BRITISH JOURNAL OF HOSPITAL MEDICINE

ARTICLE

# Evaluation of Sepsis Severity Using Combined High-Density Lipoprotein and Red Cell Distribution Width Indicators

Yan Gao[1], Yao Chen[2,*], Li Gao[3]

[1]Intensive Care Unit, The Second People's Hospital of Jingdezhen, Jingdezhen, Jiangxi, China
[2]Hemodialysis Unit, The Second People's Hospital of Jingdezhen, Jingdezhen, Jiangxi, China
[3]Department of General Medicine, The Second People's Hospital of Jingdezhen, Jingdezhen, Jiangxi, China
*Correspondence: chenyao987666@163.com (Yao Chen)

## Abstract

**Aims/Background** Sepsis is a life-threatening condition resulting from dysregulated immune responses to infection, leading to organ dysfunction. High-density lipoprotein (HDL) and red cell distribution width (RDW) have shown significant correlations with sepsis severity, yet the combined prognostic value of HDL and RDW in evaluating sepsis severity and outcomes remains unclear. This study examines the relationship between HDL and RDW levels and sepsis severity, as well as evaluates the combined utility of these markers in predicting disease severity and patient outcomes.

**Methods** This retrospective study included 103 patients diagnosed with sepsis. Clinical data, including HDL and RDW levels, were collected for analysis. Patients were divided into shock and non-shock groups based on the presence of septic shock and into survival and death groups based on 30-day in-hospital mortality. Multivariate logistic regression was used to identify factors influencing sepsis severity and prognosis, while the predictive value of HDL in combination with RDW was evaluated using receiver operating characteristic (ROC) curve analysis.

**Results** Multivariate analysis identified sequential organ failure assessment (SOFA) score (OR = 6.566), interleukin-6 (IL-6) (OR = 2.568), HDL (OR = 0.864), and RDW (OR = 4.052) as independent predictors of sepsis severity ($p < 0.05$ for all). ROC analysis demonstrated that HDL combined with RDW yielded the highest diagnostic accuracy for sepsis severity, with an area under curve (AUC) of 0.962, sensitivity of 97.56%, and specificity of 91.94%. Additionally, SOFA score (OR = 2.354), interleukin-6 (IL-6) (OR = 1.446), HDL (OR = 0.870), and RDW (OR = 3.502) were independent prognostic indicators ($p < 0.05$ for all). ROC analysis for prognosis showed that HDL combined with RDW had the highest predictive efficacy for the prognosis of sepsis, with an AUC of 0.922, sensitivity of 79.31%, and specificity of 93.24%.

**Conclusion** The combination of HDL and RDW is a robust indicator for the evaluation of sepsis severity and is a valuable prognostic tool for assessing 30-day mortality risk in sepsis patients.

**Key words: sepsis; high-density lipoprotein; red cell distribution width; severity; prognosis; evaluation**

**Submitted: 30 July 2024 Revised: 5 November 2024 Accepted: 11 November 2024**

**How to cite this article:**
Gao Y, Chen Y, Gao L. Evaluation of Sepsis Severity Using Combined High-Density Lipoprotein and Red Cell Distribution Width Indicators. Br J Hosp Med. 2024. https://doi.org/10.12968/hmed.2024.0473



## Introduction

Sepsis is characterized by organ dysfunction resulting from an abnormal immune response to infection, with the uncontrolled systemic inflammatory response being the primary cause of multiple organ dysfunction. This inflammatory dysregulation leads to elevated levels of inflammatory mediators, posing a severe risk

to patient survival (Liu et al, 2022; Yang et al, 2023). Despite advances in clinical treatment, the mortality rate for sepsis remains high, ranging from 30%–70%. Early identification of sepsis severity and prognosis, followed by timely and effective therapeutic interventions, is crucial for improving patient outcomes (Bauer et al, 2020; Weng et al, 2023).

Traditionally, sepsis severity has been assessed using scoring systems such as the sequential organ failure assessment (SOFA) score and the acute physiology and chronic health evaluation (APACHE II). However, these scoring systems are complex and may delay early disease evaluation, limiting their utility for rapid clinical decision-making (Asai et al, 2021; Sevransky et al, 2021). Recent studies have shown that in sepsis patients, especially those with septic shock, serum levels of high-density lipoprotein (HDL) are significantly reduced, while the level of red cell distribution width (RDW) is markedly elevated. Furthermore, HDL and RDW levels have shown high sensitivity and specificity in the evaluation of sepsis prognosis, suggesting that changes in these biomarkers may be valuable for evaluating disease severity and prognosis (Rohatgi et al, 2021; Stasi et al, 2021; Xu et al, 2023a).

While previous research has explored the prognostic value of HDL or RDW individually or in combination with other clinical indicators, few studies have specifically investigated the combined use of HDL and RDW in the assessment of sepsis severity (Barker et al, 2021; Liu et al, 2023; Xu and Qi, 2023b; Zhang et al, 2022). This study aimed to determine the sensitivity and specificity of HDL combined with RDW to predict sepsis severity and assess the disease prognosis.

# Methods

## General Information

This retrospective study included 103 sepsis patients treated in the Intensive Care Unit (ICU) of the Second People's Hospital of Jingdezhen, Jiangxi Province, between January 2015 and January 2020. The study was approved by the Ethics Committee of the Second People's Hospital of Jingdezhen (Ethics Approval Number: 2021-LLSWJWKY-009). This study was conducted in line with the principles of the Helsinki Declaration, and informed consent was obtained from all participants.

Inclusion criteria: (1) In line with the diagnostic criteria for sepsis, as per Singer et al (2016), with a SOFA score increase of $\geq$2 points from baseline due to infection-related inflammation. (2) Patients aged $\geq$18 years. (3) ICU admission for $\geq$24 hours. (4) Availability of complete clinical data.

Exclusion criteria: (1) Pregnant or lactating women. (2) Patients with hematologic or immune system disorders. (3) Patients with acute cardiovascular or cerebrovascular diseases. (4) Patients with malignant tumors. (5) Patients with gastrointestinal bleeding. (6) Patients who have undergone splenectomy. (7) Patients who have discontinued treatment. (8) Patients with severe liver disease or nephrotic syndrome. (9) Patients with a history of organ transplantation.

### Data Collection and General Information

General patient information was collected from electronic medical records, including age, sex, and comorbidities. SOFA and APACHE II scores were evaluated upon admission. The SOFA score (range: 0–24) evaluates multiple organ systems, such as the respiratory system, central nervous system, and cardiovascular system, with higher scores indicating more severe disease. The APACHE II score (range: 0–71) includes assessments of acute physiology, age, and chronic health conditions, with higher scores correlating with greater disease severity.

### Clinical Data Collection

Patient data, including temperature, respiratory rate, blood pressure, and urine output, were recorded within 24 hours of admission. Fasting blood samples collected within 24 hours of admission were analyzed in the laboratory for levels of platelets (PLT), neutrophil (N), D-dimer (DD), procalcitonin (PCT), interleukin-6 (IL-6), white blood cell count (WBC), C-reactive protein (CRP), HDL, RDW, and other relevant biomarkers.

### Grouping Method

Patients were divided into groups based on disease severity: a shock group (41 cases) and a non-shock group (62 cases), according to the presence of septic shock (Evans et al, 2021). Additionally, patients were divided into a survival group (74 cases) and a death group (29 cases) based on survival within 30 days of hospitalization. The study flowchart that outlines the key steps in the research process, from patient selection to data analysis, is presented in Fig. 1.

### Statistical Methods

Data were analyzed using SPSS 25.0 statistical software (IBM Corp., Armonk, NY, USA). Categorical data were expressed as frequencies (n, %) and analyzed using the chi-square ($\chi^2$) test for nominal variables or rank-sum test for ordinal variable (Z). Continuous variables with normal distribution were expressed as mean $\pm$ standard deviation ($\bar{x} \pm s$) and analyzed using the *t*-test. Logistic regression was used to identify factors influencing sepsis severity and prognosis. The predictive value of HDL combined with RDW for sepsis severity and prognosis was evaluated using receiver operating characteristic (ROC) curve analysis. A $p$-value $< 0.05$ was considered statistically significant.

## Results

### Logistic Regression Analysis of Factors Influencing Sepsis Severity

Baseline data for patients in the shock and non-shock groups are presented in **Supplementary Table 1**, while the assignment of factors related to sepsis severity is shown in Table 1. Univariate logistic regression analysis revealed statistically significant differences in SOFA score, APACHE II score, DD, IL-6, CRP, HDL, and RDW levels ($p < 0.05$ for all comparisons). Multivariate logistic regression analysis identified SOFA score (OR = 6.566), IL-6 (OR = 2.568), HDL (OR =

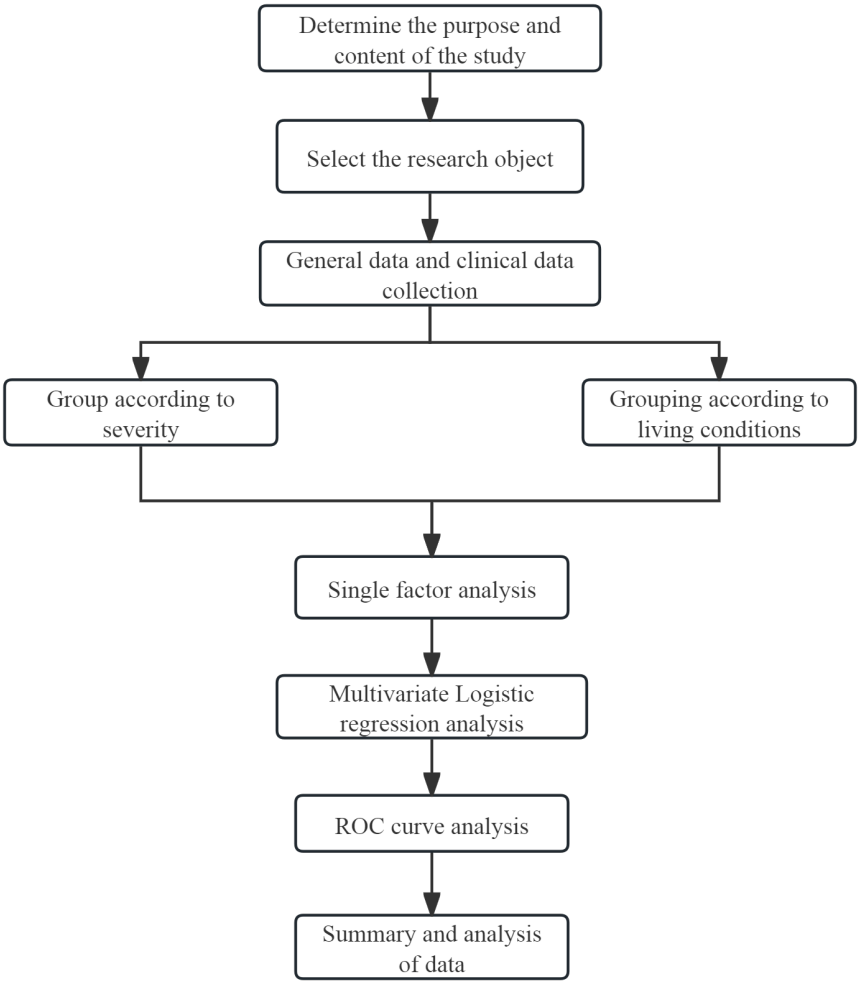


**Fig. 1. Study flowchart.** ROC, receiver operating characteristic.

0.864), and RDW (OR = 4.052) as independent predictors for sepsis severity ($p < 0.05$ for all), as shown in Table 2.

## ROC Curve Analysis for Predicting Sepsis Severity

A binary logistic regression was constructed to assess the predictive power of HDL and RDW for sepsis severity: Logit(P) = 0.759 – 1.029 X_HDL + 0.800 X_RDW. The Hosmer-Lemeshow test the result ($\chi^2 = 8.629$, $p = 0.375$) indicating that the model had high goodness of fit. The ROC curve analysis showed that HDL combined with RDW achieved the highest diagnostic efficacy for predicting sepsis severity, with an area under curve (AUC) of 0.962, sensitivity of 97.56%, and specificity of 91.94% (Table 3 and Fig. 2).

## Multivariate Logistic Regression Analysis of Factors Influencing Sepsis Prognosis

Baseline data for sepsis patients in the survival and death groups are shown in **Supplementary Table 2**, with the assignment of prognosis-related factors shown

**Table 1. Definition and assignment of severity-related factors.**

| Factor | Name | Assignment method |
|---|---|---|
| Septic shock occurrence | Y | Yes = 1, No = 0 |
| SOFA score | X1 | Continuous variable |
| APACHE II score | X2 | Continuous variable |
| DD | X3 | Continuous variable |
| IL-6 | X4 | Continuous variable |
| CRP | X5 | Continuous variable |
| HDL | X6 | Continuous variable |
| RDW | X7 | Continuous variable |

SOFA, sequential organ failure assessment score; APACHE II, acute physiology and chronic health evaluation; DD, D-dimer; IL-6, interleukin-6; CRP, C-reactive protein; HDL, high-density lipoprotein; RDW, red cell distribution width.

**Table 2. Logistic regression analysis of factors influencing sepsis severity.**

| Variable | Univariate analysis | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|
| | $\beta$ | *p*-value | OR (95% CI) | $\beta$ | *p*-value | OR (95% CI) |
| SOFA score | 0.608 | <0.001 | 1.836 (1.367–2.466) | 1.882 | 0.031 | 6.566 (1.193–36.146) |
| APACHE II score | 0.187 | <0.001 | 1.206 (1.101–1.320) | 0.274 | 0.284 | 1.315 (0.797–2.170) |
| DD | 1.826 | 0.004 | 6.212 (1.786–21.605) | 0.253 | 0.366 | 1.288 (0.744–2.227) |
| IL-6 | 0.591 | <0.001 | 1.807 (1.427–2.287) | 0.943 | 0.040 | 2.568 (1.044–6.317) |
| CRP | 0.088 | 0.001 | 1.092 (1.037–1.150) | 0.094 | 0.379 | 1.098 (0.891–1.354) |
| HDL | –1.063 | <0.001 | 0.345 (0.231–0.517) | –0.146 | 0.011 | 0.864 (0.772–0.967) |
| RDW | 0.721 | <0.001 | 2.056 (1.524–2.773) | 1.399 | 0.025 | 4.052 (1.193–13.756) |

in **Supplementary Table 3**. Univariate logistic regression analysis indicated statistically significant differences in SOFA score, APACHE II score, DD, PCT, IL-6, CRP, HDL, and RDW levels between the groups ($p < 0.05$ for all). In the multivariate logistic regression, SOFA score (OR = 2.354), IL-6 (OR = 1.446), HDL (OR = 0.870), and RDW (OR = 3.502) emerged as independent predictors the prognosis of sepsis ($p < 0.05$ for all), as shown in Table 4.

## ROC Curve Analysis for Predicting Sepsis Prognosis Using HDL and RDW

To evaluate the predictive efficacy of HDL and RDW for sepsis prognosis, the two indicators were incorporated into a binary logistic regression model: Logit(P) = –3.663 – 0.745 X_HDL + 0.832 X_RDW. The Hosmer-Lemeshow test ($\chi^2 = 2.993$, $p = 0.939$) indicated a high goodness of fit for the model. ROC curve analysis showed that the combination of HDL and RDW provided the highest predictive efficacy for sepsis prognosis, yielding an AUC of 0.922, sensitivity of 79.31%, and specificity of 93.24%, as illustrated in Table 5 and Fig. 3.

**Table 3. Diagnostic performance of indicators in the prediction of sepsis severity.**

| Indicator | AUC | Sensitivity (%) | Specificity (%) | *p*-value | 95% CI | Youden index |
|---|---|---|---|---|---|---|
| SOFA score | 0.760 | 58.54 | 83.87 | <0.001 | 0.666–0.839 | 0.424 |
| APACHE II score | 0.780 | 65.85 | 79.03 | <0.001 | 0.688–0.856 | 0.780 |
| IL-6 | 0.855 | 85.37 | 79.03 | <0.001 | 0.772–0.917 | 0.644 |
| HDL | 0.926 | 95.12 | 85.48 | <0.001 | 0.857–0.968 | 0.806 |
| RDW | 0.818 | 78.05 | 79.03 | <0.001 | 0.730–0.887 | 0.571 |
| HDL+RDW | 0.962 | 97.56 | 91.94 | <0.001 | 0.904–0.990 | 0.895 |

AUC, area under curve.

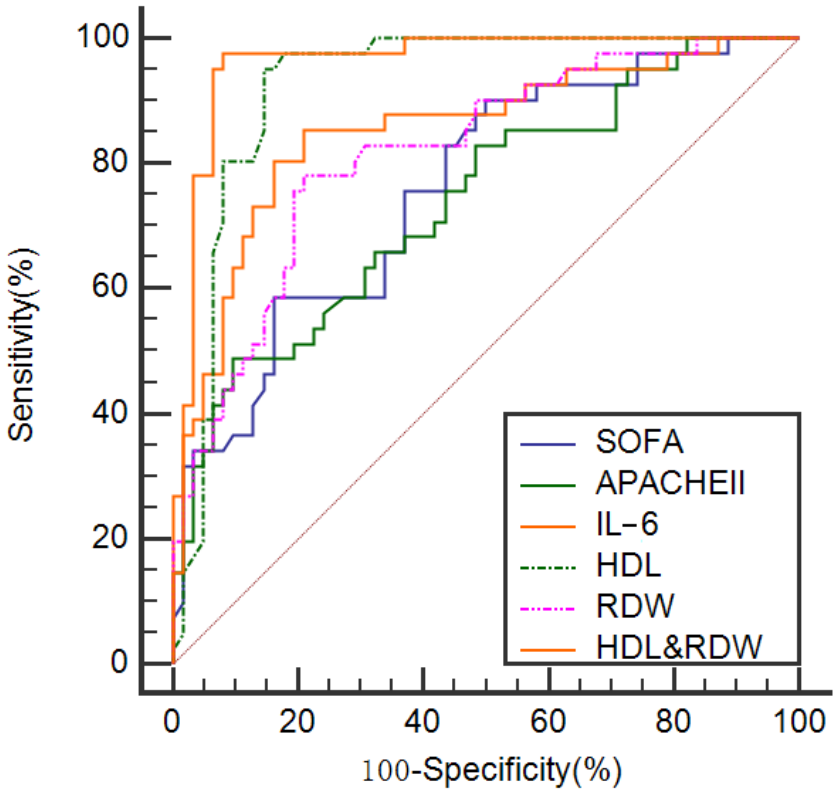


**Fig. 2. ROC curve analysis for predicting sepsis severity using indicators.**

## Discussion

Early evaluation of sepsis severity and prognosis is crucial for healthcare providers to respond promptly with appropriate treatments, potentially improving patient outcomes. In clinical settings, multiple evaluation systems such as SOFA and APACHE II scores have been widely used in the evaluation the disease severity of severe patients and predicting death mortality risk in critically ill patients. The SOFA score, for instance, has effectively been used to predict the short-term mortality rate among sepsis patients (Li et al, 2020; Palmowski et al, 2024). In this study, SOFA and APACHE II scores demonstrated high predictive value in the evaluation of disease severity and short-term mortality risk. SOFA score, by evaluating multiple organ systems, provides insights into the severity of organ dysfunction caused

**Table 4. Logistic regression analysis of factors influencing sepsis prognosis.**

| Variable | Univariate analysis | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|
| | $\beta$ | *p*-value | OR (95% CI) | $\beta$ | *p*-value | OR (95% CI) |
| SOFA score | 0.650 | <0.001 | 1.916 (1.443–2.542) | 0.856 | 0.020 | 2.354 (1.142–4.855) |
| APACHE II score | 0.263 | <0.001 | 1.300 (1.124–1.504) | 0.353 | 0.095 | 1.423 (0.940–2.153) |
| DD | 2.366 | 0.001 | 10.652 (2.657–42.704) | 1.902 | 0.140 | 6.696 (0.537–83.576) |
| PCT | 0.107 | 0.011 | 1.113 (1.025–1.208) | 0.175 | 0.184 | 1.191 (0.920–1.542) |
| IL-6 | 0.361 | <0.001 | 1.435 (1.217–1.691) | 0.368 | 0.027 | 1.446 (1.043–2.003) |
| CRP | 0.051 | 0.041 | 1.052 (1.002–1.104) | –0.020 | 0.783 | 0.980 (0.847–1.133) |
| HDL | –0.700 | <0.001 | 0.497 (0.344–0.717) | –0.139 | 0.040 | 0.870 (0.762–0.994) |
| RDW | 0.819 | <0.001 | 2.268 (1.635–3.147) | 1.253 | 0.001 | 3.502 (1.628–7.536) |

PCT, procalcitonin.

**Table 5. Predictive performance of indicators in the prediction of the prognosis of sepsis.**

| Related indicator | AUC | Sensitivity (%) | Specificity (%) | *p*-value | 95% CI | Youden index |
|---|---|---|---|---|---|---|
| SOFA score | 0.812 | 82.76 | 75.68 | <0.001 | 0.724–0.883 | 0.584 |
| APACHE II score | 0.833 | 68.97 | 89.19 | <0.001 | 0.747–0.899 | 0.582 |
| IL-6 | 0.790 | 65.52 | 87.84 | <0.001 | 0.698–0.864 | 0.534 |
| HDL | 0.776 | 82.76 | 68.92 | <0.001 | 0.683–0.852 | 0.517 |
| RDW | 0.883 | 75.86 | 91.89 | <0.001 | 0.804–0.938 | 0.678 |
| HDL+RDW | 0.922 | 79.31 | 93.24 | <0.001 | 0.852–0.966 | 0.726 |

by sepsis, while the APACHE II score monitors changes in disease status by assessing multiple clinical parameters such as respiratory and neurological function. Schertz et al (2023) also observed that the SOFA score is useful in determining prognosis and disease severity, which provides an important basis for the development and adjustment of treatment planning. In clinical practice, the APACHE II score is an important tool to improve the survival rate of severe patients and the treatment effect. Despite their utility, SOFA and APACHE II scores cannot replace conventional biochemical indicators due to their limitations, including complexity and delayed results, which can hinder rapid decision-making. A more efficient clinical marker is needed to quickly and accurately predict 30-day mortality in ICU sepsis patients (Liu et al, 2021). The relatively low predictive value of SOFA and APACHE II scores in our study may be due to the small sample size.

Sepsis is characterized by systemic multi-organ injury triggered by inflammatory responses, resulting in elevated serum biomarkers through the action of inflammatory mediators (Cong et al, 2021). Li et al (2023) showed that monitoring inflammatory markers is valuable in the assessment of disease progression and has diagnostic value for sepsis. Our study confirmed that patients with septic shock or poor prognosis had elevated IL-6 levels, which is useful in assessing disease severity and prognosis. In the inflammatory cascade associated with sepsis, inflammatory markers such as CRP and PCT are rapidly released into the bloodstream through the mediation of IL-6. Previous studies have also identified IL-6 level

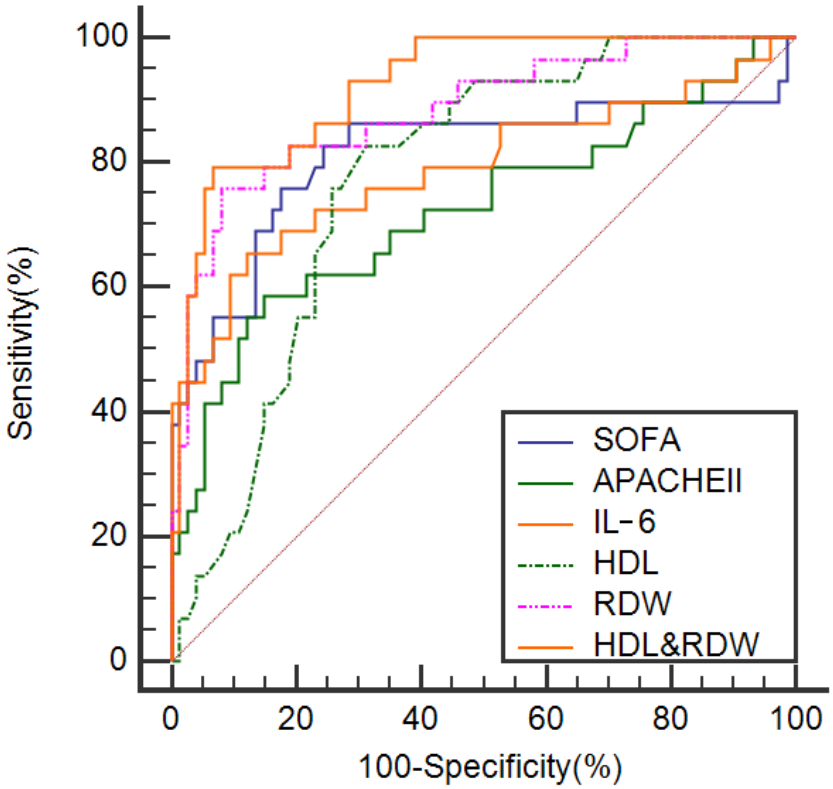


**Fig. 3. ROC curve analysis for the prediction of sepsis prognosis using indicators.**

changes as highly correlated with sepsis severity and mortality, suggesting that tracking IL-6 could inform clinical treatment strategies and enhance survival rates among severely ill sepsis patients (Hamilton et al, 2023; Peng et al, 2022).

The ROC curve analysis in our study showed that HDL and RDW are valuable predictors for the evaluation of the severity and prognosis of sepsis patients. Previous studies indicate that lipoprotein levels tend to decrease in severe sepsis or septic shock. Notably, HDL binds to endotoxins and tumor necrosis factors, with levels dropping significantly during the early stages of sepsis (Fan et al, 2020). Barber et al (2023) observed that endotoxins in septic shock patients stimulate the body to produce more inflammatory mediators such as IL-6 and tumor necrosis factor, which increases HDL binding and, thus, lowers HDL levels in critically ill patients. Additionally, RDW, a red blood cell heterogeneity measure, has been associated with more severe disease progression and is a reliable predictor of mortality in sepsis patients (Wu et al, 2022). Zhong et al (2024) suggested that infection in sepsis patients stimulates the body to produce a large number of inflammatory mediators, such as IL-6 and tumor necrosis factor, which will lead to an increase in immature red blood cells and their subsequent release into the bloodstream, thereby elevating RDW levels. He et al (2023) further observed that as the oxidative stress response intensifies, RDW levels also rise, indicating a more severe disease state and suggesting a poorer prognosis.

Given the utility of HDL and RDW as timely indicators for evaluating sepsis severity, a combined prediction model was developed using both markers in this study. ROC analysis demonstrated that HDL combined with RDW achieved high

sensitivity and specificity in evaluating sepsis severity and predicting short-term mortality, with superior predictive efficacy compared to either marker alone.

This combined evaluation of HDL and RDW offers clinicians a straightforward, practical tool for decision-making. For sepsis patients without shock, it allows for a conservative approach, reducing unnecessary medical interventions and their associated costs and risks, such as antibiotic overuse. This model supports timely and effective interventions for critically ill patients with septic shock, including early nutritional support, to reduce hospital stays and improve clinical outcomes. Thus, the HDL-RDW combination holds significant clinical value in managing sepsis (Blauw et al, 2020; Cha et al, 2022).

## Conclusion

In conclusion, combination of HDL and RDW serves as a reliable indicator for the evaluation of the disease severity in sepsis patients, and offers effective prediction of 30-day mortality risk following hospitalization. A limitation of this study is its retrospective design, with data drawn from a single-center cohort, which has been internally validated. Future research should focus on multi-center prospective studies to externally validate and strengthen the generalizability of these findings.

### Key Points

- The early severity and prognosis evaluation of sepsis can help medical staff to make accurate judgments and timely treatment of sepsis patients.
- HDL is one of the most advantageous lipoproteins that can combine with endotoxin and tumor necrosis factor, and the level of HDL can decrease obviously in the early stage of sepsis.
- Inflammatory reaction and oxidative stress reaction will cause the increase of immature red blood cells and release them into the blood, which shows that the increase of RDW level reflects the disease development and poor prognosis of sepsis patients.

## Availability of Data and Materials

The data analyzed was available on the request for the corresponding author.

## Author Contributions

YG and YC designed the research. YG and LG performed the research. LG analyzed the data. YC drafted the manuscript. All authors contributed to important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

## Ethics Approval and Consent to Participate

The study was approved by Ethics Committee of the Second People's Hospital of Jingdezhen (Ethics Approval Number: 2021-LLSWJWKY-009). This study was conducted in line with the principles of the Helsinki Declaration, and informed consent was obtained from all participants.

## Acknowledgement

Not applicable.

## Funding

This study is supported by Science and Technology Plan of Jiangxi Health Commission (202212054).

## Conflict of Interest

The authors declare no conflict of interest.

## Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://www.magonlinelibrary.com/doi/suppl/10.12968/hmed.2024.0473.

## References

Asai N, Ohashi W, Sakanashi D, Suematsu H, Kato H, Hagihara M, et al. Combination of Sequential Organ Failure Assessment (SOFA) score and Charlson Comorbidity Index (CCI) could predict the severity and prognosis of candidemia more accurately than the Acute Physiology, Age, Chronic Health Evaluation II (APACHE II) score. BMC Infectious Diseases. 2021; 21: 77. https://doi.org/10.1186/s12879-020-05719-8

Barber G, Tanic J, Leligdowicz A. Circulating protein and lipid markers of early sepsis diagnosis and prognosis: a scoping review. Current Opinion in Lipidology. 2023; 34: 70–81. https://doi.org/10.1097/MOL.0000000000000870

Barker G, Leeuwenburgh C, Brusko T, Moldawer L, Reddy ST, Guirgis FW. Lipid and Lipoprotein Dysregulation in Sepsis: Clinical and Mechanistic Insights into Chronic Critical Illness. Journal of Clinical Medicine. 2021; 10: 1693. https://doi.org/10.3390/jcm10081693

Bauer M, Gerlach H, Vogelmann T, Preissing F, Stiefel J, Adam D. Mortality in sepsis and septic shock in Europe, North America and Australia between 2009 and 2019- results from a systematic review and meta-analysis. Critical Care. 2020; 24: 239. https://doi.org/10.1186/s13054-020-02950-2

Blauw LL, Wang Y, Willems van Dijk K, Rensen PCN. A Novel Role for CETP as Immunological Gatekeeper: Raising HDL to Cure Sepsis? Trends in Endocrinology and Metabolism. 2020; 31: 334–343. https://doi.org/10.1016/j.tem.2020.01.003

Cha JK, Kim HS, Kim EJ, Lee ES, Lee JH, Song IA. Effect of Early Nutritional Support on Clinical Outcomes of Critically Ill Patients with Sepsis and Septic Shock: A Single-Center Retrospective Study. Nutrients. 2022; 14: 2318. https://doi.org/10.3390/nu14112318

Cong S, Ma T, Di X, Tian C, Zhao M, Wang K. Diagnostic value of neutrophil CD64, procalcitonin, and interleukin-6 in sepsis: a meta-analysis. BMC Infectious Diseases. 2021; 21: 384. https://doi.org/10.1186/s12879-021-06064-0

Evans L, Rhodes A, Alhazzani W, Antonelli M, Coopersmith CM, French C, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Intensive Care Medicine. 2021; 47: 1181–1247. https://doi.org/10.1007/s00134-021-06506-y

Fan Y, Chen J, Liu D, Li W, Wang H, Huang Y, et al. HDL-S1P protects endothelial function and reduces lung injury during sepsis in vivo and in vitro. The International Journal of Biochemistry & Cell Biology. 2020; 126: 105819. https://doi.org/10.1016/j.biocel.2020.105819

Hamilton FW, Thomas M, Arnold D, Palmer T, Moran E, Mentzer AJ, et al. Therapeutic potential of IL6R blockade for the treatment of sepsis and sepsis-related death: A Mendelian randomisation study. PLoS Medicine. 2023; 20: e1004174. https://doi.org/10.1371/journal.pmed.1004174

He S, Shao Y, Hu T, Liu Y. Potential value of red blood cell distribution width in predicting in-hospital mortality in intensive care US population with acute pancreatitis: a propensity score matching analysis. Scientific Reports. 2023; 13: 12841. https://doi.org/10.1038/s41598-023-40192-8

Li J, Chen Y, Li R, Zhang X, Chen T, Mei F, et al. Gut microbial metabolite hyodeoxycholic acid targets the TLR4/MD2 complex to attenuate inflammation and protect against sepsis. Molecular Therapy. 2023; 31: 1017–1032. https://doi.org/10.1016/j.ymthe.2023.01.018

Li Y, Yan C, Gan Z, Xi X, Tan Z, Li J, et al. Prognostic values of SOFA score, qSOFA score, and LODS score for patients with sepsis. Annals of Palliative Medicine. 2020; 9: 1037–1044. https://doi.org/10.21037/apm-20-984

Liu D, Huang SY, Sun JH, Zhang HC, Cai QL, Gao C, et al. Sepsis-induced immunosuppression: mechanisms, diagnosis and current treatment options. Military Medical Research. 2022; 9: 56. https://doi.org/10.1186/s40779-022-00422-y

Liu F, Yao J, Liu C, Shou S. Construction and validation of machine learning models for sepsis prediction in patients with acute pancreatitis. BMC Surgery. 2023; 23: 267. https://doi.org/10.1186/s12893-023-02151-y

Liu H, Zhang L, Xu F, Li S, Wang Z, Han D, et al. Establishment of a prognostic model for patients with sepsis based on SOFA: a retrospective cohort study. The Journal of International Medical Research. 2021; 49: 3000605211044892. https://doi.org/10.1177/03000605211044892

Palmowski L, Nowak H, Witowski A, Koos B, Wolf A, Weber M, et al. Assessing SOFA score trajectories in sepsis using machine learning: A pragmatic approach to improve the accuracy of mortality prediction. PLoS ONE. 2024; 19: e0300739. https://doi.org/10.1371/journal.pone.0300739

Peng Y, Yang Q, Gao S, Liu Z, Kong W, Bian X, et al. IL-6 protects cardiomyocytes from oxidative stress at the early stage of LPS-induced sepsis. Biochemical and Biophysical Research Communications. 2022; 603: 144–152. https://doi.org/10.1016/j.bbrc.2022.03.013

Rohatgi A, Westerterp M, von Eckardstein A, Remaley A, Rye KA. HDL in the 21st Century: A Multifunctional Roadmap for Future HDL Research. Circulation. 2021; 143: 2293–2309. https://doi.org/10.1161/CIRCULATIONAHA.120.044221

Schertz AR, Lenoir KM, Bertoni AG, Levine BJ, Mongraw-Chaffin M, Thomas KW. Sepsis Prediction Model for Determining Sepsis vs SIRS, qSOFA, and SOFA. JAMA Network Open. 2023; 6: e2329729. https://doi.org/10.1001/jamanetworkopen.2023.29729

Sevransky JE, Rothman RE, Hager DN, Bernard GR, Brown SM, Buchman TG, et al. Effect of Vitamin C, Thiamine, and Hydrocortisone on Ventilator- and Vasopressor-Free Days in Patients With Sepsis: The VICTAS Randomized Clinical Trial. JAMA. 2021; 325: 742–750. https://doi.org/10.1001/jama.2020.24505

Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016; 315: 801–810. https://doi.org/10.1001/jama.2016.0287

Stasi A, Franzin R, Fiorentino M, Squiccimarro E, Castellano G, Gesualdo L. Multifaced Roles of HDL in Sepsis and SARS-CoV-2 Infection: Renal Implications. International Journal of Molecular Sciences. 2021; 22: 5980. https://doi.org/10.3390/ijms22115980

Weng L, Xu Y, Yin P, Wang Y, Chen Y, Liu W, et al. National incidence and mortality of hospitalized sepsis in China. Critical Care. 2023; 27: 84. https://doi.org/10.1186/s13054-023-04385-x

Wu H, Liao B, Cao T, Ji T, Huang J, Ma K. Diagnostic value of RDW for the prediction of mortality in adult sepsis patients: A systematic review and meta-analysis. Frontiers in Immunology. 2022; 13: 997853. https://doi.org/10.3389/fimmu.2022.997853

Xu L, Yuan L, Chi K, Zhong D, Huang L. The role of red blood cell distribution width (RDW) in the diagnosis of pediatric sepsis. The Turkish Journal of Pediatrics. 2023a; 65: 964–972. https://doi.org/10.24953/turkjped.2023.182

Xu Y, Qi W. Association between red cell distribution width to albumin ratio and acute kidney injury in patients with sepsis: a MIMIC population-based study. International Urology and Nephrology. 2023b; 55: 2943–2950. https://doi.org/10.1007/s11255-023-03572-7

Yang J, Hao S, Huang J, Chen T, Liu R, Zhang P, et al. The application of artificial intelligence in the management of sepsis. Medical Review. 2023; 3: 369–380. https://doi.org/10.1515/mr-2023-0039

Zhang L, Huang T, Xu F, Li S, Zheng S, Lyu J, et al. Prediction of prognosis in elderly patients with sepsis based on machine learning (random survival forest). BMC Emergency Medicine. 2022; 22: 26. https://doi.org/10.1186/s12873-022-00582-z

Zhong L, Zhong Y, Chen W, Liang F, Liao Y, Zhou Y. Association between haemoglobin-to-red blood cell distribution width ratio at admission and all-cause mortality in adult patients with sepsis in an intensive care unit: a secondary analysis of the MIMIC-IV database. BMJ Open. 2024; 14: e081340. https://doi.org/10.1136/bmjopen-2023-081340