Infection and Drug Resistance Dovepress

Open Access Full Text Article ORIGINAL RESEARCH

Predictive Value of Combined Detection of Serum LGALS3BP and GDF-15 for the Prognosis of ICU Sepsis Patients

Dengliang Ji[1], Jiulong Li[2], Andong Liu[3], Ruiping Ye[4], Shengrui Zhang[5], Lin Gao[5], Zhenfei Huang[5]

[1]Department of Intensive Care Unit, Ganzhou Fifth People's Hospital, Ganzhou, Jiangxi, 341000, People's Republic of China; [2]Department of Intensive Care Unit, Ningdu County Chinese Medicine Hospital, Ganzhou, Jiangxi, 341000, People's Republic of China; [3]Department of Intensive Care Unit, Suichuan County Chinese Medicine Hospital, Jian, Jiangxi, 343000, People's Republic of China; [4]Department of Intensive Care Unit, Dingnan County First People's Hospital, Ganzhou, Jiangxi, 341000, People's Republic of China; [5]Department of Intensive Care Unit, GanZhou People's Hospital, Ganzhou, Jiangxi, 341000, People's Republic of China

Correspondence: Zhenfei Huang, Department of Intensive Care Unit, GanZhou People's Hospital, No. 16 Meiguan Avenue, Zhanggong District, Ganzhou, Jiangxi, 341000, People's Republic of China, Email fishyugz129@sina.com

Objective: This study aims to investigate the effectiveness of combining serum lectin galactoside-binding soluble 3 binding protein (LGALS3BP) with growth differentiation factor 15 (GDF-15) for predicting outcomes in sepsis patients in an intensive care unit (ICU) setting.

Methods: The study involved 208 sepsis patients from the ICU of our hospital. These patients were categorized based on their 28-day survival outcomes into two groups: 166 in the survival group and 42 in the mortality group. The serum levels of LGALS3BP and GDF-15 were measured using the ELISA technique. Pearson and Spearman methods were utilized for correlation analysis. Factors affecting mortality in ICU sepsis patients were evaluated through multivariate logistic regression analysis. The efficacy of these biomarkers in prognosis prediction was assessed using receiver operating characteristic (ROC) curve analysis.

Results: The proportion of septic shock, APACHE II score, SOFA score, and serum LGALS3BP and GDF-15 levels in ICU sepsis patients in the death group were obviously higher than those in the survival group ($P<0.05$). The severity of ICU sepsis patients, APACHE II score, and SOFA score were obviously positively correlated with serum LGALS3BP and GDF-15 levels ($P<0.05$). LGALS3BP (OR: 95% CI=2.745:1.583~4.761) and GDF-15 (OR: 95% CI=2.639:1.423~4.893) were independent risk factors for death in ICU sepsis patients ($P<0.05$). The AUC of serum LGALS3BP and GDF-15 levels alone in predicting death in ICU sepsis patients was 0.859 and 0.854, obviously lower than the AUC of the combination, 0.943 ($Z=2.704$, 2.287, $P<0.05$). The AUC for predicting mortality in ICU sepsis patients using the APACHE II and SOFA scores were 0.832 and 0.842, respectively. The differences in comparison to the AUCs of LGALS3BP and GDF-15 were not statistically significant ($P > 0.05$).

Conclusion: Serum levels of LGALS3BP and GDF-15 can both be used as predictive indicators for death in ICU sepsis patients, and their combined predictive efficacy is better.

Keywords: sepsis, intensive care unit, lectin galactoside-binding soluble 3 binding protein, growth differentiation factor 15, prognosis

Introduction

Sepsis, characterized by an uncontrolled immune reaction to infection, results in severe organ failure, posing a significant medical emergency. This condition not only leads to a high mortality rate but also leaves survivors with enduring disabilities.[1] Despite advances in our understanding of sepsis, supportive treatments including early fluid resuscitation, antibiotics, and organ support care remain the main treatment standards; therefore, the mortality rate of sepsis remains high, at about 26%.[2] This high mortality rate is partly due to poor awareness of the disease, late identification, and improper management.[3] Therefore, improving sepsis prevention, identification, and prognosis remains a global health priority, and finding biomarkers that can accurately identify high mortality risk patients early in sepsis is crucial for clinical practice. Some studies have identified prognostic biomarkers for sepsis patients, such as miRNA, human

Received: 12 June 2024
Accepted: 9 October 2024
Published: 14 October 2024

epididymis secretory protein 4, procalcitonin, and interleukin-6 etc.[4,5] However, many sepsis patients still have poor outcomes, so it is necessary to continue exploring new biomarkers to improve the accuracy of prognosis prediction. Studies on Lectin Galactoside-Binding Soluble 3 Binding Protein (LGALS3BP) have primarily concentrated on its function in cancerous growths. Since its discovery, studies have considered LGALS3BP to be associated with the diagnosis, prognosis, and treatment response of diseases.[6] And recent studies have shown that LGALS3BP is closely related to the immune system and pulmonary infectious diseases,[7] suggesting that it may be involved in the progression of sepsis. Discovered more than two decades ago, Growth Differentiation Factor 15 (GDF-15) plays a crucial role in key biological functions, including erythropoiesis, cachexia, immune system, and cellular survival.[8] Recent literature has found that GDF-15 is an established or potential biomarker in various diseases related to pulmonary and critical care medicine.[9] Both LGALS3BP and GDF-15 are associated with the immune system and the progression of pulmonary infectious diseases, suggesting that they may also play important roles in sepsis. Consequently, this research focuses on examining the prognostic significance of serum LGALS3BP and GDF-15 levels in ICU patients suffering from sepsis.

Subjects and Methods

Subjects

In this investigation, 208 patients suffering from sepsis in the ICU of our hospital, between May 2020 and July 2023, were enrolled. The participants had an average age of 49.94±10.92 years, including 113 males and 95 females. Depending on their outcomes after 28 days, they were categorized into two groups: 166 patients in the group that survived and 42 in the group that did not. The research received approval from the Hospital's Ethics Committee for Medical Research, and relatives of the patients were duly informed. Inclusion criteria: (1) Patients meeting the diagnostic criteria for sepsis and septic shock;[10] (2) Age over 18 years; (3) First-time diagnosis and treatment. Exclusion criteria: (1) Families voluntarily giving up treatment; (2) Patients with end-stage organ failures such as advanced heart failure or liver cirrhosis; (3) Patients with immune system diseases, hematological diseases, or malignant tumors; (4) Patients who received antimicrobial or immunosuppressive therapy within 3 days before admission; (5) Pregnant or breastfeeding women. See Figure 1 for the case collection flowchart.

Methods

Collection of General Data and Laboratory Indices

Baseline characteristics and laboratory parameters of the sepsis patients at the time of admission were gathered. This included demographic information such as age, body mass index (BMI), sex, diabetes, hypertension, hyperlipidemia, coronary heart disease, source of infection, and the severity of the illness. Clinical data like length of stay in ICU, platelet count (PLT), white blood cell count (WBC), levels of C-reactive protein (CRP), interleukin-6 (IL-6), as well as scores from Acute Physiology and Chronic Health Evaluation II (APACHE II) and Sequential Organ Failure Assessment (SOFA) were also recorded.

Detection of Serum LGALS3BP and GDF-15 Levels

Upon admission, venous blood samples of 10 mL were drawn from the elbow of sepsis patients within the first hour. These samples were allowed to stand at ambient temperature for approximately one hour before being centrifuged at 3000 rpm for 15 minutes (centrifuge radius being 18 cm). Post-centrifugation, the upper layer of serum was preserved and frozen at −80°C for subsequent analysis. The concentrations of LGALS3BP and GDF-15 in these serum samples were measured using the enzyme-linked immunosorbent assay (ELISA) technique. The LGALS3BP kit was provided by Shanghai Biolais Biotech Co., Ltd. (Catalog No.: BLL103030E). The GDF-15 kit was provided by Shanghai Weiao Biotech Co., Ltd. (Catalog No.: EH6207M).

Statistical Analysis

Statistical analyses were performed using IBM-SPSS version 23.0. Quantitative data were expressed as ($\bar{x} \pm s$) and subjected to *t*-test analysis. Qualitative data, on the other hand, were presented as [n (%)] and evaluated using chi-square (χ^2) and adjusted chi-square tests. Correlation between variables was assessed using both Pearson and Spearman

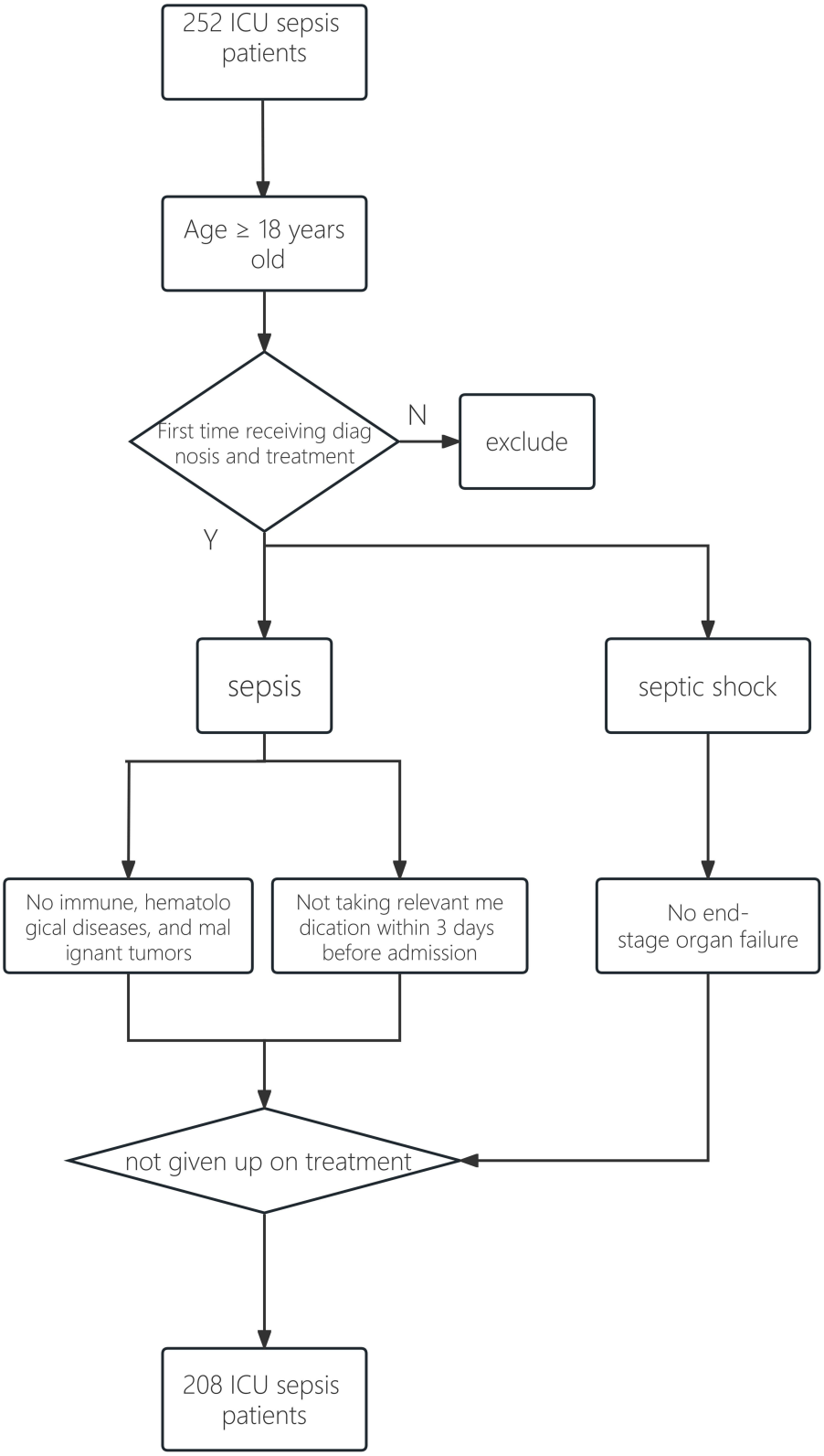

Figure 1 Case collection process diagram.

methods. To determine the factors influencing mortality in ICU sepsis patients, multifactor logistic regression analysis was employed. The effectiveness of prediction was assessed through receiver operating characteristic (ROC) curve analysis. Statistical significance was set at a P-value of less than 0.05.

Results

Comparison of General Data and Laboratory Indices Between ICU Sepsis Patients with Different Prognoses

When contrasting the characteristics of the ICU sepsis patients who survived with those who did not, in aspects such as age, BMI, sex, diabetes, hypertension, hyperlipidemia, coronary heart disease, origin of infection, duration of ICU stay, PLT, white blood cell count, CRP levels, and IL-6 levels, there were no notable statistical differences observed ($P > 0.05$). However, the incidence of septic shock, along with the APACHE II and SOFA scores, were considerably higher in the group that did not survive compared to the group that did ($P < 0.05$). See Table 1.

Comparison of Serum LGALS3BP and GDF-15 Levels Between ICU Sepsis Patients with Different Prognoses

In the group of ICU sepsis patients who succumbed, the levels of serum LGALS3BP and GDF-15 were notably elevated compared to those in the group who survived ($P < 0.05$). See Table 2.

Correlation Between General Data and Serum LGALS3BP, GDF-15 Levels in ICU Sepsis Patients

The results showed that the severity of the condition, APACHE II scores, and SOFA scores in the general data of ICU sepsis patients were significantly positively correlated with serum LGALS3BP and GDF-15 levels ($P < 0.05$). See Table 3.

Table 1 General Information and Laboratory Indicators Comparison of ICU Sepsis Patients with Different Prognoses [$(\bar{x} \pm s)$/n(%)]

Index	Survival Group (n=166)	Death Group (n=42)	t/χ^2	P
Age (years)	49.86±10.13	50.02±11.35	0.089	0.929
BMI (kg/m^2)	22.67±2.85	22.79±2.94	0.242	0.809
Male [n (%)]	90 (54.22)	23 (54.76)	0.004	0.949
Diabetes [n (%)]	12 (7.23)	5 (11.90)	0.976	0.323
Hypertension [n (%)]	39 (23.49)	15 (35.71)	2.604	0.107
Hyperlipidemia [n (%)]	18 (10.84)	8 (19.05)	2.063	0.151
Coronary heart disease[n (%)]	6 (3.61)	3 (7.14)	0.336	0.562
Infection site[n (%)]			0.041	0.998
Lung	116 (69.88)	29 (69.05)		
Urinary system	17 (10.24)	5 (11.91)		
Abdominal cavity	15 (9.04)	4 (9.52)		
Others	18 (10.84)	4 (9.52)		
Degree of illness[n (%)]			28.557	0.000
Sepsis	121 (72.89)	12 (28.57)		
Septic shock	45 (27.11)	30 (71.43)		
Time of moving into ICU (d)	10.57±3.26	10.86±3.41	0.510	0.610
PLT (ng/mL)	3.94±0.81	4.12±1.05	1.207	0.229
WBC (×10^9/L)	10.98±3.26	11.20±3.17	0.393	0.695
CRP (mg/L)	80.49±20.10	86.92±21.55	1.825	0.069
IL-6 (pg/mL)	75.48±14.96	80.17±15.34	1.806	0.072
APACHE II scores (points)	20.15±5.35	30.95±7.25	10.821	0.000
SOFA scores (points)	6.45±2.25	12.57±3.42	14.025	0.000

Abbreviations: BMI, body mass index; PLT, platelet count; WBC, white blood cell; CRP, C-reactive protein; IL-6, interleukin-6; APACHE II, acute physiology and chronic health evaluation II; SOFA, sepsis-related organ failure assessment.

Table 2 Comparison of Serum LGALS3BP and GDF-15 Levels in ICU Sepsis Patients with Different Prognoses ($\bar{x} \pm s$)

Groups	Number	LGALS3BP (ng/mL)	GDF-15 (ng/mL)
Survival group	166	80.76±20.09	2.35±0.62
Death group	42	113.58±25.14	3.27±0.70
t	–	8.967	8.365
P	–	0.000	0.000

Abbreviations: LGALS3BP, lectin galactoside-binding soluble 3 binding protein; GDF-15, growth differentiation factor 15.

Table 3 Correlation Between General Information of ICU Sepsis Patients and Serum LGALS3BP and GDF-15 Levels

Index	LGALS3BP		GDF-15	
	r	*P*	*r*	*P*
Degree of illness	0.524	0.000	0.512	0.000
APACHE II scores	0.517	0.000	0.498	0.000
SOFA scores	0.509	0.000	0.531	0.000

Abbreviations: APACHE II, acute physiology and chronic health evaluation II; SOFA, sepsis-related organ failure assessment; LGALS3BP, lectin galactoside-binding soluble 3 binding protein; GDF-15, growth differentiation factor 15.

Analysis of Mortality Determinants in ICU Sepsis Patients Using Multivariate Logistic Regression

The LGALS3BP, GDF-15, APACHE II score, and SOFA score were included in the multivariate logistic regression analysis as continuous variables, and the prognosis (death=1, survival=0) was classified as categorical variables.

Findings indicated that LGALS3BP (Odds Ratio [OR]: 95% Confidence Interval [CI]=2.745:1.583–4.761) and GDF-15 (OR: 95% CI=2.639:1.423–4.893) independently contributed to the risk of death in patients with sepsis in the ICU (P<0.05). See Table 4.

Predictive Efficacy of Serum LGALS3BP and GDF-15 Levels for Mortality in ICU Sepsis Patients

ROC curve results indicated that the AUC for predicting mortality in ICU sepsis patients was 0.859 (95% CI:0.808~0.911) and 0.854 (95% CI:0.786~0.921) for serum LGALS3BP and GDF-15 levels, respectively, far lower

Table 4 Multivariate Logistic Regression Analysis of Death Factors in ICU Sepsis Patients

Influence Factor	*β*	*SE*	*Wald*χ^2	*OR*	*95% CI*	*P*
LGALS3BP	1.010	0.281	12.913	2.745	1.583~4.761	0.000
GDF-15	0.970	0.315	9.490	2.639	1.423~4.893	0.002
Degree of illness	0.131	0.129	1.032	1.140	0.885~1.468	0.310
APACHE II scores	0.255	0.147	3.019	1.291	0.968~1.722	0.082
SOFA scores	0.266	0.160	2.768	1.305	0.954~1.786	0.096

Abbreviations: APACHE II, acute physiology and chronic health evaluation II; SOFA, sepsis-related organ failure assessment; LGALS3BP, lectin galactoside-binding soluble 3 binding protein; GDF-15, growth differentiation factor 15.

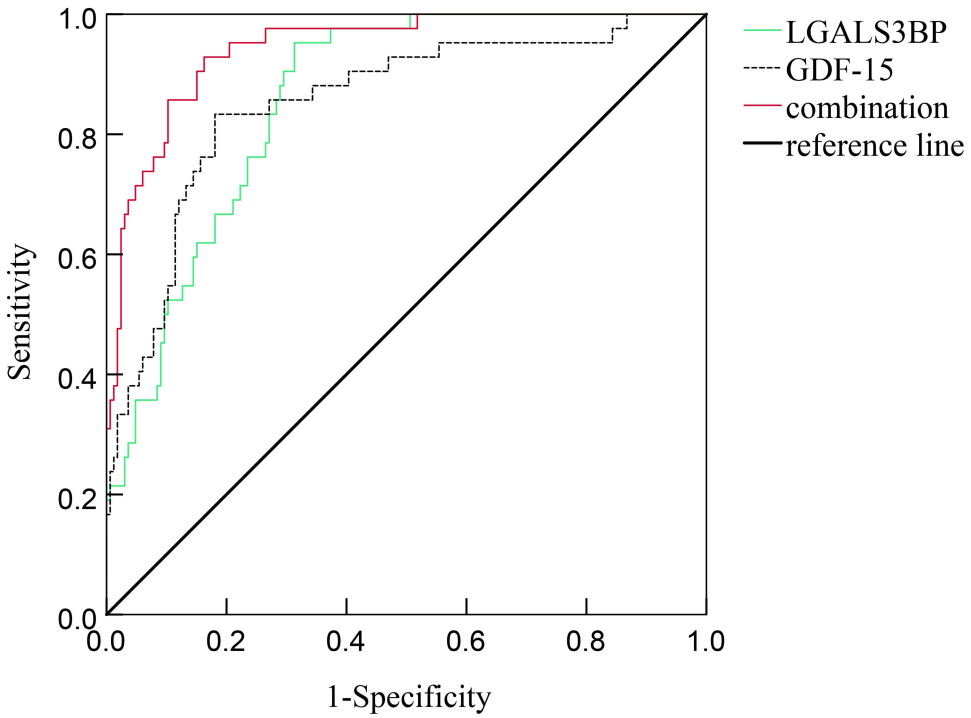

Figure 2 ROC curve of serum LGALS3BP and GDF-15 levels predicting death in ICU sepsis patients.
Abbreviations: LGALS3BP, lectin galactoside-binding soluble 3 binding protein; GDF-15, growth differentiation factor 15.

than the combined AUC of 0.943 (95% CI:0.909~0.978)(Z=2.704, 2.287, P < 0.05). The sensitivities were 95.29%, 88.12%, and 85.78%, while the specificities were 68.79%, 65.74%, and 89.29%. The cutoff values for predicting LGALS3BP and GDF-15 were 90.09 ng/mL and 2.86 ng/mL, respectively. See Figure 2 for ROC curves.

Efficacy of APACHE II and SOFA Scores in Predicting Mortality in ICU Sepsis Patients

The results of the ROC curve show that the AUCs for predicting mortality in ICU sepsis patients using the APACHE II and SOFA scores were 0.832 (95% CI: 0.761–0.908) and 0.842 (95% CI: 0.775–0.910), respectively. The sensitivities were 80.25% and 80.41%, while the specificities were 77.28% and 76.51%. The cutoff values for predicting APACHE II and SOFA scores were 25 and 8 points, respectively. The differences in the predictive AUCs between these scores and LGALS3BP and GDF-15 were not statistically significant (P > 0.05). The ROC curve is shown in Figure 3.

Discussion

After contracting sepsis, patients may exhibit symptoms such as fever, tachycardia, and rapid breathing, with the progression of the condition possibly leading to shock or multiple organ dysfunction syndrome (MODS).[11]

Presently, the treatment of sepsis is facing a critical impasse; despite the application of powerful antimicrobial treatments, the resulting inflammatory factor cascade remains irreversible, leading to the possibility of patient demise within mere days.[12] Over the past decades, many biomarkers for sepsis, including inflammatory factors, cellular proteins, and miRNAs, have been identified.[13] However, due to the complexity of sepsis etiology, the unclear pathogens involved, and the vague early clinical symptoms of sepsis patients, early diagnosis and prognosis prediction of sepsis still pose challenges.[14]

Located on chromosome 17q25, LGALS3BP is a prevalent and multifunctional secreted glycoprotein in humans, featuring a scavenger receptor cysteine-rich domain. It belongs to the β-galactoside-binding protein family.[15] Various cell types, including hematopoietic and glandular or mucosal epithelial cells, are capable of synthesizing and secreting LGALS3BP. This protein is predominantly found in human serum and other bodily fluids such as saliva, tears, breast milk, and semen,

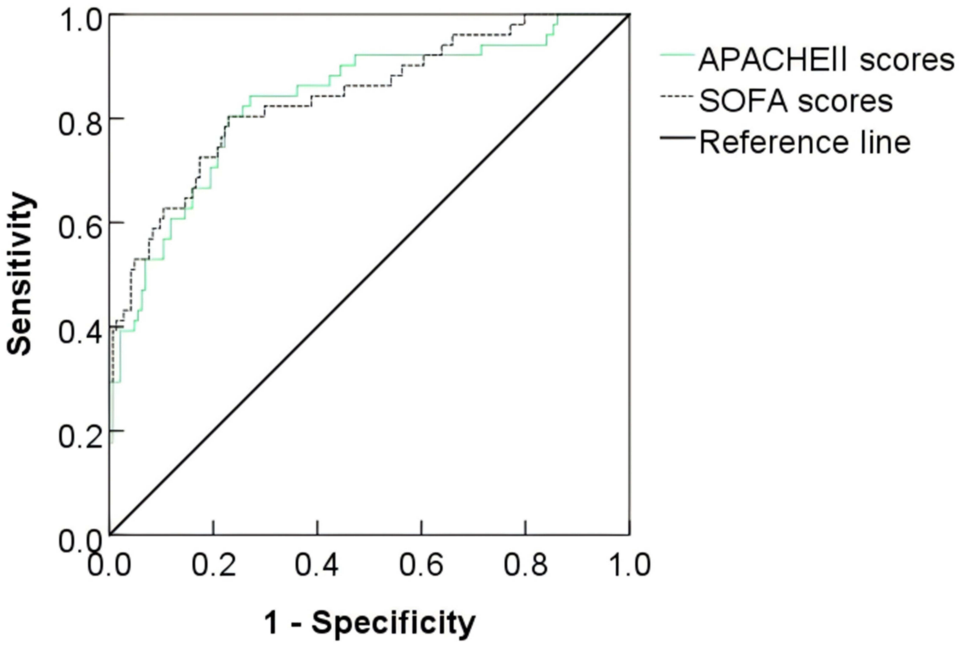

Figure 3 ROC curve of APACHE II scores and SOFA scores predicting death in ICU sepsis patients.
Abbreviations: APACHE II, acute physiology and chronic health evaluation II; SOFA, sepsis-related organ failure assessment.

playing a role in the modulation of intercellular or cell-matrix interactions.[16] Recent studies[17] indicates that LGALS3BP can prompt matrix cells to produce IL-6 in a galectin-3 dependent manner, thus contributing to the process of COVID-19 infection. Previous studies based on weighted gene co-expression network analysis have identified LGALS3BP as a biomarker for differentiating sepsis caused by Burkholderia pseudomallei.[18] Research by Luo et al[19] shows that serum LGALS3BP levels are higher in non-survivors of sepsis than in survivors, indicating its significance for prognosis. This study is consistent with the above results, identifying LGALS3BP as a risk factor for death in sepsis patients. This indicates that higher levels of LGALS3BP are correlated with an increased mortality rate in sepsis patients and could potentially act as a reliable biomarker for prognostic evaluation. The analysis suggests that the possible mechanism by which LGALS3BP participates in sepsis may be as follows: infection stress activates inflammatory signaling pathways in the body, leading to the production of a large number of inflammatory factors, which exacerbates the extent of inflammatory damage. This stimulates the excessive expression of LGALS3BP in the serum. LGALS3BP can further induce the expression of downstream inflammatory factors such as IL-6 in a galectin-3-dependent manner, triggering an inflammatory cascade reaction that contributes to disease progression and poor prognosis. ROC curve results show that LGALS3BP predicts the mortality of sepsis patients with a sensitivity of 95.29% and an AUC of 0.859. The study supports the conclusion that serum LGALS3BP levels can highly assess the poor prognosis of sepsis patients. Higher LGALS3BP levels may indicate more severe patient conditions and correspondingly higher mortality rates. However, the specificity of LGALS3BP alone is 68.79%. It is believed that LGALS3BP may primarily reflect the inflammatory damage and immune status of certain organs or tissues of the body, and its ability to reflect the overall state of the body and disease progression is limited. Therefore, it cannot be solely used as an indicator for predicting the death of sepsis patients.

GDF-15 stands out as a distinct member of the Transforming Growth Factor (TGF)-β superfamily, exhibiting low sequence similarity with other family members and unique biological roles.[20] Particularly in macrophages, GDF-15 is upregulated in response to tissue damage, inflammation, oxidative stress, and in various cancers.[21] Recent research underscores the significance of GDF-15 in forecasting overall mortality, especially in predicting cardiovascular event outcomes.[22] Moreover, GDF-15 has been shown to be a predictor of mortality in diverse situations; its levels in critically ill patients (including those with sepsis) upon ICU admission are intimately linked to organ failure and independently foretell both short-term and long-term mortality risks.[23] Research by Desmedt et al[24] also indicate that high serum GDF-

15 levels in critically ill patients correlate with sepsis, organ failure, and severity of illness. The results of this study are generally consistent with the aforementioned research. Based on previous studies, it is hypothesized that the possible mechanism of GDF-15 in sepsis is as follows: during infection in sepsis patients, GDF-15 is induced in macrophages, and cell death leads to increased secretion levels of GDF-15. The pro- or anti-proliferative characteristics of GDF-15 may influence the survival of sepsis patients, thereby increasing their risk of mortality.

The APACHE II and SOFA scores can be used to assess the severity of illness and poor prognosis in sepsis patients, and they are valuable clinical indicators in sepsis evaluation.[25,26] This study showed that the APACHE II and SOFA scores were higher in sepsis patients who ultimately died compared to those who survived. This further suggests that higher APACHE II and SOFA scores correlate with worse patient condition and increased mortality risk. However, a concern in this study is that ICU patients with sepsis typically have more severe conditions and rapid disease progression, necessitating prompt and accurate early predictions for high-risk patients to ensure their safety. Therefore, it is essential to explore new biomarkers to enhance accuracy. The ROC curve analysis indicated that the AUCs for predicting sepsis prognosis using APACHE II and SOFA scores showed no statistically significant difference compared to LGALS3BP and GDF-15. Additionally, the results from Gao et al[4] and Lai et al[5] showed that the AUCs for miR-127, human epididymis secretory protein 4, procalcitonin, and interleukin-6 in predicting sepsis prognosis were 0.748, 0.881, 0.567, and 0.589, respectively, which are generally consistent with or lower than the AUCs for LGALS3BP and GDF-15 in this study. This indicates that LGALS3BP and GDF-15 have significant evaluative value in sepsis prognosis and could assist the two scoring systems to improve prognostic accuracy in the future.

The correlation findings reveal that the concentrations of LGALS3BP and GDF-15 have a strong association with APACHE II scores, SOFA scores, and the overall severity of sepsis. This further suggests the evaluative role of LGALS3BP and GDF-15 level testing in the prognosis of sepsis. As sepsis progresses, the body's inflammatory responses and anti-inflammatory mechanisms counterbalance each other, and pathological changes such as immune function suppression and inflammatory damage in tissues and organs progressively worsen, resulting in elevated serum LGALS3BP and GDF-15 levels. The combined ROC curve results show higher predictive value for mortality in sepsis patients than LGALS3BP and GDF-15 alone, with an AUC of 0.943 and a specificity of 89.29%. However, this study also has some limitations: Initially, this study focuses on sepsis patients. To ascertain the viability of LGALS3BP and GDF-15 as biomarkers for sepsis, it is essential to contrast their patterns with those in a healthy, non-diseased population. Moreover, the sample size of this research is limited, necessitating broader and multi-center investigations for more conclusive results. Thirdly, the actual mechanisms of LGALS3BP and GDF-15 in sepsis prognosis are currently unclear. Lastly, this study did not include a healthy control group or bacteremia patients, so it cannot definitively determine whether LGALS3BP and GDF-15 can distinguish between healthy individuals, bacteremia patients, and those in this study. Further experiments are needed to verify these findings.

Conclusion

In summary, serum LGALS3BP and GDF-15 levels are abnormally elevated in the death group of ICU sepsis patients, suggesting potential application value as prognostic markers for sepsis. The combined use of LGALS3BP and GDF-15 can assist clinicians in the early prediction of prognosis in sepsis patients, providing reference for physicians in developing treatment plans.

Data Sharing Statement

The datasets used during the present study are available from the corresponding author upon reasonable request.

Ethics Approval and Consent to Participate

This study involving human participants was in accordance with the ethical standards of the Ganzhou Fifth People's Hospital research committee and with the 1964 helsinki Declaration. And obtain the informed consent form of the patient or their guardian, and sign on the informed consent form.

Consent for Publication

All authors give consent for publication.

Disclosure

The authors declared no conflicts of interest in this work.

References

1. Barber G, Tanic J, Leligdowicz A. Circulating protein and lipid markers of early sepsis diagnosis and prognosis: a scoping review. *Curr Opin Lipidol*. 2023;34(2):70–81. doi:10.1097/MOL.0000000000000870
2. Yang A, Kennedy JN, Reitz KM, et al. Time to treatment and mortality for clinical sepsis subtypes. *Crit Care*. 2023;27(1):236. doi:10.1186/s13054-023-04507-5
3. Póvoa P, Coelho L, Dal-Pizzol F, et al. How to use biomarkers of infection or sepsis at the bedside: guide to clinicians. *Intensive Care Med*. 2023;49(2):142–153.
4. Gao C, Chen H. Correlation of serum miR-127 level with severity and prognosis of sepsis. *Am J Transl Res*. 2022;14(11):7994–8001.
5. Lai X, Kang M, Chen Y, Xu F, Wang K, Cao J. Elevated serum level of human epididymal protein 4 (HE4) predicts poor prognosis in the critically ill with sepsis: a prospective observational cohort study. *Clin Biochem*. 2022;109–110:79–85. doi:10.1016/j.clinbiochem.2022.08.001
6. Capone E, Iacobelli S, Sala G. Role of galectin 3 binding protein in cancer progression: a potential novel therapeutic target. *J Transl Med*. 2021;19(1):405. doi:10.1186/s12967-021-03085-w
7. Bosquillon de Jarcy L, Akbil B, Mhlekude B, et al. 90K/LGALS3BP expression is upregulated in COVID-19 but may not restrict SARS-CoV-2 infection. *Clin Exp Med*. 2023;23(7):3689–3700. doi:10.1007/s10238-023-01077-2
8. Reyes J, Yap GS. Emerging roles of growth differentiation factor 15 in immunoregulation and pathogenesis. *J Immunol*. 2023;210(1):5–11. doi:10.4049/jimmunol.2200641
9. Wang Y, Yao P, Li K, Qin S. GDF-15 (a biomarker for metformin) and the risk of COVID-19: a two-sample Mendelian randomization study. *Medicine*. 2023;102(39):e34675. doi:10.1097/MD.0000000000034675
10. 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;49(11):e1063–e143.
11. Liu J, Wang H, Xiao H, et al. Predicting the prognosis in patients with sepsis by an endoplasmic reticulum stress gene signature. *Aging*. 2023;15(22):13434–13451. doi:10.18632/aging.205252
12. Min J, Lu J, Zhong L, Yuan M, Xu Y. The correlation study between blood urea nitrogen to serum albumin ratio and prognosis of patients with sepsis during hospitalization. *BMC Anesthesiol*. 2022;22(1):404.
13. Barichello T, Generoso JS, Singer M, Dal-Pizzol F. Biomarkers for sepsis: more than just fever and leukocytosis-a narrative review. *Crit Care*. 2022;26(1):14. doi:10.1186/s13054-021-03862-5
14. Cutrin JC, Alves-Filho JC, Ryffel B. Editorial: sepsis: studying the immune system to highlight biomarkers for diagnosis, prognosis and personalized treatments. *Front Immunol*. 2023;14:1325020. doi:10.3389/fimmu.2023.1325020
15. Cho S-H, Shim H-J, Park M-R, et al. Lgals3bp suppresses colon inflammation and tumorigenesis through the downregulation of TAK1-NF-κB signaling. *Cell Death Discov*. 2021;7(1):65. doi:10.1038/s41420-021-00447-7
16. El Bannoudi H, Cornwell M, Luttrell-Williams E, et al. Platelet LGALS3BP as a mediator of myeloid inflammation in systemic lupus erythematosus. *Arthritis Rheumatol*. 2023;75(5):711–722. doi:10.1002/art.42382
17. Messner CB, Demichev V, Wendisch D, et al. Ultra-high-throughput clinical proteomics reveals classifiers of COVID-19 infection. *Cell Syst*. 2020;11(1):11–24.e4. doi:10.1016/j.cels.2020.05.012
18. Yin L, Chen Y, Fu T, Liu L, Xia Q. Identification of candidate blood biomarkers for the diagnosis of septicaemic melioidosis based on WGCNA. *Artif Cells Nanomed Biotechnol*. 2022;50(1):252–259. doi:10.1080/21691401.2022.2126490
19. Luo M, Zhang Q, Hu Y, Sun C, Sheng Y, Deng C. LGALS3BP: a potential plasma biomarker associated with diagnosis and prognosis in patients with sepsis. *Infect Drug Resist*. 2021;14:2863–2871. doi:10.2147/IDR.S316402
20. Yin D, Yan X, Bai X, Tian A, Gao Y, Li J. Prognostic value of growth differentiation factors 15 in acute heart failure patients with preserved ejection fraction. *ESC Heart Fail*. 2023;10(2):1025–1034. doi:10.1002/ehf2.14271
21. Reyes J, Zhao Y, Pandya K, Yap GS. Growth differentiation factor-15 is an IFN-γ regulated mediator of infection-induced weight loss and the hepatic FGF21 response. *Brain Behav Immun*. 2023;116:24–33. doi:10.1016/j.bbi.2023.11.029
22. Ishak SR, Ganzoury MME, Fouda EM, et al. Serum growth differentiation factor-15 (GDF-15) is a biomarker of cardiac manifestations in children with COVID-19. *Eur J Med Res*. 2023;28(1):527. doi:10.1186/s40001-023-01514-8
23. Verhamme FM, Freeman CM, Brusselle GG, Bracke KR, Curtis JL. GDF-15 in pulmonary and critical care medicine. *Am J Respir Cell Mol Biol*. 2019;60(6):621–628. doi:10.1165/rcmb.2018-0379TR
24. Desmedt S, Desmedt V, De Vos L, Delanghe JR, Speeckaert R, Speeckaert MM. Growth differentiation factor 15: a novel biomarker with high clinical potential. *Crit Rev Clin Lab Sci*. 2019;56(5):333–350. doi:10.1080/10408363.2019.1615034
25. Liu H, Zhang L, Xu F, et al. Establishment of a prognostic model for patients with sepsis based on SOFA: a retrospective cohort study. *J Int Med Res*. 2021;49(9):3000605211044892. doi:10.1177/03000605211044892
26. Gai X, Wang Y, Gao D, Ma J, Zhang C, Wang Q. Risk factors for the prognosis of patients with sepsis in intensive care units. *PLoS One*. 2022;17(9):e0273377. doi:10.1371/journal.pone.0273377