocrit (Hct), mean corpuscular hemoglobin concentration (MCHC), alanine aminotransferase (ALT), or fibrinogen (FIB) level ($p > 0.05$) (Table 2).

Multivariate analysis

The binary logistic regression analysis included indicators with statistical significance in the univariate analysis. The results revealed that elevated Lac, CRP, CEACAM1_A, and CEACAM1_B were independent high-risk factors for early sepsis warning (Table 3).

Spearman correlation analysis

The results demonstrated that the CEACAM1_A and CEACAM1_B levels were strongly positively correlated with the severity of sepsis ($r = 1$, $r = 0.992$; $p < 0.01$). This highly significant correlation suggests that these two biomarkers may play essential roles in the progression of sepsis and could serve as valuable indicators for assessing sepsis severity.

Table 1. Characteristics of the patients (n = 144).

Characteristics	Sepsis (n = 96)	Non-sepsis (n = 48)	Statistical values z/t/x^2	p-value
Age (years)	78 (70, 84)	62 (30, 78)	-4.937	< 0.001
Gender (male/female)	72/24	24/24	-2.99	0.003
BMI (kg/m^2)	21.28 ± 4.03	22.6 ± 3.97	1.864	0.064
Hypertension	49 (51)	13 (27.1)	2.778	0.096
Cardiovascular/cerebrovascular disease	64 (66.7)	13 (27.1)	-4.474	< 0.001
Diabetes	20 (20.8)	5 (10.4)	-1.55	0.121
Bacterial infection	69 (71.9)	19 (39.6)	-3.734	< 0.001
ICU transfer within 7 days	51 (53.1)	12 (25)	-5.99	< 0.001
Death within 28 days	15 (15.6)	0	-2.883	0.004
SOFA scores	5.53 ± 5.10	0.29 ± 0.459	-9.881	< 0.001

Data are presented as mean ± SD, n (%), or median (Q1 - Q3). p-values compare sepsis vs. non-sepsis; p < 0.05 is considered significant.
BMI: body mass index, SOFA: Sequential Organ Failure Assessment.

Table 2. Comparison of peripheral blood indices in sepsis and non-sepsis groups.

Characteristics	Sepsis (n = 96)	Non-sepsis (n = 48)	Statistical values z/t/x^2	p-value
WBC ($10^9/L$)	9.82 ± 6.75	7.73 ± 3.21	-2.514	0.013
NEU ($10^9/L$)	15.37 ± 75.23	6.14 ± 2.61	-0.848	0.398
EOS ($10^9/L$)	0.02 (0, 0.1)	0.07 (0.02, 0.13)	-2.114	0.035
HCT%	37.65 ± 6.76	37.12 ± 5.13	-0.473	0.637
MCV (fL)	93.3 (90.4, 97.3)	89.7 (86.5, 92.8)	-3.899	< 0.001
RDW-CV%	14.1 (13.02, 15.2)	13.4 (12.6, 13.8)	-3.076	< 0.001
RDW-SD (fL)	46.25 (43.05, 50.1)	42 (41.12, 45.07)	-5.468	< 0.001
MCHC (g/L)	324 (312.3, 330)	325 (321, 332)	-1.028	0.279
Scr (μmol/L)	84.4 (63.7, 117.3)	66 (53.1, 76.05)	-4.09	< 0.001
BUN (mmol/L)	7.25 (6.1, 9.6)	5 (3.51, 6.85)	-4.906	< 0.001
TP (g/L)	66.94 ± 9.41	71.9 ± 9.06	3.301	0.003
ALB (g/L)	33.85 ± 6.21	41 ± 5.91	4.758	< 0.001
TBIL (μmol/L)	13.35 (10.3, 25.27)	10.2 (8.52, 14.05)	-3.761	< 0.001
ALT (U/L)	23.5 (15, 37)	20 (15.25, 32)	-0.36	0.719
AST (U/L)	30.5 (23, 54.25)	26 (23.25, 30)	-2.209	0.027
GGT (U/L)	31.9 (17.25, 62)	22.65 (12.5, 38)	-2.467	0.014
LDH (U/L)	225 (179.2, 283.7)	184 (169.2, 214)	-3.397	< 0.001
PT (s)	14.3 (13.3, 15.27)	13.3 (12.8, 13.9)	-3.74	< 0.001
FIB (g/L)	4.84 (3.84, 6.22)	4.65 (3.81, 5.8)	-0.367	0.741
D-D	1.09 (0.56, 2.38)	0.52 (0.21, 0.83)	-4.628	< 0.001
Lac (mmol/L)	2.36 (1.62, 3.7)	0.7 (0.2, 1.5)	-7.445	< 0.001
CRP (mg/L)	96.93 (37.4, 159.9)	19.1 (1.83, 60.96)	-5.454	< 0.001
PCT (ng/mL)	0.52 (0.14, 2.33)	0.095 (0.05, 0.32)	-5.051	< 0.001
NLR	7.13 (3.58, 17.38)	4.4 (3.65, 8.78)	-2.055	0.04
GCS	11.97 ± 4.02	14.6 ± 0.7	-6.27	< 0.001
CEACAM1_A	3,874.5 (1,556.75, 8,107)	629 (380, 991.25)	-8.013	< 0.001
CEACAM1_B	5,598.5 (2,149.5, 10,644)	809 (525.2, 1342)	-8.014	< 0.001

Data are presented as median (Q1 - Q3). Underlined values indicate variables included in binary logistic regression (p < 0.05). p-values compare sepsis vs. non-sepsis groups; p < 0.05 is considered significant.
MCV: mean corpuscular volume, RDW: Red Cell Distribution Width, TP: total protein, ALB: albumin, TBIL: total bilirubin, AST: aspartate aminotransferase, GGT: gamma-glutamyl transferase, DD: D-dimer, Lac: lactate, CRP: C-reactive protein, PCT: procalcitonin, NLR: neutrophil - lymphocyte ratio, GCS: Glasgow Coma Scale.

Table 3. Multivariate logistic regression analysis of sepsis risk factors.

Variables	β-value	SE value	Wald x² value	p-value	OR	95% CI
Lac (mmol/L)	1.424	0.323	19.472	< 0.001	4.154	2.207 - 7.819
CRP (mg/L)	0.012	0.004	9.289	0.002	1.012	1.004 - 1.020
PCT (ng/mL)	0.248	0.206	1.451	0.228	1.282	0.856 - 1.920
CEACAM1_A	0.001	0.000	15.933	< 0.001	1.001	1.001 - 1.002
CEACAM1_B	0.001	0.000	16.245	< 0.001	1.001	1.000 - 1.001

β: regression coefficient, SE: standard error, Wald χ^2: Wald chi-square statistic, OR: odds ratio, 95% CI: 95% confidence interval, $p < 0.05$ indicates statistical significance.

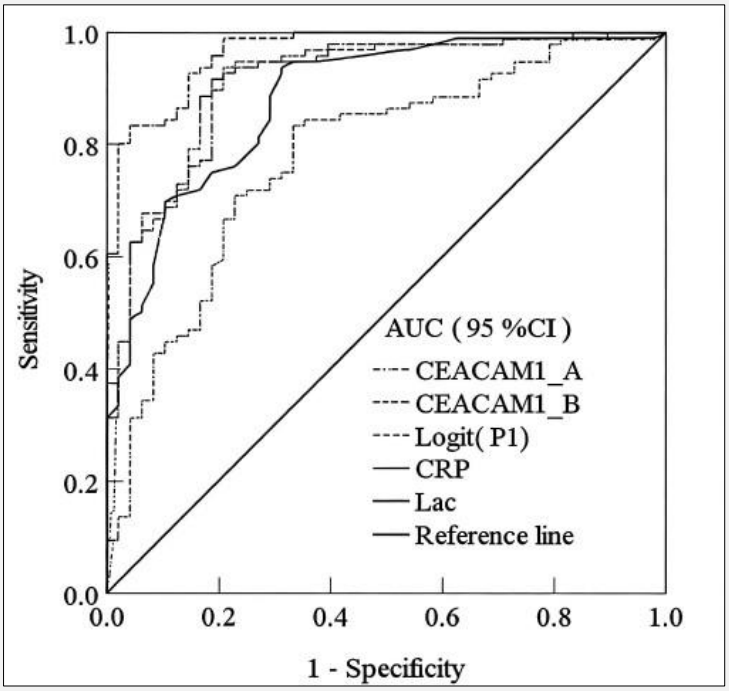

Figure 1. Area under the receiver operating characteristic (ROC) curve.

ROC curves for early prediction of sepsis. CEACAM1_A, CEACAM1_B, and their combined model (Logit(p1)) showed significant predictive value. AUC: area under the curve, CI: confidence interval, CRP: C-reactive protein, Lac: lactate.

ROC curve analysis

The area under the ROC curve (AUC) for lactate (Lac) was 0.881, with an optimal truncation value of 1.135, yielding a sensitivity of 0.938 and specificity of 0.687. For C-reactive protein (CRP), the AUC was 0.779, the truncation value was 0.515, sensitivity was 0.99, and specificity was 0.83. CEACAM1_A exhibited an AUC of 0.915, with a truncation value of 1,073.5, sensitivity of 0.938, and specificity of 0.791. CEACAM1_B had an AUC of 0.910, truncation value of 1,530, sensitivity of 0.917, and specificity of 0.812. The combined model of CEACAM1_A and CEACAM1_B (Logit(P1)) showed an AUC of 0.914, truncation value of 0.461, sensitivity of 0.938, and specificity of 0.812 (Figure 1).

Risk prediction model

On the basis of the multivariate analysis results of this study, with the occurrence of sepsis as the clinical out-

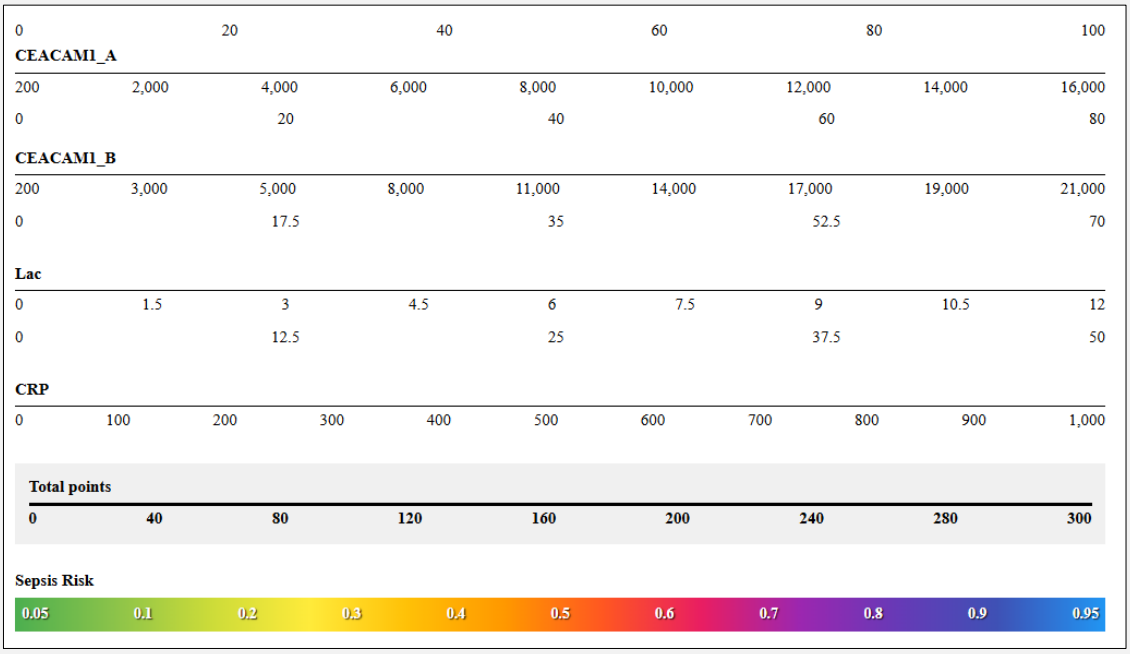

Figure 2. Nomogram model for early warning of the risk of sepsis.

Nomogram for predicting the risk of sepsis. Each variable is assigned a point value based on its contribution; total points are calculated by summing individual scores and mapped to the predicted sepsis risk. Higher total scores indicate greater risk. CEACAM1_A contributes the most and thus carries the highest point weight.

come, we established a risk nomogram integrating four independent risk factors: CEACAM1_A, CEACAM-1_B, CRP, and Lac. The nomogram demonstrated distinct hierarchical differences in the contribution of these biomarkers to the prediction model, with CEACAM1_A exhibiting the highest predictive value, followed by CEACAM1_B, Lac, and CRP. Compared with traditional inflammatory indicators, the CEACAM1 subtype is a novel biomarker that has superior predictive ability (Figure 2).

DISCUSSION

Sepsis, a syndrome characterized by a dysregulated systemic inflammatory response and organ dysfunction caused by infection, involves complex immune pathophysiological mechanisms with extensive activation and regulation of the innate and adaptive immune systems. This immune dysregulation includes an early excessive inflammatory response followed by an immunosuppressive state, subjecting patients to the dual threat of inadequate infection control and self-tissue damage 11. In recent years, with advances in precision medicine, molecular-level biomarker research has provided new perspectives for the early identification and individualized treatment of sepsis. Among various immune-related molecules 12, the immunoregulatory protein CEACAM1 and its subtypes have gained attention because of their critical roles in inflammation and infection 13.

CEACAM1_B promotes the release of reactive oxygen species (ROS) and elastase from neutrophils, directly compromising endothelial barrier integrity while increasing the release of the inflammatory cytokines TNF-α and IL-6. Activating endothelial inflammatory pathways, NF-κB and MAPK amplify the endothelial inflammatory response, upregulate the expression of the adhesion molecule ICAM-1, and stimulate the release of TNF-α and IL-6, ultimately leading to a "cytokine storm" 14. These mechanisms induce vascular endothelial injury, capillary leakage, and microcirculatory dysfunction. CEACAM1_B also promotes neutrophil adhesion and aberrant migration, mediates metabolic imbalance, and drives the progression of sepsis from localized infection to systemic inflammation and multiple organ failure 15. Specific pathogens 16, such as *Fusobacterium nucleatum*, suppress T-cell and natural killer (NK) cell functions through CEACAM1_A, weakening host immune defenses, facilitating the

spreading of infection, and exacerbating sepsis progression 17.

Studies have demonstrated that serum CEACAM1 levels progressively increase from healthy controls to patients with systemic inflammatory response syndrome (SIRS), sepsis, and septic shock. Significantly elevated serum CEACAM1 levels were observed in patients with septic shock compared with those with ordinary sepsis 18. These findings suggest that elevated CEACAM1 is closely associated with infection progression and organ dysfunction, and the gradient differences in expression levels constitute clinical evidence for CEACAM1 as an early warning biomarker 19.

In early sepsis, inflammatory factors such as interferon-γ (IFN-γ) activate CEACAM1 gene transcription through interferon regulatory factor 1 (IRF-1). IRF-1 increases overall CEACAM1 expression and specifically promotes the production of CEACAM1_A. Under activation conditions, the ITIM structure of CEACAM1_A is phosphorylated by tyrosine kinases (such as Lyn and Hck), subsequently recruiting SHP-1/SHP-2 phosphatases to form a negative feedback loop that inhibits immune cell function 20. As CEACAM1_A expression increases, this inhibitory effect is enhanced, impairing immune function 21. Specific pathogens, such as group A Streptococcus, bind to CEACAM1 through their surface proteins, particularly those that interact with CEACAM1_A, which contains ITIM domains, enhancing its immunosuppressive effects. This interaction promotes pathogen adhesion and invasion of host cells and suppresses host immune responses, facilitating infection spread. Therefore, elevated levels of CEACAM1_A and CEACAM1_B positively correlate with sepsis severity throughout disease progression. The upregulation of these proteins, especially CEACAM1_A, reflects a protective mechanism by which the body attempts to suppress excessive inflammatory responses. However, this inhibition is exploited by pathogens, ultimately resulting in immune dysfunction, preventing adequate clearance of infection, and thereby exacerbating sepsis 23. Consistent with Van der Flier M et al.'s findings, serum CEACAM1 levels were significantly higher in patients with septic shock than in healthy controls and patients with uncomplicated sepsis 0. Our study confirmed that CEACAM1_A and CEACAM1_B expression levels were significantly higher in the sepsis group than in the non-sepsis group ($p < 0.001$) and were positively correlated with disease severity ($r = 1$, $r = 0.992$). Furthermore, in early sepsis, CEACAM1_A and CEACAM1_B predominate, promoting inflammatory responses and indicating a worsening immunosuppressive state in sepsis patients. Therefore, we can infer that these novel biomarkers play important roles in sepsis progression and may serve as potential indicators for assessing the severity of early sepsis.

Compared with clinically established biomarkers, CEACAM1_A and CEACAM1_B demonstrated greater diagnostic value. In our study, the area under the curve (AUC) for predicting sepsis was 0.915 for CEACAM-1_A and 0.910 for CEACAM1_B, exceeding the AUC of CRP (0.779). This finding 0 is consistent with the study by Pierrakos et al., which revealed that traditional inflammatory markers such as CRP primarily reflect systemic inflammatory responses and are suitable for preliminary assessment of inflammatory states in primary care settings 26. However, CRP exhibits reduced sensitivity during the first 6 hours of infection and does not adequately reflect sepsis severity, whereas antibiotic or glucocorticoid therapy may affect CRP levels, potentially masking the actual inflammatory state 27. In contrast, CEACAM1 regulates endothelial cell function, vascular permeability, and leukocyte migration and is intricately linked to sepsis pathophysiology 28.

Although lactate demonstrated a relatively high predictive value in our study, with an area under the curve (AUC) of 0.881, reflecting microcirculatory dysfunction and tissue hypoxia in patients and acting synergistically with inflammatory markers to improve diagnostic accuracy and sepsis stratification, which is consistent with Bakker et al.'s research on lactate 29, its non-specificity, time delay, and sensitivity to therapeutic interventions may lead to the absence of an optimal window for early sepsis intervention.

Therefore, CEACAM1_A and CEACAM1_B, as molecular-level markers, can provide more precise information about specific pathological processes. Consequently, the development of multiparameter combined models integrated with artificial Intelligence analysis can be implemented to achieve accurate early warning and personalized treatment of sepsis. The risk nomogram constructed on the basis of CEACAM1_A, CEACAM1_B, Lac, and CRP provides an intuitive tool for clinical sepsis risk assessment. This model integrates molecular markers with clinical indicators to achieve multidimensional risk evaluation and is expected to improve the accuracy of the early identification of high-risk patients. However, CEACAM1 detection has not yet been standardized or widely applied, and the practical implementation of this model still faces technical and cost challenges.

CONCLUSION

This study confirmed that the expression levels of CEACAM1_A and CEACAM1_B are increased in sepsis patients, reflecting the immune response to infection, and that these levels are closely correlated with disease severity. These findings provide a theoretical basis for the use of CEACAM1_A and CEACAM1_B as early warning biomarkers for sepsis and further validate their potential as early diagnostic indicators. Combining CEACAM1 expression levels with traditional clinical indicators and scoring systems can significantly improve the accuracy of sepsis risk prediction, provide a reference for rational allocation of medical resources, and facilitate more timely and effective treatment for patients.

Our study has several limitations. First, this study was conducted in a single center, which may introduce potential bias and limit the generalizability of the findings. Future multicenter studies with larger sample sizes are warranted to further validate our results and enhance their robustness and applicability. Additionally, future studies should incorporate in vitro cellular experiments and animal models to further elucidate the mechanistic role of CEACAM1 in the pathophysiological progression of sepsis.

Acknowledgment:
We wish to show our gratitude to all those who were involved in this study.

Availability of Data and Materials:
The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Source of Funds:
This study was supported by the Applied Medical Research Project of Heifei Municipal Health Commission (Hwk2023zd012), Scientific Research Projects of Higher Education Institutions in Anhui Province (2024AH05 0703), the Science and Technology Project of Bengbu Medical University (2024byzd377). The Second People's Hospital of Hefei City hospital-level topics (2025y kt038).

Declaration of Interest:
The authors have no conflicts of interest to declare.

References:

1. Font MD, Thyagarajan B, Khanna AK. Sepsis and Septic Shock-Basics of diagnosis, pathophysiology and clinical decision making. Med Clin North Am 2020 Jul;104(4):573-85. (PMID: 32505253)

2. Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 2016 Feb;315(8):801-10. (PMID: 26903338)

3. Evans L, Rhodes A, Alhazzani W, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Crit Care Med 2021 Nov; 47(11):1181-247. (PMID: 34599691)

4. Lu X, Xue L, Sun W, Ye J, Zhu Z, Mei H. Identification of key pathogenic genes of sepsis based on the Gene Expression Omnibus database. Mol Med Rep 2018 Feb;17(2):3042-54. (PMID: 29257295)

5. Wang H, Len L, Hu L, Hu Y. Combining machine learning and single-cell sequencing to identify key immune genes in sepsis. Sci Rep 2025 Jan;15(1):1557. (PMID: 39789158)

6. Catton EA, Bonsor DA, Herrera C, et al. Human CEACAM1 is targeted by a Streptococcus pyogenes adhesin implicated in puerperal sepsis pathogenesis. Nat Commun 2023 Apr;14(1):2275. (PMID: 37080973)

7. Kim WM, Huang YH, Gandhi A, Blumberg RS. CEACAM1 structure and function in immunity and its therapeutic implications. Semin Immunol 2019 Apr; 42:101296. (PMID: 31604530)

8. Pierrakos C, Velissaris D, Bisdorff M, Marshall JC, Vincent JL. Biomarkers of sepsis: time for a reappraisal. Crit Care 2020 Jun;24(1):287. (PMID: 32503670)

9. Szakmany T, Fitzgerald E, Garlant HN, et al. The 'analysis of gene expression and biomarkers for point-of-care decision support in Sepsis' study; temporal clinical parameter analysis and validation of early diagnostic biomarker signatures for severe inflammation and sepsis-SIRS discrimination. Front Immunol 2024 Jan;14:1308530. (PMID: 38332914)

10. van der Poll T, van de Veerdonk FL, Scicluna BP, Netea MG. The immunopathology of sepsis and potential therapeutic targets. Nat Rev Immunol 2017 Jul;17(7):407-20. (PMID: 28436424)

11. Hotchkiss RS, Monneret G, Payen D. Sepsis-induced immunosuppression: from cellular dysfunctions to immunotherapy. Nat Rev Immunol 2013 Dec;13(12):862-74. (PMID: 24232462)

12. Delano MJ, Ward PA. The immune system's role in sepsis progression, resolution, and long-term outcome. Immunol Rev 2016 Nov;274(1):330-53. (PMID: 27782333)

13. Gray-Owen SD, Blumberg RS. CEACAM1: contact-dependent control of immunity. Nat Rev Immunol 2006 Jun;6(6):433-46. (PMID: 16724098)

14. Kuespert K, Pils S, Hauck CR. CEACAMs: their role in physiology and pathophysiology. Curr Opin Cell Biol 2006 Oct;18(5): 565-71. (PMID: 16919435)

15. Dankner M, Gray-Owen SD, Huang YH, Blumberg RS, Beauchemin N. CEACAM1 as a multi-purpose target for cancer immunotherapy. Oncoimmunology 2017 May;6(7):e1328336. (PMID: 28811967)

16. Horst AK, Najjar SM, Wagener C, Tiegs G. CEACAM1 in liver injury, metabolic and immune regulation. Int J Mol Sci 2018 Oct;19(10):3110. (PMID: 30309006)

17. Gur C, Maalouf N, Shhadeh A, et al. Fusobacterium nucleatum suppresses anti-tumor immunity by inhibiting CEACAM1. Immunity 2019 Mar;50(6):e1581531. (PMID: 31069151)

18. Boulton IC, Gray-Owen SD. Neisserial binding to CEACAM1 arrests the activation and proliferation of CD4+ T lymphocytes. Nat Immunol 2002 Mar;3(3):229-36. (PMID: 11850628)

19. Nouvenne A, Ticinesi A, Folesani G, et al. The association of serum procalcitonin and high-sensitivity C-reactive protein with pneumonia in elderly multimorbid patients with respiratory symptoms: retrospective cohort study. BMC Geriatr 2016 Jan 15;16: 16. (PMID: 26772604)

20. Peters EJ, Frydland MS, Hassager C, et al. Biomarker patterns in patients with cardiogenic shock versus septic shock. Int J Cardiol Heart Vasc 2024 May;52:101424. (PMID: 38784047)

21. Chen CJ, Shively JE. The cell-cell adhesion molecule carcinoembryonic antigen-related cellular adhesion molecule 1 inhibits IL-2 production and proliferation in human T cells by association with Src homology protein-1 and down-regulates IL-2 receptor. J Immunol 2004 Mar;172(6):3544-52. (PMID: 15004155)

22. Aziz M, Jacob A, Matsuda A, Wang P. Review: milk fat globule-EGF factor 8 expression, function and plausible signal transduction in resolving inflammation. Apoptosis 2011 Nov;16(11): 1077-86. (PMID: 21901532)

23. Nagaishi T, Pao L, Lin SH, et al. SHP1 phosphatase-dependent T cell inhibition by CEACAM1 adhesion molecule isoforms. Immunity 2006;25(5):769-81. (PMID: 17081782)

24. Van der Flier M, Sharma DB, Estevão S, et al. Increased CD4(+) T cell co-inhibitory immune receptor CEACAM1 in neonatal sepsis and soluble-CEACAM1 in meningococcal sepsis: a role in sepsis-associated immune suppression? PLoS One 2013 Jul 22; 8(7):e68294. (PMID: 23894299)

25. Pierrakos C, Vincent JL. Sepsis biomarkers: a review. Crit Care 2010 Jan;14(1):R15. (PMID: 20144219)

26. Klaile E, Müller MM, Schäfer MR, et al. Binding of Candida albicans to human CEACAM1 and CEACAM6 modulates the inflammatory response of intestinal epithelial cells. mBio 2017 Mar;8(2):e02142-16. (PMID: 28292985)

27. Huang YH, Zhu C, Kondo Y, et al. CEACAM1 regulates TIM-3-mediated tolerance and exhaustion. Nature 2015 Jan;517(7534): 386-90. (PMID: 25363763)

28. Póvoa P, Salluh JIF. Biomarker-guided antibiotic therapy in adult critically ill patients: a critical review. Ann Intensive Care 2012 Jul;2(1):32. (PMID: 22824162)

29. Bakker J, Nijsten MW, Jansen TC. Clinical use of lactate monitoring in critically ill patients. Ann Intensive Care 2013 Mar;3(1): 12. (PMID: 23618496)

30. Ludewig P, Sedlacik J, Gelderblom M, et al. Carcinoembryonic antigen-related cell adhesion molecule 1 inhibits MMP-9-mediated blood-brain-barrier breakdown in a mouse model for ischemic stroke. Circ Res 2013 Oct;113(8):1013-22.
(PMID: 23780386)