Risk factors of acute kidney injury, septic shock and acute respiratory distress syndrome in patients with blood culture-positive sepsis

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Abstract. Sepsis, a condition characterized by a dysregulated host response to infection, can progress to septic shock and lead to various complications. The present study aimed to identify risk factors for the early clinical identification of sepsis patients at heightened risk of complications. In the present study, a total of 383 hospitalized patients with sepsis and positive blood cultures were enrolled. Demographic characteristics, laboratory findings at admission and treatment outcomes were collected and analyzed. Among the 383 sepsis patients, 165 were diagnosed with acute kidney injury (AKI). Patients with AKI exhibited significantly lower platelet counts, elevated procalcitonin levels and higher Sequential Organ Failure Assessment (SOFA) scores. Logistic regression analysis identified the SOFA score [odds ratio (OR)=1.269, 95% confidence interval (CI): 1.067-1.510, P=0.007) as an independent predictor of AKI. Furthermore, patients with septic shock had lower platelet counts and higher white blood cell counts at admission. Multivariable analysis revealed that age (OR=1.024, 95% CI: 1.001-1.047, P=0.039), procalcitonin (OR=1.018, 95% CI: 1.003-1.032, P=0.015), SOFA score (OR=1.465, 95% CI: 1.248-1.719, P<0.001) and Pitt bacteremia score (OR=1.437, 95% CI: 1.204-1.716, P<0.001) were independently associated with septic shock. In addition, sepsis patients with acute respiratory distress syndrome (ARDS) were observed to have lower platelet counts, higher body weight and elevated alanine aminotransferase levels. Multivariable analysis identified the SOFA score (OR=1.177, 95% CI: 1.095-1.265, P<0.001) and body weight (OR=1.030, 95% CI: 1.007-1.054, P=0.010) as independent predictors of ARDS. The present study highlights the risk factors associated with AKI, ARDS and septic shock in sepsis patients with positive blood cultures. Early identification and close monitoring of these factors are crucial for improving outcomes in sepsis management.

Introduction

Sepsis, a life-threatening syndrome resulting from a dysregulated host response to infections, can progress to septic shock and various complications. This poses a major global health challenge owing to the elevated morbidity and mortality rates of sepsis (1-4). A retrospective analysis conducted in 2014 revealed that sepsis was implicated in 35% of hospital deaths in the United States (3). Globally, an estimated 48.9 million sepsis cases with 11.0 million sepsis-related deaths occurred in 2017, contributing to ~20% of global mortality (2). These data emphasize the critical need to analyze factors associated with poor prognosis in sepsis.

Patients with sepsis often experience complications, such as acute kidney injury (AKI), septic shock and acute respiratory distress syndrome (ARDS), leading to a worse prognosis compared with others (5-7). In AKI, controversies surround the treatment because of an inadequate understanding of its pathophysiological mechanisms (8,9). Septic shock, a subtype of sepsis, is characterized by circulatory failure and abnormal cell metabolism, which significantly decreases the prognosis of patients with sepsis, posing a substantial economic burden (10,11). Early detection of septic shock is challenging but crucial for improving patient outcomes. ARDS is the most common and early complication of sepsis (12). Identifying risk factors for these complications is urgently needed to facilitate early intervention and personalized treatment, thereby enhancing the clinical treatment success rate.

Several models are currently available to predict sepsis. The Early Warning Score (EWS) (13), calculated from a

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Table I. Demographics and clinical characteristics of All patient with or without AKI.

Characteristic	Non-AKI group	AKI group	P-value
Sample size	218	165	-
Sex, male (%)	129 (59.2)	110 (66.7)	0.134
Age, years	60.56±17.45	63.2±16.72	0.163
Height, cm	164.00±8.05	165.32±7.19	0.098
Weight, kg	61.12±11.90	63.45±11.51	0.055
CVD, n (%)	76 (34.9)	66 (40.0)	0.303
T2DM, n (%)	48 (22.0)	38 (23.0)	0.814
WBC, 10^9/l	13.37±8.57	14.18±8.85	0.367
PLT, 10^9/l	187.37±112.97	138.84±114.14	<0.001
CRP, mg/l	88.10±58.92	110.76±69.01	0.002
PCT, ng/ml	2.60 (0.38, 17.13)	15.54 (1.95, 76.16)	<0.001
PT, sec	15.08±3.17	16.86±4.47	<0.001
FIB, g/l	4.34±1.89	4.38±2.11	0.858
ALT, U/l	16.00 (31.00, 75.75)	36.00 (21.00, 82.50)	0.094
ALB, g/l	30.13±5.82	29.17±6.36	0.138
BUN, mmol/l	8.47±4.29	16.37±9.56	<0.001
SOFA score	6.31±3.57	9.79±4.06	<0.001
PITT	3.26±2.83	4.25±2.93	0.001
Pathogens, n (%)			0.554
E. coli	39 (17.9)	39 (23.6)	
K. pneumoniae	39 (17.9)	29 (17.6)	
S. aureus	24 (11.0)	15 (9.1)	
Others	116 (53.2)	82 (49.7)	

AKI, acute kidney injury; CVD, cardiovascular disease; T2DM, type 2 diabetes; WBC, white blood cells; PLT, platelets; CRP, C-reactive protein; PCT, procalcitonin; PT, prothrombin time; FIB, fibrinogen; ALT, alanine aminotransferase; ALB, albumin; BUN, blood urea nitrogen; SOFA, Sequential Organ Failure Assessment; PITT, Pitt bacteremia score.

patient's vital signs and mental status, is widely used to identify patients with acute deterioration. Additionally, the Quick Sequential Organ Failure Assessment (qSOFA) and the National Early Warning Score (NEWS) are commonly employed for sepsis identification and mortality prediction (14). Notably, the National Health Service in England has adopted a NEWS score of ≥5 to indicate possible sepsis (15). Despite these advances, predictive markers and models of sepsis-related complications remain insufficient. For AKI, the Acute Disease Quality Initiative 23 Consensus Conference recommends combining damage and functional biomarkers to improve the sensitivity of AKI definitions (16). Similarly, early detection of ARDS is crucial, as sepsis and ARDS are independently associated with higher incidence, mortality and prolonged hospital stays (17,18). Currently, no evidence or consensus exists on screening patients for ARDS (19). Therefore, studying the risk factors of sepsis-related complications is essential.

However, to analyze the factors related to the prognosis of sepsis, it is necessary to distinguish between different types of sepsis because the factors influencing each type may vary. Based on blood culture results, sepsis can be categorized into culture-negative and culture-positive (20). Various factors influence these culture results, including hospital laboratory conditions and host-specific factors. Notably, a negative culture may result from pathogens requiring fastidious conditions that are difficult to culture. Subtle differences between culture-negative and culture-positive sepsis have been reported, such as longer hospital stays and extended mechanical ventilation in patients with culture-positive sepsis (21). To evaluate patient prognoses more accurately, the present study focused exclusively on patients with sepsis and positive blood cultures. This approach allowed it to narrow the research scope and thoroughly investigate sepsis management and outcomes.

Therefore, the present study focused on sepsis patients with positive blood cultures, investigating the relationship between their clinical and demographic characteristics and the occurrence of complications. The objective was to identify risk factors for the early clinical identification of sepsis patients at elevated risk of complications, thereby providing evidence-based insights to enhance the management of sepsis.

Materials and methods

Study population. The present retrospective observational study was approved by the Ethics Committee of The First Affiliated Hospital of Xiamen University (Fujian, China; approval no. 2022-037). Written informed consent was obtained from all patients upon admission. A total of 383 hospitalized patients with

Table II. Univariate and multivariate analysis for AKI in sepsis patients.

	Univariate analysis			Multivariate analysis		
Variable	OR	95% CI	P-value	OR	95% CI	P-value
Sex, male vs. female	0.725	0.475-1.105	0.134			
Age, years	1.009	0.997-1.021	0.164			
Height, cm	1.023	0.996-1.050	0.099	1.010	0.957-1.065	0.722
Weight, kg	1.017	1.000-1.035	0.056	1.032	0.999-1.066	0.061
CVD, yes vs. no	1.246	0.820-1.892	0.303			
T2DM, yes vs. no	1.060	0.653-1.719	0.814			
WBC, 10^9/l	1.011	0.988-1.035	0.367			
PLT, 10^9/l	0.996	0.994-0.998	<0.001	0.999	0.995-1.003	0.638
CRP, mg/l	1.006	1.002-1.009	0.003	0.995	0.988-1.002	0.189
PCT, ng/ml	1.020	1.013-1.027	<0.001	1.007	0.992-1.023	0.362
PT, sec	1.153	1.078-1.234	<0.001	0.937	0.810-1.085	0.384
FIB, g/l	1.010	0.910-1.120	0.858			
ALT, U/l	1.000	0.999-1.001	0.987			
ALB, g/l	0.974	0.940-1.009	0.139			
BUN, mmol/l	1.210	1.154-1.268	<0.001	1.059	0.983-1.142	0.133
SOFA score	1.263	1.189-1.342	<0.001	1.269	1.067-1.510	0.007
PITT	1.127	1.049-1.211	0.001	0.949	0.793-1.136	0.570

AKI, acute kidney injury; OR, odds ratio; CI, confidence interval; CVD, cardiovascular disease; T2DM, type 2 diabetes; WBC, white blood cells; PLT, platelets; CRP, C-reactive protein; PCT, procalcitonin; PT, prothrombin time; FIB, fibrinogen; ALT, alanine aminotransferase; ALB, albumin; BUN, blood urea nitrogen; SOFA, Sequential Organ Failure Assessment; PITT, Pitt bacteremia score.

sepsis confirmed by positive blood cultures were enrolled from the Intensive Care Unit (The First Affiliated Hospital of Xiamen University, Fujian, China) between January 2015 and December 2022. The inclusion criteria for the present study were: i) a diagnosis of sepsis based on the International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) (22) and ii) positive blood culture results.

Exclusion criteria were: i) Presence of other serious underlying diseases or HIV positivity that could independently contribute to complications and ii) incomplete clinical data essential for the analysis. A total of 229 patients were excluded for not meeting the inclusion criteria and an additional 22 patients were excluded due to blood culture contamination. Thus, 383 patients were included in the final analysis, comprising 239 males and 144 females, with a median age of 64 years (range: 18-79 years). The three most commonly identified pathogens were *Escherichia coli*, *Klebsiella pneumoniae* and *Staphylococcus aureus*.

Diagnosis of complications. In the present study, the diagnosis of ARDS followed the 2012 Berlin definition (23), which defines ARDS as a condition where $PaO_2/FiO_2 \leq 300$. Septic shock is diagnosed if, after fluid resuscitation, vasopressors are still necessary to maintain the mean arterial pressure at ≥65 mmHg serum lactate level >2 mmol/l. The diagnosis of AKI adhered to the KDIGO guidelines (24), defined as an increase in serum creatinine (CRE) by ≥26.5 μmol/l within 48 h, a ≥1.5-fold increase in CRE compared to the baseline value within 7 days, or a urine output <0.5 ml/(kg·h) for 6 h.

Laboratory test and biomarkers. Blood samples were promptly collected and analyzed using the Sysmex SE-9000 analyzer (Sysmex UK Ltd.) for Complete Blood Count and the Olympus AU5400 analyzer (Olympus Corporation) for biochemical examination. Demographic characteristics, laboratory results upon admission and treatment outcomes were retrieved from the electronic medical records system. All laboratory tests included in the analysis were conducted within the first 24 h of sepsis diagnosis to ensure relevance to early sepsis management and prognosis.

Statistical analysis. Continuous variables with normal distributions were expressed as mean ± standard deviation and their means were compared using the independent samples t-test. For non-normally distributed continuous variables, such as procalcitonin and alanine transaminase levels, data were presented as medians with interquartile ranges (25th percentile, 75th percentile) and comparisons were performed using non-parametric tests. Categorical variables were reported as frequencies and percentages and comparisons were made using the χ^2 test for variables such as sex, the proportion of patients with cardiovascular disease, type 2 diabetes mellitus and pathogens identified. For all enrolled patients, univariate and multivariate logistic regression analyses were conducted to determine independent risk factors. Variables with a P-value <0.1 in the univariate analysis were included in the multivariate model for further evaluation. The results of logistic regression analyses were reported as odds ratios (OR) with their corresponding 95% confidence intervals (CI). All statistical

Table III. Demographics and clinical data of all patient with or without septic shock.

Characteristic	Non-septic shock group	Septic shock group	P-value
Sample size	144	239	-
Sex, male (%)	80 (55.6)	159 (66.5)	0.032
Age, year	59.08±17.76	63.15±16.64	0.025
Height, cm	163.67±7.64	165.10±7.71	0.078
Weight, kg	62.61±11.76	61.82±11.80	0.525
CVD, n (%)	53 (36.8)	89 (37.2)	0.932
T2DM, n (%)	40 (27.8)	46 (19.2)	0.053
WBC, 10^9/l	12.42±6.04	14.49±9.89	0.011
PLT, 10^9/l	196.12±119.83	148.66±109.92	<0.001
CRP, mg/l	87.91±64.39	103.56±63.68	0.041
PCT, ng/ml	1.36 (0.26, 14.42)	9.19 (1.39, 51.85)	<0.001
PT, sec	15.03±3.34	16.35±4.11	0.001
FIB, g/l	4.67±1.89	4.17±2.02	0.018
ALT, U/l	30.50 (16.00, 60.00)	35.50 (18.75, 88.50)	0.055
ALB, g/l	30.57±6.15	29.18±5.97	0.035
BUN, mmol/l	10.63±8.59	12.77±7.74	0.014
SOFA score	4.67±2.61	9.70±3.75	<0.001
PITT,	1.76±2.20	4.85±2.67	<0.001
Pathogens, n (%)			0.817
E. coli	26 (18.1)	52 (21.8)	
K. pneumoniae	26 (18.1)	42 (17.6)	
S. aureus	14 (9.7)	25 (10.5)	
Others	78 (54.2)	120 (50.2)	

CVD, cardiovascular disease; T2DM, type 2 diabetes; WBC, white blood cells; PLT, platelets; CRP, C-reactive protein; PCT, procalcitonin; PT, prothrombin time; FIB, fibrinogen; ALT, alanine aminotransferase; ALB, albumin; BUN, blood urea nitrogen; SOFA, Sequential Organ Failure Assessment; PITT, Pitt bacteremia score.

analyses were performed using SPSS software version 26.0 (IBM Corp.). P<0.05 was considered to indicate a statistically significant difference.

Results

Risk factors associated with AKI in blood culture-positive sepsis patients. A total of 383 sepsis patients with positive blood cultures were included in the present study. Patients with AKI demonstrated significantly elevated levels of C-reactive protein (CRP; 88.10±58.92 vs. 110.76±69.01; P=0.002), reduced platelet counts (PLT; 187.37±112.97 vs. 138.84±114.14, P<0.001) and higher SOFA scores (6.31±3.57 vs. 9.79±4.06, P<0.001), as shown in Table I.

Logistic regression analysis was performed to identify independent risk factors for AKI (Table II). While PLT, procalcitonin (PCT) and SOFA score were identified as potential risk factors, only the SOFA score (OR=1.269, 95% CI: 1.067-1.510, P=0.007) emerged as an independent predictor of AKI in blood culture-positive sepsis patients.

Risk factors associated with septic shock in blood culture-positive sepsis patients. The present study next identified several factors associated with septic shock among the 383 blood culture-positive sepsis patients. Patients with septic shock exhibited significantly lower PLT (196.12±119.83 vs. 148.66±109.92; P<0.001) and higher WBC on admission (12.42±6.04 vs. 14.49±9.89; P=0.011), as shown in Table III.

Further investigation into independent predictors of septic shock was conducted through logistic regression analysis (Table IV). The results demonstrated that age (OR=1.024, 95% CI: 1.001-1.047, P=0.039), PCT (OR=1.018, 95% CI: 1.003-1.032, P=0.015), SOFA score (OR=1.465, 95% CI: 1.248-1.719, P<0.001) and Pitt bacteremia score (PITT) score (OR=1.437, 95% CI: 1.204-1.716, P<0.001) were independently associated with septic shock.

Risk factors associated with ARDS in blood culture-positive sepsis patients. Patients with ARDS were observed to have significantly lower PLT (191.57±115.22 vs. 156.11±114.75, P=0.007), higher body weight (59.57±11.35 vs. 63.15±11.81, P=0.007) and elevated ALT levels, as shown in Table V.

To identify independent predictors of ARDS, we performed multivariate logistic regression analysis (Table VI). The results highlighted the SOFA score (OR=1.177, 95% CI: 1.095-1.265, P<0.001) and body weight (OR=1.030, 95% CI: 1.007-1.054, P=0.010) as robust independent risk factors for ARDS in blood culture-positive sepsis patients.

Table IV. Univariate and multivariate analysis for septic shock in sepsis patients.

	Univariate analysis			Multivariate analysis		
Variable	OR	95% CI	P-value	OR	95% CI	P-value
Sex, male vs. female	0.629	0.411-0.962	0.032	1.586	0.511-4.920	0.425
Age, years	1.014	1.002-1.026	0.025	1.024	1.001-1.047	0.039
Height, cm	1.025	0.997-1.053	0.079	1.031	0.966-1.099	0.359
Weight, kg	0.994	0.977-1.012	0.524			
CVD, yes vs. no	1.019	0.664-1.563	0.932			
T2DM, yes vs. no	0.620	0.381-1.008	0.054	0.482	0.196-1.183	0.111
WBC, 10^9/l	1.031	1.004-1.058	0.025	1.016	0.967-1.068	0.521
PLT, 10^9/l	0.996	0.995-0.998	<0.001	1.003	1.000-1.007	0.079
CRP, mg/l	1.004	1.000-1.008	0.042	1.005	0.998-1.012	0.144
PCT, ng/ml	1.015	1.008-1.023	<0.001	1.018	1.003-1.032	0.015
PT, sec	1.117	1.042-1.198	0.002	0.944	0.823-1.083	0.410
FIB, g/l	0.880	0.791-0.979	0.019	0.847	0.685-1.049	0.128
ALT, U/l	1.001	1.000-1.003	0.108			
ALB, g/l	0.962	0.928-0.998	0.037	0.971	0.911-1.034	0.358
BUN, mmol/l	1.036	1.007-1.067	0.016	0.957	0.913-1.002	0.059
SOFA score	1.633	1.474-1.808	<0.001	1.465	1.248-1.719	<0.001
PITT	1.700	1.514-1.909	<0.001	1.437	1.204-1.716	<0.001

OR, odds ratio; CI, confidence interval; CVD, cardiovascular disease; T2DM, type 2 diabetes; WBC, white blood cells; PLT, platelets; CRP, C-reactive protein; PCT, procalcitonin; PT, prothrombin time; FIB, fibrinogen; ALT, alanine aminotransferase; ALB, albumin; BUN, blood urea nitrogen; SOFA, Sequential Organ Failure Assessment; PITT, Pitt bacteremia score.

Discussion

The present study identified key factors associated with complications in sepsis patients. For AKI, the SOFA score emerged as the independent predictor. Septic shock was independently associated with age, PCT level, PITT score and SOFA score. Similarly, for ARDS, independent factors included body weight and the SOFA score.

Culture-negative sepsis presents exceptional diagnostic challenges for clinicians and microbiologists, raising concerns about the accuracy and applicability of current sepsis definitions (25). Blood cultures may be negative for various reasons, such as sepsis or septic shock caused by atypical or non-culturable pathogens. Previous studies have indicated some subtle differences between blood culture-positive and culture-negative sepsis (26,27). While previous study suggests no statistically significant difference between culture-positive and culture-negative patients in terms of all-cause mortality, the need for mechanical ventilation, or renal replacement therapy requirements, or ICU length of stay (21). Another study observed longer hospital stays and extended mechanical ventilation in the culture-positive sepsis patients (27). The present study specifically focused on septic patients with positive blood cultures. This decision allowed it to narrow its scope and delve deeper into understanding specific aspects of sepsis management and outcomes.

Few comparative studies have investigated AKI or ARDS in patients with sepsis and either positive or negative blood cultures. A meta-analysis of 47 studies examining sepsis-related AKI found that a positive blood culture was an independent risk factor for AKI in patients with sepsis (OR=1.6; 95% CI: 1.35-1.89) (28). Similarly, another study confirmed that patients with positive cultures were more likely to develop ARDS than those with negative cultures (44.9% vs. 34.9%; P=0.013) (29). These findings suggest that complications are more common in patients with sepsis and positive blood cultures, highlighting the need for close, continuous monitoring.

AKI is a frequent complication in patients with sepsis, but its pathophysiological mechanisms are unclear. Funahashi *et al* (30). found that leukocyte infiltration was widespread in the renal tissues of mice with sepsis. Notably, the present study also found reduced Ly6B+ monocyte infiltration after miR-146a plasmid treatment. Previous studies have also implied that obesity significantly raises the risk of chronic kidney disease (31,32). The contribution of adipose tissue to renal injury in obesity is gaining prominence; however, the molecular mechanisms underlying these two conditions remain incompletely understood. Within the context of obesity, alterations in lipotoxicity and the secretory profile of adipose tissue drive inflammation, oxidative stress and fibrosis in the kidney, resulting in impaired renal function (33,34). Several studies have underlined the importance of weight loss in enhancing kidney function markers (35-37). Although the mechanisms underlying sepsis-associated AKI remain elusive, the inflammatory cascade characteristics of sepsis appear to play a crucial role in its pathogenesis (38). Traditional theories

Table V. Demographics and clinical data of all patient with or without ARDS.

Characteristic	Non-ARDS group	ARDS group	P-value
Sample size	110	273	-
Sex, male (%)	60 (54.5)	179 (65.6)	0.044
Age, year	62.34±19.22	61.33±16.29	0.604
Height, cm	163.54±7.97	164.98±7.57	0.097
Weight, kg	59.57±11.35	63.15±11.81	0.007
CVD, n (%)	39 (35.5)	103 (37.7)	0.677
T2DM, n (%)	29 (26.4)	57 (20.9)	0.244
WBC, 10^9/l	13.62±9.55	13.75±8.34	0.896
PLT, 10^9/l	191.57±115.22	156.11±114.75	0.007
CRP, mg/l	88.89±60.83	101.33±65.43	0.128
PCT, ng/ml	3.83 (0.64, 40.23)	5.09 (0.60, 34.90)	0.913
PT, sec	15.87±5.09	15.85±3.32	0.965
FIB, g/l	4.16±1.75	4.44±2.06	0.228
ALT, U/l	25.5 (14.25, 58.25)	37.5 (20.25, 86.50)	0.002
ALB, g/l	29.27±6.77	29.87±5.80	0.409
BUN, mmol/l	12.69±7.98	11.68±8.18	0.282
SOFA score	6.06±3.54	8.51±4.19	<0.001
PITT	3.47±2.89	3.77±2.93	0.363
Pathogens, n (%)			0.691
E. coli	24 (21.8)	54 (19.8)	
K. pneumoniae	16 (14.5)	52 (19.0)	
S. aureus	13 (11.8)	26 (9.5)	
Others	57 (51.8)	141 (51.6)	

ARDS, acute respiratory distress syndrome; CVD, cardiovascular disease; T2DM, type 2 diabetes; WBC, white blood cells; PLT, platelets; CRP, C-reactive protein; PCT, procalcitonin; PT, prothrombin time; FIB, fibrinogen; ALT, alanine aminotransferase; ALB, albumin; BUN, blood urea nitrogen; SOFA, Sequential Organ Failure Assessment; PITT, Pitt bacteremia score.

primarily attribute this condition to tissue hypoperfusion, leading to renal ischemia and acute tubular necrosis. However, AKI in patients with mild infection and early sepsis without cardiac output impairment challenges this view (39). The current understanding suggests that the mechanism is not solely hypoperfusion-dependent but involves multiple factors, including nephron inflammation, glomerular dysfunction due to ischemia-reperfusion injury, oxidative stress, tubular damage mediated by cytokines and chemokines and apoptosis in tubular and mesenchymal cells (40). Hence, the key contributors to sepsis-associated AKI may include impaired renal microvascular oxygenation, dysregulated immune responses and cellular dysfunction. The present study found that patients with AKI had a higher body weight, although the P-value was only 0.055. Additionally, it was observed that patients with AKI had prolonged PT, lower PLT counts and elevated PCT and CRP levels. Thus, the specific mechanisms underlying these associations require further research and exploration.

The primary mechanisms underlying ARDS in sepsis involve leukocyte and platelet recruitment, endothelial injury and oxidative stress. In the present study, the PLT and ALT levels were associated with the development of ARDS. Platelets are sensitive to environmental changes and are critical in immune response activation (41,42). Activated platelets release substances that aid in pathogen elimination and immune system activation. The interaction between CD40L and immune cell CD40 plays a role in the activation, proliferation and differentiation of helper T cells (43). In animal models, Zhang *et al* (44). discovered that cold-inducible RNA-binding protein can impede ICAM-1-mediated platelet-endothelial-neutrophil interactions in lung tissue, enhancing animal survival time and reducing hypoxia. Furthermore, Yu *et al* (45) observed that membranous vesicles and platelet particles released during platelet activation contribute to increased levels of TNF-α and IL-1β inflammatory factors in the alveoli. This triggers neutrophil infiltration in extravascular areas and results in acute lung injury. In sepsis, the release of numerous pro-inflammatory substances can lead to vascular endothelial dysfunction, increase pulmonary microvascular permeability and drive the development and progression of ARDS (46). Lung injury triggers the recruitment of innate immune cells, such as neutrophils and monocytes, to the alveolar space, causing damage to the alveolar epithelium and endothelium (47). This is because the host's immune response is not consistently hyperactive. In the later stages of the disease, owing to the immune system's negative feedback and exhaustion, a state of immune paralysis may develop (48). A complex interplay among the signaling pathways, inflammatory cytokines, recruited immune cells,

Table VI. Univariate and multivariate analysis for ARDS in sepsis patients.

	Univariate analysis			Multivariate analysis		
Variable	95% CI	P-value	95% CI	P-value	95% CI	P-value
Sex, male vs. female	0.630	0.402-0.989	0.045	0.842	0.409-1.735	0.642
Age, years	0.997	0.984-1.010	0.603			
Height, cm	1.025	0.996-1.055	0.098	0.991	0.945-1.039	0.705
Weight, kg	1.027	1.007-1.048	0.008	1.030	1.007-1.054	0.010
CVD, yes vs. no	1.103	0.696-1.749	0.677			
T2DM, yes vs. no	0.737	0.440-1.233	0.245			
WBC, 10^9/l	1.002	0.976-1.028	0.896			
PLT, 10^9/l	0.997	0.996-0.999	0.008	1.000	0.997-1.002	0.701
CRP, mg/l	1.003	0.999-1.007	0.129			
PCT, ng/ml	0.999	0.992-1.006	0.757			
PT, sec	0.999	0.942-1.059	0.965			
FIB, g/l	1.075	0.956-1.210	0.228			
ALT, U/l	1.001	0.999-1.003	0.179			
ALB, g/l	1.017	0.978-1.057	0.408			
BUN, mmol/l	0.985	0.959-1.012	0.283			
SOFA score	1.175	1.104-1.251	<0.001	1.177	1.095-1.265	<0.001
PITT	1.037	0.960-1.120	0.362			

ARDS, acute respiratory distress syndrome; CVD, cardiovascular disease; T2DM, type 2 diabetes; WBC, white blood cells; PLT, platelets; CRP, C-reactive protein; PCT, procalcitonin; PT, prothrombin time; FIB, fibrinogen; ALT, alanine aminotransferase; ALB, albumin; BUN, blood urea nitrogen; SOFA, Sequential Organ Failure Assessment; PITT, Pitt bacteremia score.

immune paralysis and the complement system may contribute to the cascade of inflammatory reactions underlying sepsis and the associated ARDS. However, in the multivariate analysis, only the SOFA score and weight were identified as independent factors associated with ARDS. This may be because the SOFA score includes PLT counts, which obscures the effect of PLTs on ARDS. The present study further underscored the crucial role of the SOFA score in the clinical management of sepsis.

The SOFA score also proved effective as an independent factor for septic shock, reinforcing its vital role in managing sepsis patients. In the present study, SOFA score was confirmed to be an independent relevant factor both in ARDS, AKI and septic shock. Covering six organ systems, the SOFA score provides a comprehensive assessment of organ functions, crucial for navigating the complex pathophysiology of sepsis (49-51). High clinical SOFA scores demand special attention for disease progression and outcomes.

The present study analyzed clinical variables to identify independent factors associated with sepsis-related complications such as AKI, ARDS and septic shock. It also adopted the widely recognized SOFA score to assess organ dysfunction, providing a basis for predicting outcomes. The aim was to offer practical insights by highlighting specific risk factors that clinicians can prioritize in treatment decisions, thereby enhancing the prospects for personalized care and improved patient outcomes.

The present study had some limitations. First, it is a retrospective study and all patients were enrolled from a single center, inevitably introducing bias. Second, data were sourced from electronic medical records. Relying on this method for demographic and treatment data carries the risk of potential incompleteness or inaccuracies. To address this issue, a two-author cross-validation approach was implemented for data extraction. Moreover, owing to objective constraints, the present study did not include the time from blood culture testing to the reporting of positive blood culture results in the analysis. Third, because of the retrospective design of The present study, it was only able to continuously include all eligible cases to ensure robust observations and a comprehensive analysis. Therefore, a prospective multicenter study is needed. The time from admission to blood culture results should be included as a variable to evaluate the risk factors related to complications in patients with sepsis.

The present study identified key risk factors associated with sepsis-related complications in patients with positive blood cultures. The results revealed that the SOFA score was an independent factor of AKI. Additionally, age, PCT level and the PITT and SOFA scores were identified as independent predictors of septic shock. The SOFA score and weight were identified as independent risk factors for ARDS. These findings underline the importance of the early identification and monitoring of these risk factors in sepsis management to improve patient outcomes.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

YH and HO designed the study. YH, CZ, YF and JZ analyzed and interpreted the data from patients with sepsis. YF and HO were major contributors in writing the manuscript. JZ and HO reviewed and edited the manuscript. YH and YF confirm the authenticity of all the raw data. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

The present retrospective study was approved by the Ethics Committee of The First Affiliated Hospital of Xiamen University (Fujian, China; approval no. 2022-037). Written informed consent was obtained from all patients upon admission.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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