ORIGINAL RESEARCH

A Nomogram for Diagnosing Ventilator-Associated Pneumonia Using Circulating Inflammation Indicators in ICU Patients

Jiajia Yang ^[],^{*}, Weiyuan Bao^{2,*}, Hongmei Wang¹, Jie Zhou³, Qiang Hu⁴, Ying Wang¹, Yuancheng Li⁵

¹Department of Infection Management, The Affiliated Suzhou Hospital of Nanjing Medical University, Suzhou Municipal Hospital, Gusu School, Nanjing Medical University, Suzhou, 215008, People's Republic of China; ²Department of Logistics Support, The Affiliated Suzhou Hospital of Nanjing Medical University, Suzhou Municipal Hospital, Gusu School, Nanjing Medical University, Suzhou, 215008, People's Republic of China; ³Intensive care unit, The Affiliated Suzhou Hospital of Nanjing Medical University, Suzhou Municipal Hospital, Gusu School, Nanjing Medical University, Suzhou, 215008, People's Republic of China; ⁴Department of Respiratory and Critical Care Medicine, The Affiliated Suzhou Hospital of Nanjing Medical University, Suzhou Municipal Hospital, Gusu School, Nanjing Medical University, Suzhou 215008, People's Republic of China; ⁴Department of Respiratory and Critical Care Medicine, The Affiliated Suzhou Hospital of Nanjing Medical University, Suzhou 215008, People's Republic of China; ⁵Institute of Dermatology, Chinese Academy of Medical Sciences and Peking Union Medical College, Jiangsu Key Laboratory of Molecular Biology for Skin Diseases and STIs, Nanjing, 210042, People's Republic of China

 $\ensuremath{^*\text{These}}$ authors contributed equally to this work

Correspondence: Ying Wang, Department of Infection Management, The Affiliated Suzhou Hospital of Nanjing Medical University, Suzhou Municipal Hospital, Gusu School, Nanjing Medical University, No. 242, Guangji Road, Suzhou, 215008, People's Republic of China, Email wangy830224@sina.com; Yuancheng Li, Institute of Dermatology, Chinese Academy of Medical Sciences and Peking Union Medical College, Jiangsu Key Laboratory of Molecular Biology for Skin Diseases and STIs, Nanjing, Jiangsu, 210042, People's Republic of China, Email ycli@pumcderm.cams.cn

Purpose: To construct a risk nomogram model of ventilator-associated pneumonia (VAP) patients with mechanical ventilation in the intensive care unit (ICU) based on peripheral blood inflammatory indicators and to evaluate its diagnostic value.

Patients and Methods: A matched 1:2 case: control study was conducted. Fifty-five mechanically ventilated patients with VAP and 113 patients without VAP were admitted to the ICU of Suzhou City Hospital with mechanical ventilation from January 2022 to June 2023 and were retrospectively included as study subjects. Clinical data and laboratory indicators of all patients were collected; the neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), lymphocyte to monocyte ratio (LMR), systemic immunoin-flammatory index (SII), and systemic inflammatory response index (SIRI) were calculated, and endotracheal aspirate (ETA) culture results of VAP patients were recorded.

Results: There were 61 pathogenic bacteria cultured in the ETA samples of 55 VAP patients, including 56 gram-negative bacilli, 4 grampositive cocci, and 1 fungus. The proportions of hypoproteinemia, procalcitonin (PCT), NLR, PLR, SII, and SIRI in VAP patients were significantly higher than those in non-VAP patients, with statistical significance (P < 0.05). Univariate and multivariate logistic regression analyses showed that hypoproteinemia, PCT, NLR, PLR, and SIRI were independent influencing factors for VAP in ICU patients (P < 0.05). The ROC curve analysis results showed that the area under the curve of the model for diagnosing VAP in ICU patients was 0.894 [(95% CI = 0.844–0.945), P < 0.001], and the sensitivity and specificity were 87.3% and 74.3%, respectively. The calibration curve shows that the model has good accuracy, and the clinical decision curve indicates that the clinical net benefit rate is higher when the model is used to diagnose VAP. **Conclusion:** Hypoproteinemia, PCT, NLR, PLR, and SIRI are the independent risk factors for VAP in ICU patients. The nomogram model constructed based on these easily accessible indicators may provide a promising tool for the early diagnosis of VAP in ICU patients, while requires further refinement for routine clinical use.

Keywords: ventilator-associated pneumonia, neutrophil to lymphocyte ratio, platelet to lymphocyte ratio, systemic inflammatory response index, nomogram model, intensive care unit

Introduction

Ventilator-associated pneumonia (VAP) is defined as pneumonia that occurs 48 hours after the establishment of artificial airways (endotracheal intubation or tracheotomy) and mechanical ventilation, including those who have used artificial

4615

airways for mechanical ventilation within 48 hours of pneumonia. It is the most common hospital-acquired infection in the intensive care unit (ICU).¹ The incidence of VAP in ICUs was found to be 2.5%–40% in a prospective research that was carried out in 36 countries.² A survey conducted in China revealed that the prevalence of VAP was 8.9 instances per 1000 mechanical ventilation days in 17,358 ICU patients across 46 institutions, and the incidence of VAP in patients on mechanical ventilation ranged from 9.7% to 48.4%.³ The incidence of VAP will not only result in increased costs for patients, hospitals, and the health care system due to extended periods of mechanical ventilation, ICU treatment, and hospitalization, but it will also raise the risk of atelectasis, ventilator-related lung injury, airway obstruction, and other complications.⁴ Furthermore, a delayed identification of VAP will make it more difficult to treat patients or encourage the abuse of broad-spectrum antibiotics, which would have a negative impact on their prognosis.⁵ In order to improve the patient's health and prognosis, early identification and treatment of VAP are therefore critical.

The microbiological finding of pathogenic microorganisms and the consistency of lung histopathology are usually considered as the gold standard for the diagnosis of VAP.⁶ However, this diagnostic procedure is invasive and hard to accept by patients and clinicians, and clinical use is tough. Currently, the diagnosis of VAP is mostly based on laboratory test results, clinical manifestations, and imaging examination. However, clinical features assessment are subjective, and the imaging findings are lack of specificity. Although the results of etiological tests provide a solid foundation for the diagnosis of VAP, they are not conducive to the early diagnosis of VAP since they take a lot of time. The clinical pulmonary infection score (CPIS) has been reported to be applicable in the diagnosis of VAP.⁷ However, some experts recommend against using CPIS for the routine diagnosis of VAP because it may lead to the overuse of antibiotics.^{8,9} Therefore, it is of great significance to further search for early diagnostic markers of VAP. It has been observed that inflammatory markers closely linked to infection, such as peripheral blood leukocyte count, high-sensitivity C-reactive protein (hs-CRP) and procalcitonin (PCT).¹⁰⁻¹² Neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), lymphocyte to monocyte ratio (LMR), systemic immune inflammatory index (SII), and systemic inflammatory response index (SIRI) are composite inflammatory indicators that have been widely concerned in recent years and have been confirmed to play a certain role in the diagnosis of a variety of infectious complications.^{13,14} These markers can be obtained directly or indirectly through peripheral blood routine or biochemical analysis, both of which have the benefits of being quick, simple, and non-invasive.

According to previous research,^{15,16} multi-inflammatory markers combinations are useful in diagnosing bacterial bloodstream infections, neonatal sepsis, and other conditions. The nomogram model is a visual model that is created by integrating various elements based on multivariate regression analysis, and can be used in clinical practice for prognosis evaluation, risk prediction, and disease diagnosis.^{17–19} Thus, to offer a novel concept for the early identification of VAP, this study examined the association between peripheral blood inflammatory markers and VAP in ICU patients and created a nomogram model.

Materials and Methods

Study Population

The retrospective investigation included patients on mechanical ventilation who were admitted to the ICU at Suzhou Hospital Affiliated to Nanjing Medical University between January 2022 and June 2023. The inclusion criteria were as follows: (1) the duration of mechanical ventilation exceeded 48 hours; (2) the age was ≥ 18 years old; (3) the clinical data and laboratory examination indexes were complete and available. The following patients were excluded: (1) pulmonary infection that developed prior to or within 48 hours of mechanical ventilation; (2) ventilator-assisted treatment prior to ICU admission; (3) non-pulmonary infection patients prior to data collection completion; and (3) patients with severe immune deficiency. VAP was defined based on the criteria in the Chinese Guidelines for the Diagnosis and Treatment of Hospital-acquired Pneumonia and Ventilator-associated Pneumonia in Adults (2018 edition).²⁰ To meet the criteria, a chest X-ray or CT scan must show a new or growing infiltrate, consolidation, or ground glass opacity, along with two or more of the following: (I) fever >38 °C; (II) purulent airway secretions; (III) peripheral white blood cell count >10×10⁹/L or <4×10⁹/L. On the basis of the above, VAP can be defined when the microbiological cultures of lower respiratory tract specimens are positive.

Finally, 55 patients with VAP were included in case group, and 113 patients without VAP matching the gender and age of the case group were included as the control group. This study was conducted in accordance with the Declaration of Helsinki and approved by The Affiliated Suzhou Hospital of Nanjing Medical University Ethical Review Committee (K-2024-097-H01). The written informed consent was waived because of the retrospective nature of our study. During the data collection, personally identifiable information such as names, addresses and phone numbers of the study participants were never recorded. The collected data were kept confidentially and used only for the purpose of the study.

Collection of Clinical Data and Laboratory Indicators

The medical records and laboratory system were examined. Gender, age, fever, hypoproteinemia, WBC, hs-CRP, PCT, neutrophil, lymphocyte, platelet, and monocyte counts of each subject were gathered, and NLR, PLR, LMR, SII, and SIRI were computed. NLR = neutrophil/lymphocyte, PLR = platelet/lymphocyte, LMR = lymphocyte/monocyte ratio, SII = platelet × neutrophil/lymphocyte, SIRI = neutrophil count × monocyte count/lymphocyte count. For the VAP group, the clinical data, laboratory examination values, and endotracheal aspirate (ETA) culture pathogen detection results were selected within 24 hours before diagnosis; while for the non-VAP group, the last examination values within 3 to 7 days after mechanical ventilation were selected. CPIS was calculated according to the criteria established by Pugin et al²¹ in 1991, utilizing the patient's body temperature, white blood cell count, airway secretions, oxygenation index, imaging characteristics, and the culture of airway secretions during the same time. A patient was deemed to have VAP when the score exceeded 6.

Statistical Analysis

All statistical analysis processes were processed by SPSS 27.0 software and R software (R4.1.2). For continuous variables conforming to normal distribution, mean \pm standard deviation was used for description, and a *t*-test was used for comparison between groups; for continuous variables not conforming to normal distribution, median and upper and lower quartiles were used for description, and a Mann–Whitney *U*-test was used for comparison between groups. Qualitative data were expressed as frequency and percentage, and the χ^2 -test was used for comparison between groups. The variance inflation factor (VIF) was used to assess multicollinearity between variables. Univariate and multivariate logistic regression analyses were used to assess the association between variables and the presence of VAP. Based on the independent risk factors screened by multivariate logistic regression analysis, a diagnostic model was constructed and a nomogram was drawn. The receiver operating characteristic (ROC) curve was used to evaluate the diagnostic value of the nomogram model, and the Bootstrap method was used to verify the nomogram by 1000 resampling, and the calibration curve was drawn to evaluate the accuracy of the model. The clinical validity of the model was assessed using clinical decision curve analysis. The difference was considered statistically significant when the two-sided P value was < 0.05.

Results

Incidence of VAP in ICU Patients and Distribution Characteristics of Pathogens

Of the 168 patients, 113 (67.26%) did not develop VAP, while 55 (32.74%) did. From the ETA samples of 55 patients diagnosed with VAP, 61 strains of pathogenic bacteria were identified, comprising 60 bacterial strains (98.36%) and 1 fungal strain (1.64%). Out of 60 bacterial strains, 56 (93.33%) were gram-negative bacilli and 4 (6.67%) were grampositive coccus, as demonstrated in Figure 1. There were 20 strains of Acinetobacter baumannii (33. 34%), 17 strains of Klebsiella pneumoniae (28. 33%), 17 strains of Pseudomonas aeruginosa (28. 33%), 3 strains of Staphylococcus aureus (5. 00%), 2 strains of Escherichia coli (3. 33%) and 1 strain of Streptococcus pneumoniae (1. 67%). The detection of 43 strains of multi-resistant bacteria was made up of 18 strains of carbapenem-resistant Acinetobacter baumannii (CRAB) (30.0%), 13 strains of carbapenem-resistant Klebsiella pneumoniae (CRKP) (21.67%), 10 strains of carbapenem-resistant Pseudomonas aeruginosa (CRPA) (16.67%), and 2 (3.33%) strains of methicillin-resistant Staphylococcus aureus (MRSA).

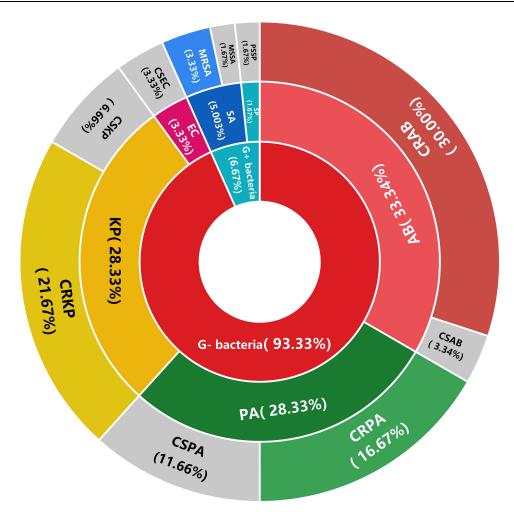


Figure I Distribution characteristics of bacterial strains.

Comparison of General Data and Peripheral Blood Inflammatory Indicators Between Patients with and without VAP

As shown in Table 1, there was no significant difference in gender, age, fever, WBC, hs-CRP, or LMR between patients with and without VAP (P > 0.05). However, the proportion of hypoproteinemia, PCT, NLR, PLR, SII, and SIRI in VAP patients was significantly higher than that in non-VAP patients, and the difference was statistically significant (P < 0.05).

Univariate and Multivariate Logistic Regression Analysis of VAP

Assign values to all variables (Table 2). Univariate logistic regression analysis revealed a significant correlation between the incidence of VAP and hypoproteinemia, PCT, NLR, PLR, SII, and SIRI (P < 0.05). Multivariate logistic regression analysis indicated that hypoproteinemia, PCT, NLR, PLR, and SIRI were the independent influencing factors of VAP (P < 0.05), as shown in Table 3.

ROC Curve Analysis of Each Variable for Diagnosis of VAP

Based on the ROC curve analysis and AUC values, the hypoproteinemia (AUC: 0.686, 95% CI: 0.600 ~ 0.773), PCT (AUC: 0.736, 95% CI: 0.651 ~ 0.822, cutoff value: 0.29 μ g/L), NLR (AUC: 0.708, 95% CI:0.608 ~ 0.808, cutoff value: 5.85), PLR (AUC: 0.603, 95% CI:0.502 ~ 0.704, cutoff value: 210.82) and SIRI (AUC:0.647, 95% CI: 0.650–0.764, cutoff value: 4.13) showed mediocre predictive ability for VAP in ICU patients with mechanical ventilation (Figure 2). Details of the optimal cutoff, sensitivity and specificity rates are demonstrated in Table 4.

Characteristics	Non-VAP Group (n=113)	VAP Group (n=55)	χ ² /t/Ζ	Р
Gender (male/female)	72/41	33/22	0.218	0.641
Age (years)	56.24±9.19	57.50±9.80	0.820	0.414
Fever (yes/no)	60/53	33/22	0.713	0.398
Hypoproteinemia (yes/no)	36/77	38/17	20.808	<0.001
WBC count (×10 ⁹ /L)	8.93 (5.90, 12.27)	11.60 (4.65, 14.89)	1.644	0.100
hs-CRP (mg/L)	23.94 (11.85, 39.26)	29.06 (17.10, 48.87)	1.529	0.126
PCT (µg/L)	0.17 (0.09, 0.27)	0.32 (0.21, 0.42)	4.964	<0.001
NLR	3.93 (3.00, 5.22)	6.21 (3.38, 8.86)	4.372	<0.001
PLR	174.34 (139.84, 210.68)	211.36 (138.92, 258.80)	2.165	0.009
LMR	4.55 (3.20, 6.04)	4.23 (2.58, 5.63)	1.497	0.134
SII	1377.59 (902.04, 1972.56)	2014.38 (1243.57, 2873.29)	3.047	0.002
SIRI	2.68 (1.82, 3.77)	4.42 (1.92, 5.96)	3.079	0.002
CPIS	5.73±1.72	7.87±1.60	7.756	<0.001

 Table I Comparison of General Data, Peripheral Blood Inflammatory Indicators and CPIS Between

 VAP and Non-VAP Patients

Table 2 Variable Assignments

Variables	Assignment		
Gender	Female=1; male=2		
Age (years)	Continuous variable		
Fever	No=1; Yes=2		
Hypoproteinemia	No=1; Yes=2		
WBC count (×10 ⁹ /L)	Continuous variable		
hs-CRP (mg/L)	Continuous variable		
PCT (µg/L)	Continuous variable		
NLR	Continuous variable		
PLR	Continuous variable		
LMR	Continuous variable		
SII	Continuous variable		
SIRI	Continuous variable		

Table 3 Univariate and Multivariate Logistic Regression Analysis of VAP Occurrence

Variables	Univariate Analysis		Multivariate Analysis			
	OR	95% CI	Р	OR	95% CI	Р
Gender	1.171	0.604~2.269	0.641			
Age (years)	1.015	0.980~1.050	0.411			
Fever	1.325	0.689~2.548	0.399			
Hypoproteinemia	5.913	2.920~11.973	<0.001	5.008	1.945~12.895	0.001
WBC count (×10 ⁹ /L)	1.068	0.999~1.141	0.052	1.092	0.993~1.201	0.069
hs-CRP (mg/L)	1.013	0.997~1.030	0.116			
PCT (µg/L)	1.927	1.477~2.514	<0.001	1.814	1.281~2.570	0.001
NLR	1.479	1.267~1.726	<0.001	1.575	1.287~1.928	<0.001
PLR	1.007	1.002~1.011	0.005	1.007	1.001~1.013	0.019
LMR	0.872	0.734~1.036	0.120			
SII	1.001	1.000~1.001	0.001	1.000	1.000~1.001	0.942
SIRI	1.524	1.240~1.873	<0.001	I.430	1.122~1.821	0.004

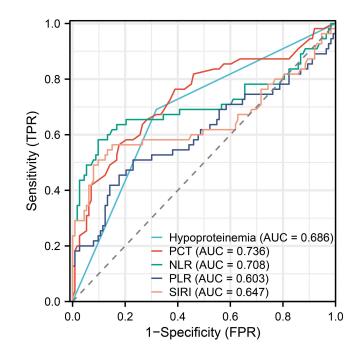


Figure 2 ROC curve analysis of each variable for diagnosis of VAP.

Establishment and Verification of Nomogram Model

The nomogram of VAP in ICU patients was drawn based on the five variables screened by multivariate logistic regression analysis, as shown in Figure 3A. According to the specific value of each variable, the total score was obtained by adding the scores of each variable to obtain the probability of VAP in ICU patients.

As shown in Figure 3B, the diagnostic value of the nomogram model was assessed by ROC curve analysis, yielding an AUC of 0.894 [(95% CI = 0.844–0.945), P < 0.001], a sensitivity of 87.3%, and a specificity of 74.3%. The AUC of the ROC curve for CPIS > 6 in diagnosing VAP was 0.822 [(95% CI = 0.758–0.887), P < 0.001]; sensitivity and specificity were 94.5% and 69.9%, respectively. The nomogram was internally verified using the Bootstrap technique. Figure 3C illustrates the calibration curve that was produced by repeatedly sampling the original data 1000 times. It revealed a mean absolute error of 0.028 and a probability of VAP in ICU patients that the model diagnosed was consistent with the actual probability, indicating a high degree of diagnostic accuracy.

Evaluation of the Clinical Validity of the Nomogram Model

The results of the decision curve analysis showed that the net benefit of the nomogram model constructed in this study was higher above the two critical lines, that is, the threshold value was > 10%, which was helpful for clinical decision-making, as illustrated in Figure 3D.

Variables	AUC	95% CI	Р	Cutoff Value	Sensitivity	Specificity
Hypoproteinemia	0.686	0.600 ~ 0.773	<0.001	-	69.1%	68.1%
PCT (µg/L)	0.736	0.651 ~ 0.822	<0.001	0.29	56.4%	82.3%
NLR	0.708	0.608 ~ 0.808	<0.001	5.85	58.2%	90.3%
PLR	0.603	0.502 ~ 0.704	0.030	210.82	50.9%	77.0%
SIRI	0.647	0.542 ~ 0.751	0.002	4.13	56.4%	85.0%

Table 4 ROC Curve Analysis of VAP Diagnosis for Each Variable

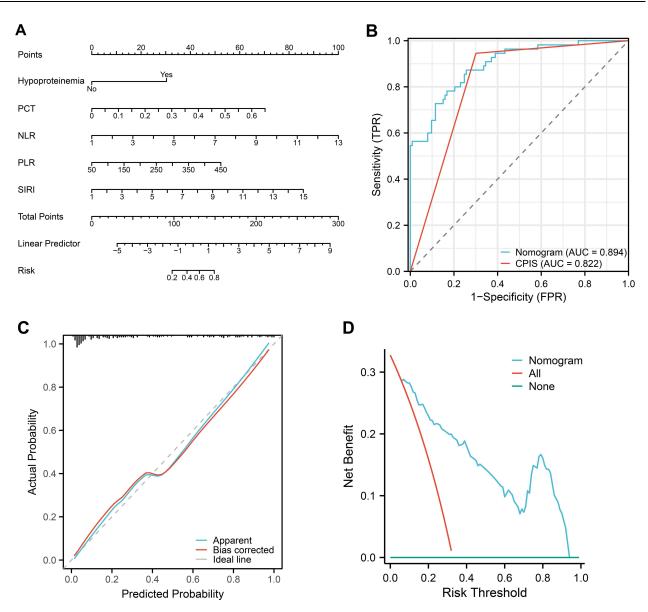


Figure 3 Establishment and verification of nomogram. (**A**) Nomogram for diagnosing VAP. An example of the application of the model: a patient had hypoproteinemia, with the PCT of 0.27 µg/L, the NLR of 3.42, the PLR of 191.85, and the SIRI of 2.71. The corresponding scores were 30, 28, 20, 18, and 10 points, respectively. Therefore, the total scores were 106 points, indicating that the estimated probability of developing VAP in this case was 30%.; (**B**) ROC curves analysis of nomogram and CPIS; (**C**) Calibration curve; (**D**) Clinical decision curve.

Discussion

VAP is the most prevalent hospital-acquired infection in the ICU, and it is strongly linked to the poor prognosis of patients.⁵ Gram-negative bacteria, such as Acinetobacter baumannii, Pseudomonas aeruginosa, Klebsiella pneumoniae, and Escherichia coli, account for the majority of frequent infections associated with VAP in China,²² and most of the pathogens are multidrug-resistant bacteria. In this investigation, similar outcomes were also attained. Gram-negative bacteria constituted the majority of the pathogenic bacteria found in VAP patients, with a comparatively high percentage of multi-drug resistant bacteria. When pathogenic bacteria invade the lungs, the lung tissue will cause local inflammatory reaction under the influence of infectious pathogenic bacteria and toxins secreted by pathogenic bacteria. This process stimulates alveolar monocytes and giant cells to release a variety of inflammatory mediators to further participate in the inflammatory response.²³ Albumin, WBC, hs-CRP, PCT, NLR, PLR, LMR, SII and SIRI are all related to the level of inflammation. In this study, we examined the correlation and diagnostic utility of these indicators with the incidence of

VAP in ICU patients. According to the findings, hypoproteinemia, PCT, NLR, PLR, and SIRI were independent risk factors for VAP. The nomogram model created by combining these indexes also demonstrated good diagnostic performance and clinical application value.

In this study, we discovered that we discovered that compared to non-VAP patients, the percentage of patients with VAP who had hypoproteinemia and their levels of PCT, NLR, PLR, SII, and SIRI were considerably greater. Subsequent univariate and multivariate logistic regression analysis results demonstrated that hypoproteinemia, PCT, NLR, PLR, and SIRI were independent risk factors for the development of VAP in ICU patients. Serum albumin levels less than 30 g/L are considered hypoproteinemia in patients and are suggestive of malnourishment and compromised immune function.²⁴ Albumin has antioxidant properties and may be involved in scavenging oxygen radicals in the pathogenesis of inflammatory diseases. A previous study have shown that hypoproteinemia is closely associated with the development of infections and inflammation, and can indicate the extent to which an organism is under inflammatory stress.²⁵ When an organism suffers from inflammation, capillary permeability rises and plasma albumin extravasates, causing oedema in the interstitial space between tissues and an increase in albumin's volume of distribution. In addition, the inflammatory condition shortens albumin's half-life, resulting in a decrease in albumin levels overall.²⁶ According to Boh et al²⁷ individuals with hypoalbuminemia were far more likely than those with normal albumin levels to get pneumonia and surgical site infections. PCT is an immunoreactive protein, and is normally found in very low concentrations in plasma under normal physiological conditions. However, when the body is infected with bacteria, the cells quickly secrete PCT to counteract the bacterial endotoxin, which results in a marked increase in PCT concentration in plasma.²⁸ According to multiple studies,²⁹⁻³¹ PCT is a significant predictor of bacterial infection and infection severity. Furthermore, a recent study found that the use of PCT showed superior sensitivity and specificity than WBC and CRP in identifying bacterial infections, which may be attributed to the longer biological half-life of PCT.³²

Recent substantial researches have demonstrated the value of composite inflammatory indicators, including NLR, PLR, and SIRI, in the detection of lung infections, bloodstream infections, and urinary tract infections.^{12,14,33,34} Neutrophils and lymphocytes have distinct functions in the body's inflammatory response; the former are inflammation activators, while the latter are inflammation regulators.³⁵ Since the balance between neutrophils and lymphocytes has been upset during the body's early inflammatory reaction, NLR might more precisely reflect the inflammatory response of the organism. Platelets are produced by distinct isoploid mature megakaryocytes, which are the source of several inflammatory mediators, thus platelet counts are raised before inflammatory mediator levels rise as a result of a sharp rise in megakaryocyte population. Therefore, in the early stage of inflammation, PLR has a more pronounced response to the emergence of inflammation in the body. A study by Xie et al³³ reported that elevated NLR in mechanically ventilated patients with malignant tumours significantly increased the risk of VAP. Additionally, a study by Chen et al¹² revealed that high NLR and PLR had a prognostic value for a bad 28-day prognosis for patients and might considerably increase the likelihood of VAP in critically ill patients. SIRI is a unique composite inflammatory biomarker based on neutrophil, monocyte, and lymphocyte counts that can comprehensively reflect the inflammatory status of the body. Previous research has validated that SIRI has good efficacy in the early diagnosis of catheter-associated bloodstream infections in haemodialysis patients.¹⁴ Furthermore, a research by Wang et al³⁶ demonstrated a correlation between SIRI and lung infection rates in cerebral hemorrhage patients. Another study indicated that combining SIRI with other inflammatory indicators could enhance the diagnostic usefulness of periprosthetic joint infections, but utilizing SIRI alone had a limited diagnostic impact.¹³

The findings of this study showed that although hypoproteinemia, PCT, NLR, PLR and SIRI were closely related to the occurrence of VAP in ICU patients, their ability to independently diagnose VAP in these patients was only mediocre. While PCT, NLR, and SIRI had good specificity (82.3%, 90.3%, and 85.0%, respectively) in independently identifying VAP, their sensitivity was relatively poor (all below 60%). In order to further visualize the diagnostic effect of the combined application of multiple variables, we further created a nomogram model based on these indicators. The nomogram model's sensitivity and specificity for identifying VAP in ICU patients were 87.3% and 74.3%, respectively, according to ROC curve analysis. Although the specificity of the diagnosis of VAP is slightly lower than that of each index alone, the sensitivity of the model is significantly improved, and it has a good degree of differentiation. Further internal validation results show that the model has good accuracy, and the results of clinical decision curve analysis suggest that the clinical net benefit rate of using this model to diagnose VAP is higher.

We excluded patients who had developed other site infections from the non-VAP group when screening subjects. The inflammatory markers researched in this study are not specific to pulmonary infection and may also be elevated in other systemic infections. This could potentially explain why the specificity of the nomogram model in diagnosing VAP is relatively ordinary. However, not excluding patients with other infections from the non-VAP group may limit the model's sensitivity to diagnose VAP. In practical applications, physicians need to weigh sensitivity and specificity based on the specific patient's situation. High sensitivity means fewer patients are missed, which is particularly important for the diagnosis of VAP patients, as missed diagnosis can lead to worsening of the condition or improper treatment. High specificity means a lower rate of misdiagnosis, which helps to avoid unnecessary treatment and waste of medical resources. We think that for patients with suspected VAP, higher sensitivity may need to be prioritized to ensure that the diagnosis is not missed. However, the specificity should not be too low; otherwise, the number of misdiagnosed patients will increase, leading to the increase in unnecessary use of antibiotics. In this study, the nomogram model had lower sensitivity (87.3% vs 94.5%) but higher specificity (74.3% vs 69.9%) than CPIS in diagnosing VAP in ICU patients. Compared to some parts of CPIS, the indicators in the nomogram model created in this study are easier to get, less expensive, and more doable for clinicians to use. Due to the low specificity of CPIS in the diagnosis of VAP in ICU patients, it may lead to excessive use of antibiotics and have more adverse consequences.³⁷ So some guidelines have not recommended the application of CPIS in the diagnosis of VAP or hospital-acquired pneumonia (HAP).^{8,9,38}

Limitations and Future Perspectives

This study has certain limitations. Firstly, selection bias and limited generalizability of the findings are unavoidable in this study due to the single-center design and relatively small sample size of the study. Secondly, some patients may have received antibiotics before admission to the ICU, and the kind and quantity of antibiotics that patients take may have an impact on the peripheral blood inflammatory markers that were examined. Thirdly, because this study is a retrospective survey, patients with incomplete examination data were excluded during the patient's admission process. Conversely, patients with more severe disease and a higher risk of VAP frequently had more complete examination data and were therefore more likely to be included in the study, which may resulted in a certain amount of bias. Finally, although internal validation was performed, external validation was lacking since no external data were available for us. Despite some limitations of our study, it does not prevent the value of this model in helping clinicians identify patients with VAP. In the future, we will further conduct multicenter, large-sample, and prospective studies and include more influencing factors, such as the use of antibiotics and dynamic changes in inflammatory indicators, to obtain more accurate and innovative results. In addition, to expand the application of the model in clinical practice, an online calculator would be considered to be established in the future.

Conclusion

In summary, hypoproteinemia, PCT, NLR, PLR, and SIRI are independent risk factors for the occurrence of VAP in ICU patients. The nomogram model constructed based on these easily accessible indicators may provide a promising tool for the early diagnosis of VAP in ICU patients, while requires further refinement for routine clinical use.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

Acknowledgments

Jiajia Yang and Weiyuan Bao are co-first authors for this study. We are appreciative of the study participants as well as the help from the physicians.

Funding

This work was supported by the Suzhou Science and Technology Project (SKY2023205) and Suzhou infection management special research project (SZSYYXH-2023-YB7).

Disclosure

The authors declare that there are no conflicts of interest in this work.

References

- 1. Rangelova V, Kevorkyan A, Raycheva R, Krasteva M. Ventilator-Associated Pneumonia in the Neonatal Intensive Care Unit-Incidence and Strategies for Prevention. *Diagnostics*. 2024;14(3):240. doi:10.3390/diagnostics14030240
- 2. Rosenthal VD, Bijie H, Maki DG, et al. International Nosocomial Infection Control Consortium (INICC) report, data summary of 36 countries, for 2004-2009. Am J Infect Control. 2012;40(5):396–407. doi:10.1016/j.ajic.2011.05.020
- 3. Gao X, Hu B, Cui Y, et al. Multicenter prospective surveillance of the incidence of ventilator-associated pneumonia in 46 hospitals in mainland China. *Chin J Infect Control*. 2015;8:540–543. doi:10.3969/j.issn.1671-9638.2015.08.008
- 4. Mohamed HT, Farhan Alenezi Sr WA, Alanzi MAA, Saleh Alsuqub FI, Salem Alhazmi SA, Mohammed Alhazmi OM. Prevalence of Ventilator-Associated Pneumonia in Children Admitted to Pediatric Intensive Care Units in the Middle East: a Systematic Review. Cureus. 2023;15(12): e51230. doi:10.7759/cureus.51230
- 5. Gan W, Chen Z, Tao Z, Li W. Constructing a Nomogram Model to Estimate the Risk of Ventilator-Associated Pneumonia for Elderly Patients in the Intensive Care Unit. *Adv Respir Med.* 2024;92(1):77–88. doi:10.3390/arm92010010
- 6. Martin-Loeches I. Current Concepts in Community and Ventilator Associated Lower Respiratory Tract Infections in ICU Patients. *antibiotics*. 2020;9(7):380. doi:10.3390/antibiotics9070380
- Gunalan A, Sistla S, Sastry AS, Venkateswaran R. Concordance between the National Healthcare Safety Network (NHSN) Surveillance Criteria and Clinical Pulmonary Infection Score (CPIS) Criteria for Diagnosis of Ventilator-associated Pneumonia (VAP). *Indian J Crit Care Med.* 2021;25 (3):296–298. doi:10.5005/jp-journals-10071-23753
- Erb CT, Patel B, Orr JE, et al. Management of Adults with Hospital-acquired and Ventilator-associated Pneumonia. Ann Am Thorac Soc. 2016;13 (12):2258–2260. doi:10.1513/AnnalsATS.201608-641CME
- 9. Leone M, Bouadma L, Bouhemad B, et al. Brief summary of French guidelines for the prevention, diagnosis and treatment of hospital-acquired pneumonia in ICU. Ann Intensive Care. 2018;8(1):104. doi:10.1186/s13613-018-0444-0
- 10. Song YY, Zhang B, Gu JW, Zhang YJ, Wang Y. The predictive value of procalcitonin in ventilator-associated pneumonia after cardiac valve replacement. *Scand J Clin Lab Invest.* 2020;80(5):423–426. doi:10.1080/00365513.2020.1762242
- 11. Zhang P, Xia G, Dai L, Cheng Y, Wang Z. Laryngoscope-assisted and cotton ball wiping methods in prevention of oral and pulmonary infection in patients receiving mechanical ventilation and the influence on hypersensitive C-reactive protein and procalcitonin. *Exp Ther Med.* 2019;18 (1):531–536. doi:10.3892/etm.2019.7614
- 12. Chen Y, Liu X. The value of serum PCT, NLR, PLR and CPIS score in the diagnosis and short-term prognosis of ventilator-associated pneumonia in critically ill patients. *Chin J Hospital Infect*. 2023;33(13):1935–1939. doi:10.11816/cn.ni.2023-221452
- 13. Chen W, Dai Z, Yang H. To evaluate the value of systemic immune inflammation index and systemic inflammatory response index in the diagnosis of periprosthetic joint infection. *Chin J Exp Surg.* 2023;40(8):1630–1633. doi:10.3760/cma.j.cn421213-20230117-01017
- Yang J, Wang H, Hua Q, Wu J, Wang Y. Diagnostic Value of Systemic Inflammatory Response Index for Catheter-Related Bloodstream Infection in Patients Undergoing Haemodialysis. J Immunol Res. 2022;2022:7453354. doi:10.1155/2022/7453354
- 15. He X, He Z, Liu Y, et A. The value of a nomogram model based on peripheral blood inflammatory markers in the early diagnosis of neonatal sepsis. *Lb Med.* 2022;37(10):921–927. doi:10.3969/j.issn.1673-8640.2022.010.003
- Liu J, Cai X, Huang L. Comparative analysis and combined application evaluation of several inflammatory markers in the prediction and diagnosis of bacterial bloodstream infection. *Chin J Antibiot*. 2022;47(8):849–853. doi:10.3969/j.issn.1001-8689.2022.08.016
- 17. Cheng H, Li J, Wei F, et al. A risk nomogram for predicting prolonged intensive care unit stays in patients with chronic obstructive pulmonary disease. *Front Med Lausanne*. 2023;10:1177786. doi:10.3389/fmed.2023.1177786
- Pei Y, Huang Y, Pan X, et al. Nomogram for predicting 90-day mortality in patients with Acinetobacter baumannii-caused hospital-acquired and ventilator-associated pneumonia in the respiratory intensive care unit. J Int Med Res. 2023;51(3):3000605231161481. doi:10.1177/03000605231161481
- Zhang X, Shen ZL, Duan XZ, et al. Postoperative Pneumonia in Geriatric Patients With a Hip Fracture: incidence, Risk Factors and a Predictive Nomogram. Geriatr Orthop Surg Rehabil. 2022;13:21514593221083824. doi:10.1177/21514593221083824
- 20. Shi Y, Huang Y, Zhang TT, et al. Chinese guidelines for the diagnosis and treatment of hospital-acquired pneumonia and ventilator-associated pneumonia in adults (2018 Edition). J Thorac Dis. 2019;11(6):2581–2616. doi:10.21037/jtd.2019.06.09
- Pugin J, Auckenthaler R, Mili N, Janssens JP, Lew PD, Suter PM. Diagnosis of ventilator-associated pneumonia by bacteriologic analysis of bronchoscopic and nonbronchoscopic "blind" bronchoalveolar lavage fluid. Am Rev Respir Dis. 1991;143(5):1121–1129. doi:10.1164/ajrccm/143.5_Pt_1.1121
- 22. Xie J, Yang Y, Huang Y, et al. The Current Epidemiological Landscape of Ventilator-associated Pneumonia in the Intensive Care Unit: a Multicenter Prospective Observational Study in China. *Clin Infect Dis*. 2018;67(suppl_2):S153-s161. doi:10.1093/cid/ciy692
- 23. Chukamnerd A, Saipetch N, Singkhamanan K, et al. Association of biofilm formation, antimicrobial resistance, clinical characteristics, and clinical outcomes among Acinetobacter baumannii isolates from patients with ventilator-associated pneumonia. *Clin Respir J.* 2024;18(1):e13732. doi:10.1111/crj.13732
- 24. Zhou H, Wang H, Ye Q, et A. Construction of a risk prediction model for ventilator-associated pneumonia in neurosurgical ICU patients. *Nursing Research*. 2022;36(23):4174–4180. doi:10.12102/j.issn.1009-6493.2022.23.007
- 25. Khan AM, Aslam SM. Comparison of qSOFA Score, SIRS Criteria, and SOFA Score as predictors of mortality in patients with sepsis. *Ghana Med* J. 2022;56(3):191–197. doi:10.4314/gmj.v56i3.9
- 26. Paul BR, De UK, Sarkar VK, et al. Effect of systemic inflammatory response syndrome on thrombocytogram, acute phase proteins, electrolytes, acid-base indices and cytokine expression in naturally canine parvovirus infected dogs. *Vet Immunol Immunopathol*. 2023;259:110598. doi:10.1016/j.vetimm.2023.110598
- Bohl DD, Shen MR, Kayupov E, Della Valle CJ. Hypoalbuminemia Independently Predicts Surgical Site Infection, Pneumonia, Length of Stay, and Readmission After Total Joint Arthroplasty. J Arthroplasty. 2016;31(1):15–21. doi:10.1016/j.arth.2015.08.028

- Qin S, He X, Wang H. The value of peripheral blood PCT IL-17 and sTREM-1 detection in the early diagnosis of ventilator-associated pneumonia. Emergency Medicine in China. 2017;37(5):427–432. doi:10.3969/j.issn.1002-1949.2017.05.010
- Cui N, Zhang YY, Sun T, Lv XW, Dong XM, Chen N. Utilizing procalcitonin, C-reactive protein, and serum amyloid A in combination for diagnosing sepsis due to urinary tract infection. *Int Urol Nephrol.* 2024;56(7):2141–2146. doi:10.1007/s11255-024-03959-0
- 30. Li D, Zhu Y. Predictive Value of Systemic Immune Inflammation Index in Septic Patients with Acute Kidney Injury. Arch Esp Urol. 2024;77 (1):67–71. doi:10.56434/j.arch.esp.urol.20247701.9
- 31. Zaki HA, Bensliman S, Bashir K, et al. Accuracy of procalcitonin for diagnosing sepsis in adult patients admitted to the emergency department: a systematic review and meta-analysis. *Syst Rev.* 2024;13(1):37. doi:10.1186/s13643-023-02432-w
- 32. Kott M, Bewig B, Zick G, et al. Elevation of procalcitonin after implantation of an interventional lung assist device in critically ill patients. *Asaio J*. 2014;60(2):249–253. doi:10.1097/mat.0000000000041
- 33. Xie Z, Wei B, Li Y. A nested case-control study on the association between neutrophil-to-lymphocyte ratio in malignant tumors and ventilator-associated pneumonia. *Chinese Critical Care Emergency Medicine*. 2021;33(2):165–168. doi:10.3760/cma.j.cn121430-20200429-00350
- 34. Asik Z. The Role of the NLR and PLR in Urinary Tract Infection. Clin Lab. 2021;67(10):133. doi:10.7754/Clin.Lab.2021.210133
- 35. Manchal N, Siriwardena M, Hay K, Shekar K, McNamara JF. Assessment of the Clinical Pulmonary Infection Scores for prediction of ventilator associated pneumonia in patients with out of hospital cardiac arrest. *Infect Dis Health*. 2021;26(1):48–54. doi:10.1016/j.idh.2020.09.001
- 36. Wang RH, Wen WX, Jiang ZP, et al. The clinical value of neutrophil-to-lymphocyte ratio (NLR), systemic immune-inflammation index (SII), platelet-to-lymphocyte ratio (PLR) and systemic inflammation response index (SIRI) for predicting the occurrence and severity of pneumonia in patients with intracerebral hemorrhage. *Front Immunol.* 2023;14:1115031. doi:10.3389/fimmu.2023.1115031
- Luyt CE, Chastre J, Fagon JY. Value of the clinical pulmonary infection score for the identification and management of ventilator-associated pneumonia. *Intensive Care Med.* 2004;30(5):844–852. doi:10.1007/s00134-003-2125-0
- Leone M, Bouadma L, Bouhemad B, et al. Hospital-acquired pneumonia in ICU. Anaesth Crit Care Pain Med. 2018;37(1):83–98. doi:10.1016/j. accpm.2017.11.006

Journal of Inflammation Research

Dovepress Taylor & Francis Group

Publish your work in this journal

The Journal of Inflammation Research is an international, peer-reviewed open-access journal that welcomes laboratory and clinical findings on the molecular basis, cell biology and pharmacology of inflammation including original research, reviews, symposium reports, hypothesis formation and commentaries on: acute/chronic inflammation; mediators of inflammation; cellular processes; molecular mechanisms; pharmacology and novel anti-inflammatory drugs; clinical conditions involving inflammation. The manuscript management system is completely online and includes a very quick and fair peer-review system. Visit http://www.dovepress.com/testimonials.php to read real quotes from published authors.

Submit your manuscript here: https://www.dovepress.com/journal-of-inflammation-research-journal