Infection and Drug Resistance

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ORIGINAL RESEARCH

Integrated SIRI and Lipid Profile for Early Prediction of Bloodstream Infection in AML During Induction Chemotherapy

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Purpose: Bloodstream infections (BSIs), a frequent and life-threatening complication during acute myeloid leukemia (AML) induction chemotherapy, carry high mortality; however, current predictive models lack robust combined inflammatory-metabolic biomarkers.

Patients and Methods: We conducted a retrospective analysis of 225 AML patients (2020–2024). The systemic inflammation response index (SIRI) and lipids measured at baseline. BSIs were confirmed according to Centers for Disease Control and Prevention/ National Healthcare Safety Network (CDC/NHSN) criteria during neutropenia. Predictors selected via univariate analysis ($P<0.05$) and multivariable logistic regression using backward selection based on the Akaike information criterion (AIC). A nomogram was constructed. Model validation included receiver operating characteristic curve analysis and area under the curve (ROC-AUC), calibration curves (1,000× bootstrap), and decision curve analysis (DCA).

Results: Among 225 AML patients, BSIs incidence was 24% (54/225). Patients with BSIs exhibited significantly elevated systemic inflammation (SIRI: 2.52 ± 0.38 vs 1.57 ± 0.29; $P<0.001$) and atherogenic dyslipidemia, characterized by higher low-density lipoprotein cholesterol (LDL-C: 3.43 ± 0.91 vs 2.56 ± 0.72 mmol/L; $P<0.001$) and lower high-density lipoprotein cholesterol (HDL-C: 0.61 ± 0.19 vs 0.92 ± 0.25 mmol/L; $P<0.001$). The SIRI-lipid nomogram incorporated six independent predictors, including SIRI (OR=3.36, 95% CI 2.00–6.07), LDL-C (OR=5.98, 95% CI 2.84–14.13) and HDL-C (OR=0.06, 95% CI 0.01–0.64). The nomogram achieved an AUC of 0.926 (95% CI 0.879–0.973) and demonstrated excellent calibration, with a mean absolute calibration error of 0.014 based on 1000 bootstrap samples. DCA showed clinical utility across decision thresholds. SIRI remained an independent predictor of BSIs after multivariable adjustment (OR=3.28) and correlated with prolonged hospitalization ($P=0.007$).

Conclusion: The SIRI-lipid integrated nomogram provides clinically applicable prediction of BSIs risk in AML induction therapy, with validated clinical utility. Elevated SIRI combined with atherogenic dyslipidemia, characterized by high LDL-C and low HDL-C, represents actionable risk indicators enabling early clinical interventions.

Keywords: dyslipidemia, inflammatory biomarkers, nomogram, risk prediction, treatment-related complication

Introduction

Leukemia imposes a substantial global health burden, with over 470,000 new cases and 310,000 deaths reported worldwide in 2022.[1] Acute myeloid leukemia (AML), an aggressive hematologic malignancy, is characterized by uncontrolled proliferation and differentiation arrest of leukemic blasts, leading to bone marrow failure and life-threatening complications including severe infections, hemorrhage, and anemia. Notably, the profound neutropenia during the myelosuppressive phase following intensive induction chemotherapy, compounded by rising antimicrobial resistance, renders bloodstream infections (BSIs) a critical complication in AML patients.[2–4] BSIs occur when pathogens invade the bloodstream and multiply, potentially leading to systemic inflammatory response, severe sepsis, or multi-organ dysfunction. In AML patients, the risk of BSIs is heightened due to a combination of factors: the breakdown of natural mucosal barriers, prolonged neutropenia from both the disease and its treatment, and the frequent use of invasive medical

Received: 3 August 2025
Accepted: 16 November 2025
Published: 27 December 2025

devices (eg, central venous catheters). These infections significantly increase mortality, prolong hospitalization, and compromise cancer treatment schedules,[5–7] with an alarming daily incidence and substantial mortality rate reported in patients with hematologic malignancies.[8] Early identification of high-risk patients is thus imperative for optimizing prophylactic strategies and implementing timely interventions, yet current predictive tools remain suboptimal.

Emerging evidence links hypolipidemia—particularly reduced levels of high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C)—to heightened susceptibility to infections and poor prognosis in both general populations and septic patients, suggesting their predictive potential.[9,10] Lipids, particularly HDL-C, play a role in modulating the immune response by binding to and neutralizing pathogens like lipopolysaccharides (LPS), thereby potentially mitigating the severity of the systemic inflammatory response during sepsis.

Concurrently, the systemic inflammation response index (SIRI), a composite biomarker reflecting neutrophil, monocyte, and lymphocyte dynamics, has shown promise in forecasting infectious outcomes.[11] As a dynamic indicator of systemic inflammation, SIRI may effectively mirror the altered immune state and elevated risk of infection complications in immunocompromised AML patients. Nevertheless, data exploring the association of SIRI and comprehensive lipid profiles with BSI risk during induction chemotherapy in immunocompromised AML cohorts are strikingly limited.

To address this knowledge gap, we developed and validated a novel risk prediction model integrating SIRI and lipid parameters to stratify BSI risk during hospitalization in AML patients undergoing standard induction chemotherapy, aiming to provide a practical clinical tool for early high-risk identification.

Materials and Methods

Study Population

This retrospective cohort study enrolled 272 adult AML patients who received first-time "3+7" induction chemotherapy (anthracycline/anthraquinone and cytarabine) at the First Affiliated Hospital of Guangxi Medical University between January 2020 and December 2024. Inclusion criteria: (1) Newly diagnosed AML per WHO 2022 classification of hematopoietic tumors; (2) Completion of full-course "3+7" chemotherapy; (3) No antibiotic exposure 72 hours prior to initial blood culture; (4) Complete baseline demographic and clinical data. Exclusion criteria: (1) Pregnancy or lactation; (2) Active concurrent malignancies; (3) Pre-chemotherapy active infection; (4) Missing key laboratory parameters; (5) Severe immunodeficiency or chronic high-dose immunosuppression; (6) Significant hepatic/renal dysfunction or documented dyslipidemia.

Following the exclusion of patients with secondary malignancies (n=18), pregnancy/lactation (n=3), or critical missing data (n=26), 225 eligible patients were included in the final analysis. Participants were categorized into bloodstream infection (BSIs, n=54) and non-BSIs (n=171) groups according to BSIs occurrence during post-chemotherapy myelosuppression. This study was conducted in accordance with the Declaration of Helsinki. The protocol was approved by the Institutional Ethics Committee of the First Affiliated Hospital of Guangxi Medical University (Approval No: 2024-S321-01). Patient screening flow is detailed in Figure 1.

Data Collection

Data were extracted from the Hospital Information System (HIS), encompassing demographics, lifestyle factors, comorbidities, laboratory results (including complete blood count, liver function tests, lipid profiles, and lymphocyte subsets), along with length of stay. Fasting blood samples collected at admission were analyzed using automated hematology, clinical chemistry (Roche), and flow cytometry (BD FACSCanto™ II) platforms.

Outcome Definition

Bloodstream infections (BSIs) were defined per CDC/NHSN surveillance criteria as: (1) Clinical criteria: Temperature >38.0°C with ≥1 sign (rigors or hypotension [systolic BP ≤90 mmHg]); (2) Microbiological criteria: ≥1 blood culture yielding a recognized pathogen, OR≥2 blood cultures with skin commensals from separate venipunctures within 48h,[12] such as coagulase-negative staphylococci.

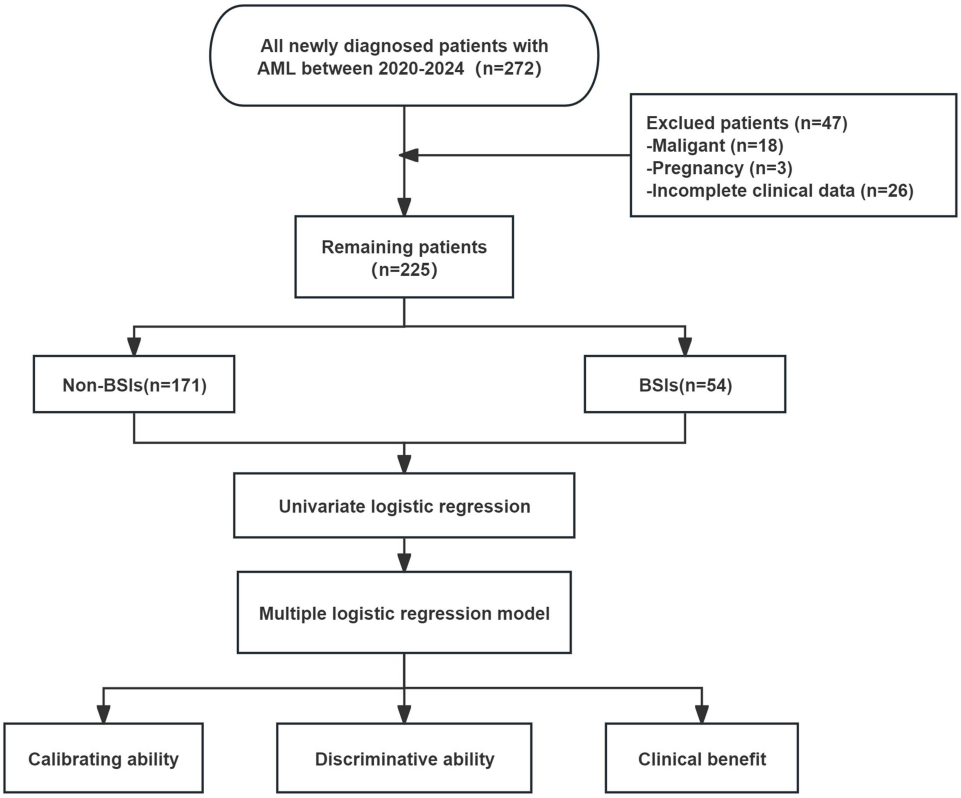

Figure 1 The procedure of the study.

Definition of Exposure Variable

The Systemic Inflammation Response Index (SIRI) is a novel biomarker reflecting the equilibrium between inflammatory activation and immune status in malignancies and inflammatory diseases.[13] SIRI has demonstrated significant prognostic potential for predicting clinical outcomes in both infectious (eg, pneumonia) and oncological contexts.[14–16] It is calculated as: SIRI = (Neutrophil count × Monocyte count)/Lymphocyte count (all parameters measured in $\times 10^9$/L units).

Definition of Covariates

Based on established BSIs risk factors, covariates included sex, age, BMI, smoking status, alcohol consumption, diabetes, coronary artery disease (CAD), and hypertension. Definitions aligned with National Health and Nutrition Examination Survey (NHANES 2021–2023) criteria: Smoking: Current smoker (l>100 lifetime cigarettes with current daily/intermittent use); Non-smoker (≤100 lifetime cigarettes). Alcohol use: Drinker (>2 drinking occasions/year AND ≥12 standard drinks*); Non-drinker (≤2 occasions/year OR <12 drinks/year). Standard drink = 12 oz beer/5 oz wine/1.5 oz liquor. Disease histories were clinically verified: Diabetes: WHO criteria (any of: fasting glucose ≥7.0 mmol/L, OGTT 2-h glucose ≥11.1 mmol/L, HbA1c ≥6.5%, or glucose-lowering therapy). CAD: Documented myocardial infarction, coronary revascularization (PCI/CABG), OR angiographic stenosis ≥70%. Hypertension: Office blood pressure ≥140/90 mmHg OR antihypertensive medication use (ESC/ACC guidelines). All data underwent source document verification.

Statistical Analysis

Analyses used SPSS 21.0 and R 4.3.2. For continuous variables, results were presented as mean ± standard deviation (SD) or median (IQR) as appropriate. Categorical variables were presented by numbers with percentages (%). Continuous variables were assessed for normality test and analyzed using *t*-test or Mann–Whitney *U*-test. For categorical variables, chi-square test or two-tailed Fisher's exact test was employed appropriately.

https://doi.org/10.2147/IDR.S557948

Variables with P<0.05 in univariate logistic regression were entered into multivariable logistic analysis. Final predictors were identified via backward stepwise selection and incorporated into a nomogram. Model performance was assessed by ROC-AUC and decision curve analysis (DCA). Statistical significance was defined as *P*<0.05 (two-sided tests).

Results

Baseline Characteristics

Demographic and laboratory features are presented in Table 1. A total of 225 patients were collected in this study, 113 (50.22%) were male, 112 (49.78%) were female. Most of the overall population did not have hypertension (63.56%), diabetes (80.00%) or coronary heart disease (90.22%). Mean age of the overall population was 47.45 ± 11.38 years, BMI was 23.51 ± 3.41 kg/m^2, LOS was 20.38 ± 7.68 days. The mean values of SIRI were 1.57 ± 0.95. The mean values of TC, TG, HDL-C and LDL-C were 4.04 ± 0.99, 2.01 ± 0.74, 0.92 ± 0.28 and 2.56 ± 0.83 mmol/L. Age (P<0.001), BMI *(P*<0.001), smoking (*P*=0.031) and LOS (*P*<0.001) differed significantly between BSIs group and Non-BSIs group. In addition, SIRI (*P*<0.001), TG (*P*<0.001) and LDL-C (*P*<0.001) were significantly higher in the BSIs group than in the Non-BSIs group; TC (*P*=0.001) and HDL-C (*P*<0.001) were significantly lower in the BSIs group than in the Non-BSIs group.

Univariate and Multiple Logistic Regression Analysis of BSIs

As shown in Table 2, univariate logistic regression analysis showed that age, BMI, smoking, SIRI, TC, TG, HDL-C and LDL-C were significant influencing factors (all *P*<0.05). Multiple logistic regression (Model 1) showed that SIRI (OR=3.18, 95% CI: 1.87–5.79, *P*<0.001) was significant risk factor of BSIs. To refine the predictive model, optimized model (Model 2) using backward stepwise regression also showed SIRI (OR=3.36, 95% CI: 2.00–6.07, *P*<0.001) was

Table 1 Baseline Characteristics

Variables	Total (n=225)	Non-BSIs Group (n=171)	BSIs Group (n=54)	*P*
Sex, n (%)				0.667
Male	113 (50.22%)	84 (49.12%)	29 (53.70%)	
Female	112 (49.78%)	87 (50.88%)	25 (46.30%)	
Age, (years) [SD]	47.45 ± 11.38	45.25 ± 10.96	54.43 ± 9.87	<0.001
High, (cm) [SD]	162.23 ± 8.22	161.35 ± 8.49	165.04 ± 6.61	0.001
Weight, (kg) [SD]	62.15 ± 11.63	60.37 ± 11.64	67.78 ± 9.75	<0.001
BMI, (kg/m2) [SD]	23.51 ± 3.41	23.09 ± 3.45	24.85 ± 2.91	<0.001
Hypertension, n(%)				0.360
No	143 (63.56%)	112 (65.50%)	31 (57.41%)	
Yes	82 (36.44%)	59 (34.50%)	23 (42.59%)	
Diabetes, n (%)				0.785
No	180 (80.00%)	138 (80.70%)	42 (77.78%)	
Yes	45 (20.00%)	33 (19.30%)	12 (22.22%)	
Coronary heart disease, n (%)				0.091
No	203 (90.22%)	158 (92.40%)	45 (83.33%)	
Yes	22 (9.78%)	13 (7.60%)	9 (16.67%)	
Smoking, n (%)				0.031
No	165 (73.33%)	132 (77.19%)	33 (61.11%)	
Yes	60 (26.67%)	39 (22.81%)	21 (38.89%)	
Drinking, n (%)				0.137
No	173 (76.89%)	136 (79.53%)	37 (68.52%)	
Yes	52 (23.11%)	35 (20.47%)	17 (31.48%)	
LOS, (days) [SD]	20.38 ± 7.68	19.13 ± 6.99	24.31 ± 8.50	<0.001

(*Continued*)

Table 1 (Continued).

Variables	Total (n=225)	Non-BSIs Group (n=171)	BSIs Group (n=54)	*P*
Laboratory features				
CD3+, (cells/μL) [SD]	70.52 ± 11.28	70.43 ± 11.64	70.83 ± 10.12	0.807
CD19+, (cells/μL) [SD]	16.33 ± 9.94	15.76 ± 10.31	18.14 ± 8.47	0.090
CD3+CD4+, (cells/μL) [SD]	41.93 ± 10.84	41.86 ± 11.76	42.16 ± 7.25	0.820
CD3+CD8+, (cells/μL) [SD]	24.87 ± 7.27	24.49 ± 7.27	26.06 ± 7.24	0.170
CD56+, (cells/μL) [SD]	13.04 ± 8.38	12.74 ± 8.30	13.98 ± 8.67	0.361
PLT, (10^9/L) [SD]	96.92 ± 36.08	96.16 ± 39.39	99.34 ± 22.72	0.461
NEU, (10^9/L) [SD]	2.20 ± 1.04	2.04 ± 1.06	2.71 ± 0.77	<0.001
MONO, (10^9/L) [SD]	1.05 ± 0.41	0.96 ± 0.41	1.34 ± 0.26	<0.001
LYM, (10^9/L) [SD]	1.55 ± 0.61	1.50 ± 0.66	1.71 ± 0.37	0.005
SIRI	1.57 ± 0.95	1.38 ± 0.89	2.21 ± 0.85	<0.001
ALB, (g/L) [SD]	38.57 ± 5.11	38.81 ± 5.03	37.80 ± 5.32	0.220
TC, (mmol/L) [SD]	4.04 ± 0.99	4.17 ± 0.97	3.64 ± 0.96	0.001
TG, (mmol/L) [SD]	1.93 (0.73)	1.79 ± 0.67	2.37 (0.72)	<0.001
HDL-C, (mmol/L) [SD]	0.92 ± 0.28	0.96 ± 0.28	0.80 ± 0.23	<0.001
LDL-C, (mmol/L) [SD]	2.56 ± 0.83	2.43 ± 0.82	3.01 ± 0.68	<0.001

Note: Mean ± SD for continuous variables and % for categorical variables. Neutrophils count * Monocyte count / Lymphocyte count.
Abbreviations: BSIs, bloodstream infections; BMI, body mass index; LOS, length of stay; CD3+, cluster of differentiation 3 positive T cells; CD19+, cluster of differentiation 19 positive B cells; CD3+CD4+, cluster of differentiation 3 and cluster of differentiation 4 co-positive T helper cells; CD3+CD8+, cluster of differentiation 3 and cluster of differentiation 8 co-positive T helper cells; CD56+, cluster of differentiation 56 positive NK cells; PLT, platelets count; NEU, neutrophils count; MONO, monocyte count; LYM, lymphocyte count; SIRI, systemic inflammatory response index; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

Table 2 Univariate and Multiple Logistic Regression Analysis

Variables	Univariate Analysis		Multiple Analysis of Model 1		Multiple Analysis of Model 2	
	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
Sex, n (%)						
Male	Reference					
Female	0.83 (0.45, 1.54)	0.562				
Age, (years) [SD]	1.09 (1.05, 1.13)	<0.001	1.11 (1.06, 1.18)	<0.001	1.12 (1.06, 1.18)	<0.001
BMI, (kg/m2) [SD]	1.17 (1.06, 1.29)	<0.001	1.14 (0.99, 1.33)	0.077		
Hypertension, n (%)						
No	Reference					
Yes	1.41 (0.75, 2.63)	0.288				
Diabetes, n (%)						
No	Reference					
Yes	1.20 (0.55, 2.49)	0.635				
Coronary heart disease, n (%)						
No	Reference					
Yes	2.43 (0.94, 6.06)	0.067				
Smoking, n (%)						
No	Reference					
Yes	2.15 (1.11, 4.14)	0.024	1.41 (0.48, 4.00)	0.517		
Drinking, n (%)						
No	Reference					
Yes	1.79 (0.88, 3.53)	0.104				

(*Continued*)

https://doi.org/10.2147/IDR.S557948

Table 2 (Continued).

Variables	Univariate Analysis		Multiple Analysis of Model 1		Multiple Analysis of Model 2	
	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
CD3+, (cells/μL) [SD]	1.00 (0.98, 1.03)	0.819				
CD19+, (cells/μL) [SD]	1.02 (0.99, 1.05)	0.129				
CD3+CD4+, (cells/μL) [SD]	1.00 (0.97, 1.03)	0.857				
CD3+CD8+, (cells/μL) [SD]	1.03 (0.99, 1.07)	0.170				
CD56+, (cells/μL) [SD]	1.02 (0.98, 1.05)	0.349				
PLT, (10^9/L) [SD]	1.00 (0.99, 1.01)	0.571				
SIRI	2.52 (1.78, 3.56)	<0.001	3.18 (1.87, 5.79)	<0.001	3.36 (2.00, 6.07)	<0.001
ALB, (g/L) [SD]	0.96 (0.91, 1.02)	0.205				
TC, (mmol/L) [SD]	0.55 (0.39, 0.79)	0.001	0.30 (0.13, 0.63)	0.003	0.32 (0.14, 0.66)	0.004
TG, (mmol/L) [SD]	3.33 (2.02, 5.48)	<0.001	3.91 (1.81, 9.54)	<0.001	3.99 (1.83, 9.59)	<0.001
HDL-C, (mmol/L) [SD]	0.07 (0.02, 0.28)	<0.001	0.10 (0.01, 1.17)	0.076	0.06 (0.01, 0.64)	0.024
LDL-C, (mmol/L) [SD]	2.41 (1.60, 3.62)	<0.001	6.48 (2.99, 15.99)	<0.001	5.98 (2.84, 14.13)	<0.001

Note: Neutrophils count * Monocyte count / Lymphocyte count.

Abbreviations: BSIs, bloodstream infections; BMI, body mass index; LOS, length of stay; CD3+, cluster of differentiation 3 positive T cells; CD19+, cluster of differentiation 19 positive B cells; CD3+CD4+, cluster of differentiation 3 and cluster of differentiation 4 co-positive T helper cells; CD3+CD8+, cluster of differentiation 3 and cluster of differentiation 8 co-positive T helper cells; CD56+, cluster of differentiation 56 positive NK cells; PLT, platelets count; NEU, neutrophils count; MONO, monocyte count; LYM, lymphocyte count; SIRI, systemic inflammatory response index; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

significant risk factor. In addition, the result showed that age (OR=1.12, 95% CI: 1.06–1.18, *P*<0.001), TC (OR=0.32, 95% CI: 0.14–0.66, *P*=0.004), TG (OR=3.99, 95% CI: 1.83–9.59, *P*=0.003), HDL-C (OR=0.06, 95% CI: 0.01–0.64, *P*=0.024) and LDL-C (OR=5.98, 95% CI: 2.84–14.13, *P*<0.001) were significant influencing factors of BSIs.

Nomogram to Predict BSIs

Based on Model 2, we developed a nomogram (Figure 2) to predict BSIs risk. The model demonstrates a C-index of 0.926 and an AIC value of 135. Higher age, higher SIRI, lower TC, higher TG, lower HDL-C and higher LDL-C were risk factors of BSIs. Using the nomogram, doctors assign points based on patient characteristics. Summing these yields a total score corresponding to a BSIs risk probability. Higher totals indicate greater risk, enabling stratified management and personalized interventions. The study used constructed calibration curves (1000 times) to analyze the deviations between the predicted values and the actual values. The solid line depicts the model's predicted probabilities, while the dashed diagonal represents perfect calibration. Better predictive accuracy is reflected by closer alignment between these lines. As shown in Figure 3A, the absolute error between the simulated and actual curves was 0.014, demonstrating that their trajectories were highly consistent, which showed a good agreement between the predicted values and the actual values. The nomogram achieved a strong discriminatory ability, reflected by an AUC of 0.926 (95% CI: 0.879–0.973), and with a sensitivity of 0.854 and a specificity of 0.889 (Figure 3B). DCA revealed the nomogram's superior net clinical benefit versus "treat-all" and "treat-none" strategies across threshold probabilities (5% to 100%), supporting its adoption in clinical practice (Figure 4).

Relationship Between SIRI and BSIs

In the overall population, a significant positive association between SIRI and BSIs was observed using univariate logistic regression (OR=2.52, 95% CI: 1.78–3.56, *P*<0.001) (Model 1). Adjustment for age, sex, and BMI yielded similar results (OR=2.61, 95% CI: 1.76–3.88, *P*<0.001) (Model 2). Even after full covariate adjustment (Model 3), the association remained statistically significant (OR=3.28, 95% CI: 1.76–6.11, *P*<0.001), as shown in Table 3.

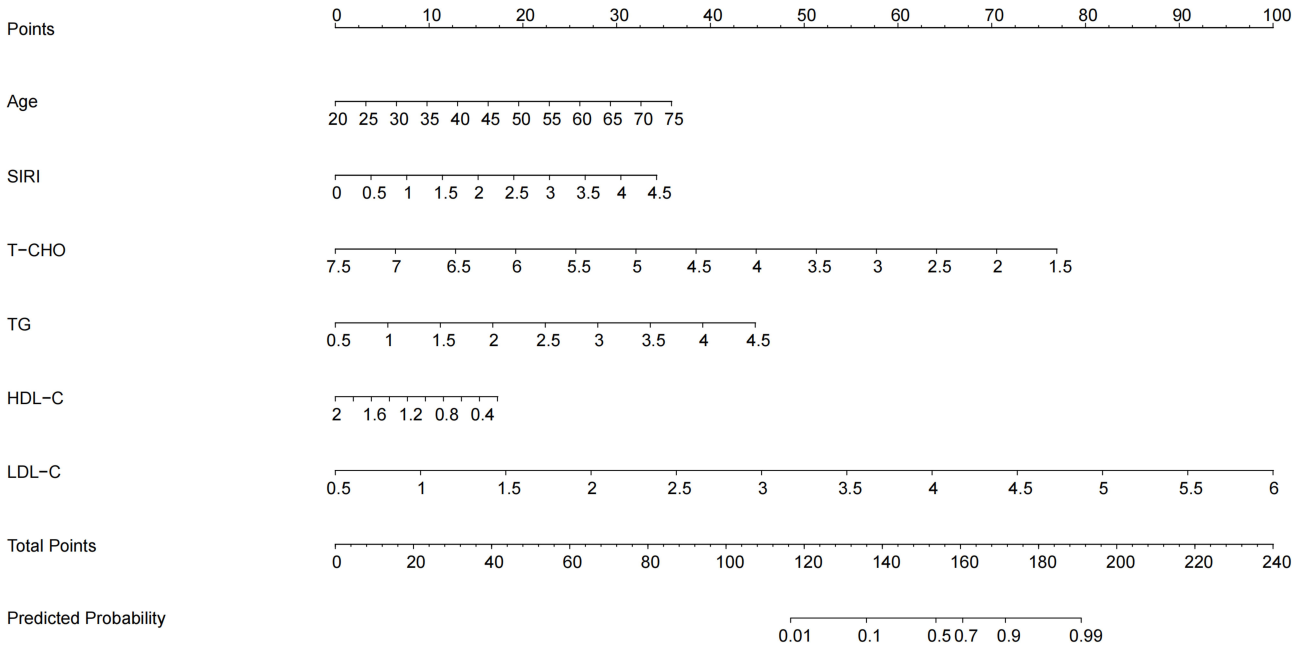

Figure 2 The nomogram model of BSIs.

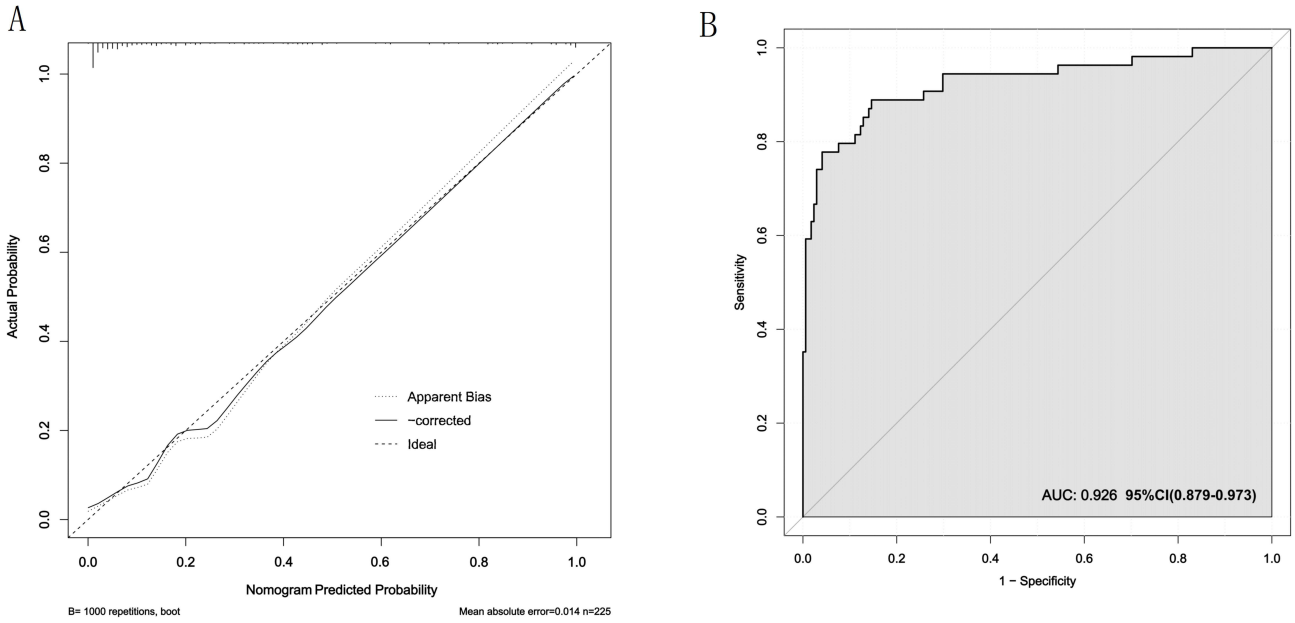

Figure 3 The calibration curve and the ROC curve of the nomogram model. (**A**) calibration curve; (**B**) ROC curve.

Correlation Between SIRI and LOS

In addition, this study used Spearman's analysis to assess the correlation between SIRI and LOS of patients with acute myeloid leukemia. The result indicated a significant positive correlation between SIRI and LOS (R = 0.18, *P*=0.007) (Figure 5).

Discussion

Acute leukemia (AL) patients are at high risk of life-threatening BSIs due to treatment-induced immunosuppression, bone marrow suppression, and neutropenia.[3] While molecular diagnostics (eg, PCR and NGS) offer rapid pathogen

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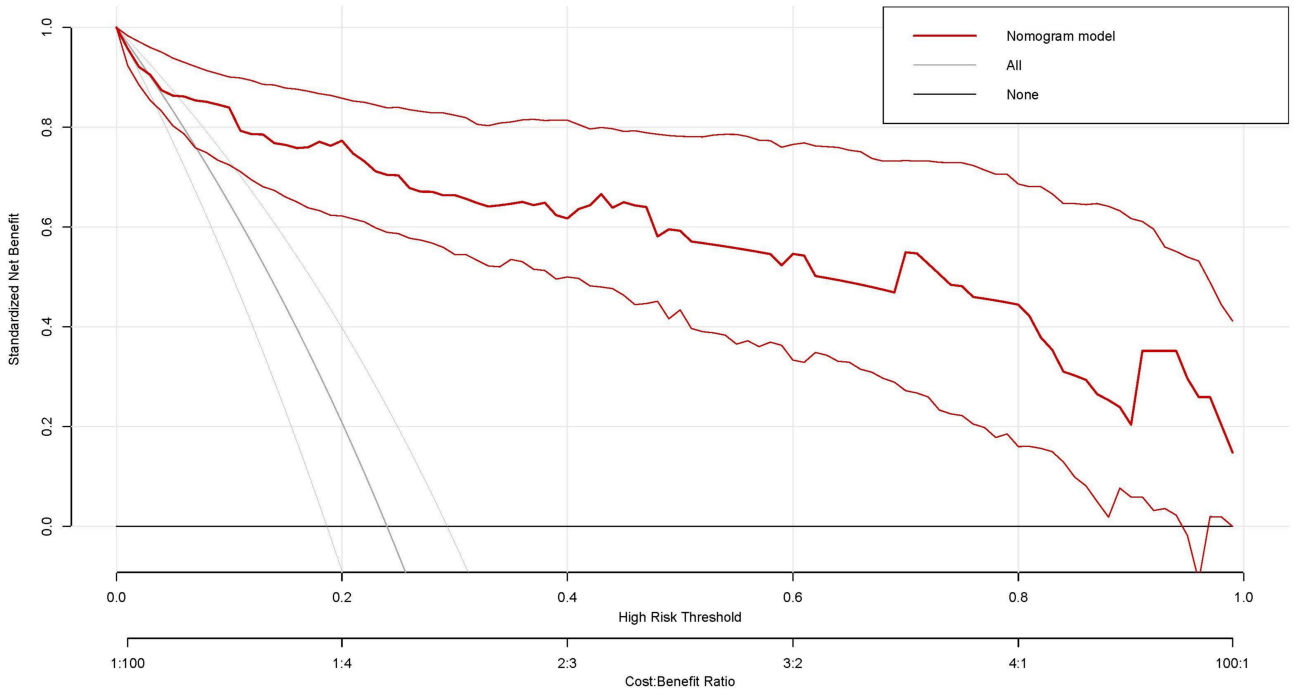

Figure 4 The The decision curve of the nomogram model.

identification, their limitations and the 48- to 72-hour delay in blood culture results underscore an urgent need for reliable early BSIs biomarkers.[17,18] This diagnostic delay underscores the critical need for more reliable indicators to enable early detection and assessment of bloodstream infections. This study identified a positive correlation between SIRI levels, blood lipid levels and the incidence of BSIs.

SIRI was significantly elevated in BSIs patients (P<0.001) and independently associated with BSIs risk across all regression models (OR=3.28, 95% CI: 1.76–6.11 after full adjustment). Current researches indicated that a chronic inflammatory state significantly weakens the body's defense capabilities, making individuals more susceptible to bloodstream infections; however, the predictive power of these markers has been insufficient (NLR of AUC: 0.678;[19] PLR of AUC: 0.837).[20] SIRI comprehensively incorporates multiple inflammatory indicators such as neutrophils, monocytes, and lymphocytes, offering a more comprehensive reflection of the chronic inflammatory state.[11] Additionally, SIR is derived from routine blood tests, offering a low-cost and easy-to-use approach with promising potential for widespread adoption. SIRI is a novel inflammatory marker that can be used for the early assessment of disease severity. Ding et al identified that SIRI may serve as a novel, reliable, and independent prognostic predictor for patients with locally advanced rectal cancer who underwent surgery following neoadjuvant chemoradiotherapy (Neo-CRT).[21] Chen et al had demonstrated that SIR was a valid inflammatory marker for assessing hyperuricemia in Chinese rural women.[22] A recent study had indicated that SIRI was also linked to coronary heart disease.[23] This study pioneered the application of SIRI for early diagnosis of BSIs in hospitalized AML patients, demonstrating high diagnostic efficacy (AUC: 0.926). Therefore, SIRI

Table 3 The Relationship Between SIRI Levels and BSI Risk Was Examined Using Logistic Regression Analysis

	Model 1		Model 2		Model 3	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
SIRI	2.52(1.78~3.56)	< 0.001	2.61 (1.76 ~3.88)	< 0.001	3.28 (1.76~6.11)	< 0.001

Notes: Model 1: No covariates were adjusted; Model 2: Adjusted for age, sex, and BMI; Model 3: Adjusted for age, sex, BMI, hypertension, diabetes, coronary heart disease, smoking, drinking, T-CHO, TG, HDL-C, LDL-C.
Abbreviations: OR, odds ratio; CI, Confidence interval.

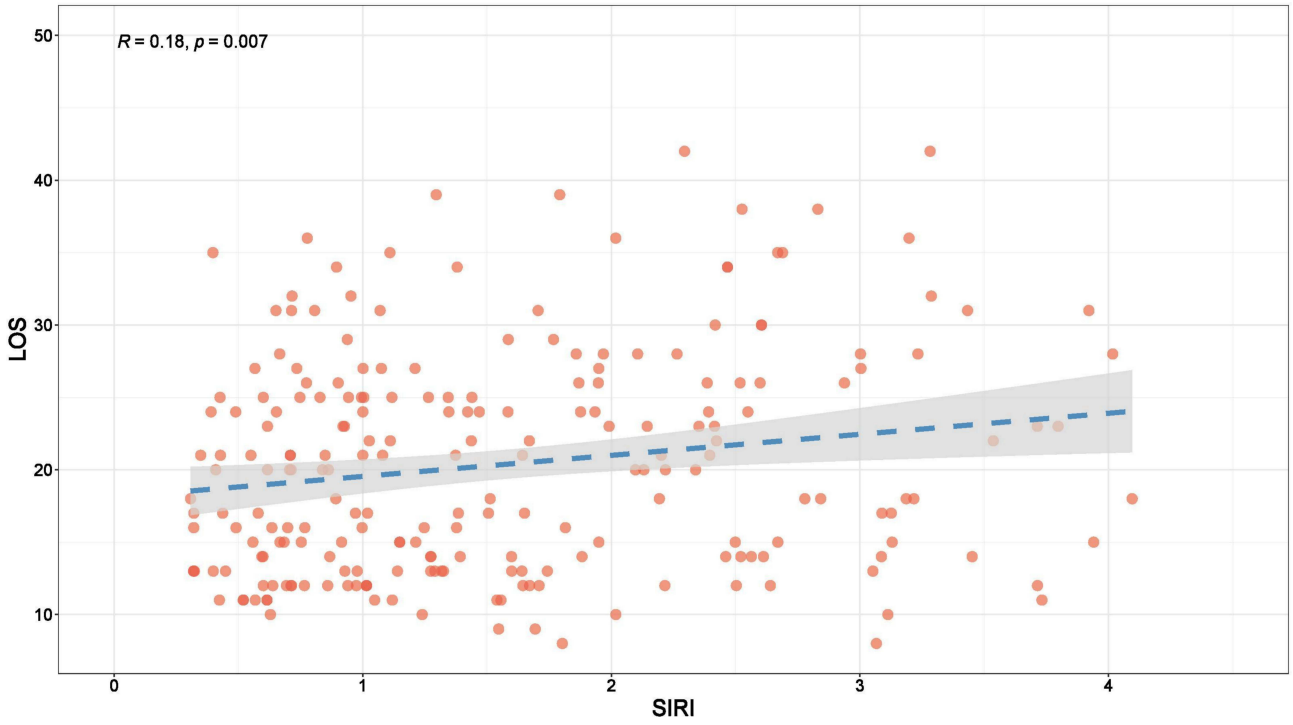

Figure 5 Correlation between SIRI and LOS.

can serve as a novel indicator for early diagnosis of BSIs in hospitalized AML patients. Neutrophils are the first line of defense against bacterial invasions, while monocytes/macrophages participate in phagocytosis and antigen presentation. Lymphocytes, particularly T cells, are crucial for adaptive immunity. Therefore, an elevated SIRI represents an imbalance where pro-inflammatory forces may be dominant, yet ineffective, and adaptive immunity is compromised, collectively creating a permissive environment for microbial dissemination into the bloodstream.[24,25] The mechanisms underlying the relationship between SIRI and BSIs may be as follows: 1) Prolonged inflammation depletes immune resources (eg, diminished function and exhaustion of persistently activated immune cells), leading to impaired responses to new pathogen. For instance, the phagocytic and bactericidal capacities of neutrophils and macrophages are reduced.[26] 2) The chronic inflammatory environment may cause an imbalance in immune responses (eg, persistently high levels of TNF-α and IL-6 coupled with compensatory increases in anti-inflammatory responses), hindering the effective coordinated clearance of pathogens.[27] 3) Chronic inflammation compromises mucosal barriers in the gut and respiratory tract, allowing commensal bacteria to more readily penetrate these barriers and enter the bloodstream.[28] 4) The chronic inflammatory environment may alter the local microbial ecology, increasing opportunities for colonization by certain pathogenic bacteria.[29] Furthermore, SIRI positively correlated with prolonged hospital stays (R=0.18, P = 0.007), suggesting its role in reflecting clinical burden.

In recent years, scientists' observations have indicated lipid levels change rapidly in the early stages of sepsis and may predict the prognosis of sepsis.[30] This study also found TC, TG, HDL-C and LDL-C were associated with BSIs in hospitalized AML patients. HDL-C possesses several direct anti-infective properties. It can bind to and neutralize lipopolysaccharide (LPS), a key component of the outer membrane of Gram-negative bacteria, thereby preventing the activation of pro-inflammatory cytokines and reducing the risk of septic shock.[31,32] Chen et al have demonstrated that LDL-C is a significant risk factor for sepsis, while HDL-C have been identified as protective factors,[33] their conclusions demonstrate homogeneity with the findings of this study. The multifaceted role of HDL-C encompasses anti-inflammatory, anti-apoptotic, and neutralizing properties, including bacterial cell wall lipopolysaccharides and lipoteichoic acids.[34] HDL-C neutralizes endotoxin (LPS) through apolipoprotein A1 (ApoA1), and low HDL-C levels weaken this protective effect, thereby exacerbating the risk of BSIs.[35]

https://doi.org/10.2147/IDR.S557948

TC serves as a critical component of cell membranes and lipid rafts, participating in immune receptor signaling (eg, Toll-like receptors). Low TC levels lead to impaired lymphocyte activation and reduced macrophage phagocytic capacity, thereby diminishing pathogen clearance efficiency.[36] Elevated TG increases the free fatty acid (FFA) release, activating the TLR4/NF-κB pathway. This triggers sustained production of pro-inflammatory cytokines (eg, TNF-α, IL-6), compromising endothelial barrier integrity and thereby promoting bacterial entry into the bloodstream.[37] Moreover, environment of higher TG levels increases blood viscosity, causing microcirculatory impairment that further aggravates tissue ischemia and compromises barrier function. LDL-C is oxidized to form ox-LDL beneath the vascular endothelium, which promotes monocyte infiltration and their transformation into foam cells, compromising endothelial integrity. Chronic infections (eg, *Helicobacter pylori*) synergize with ox-LDL to exacerbate endothelial damage, facilitating commensal bacterial breaching of the barrier and entry into circulation.[38]

However, this study also has limitations. First, as a single-center study without external validation, the conclusions may lack reliability. Second, the small sample size (n=225) may be underpowered to detect true effects, potentially leading to imprecise conclusions. Third, the variables investigated in this study were relatively limited, and critical factors such as IL-6 were not examined. Fourth, although prophylactic antibiotic use significantly impacts the incidence of bacteremia, this factor was not collected or analyzed in our study. Finally, this study only examined associations between SIRI, lipid profiles, and BSIs without establishing causal relationships. In light of these limitations, multi-center, large-scale prospective studies are warranted to validate the conclusions of this research in the future.

Conclusion

This study developed and validated the first SIRI-lipid nomogram for predicting bloodstream infection risk in AML patients undergoing induction chemotherapy. The model integrates six independent predictors—SIRI, age, TC, TG, HDL-C, and LDL-C—demonstrating exceptional discrimination (AUC=0.926) and calibration. Decision curve analysis confirmed superior clinical utility over default strategies across threshold probabilities. Critically, SIRI emerged as a robust independent predictor of BSIs and prolonged hospitalization. These findings advocate for incorporating inflammatory-metabolic biomarkers into risk stratification protocols to guide targeted prophylaxis and resource allocation.

Ethics Statement

Our research complies with the principles of the Declaration of Helsinki. The study design and procedures were reviewed and approved by the Ethics Committee of the First Affiliated Hospital of Guangxi Medical University (Approval No: 2024-S321-01).

Acknowledgments

The authors acknowledge the general support received for this research.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Consent for Publication

Written informed consent was obtained from all individual participants included in the study for the publication of any potentially identifiable data or images. All personal identifiers have been removed or anonymized to protect participant privacy.

Funding

This work was supported by the Development and Promotion of Appropriate Technology for Healthcare in Guangxi Project [grant number S2023066] and Self-Funded Plan Projects of Guangxi Health Commission [grant number Z-A20240541; Z-A20230545].

Disclosure

The authors report no conflicts of interest in this work.

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