Infection and Drug Resistance

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ORIGINAL RESEARCH

LASSO-Based Machine Learning Algorithm for Prediction of PICS Associated with Sepsis

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Introduction: This study aims to establish a comprehensive, multi-level approach for tackling tropical diseases by proactively anticipating and managing Persistent Inflammation, Immunosuppression, and Catabolism Syndrome (PICS) within the initial 14 days of Intensive Care Unit (ICU) admission. The primary objective is to amalgamate a diverse array of indicators and pathogenic microbial data to pinpoint pivotal predictive variables, enabling effective intervention specifically tailored to the context of tropical diseases.

Methods: A focused analysis was conducted on 1733 patients admitted to the ICU between December 2016 and July 2019. Utilizing the Least Absolute Shrinkage and Selection Operator (LASSO) regression, disease severity and laboratory indices were scrutinized. The identified variables served as the foundation for constructing a predictive model designed to forecast the occurrence of PICS.

Results: Among the subjects, 13.79% met the diagnostic criteria for PICS, correlating with a mortality rate of 38.08%. Key variables, including red-cell distribution width coefficient of variation (RDW-CV), hemofiltration (HF), mechanical ventilation (MV), Norepinephrine (NE), lactic acidosis, and multiple-drug resistant bacteria (MDR) infection, were identified through LASSO regression. The resulting predictive model exhibited a robust performance with an Area Under the Curve (AUC) of 0.828, an accuracy of 0.862, and a specificity of 0.977. Subsequent validation in an independent cohort yielded an AUC of 0.848.

Discussion: The acquisition of RDW-CV, HF requirement, MV requirement, NE requirement, lactic acidosis, and MDR upon ICU admission emerges as a pivotal factor for prognosticating PICS onset in the context of tropical diseases. This study highlights the potential for significant improvements in clinical outcomes through the implementation of timely and targeted interventions tailored specifically to the challenges posed by tropical diseases.

Keywords: sepsis, persistent inflammation immunosuppression catabolism syndrome, LASSO regression, mortality, predictive model

Introduction

Sepsis is a life-threatening organ dysfunction caused by the dysregulated response of the body to infection. A subset of sepsis patients would undergo a complex transition into chronic critical illness (CCI), marked by persistent inflammation, immune anomalies, and metabolic dysfunction syndrome, collectively termed Persistent Inflammation, Immunosuppression, and Catabolism Syndrome (PICS).[1] PICS is notably prevalent among specific demographics, including the elderly, traumatized, and postoperative patients, presenting heightened morbidity and mortality rates.[2] Advances in life-saving interventions for

Received: 10 April 2024
Accepted: 20 June 2024
Published: 1 July 2024

sepsis and trauma have significantly reduced early morbidity and mortality rates, contributing to the emergence of CCI and PICS as ongoing healthcare challenges.[3] Patients grappling with PICS encounter substantial hurdles, encompassing rapid weight loss, compromised nutritional status, prolonged immunosuppression, and recurrent nosocomial infections, leading to extended hospitalizations and escalated mortality rates.[4] A noteworthy study illuminated a concerning trend in mortality rates following severe trauma. While in-hospital mortality showed a steady decline over 13 years, the subsequent three-year mortality rate nearly tripled that figure Factors such as advanced age and discharge to home, rather than a rehabilitation facility, emerged as robust predictors of long-term mortality, underscoring the complexity and implications of chronic critical illness.[5] Despite its clinical significance, epidemiological data on PICS remains limited. One investigation estimated the incidence of PICS at approximately 2.5%, highlighting the need for a more comprehensive understanding of its prevalence and impact on diverse patient populations.[6] Notably, the occurrence of PICS exhibits regional and intensive care unit (ICU) variability, with the occurrence rate among polytrauma patients measured at 4.7 per 1000.[7] Approximately 50% of septic patients in the ICU eventually develop PICS, emphasizing the critical need for predictive models and intervention strategies.[8] Diagnostic criteria for PICS involve ICU stays exceeding 14 days, persistent inflammatory response indicated by C-reactive protein (CRP) levels >1.5 mg/dL, immunosuppression characterized by total peripheral blood lymphocyte count <0.8 × 10^9/L, and catabolic disorders identified by serum albumin levels <30 g/L, creatinine/height index <80%, and body weight loss exceeding 10% during hospitalization or a body mass index <18 kg/m2.[9] While the threshold for C-reactive protein has been debated, a diagnostic cutoff of >1.5 mg/dL was selected, aligned with other PICS markers, for retrospective patient assessment.[10] Indicators collected upon ICU admission, along with information about causative pathogens, serve as the foundation for predicting PICS following a 14-day hospital stay. This comprehensive approach aims to identify key predictive factors amenable to intervention, emphasizing the urgency of refining clinical strategies to address the complex trajectory of patients evolving into chronic critical illness, particularly in the context of tropical diseases prevalent in diverse populations.

Materials and Methods

Study Design and Ethical Considerations

The study was conducted per the guidelines of the Declaration of Helsinki. This retrospective investigation, spanning from December 2016 to July 2019, sourced patient data from the Department of Critical Care at Shenzhen People's Hospital. Ethical clearance, obtained from the Medical Research Ethics Committee, Shenzhen People's Hospital communicated through letter no LL-KY-2019508, included a waiver for signed informed consent forms, in accordance with the Helsinki Declaration.

Patient Selection and Diagnostic Criteria

Aligned with Sepsis-3.0 diagnostic criteria, a meticulous sepsis screening process was conducted, integrating chest X-ray, lung CT scans, and assessment for abdominal, biliary, urinary tract, and bloodstream infections. Inclusion criteria comprised specific parameters for sepsis diagnosis. PICS diagnosis required meeting specific criteria after an ICU stay exceeding 14 days. Patients devoid of observable lesions underwent screening based on their receipt of carbapenem antibiotics upon ICU admission. Clinical and laboratory findings were evaluated, encompassing: 1) Respiratory rate surpassing 20 breaths per minute or necessitating mechanical ventilation, where patients requiring mechanical ventilation due to respiratory failure were categorized under "MV requirement"; 2) Serum creatinine levels exceeding 144 μmol/L or necessitating blood purification therapy, with patients undergoing hemofiltration classified as "HF requirement"; 3) Total bilirubin levels surpassing 34.1 μmol/L; 4) Mean arterial pressure (MAP) falling below 60 mmHg or requiring norepinephrine as a vasopressor to sustain blood pressure in instances of circulatory failure, with patients undergoing norepinephrine treatment identified as "NE requirement"; 5) Platelet count dropping below 100 × 10^9/L. Patients with documented infections and/or utilization of carbapenem antibiotics, along with a minimum of two clinical and laboratory findings, were categorized as having sepsis and were included in the study. Furthermore, a white blood cell counts exceeding 12 × 10^9/L or falling below 4 × 10^9/L served as an additional diagnostic criterion for sepsis. A patient who remained in the ICU for over 14 days and concurrently met the following three criteria could be diagnosed with Persistent Inflammatory Immunosuppression Catabolic Syndrome (PICS): (1) C-reactive protein level surpassing

150 mg/L; (2) Lymphocyte count below $0.8x10^9$/L; (3) Serum albumin level below 30g/L. Lactacidosis was defined as lactate levels exceeding 1.5 mmol/L.

Intervention Strategies and Observational Parameters

Upon ICU admission, a comprehensive approach was adopted, including blood cultures, empirical antimicrobial therapy, and dynamic adjustments based on organ failure severity. Subsequent adjustments were made to antibiotic administration, other pharmacological interventions, and organ support strategies in response to alterations in patient condition and microbial cultures. The Sequential Organ Failure Assessment (SOFA) score was computed using the amassed data, capturing diverse parameters including elevated lactate levels (≥1.5 mmol/L), positive cultures indicative of multidrug-resistant microorganisms, duration of ICU stays (measured in days), mechanical ventilation duration (measured in hours), and ultimate clinical outcomes (recovery or mortality). Moreover, additional laboratory indicators upon ICU admission were recorded.

Statistical Analysis

In addition to conventional statistical methods, technical advancements were employed. LASSO regression identified prognostic risk factors, ensuring model parsimony and enhanced interpretability. ROC curve analysis, accompanied by bootstrap resampling, assessed the model's robustness. Optimal threshold determination and diagnostic metrics calculation were enhanced through rigorous computational methods.

Technical Advancements

Beyond traditional statistical analyses, the study leveraged cutting-edge techniques. LASSO regression, a machine learning approach, facilitated the identification of pivotal prognostic factors, enhancing model accuracy. Computational tools, such as Empower Stats software 4.2 (R language) X&Y Solutions, Inc., Boston, MA, USA, provided a sophisticated platform for efficient data analysis, ensuring statistical rigor. To investigate clinical and laboratory indicators manifesting discrepancies between the two cohorts, the LASSO regression method was applied. The objective was to pinpoint noteworthy prognostic risk factors in sepsis, construct a predictive model, and gauge its predictive efficacy through receiver operating characteristic (ROC) curve analysis. The area under the curve (AUC) of the risk factor model for mortality prognosis was computed, accompanied by the confidence interval. Significance testing was executed utilizing non-parametric bootstrap resampling with 500 iterations. The optimal threshold was determined for assessing diagnostic specificity, sensitivity, accuracy, positive and negative likelihood ratios, as well as positive and negative predictive values. Discrimination and calibration analyses were performed to assess the predictive potential of the developed model. Furthermore, decision curve analyses (DCA) were harnessed to corroborate the clinical utility of the nomogram. Statistical significance was defined as $p < 0.05$. Data analysis and statistical procedures were conducted employing Empower Stats software 4.2 (R language).

Results

Baseline Demographic Comparison

A total of 1733 patients fulfilled the diagnostic criteria of sepsis 3.0 and were encompassed in the study, with 239 meeting the criteria for PICS diagnosis. Within this cohort, 1013 were male and 720 were female, with an average age of 61.76 ± 20.34 years. Primary diagnoses predominantly involved pulmonary infections, while additional infectious sites encompassed the abdominal cavity, biliary tract, urinary tract, and septic conditions. The prevalence of drug-resistant bacterial infections within the PICS group exhibited a substantial elevation compared to the non-PICS group ($p<0.001$). Analysis of severity between the two patient groups unveiled significantly heightened rates of MV requirement, NE requirement, HF requirement, and hyperlactatemia within the PICS group relative to the non-PICS group ($p<0.001$). Examination of laboratory indicators disclosed that patients in the PICS cohort displayed elevated RDW-CV levels (16.67 ± 3.32 vs 15.29 ± 2.94, $p<0.001$), decreased CHOL and HDL levels, and extended APTT durations when compared to the non-PICS counterparts. Detailed comparisons of these indicators are tabulated in Table 1. From a clinical outcomes perspective, the mortality rate within the PICS group surpassed that of the non-PICS group (38.08% vs 19.48%, $p<0.001$), concomitant with prolonged ICU stays and MV durations ($p<0.001$).

Table 1 Demographic Characteristics of the Patients

	Non-PICS (n=1494) (%)	PICS (N=239) (%)	p-value
Gender			<0.001
Male (n, %)	847 (56.69)	166 (69.46)	
Female (n, %)	647 (43.31)	73 (30.54)	
Age, year, (M±Sd)	61.33 (20.42)	64.41 (19.62)	0.029
Diagnosis			
Pneumonia (n, %)	949 (63.52)	149 (62.34)	0.726
Abdominal infection (n, %)	69 (4.62)	14 (5.86)	0.405
Biliary infection (n, %)	23 (1.54)	3 (1.26)	0.737
Urinary tract infection (n, %)	7 (0.47)	1 (0.42)	0.915
Septicaemia (n, %)	143 (9.57)	77 (32.22)	<0.001
MDR (n, %)	104 (6.96)	104 (43.51)	<0.001
Severity			
SOFA Score (SD)	8.61 (3.98)	12.08 (4.60)	<0.001
MV requirement (n, %)	852 (57.03)	215 (89.96)	<0.001
NE requirement (n, %)	508 (34.00)	158 (66.11)	<0.001
HF requirement (n, %)	249 (16.67)	96 (40.17)	<0.001
Lactacidosis (n, %)	349 (23.36)	134 (56.07)	<0.001
Lab indicators			
RDW-CV (%, SD)	15.29 (2.94)	16.67 (3.32)	<0.001
CHOL (mmol/L, SD)	3.27 (1.50)	2.98 (1.16)	0.006
HDL (mmol/L, SD)	0.80 (0.40)	0.60 (0.36)	<0.001
LDL (mmol/L, SD)	1.32 (1.07)	1.40 (0.89)	0.292
TG (mmol/L, SD)	1.95 (0.95)	1.65 (1.38)	0.644
PLT (x109/L, SD)	199.94 (108.56)	201.09 (122.87)	0.891
PDW (fL, SD)	12.75 (2.86)	12.99 (2.72)	0.281
MPV (fL, SD)	10.83 (1.16)	10.95 (1.11)	0.207
APTT (s, SD)	42.35 (14.68)	45.61 (20.73)	0.007
ATIII (%, SD)	66.99 (18.64)	67.41 (18.79)	0.819
HBA1C (%, SD)	6.36 (1.86)	6.60 (2.14)	0.243
WBC (x109/L, SD)	13.07 (8.61)	13.69 (8.18)	0.343
LYMPH (x109/L, SD)	1.15 (0.96)	1.02 (0.88)	0.074
Outcomes			
Death (n, %)	291 (19.48%)	91 (38.08%)	<0.001
ICU stay (median, day)	4 (2, 7)	23 (17, 34)	<0.001
MV duration (median, hour)	31.50 (14.00, 91.00)	354.00 (186.00, 543.00)	<0.001

Abbreviations: RDW-CV, Coefficient of variation of red blood cell distribution width; HF, Hemofiltration; MDR, multiple drug resistant; SOFA score, sequence organs failure assessment score; MV, mechanical ventilation; NE, norepinephrine; CHOL, total cholesterol; HDL, high density lipoprotein; LDL, low density lipoprotein; TG, triglyceride; PLT, platelet count; PDW, platelet deviation width; MPV, mean platelet volume; APTT, activated partial thromboplastin time; HBA1C, glycosylated haemoglobin; WBC, white blood cell count; LYMPH, lymphocyte count.

LASSO Regression and Indicator Selection

Based on the comparative findings presented in Table 1, the application of LASSO regression yielded six indicators demonstrating notable disparities. These indicators hold substantial predictive utility for PICS. The identified indicators encompass: multidrug-resistant (MDR) infections, lactic acidosis, mechanical ventilation (MV) requirement, hemofiltration

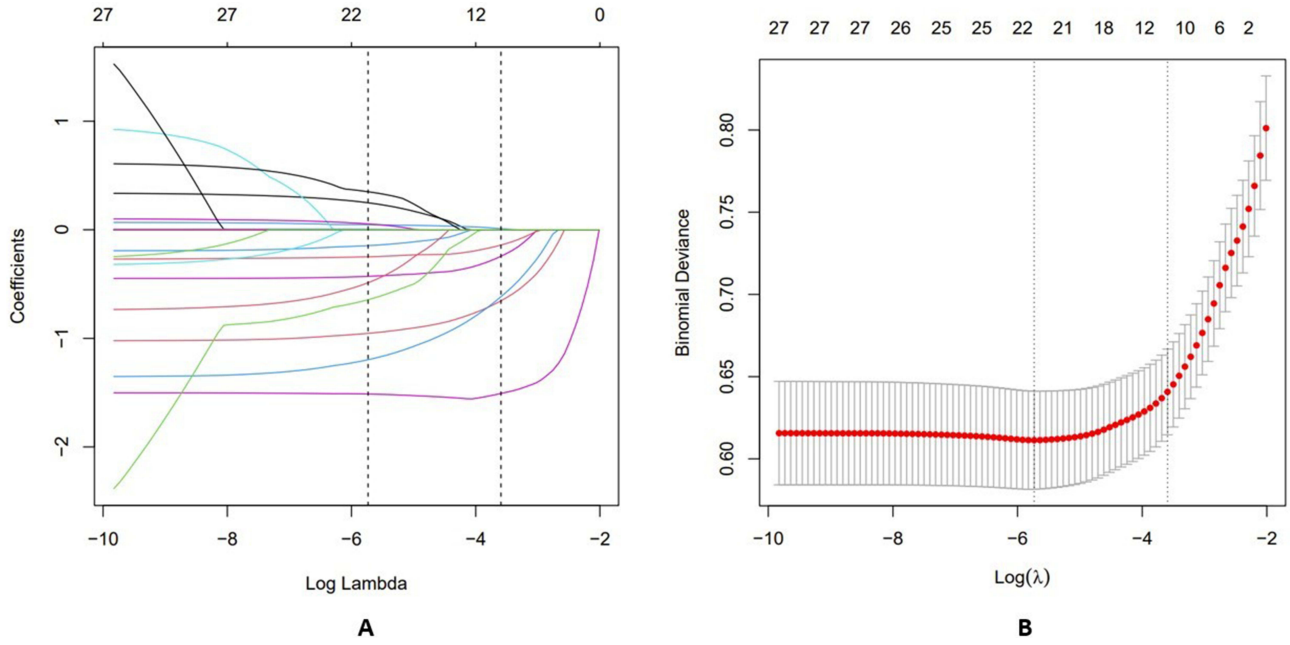

Figure 1 The LASSO regression analysis identified variables predicting PICS. (**A**) Number of non-zero coefficients in the model. (**B**) Number of variables corresponding to different λ values. Six variables were selected by LASSO regression, and constituted the basic factors of the prediction model.

(HF) requirement, noradrenaline (NE) requirement, and red cell distribution RDW-CV. A visual representation of the indicator screening process is illustrated in Figure 1A and B. Using these indicators to construct a prediction model (Table 2): −1.70148 +0.07053 x RDW-CV −0.33833 x (HF requirement=no) −1.12856 x (lactic acidosis=no) −1.69591 x (MDR=no) +1.45877 x (MV requirement=yes) −0.19913 x (NE requirement=no).

Calculation of Model Performance

The model's area under the curve (AUC) was computed as 0.828, signifying exceptional predictive efficacy (Figure 2A). For model validation, 25% of patients from this cohort were randomly designated as the validation set (V set). The AUC of the model within the V set was established as 0.847 (Figure 2B). The predictive model exhibited an accuracy of 0.862, a sensitivity of 0.278, and a specificity of 0.977.

Calibration and Clinical Utility

Based on forecasted probabilities, the data was stratified into deciles, generating ten distinct groups. Observed and predicted values for each group were graphically depicted, utilizing line graphs for separate representation. This visual

Table 2 Predicting Indicators Screened from LASSO Regression

	Estimate	Std. Error	z value	OR	95% CI		*p*-value
					lower	upper	
(Intercept)	−1.7015	0.6196	−2.7463	0.18	0.05	0.61	0.0060
RDW-CV	0.0705	0.0299	2.3598	1.07	1.01	1.14	0.0183
HF requirement=no	−0.3383	0.2114	−1.6005	0.71	0.47	1.08	0.1095
lactic acidosis=no	−1.1286	0.1864	−6.0529	0.32	0.22	0.47	<0.0001
MDR=no	−1.6959	0.2096	−8.0903	0.18	0.12	0.28	<0.0001
MV requirement=yes	1.4588	0.2800	5.2090	4.30	2.48	7.45	<0.0001
NE requirement=no	−0.1991	0.2033	−0.9797	0.82	0.55	1.22	0.3272

Abbreviations: RDW-CV, Coefficient of variation of red blood cell distribution width; HF, Hemofiltration; MDR, multiple drug resistant; MV, mechanical ventilation; NE, norepinephrine.

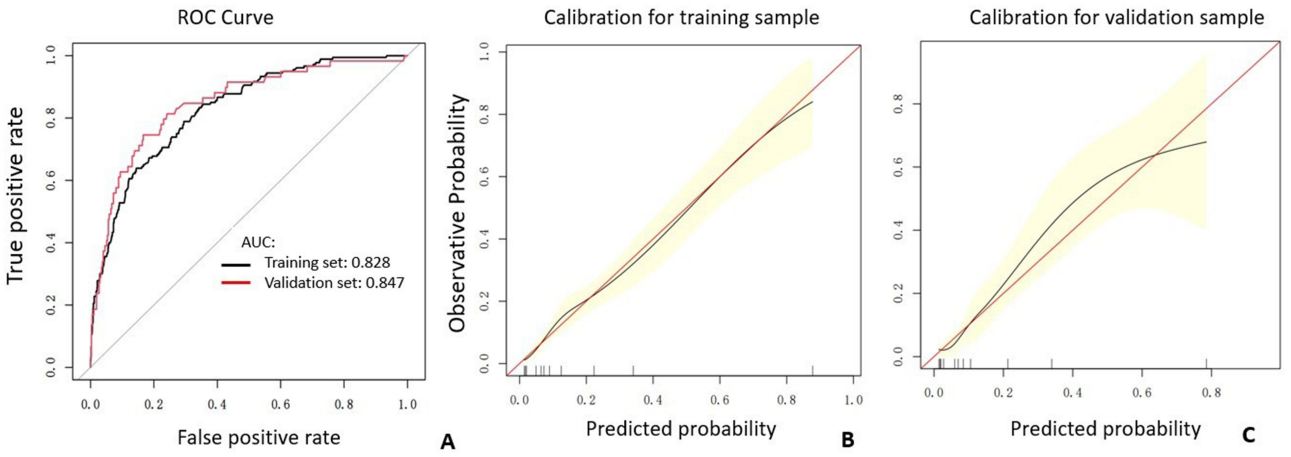

Figure 2 The predictive values of the model of machine learning algorithm. (**A**) The AUCs of training and validation sets. The AUC of training data to predict ICU mortality was 0.828, while that of validation group was 0.847. (**B**) The calibration of training set. (**C**) The calibration of validation set.

format effectively delineated disparities between actual observed values and model-derived predictions within each group. This approach facilitated a comprehensive evaluation of the model's calibration performance. The close alignment observed between actual and predicted values across the groups substantiated a well-calibrated predictive model (Figure 2B and C). To validate study findings, decision curve analysis (DCA) was employed. This analysis illustrated that models developed from the primary cohorts exhibited a threshold probability spanning 0.15 to 0.80 (Figure 3A). Within this probability range, the model's predictive performance surpassed that of individual predictors within the cohort. The DCA curve for validation data mirrored that of the training data, further corroborating the model's advantageous predictive impact (Figure 3B).

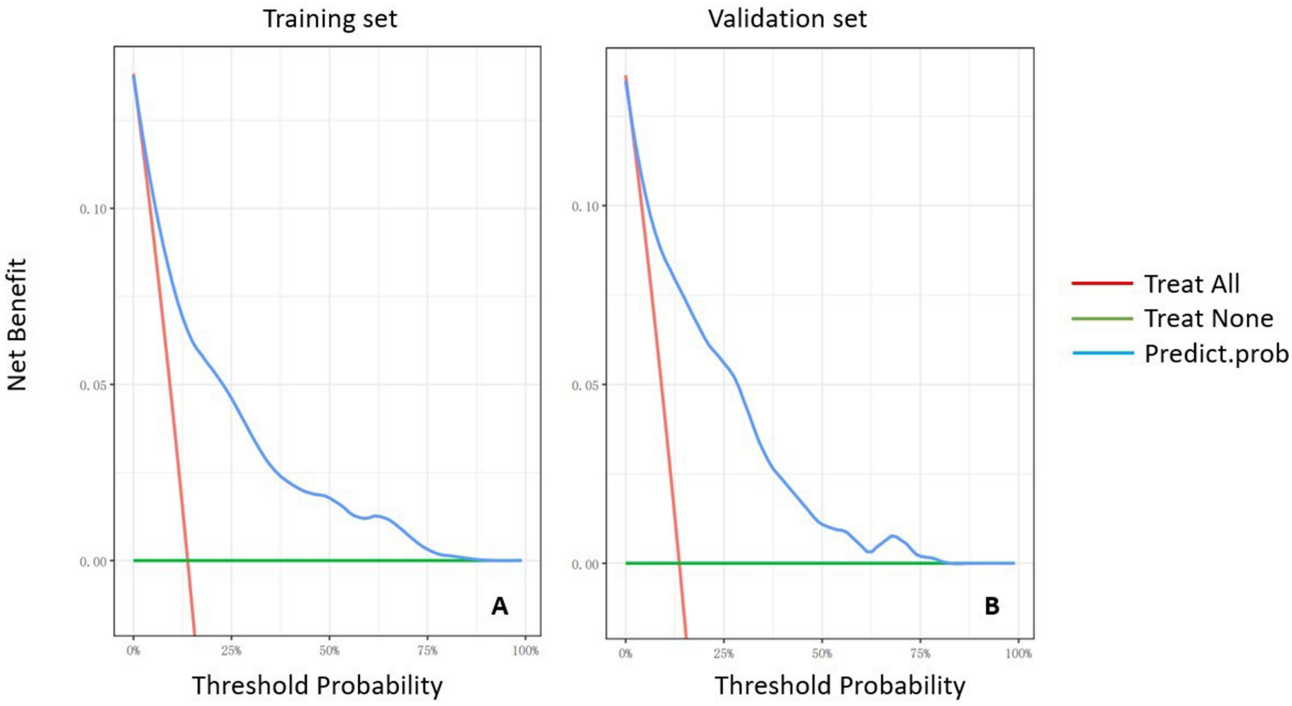

Figure 3 Decision curve analysis (DCA) of the prediction model. (**A**) The DCA curve of training set. (**B**) The DCA curve of validation set. Within this probability range of 0.15 to 0.80, the predictive performance of the model surpassed that of individual predictors within the cohort. The DCA curve of the validation data resembled that of the training data, further confirming the model's favorable predictive effect.

Discussion

Sepsis, a systemic ailment with severe multi-organ dysfunction, often leads to a substantial case fatality rate.[11] The PICS represents a critical subset, particularly prevalent among sepsis patients in intensive care units (ICUs).[8] While the majority of sepsis patients manage to recover, a subset experiences a deteriorating trajectory, ultimately leading to mortality. Among these individuals, a fraction develops persistent PICS.[1] The PICS represents a critical subset, particularly prevalent among sepsis patients in intensive care ICU. Furthermore, patients afflicted by PICS exhibit an augmented case fatality rate. Despite advancements in resuscitation techniques, the long-term prognosis remains unfavourable for a significant subset of patients.[12] Consequently, the diagnosis and prediction of PICS hold considerable clinical significance. Thus, prognosticating PICS through routine assessments could prove pivotal in enhancing patient outcomes. In our sepsis cohort, 14% (n=239) developed PICS within 14 days of ICU admission, exhibiting significantly elevated case fatality rates, prolonged ICU stays, and mechanical ventilation durations compared to their non-PICS. Clinical outcomes for PICS patients were notably worse. While gender, age, disease severity, and specific laboratory indicators upon ICU admission exhibited statistically significant differences between the PICS and non-PICS cohorts, LASSO regression analysis revealed that merely six factors entered the predictive model. Constructing a predictive model based on these six factors resulted in a diagnostic area under the ROC curve (AUC) of 0.828, indicating robust diagnostic efficacy. Despite the relatively modest sensitivity, the specificity reached a substantial value of 0.977. The model demonstrated an AUC of 0.828, with substantial specificity (0.977). Internal validation confirmed its diagnostic efficacy (AUC 0.847), and DCA validated its clinical utility. Numerous investigations have sought to forecast PICS using scoring systems and serum albumin integration, yielding an AUC of approximately 0.8381. Our non-comprehensive approach underscores the potential significance of six identified factors for PICS prediction. Further explorations have leveraged cytokines and biomarkers to anticipate PICS and CCI.[13] Additionally, dyslipidemia, notably diminished high-density lipoprotein (HDL), has emerged as a candidate predictor for PICS and CCI.[14] Diminished HDL reduction has been posited as a predictor for PICS development,[15] and advanced age has also surfaced as a pivotal factor in PICS onset.[13] These insights stem from several smaller-scale clinical inquiries. Within our own cohort, we discerned that PICS-afflicted patients exhibited advanced age and diminished HDL levels. It is pertinent to note, however, that LASSO regression analysis did not ascribe statistical significance to these two factors. Studies have also utilized indicators associated with PICS diagnosis to prognosticate the syndrome. Notable among these indicators are C-reactive protein, serum albumin levels, and the occurrence of hospital-acquired infections within seven days post-admission, which were amalgamated into a scoring system. Nevertheless, the predictive value of this system for PICS was moderately efficacious (AUC 0.74),[16] yet it does not exhibit the same robustness as the amalgamation of factors identified in our study. Furthermore, our investigation highlighted the heightened significance of elevated Red Cell Distribution RDW-CV and a positive mechanical ventilation (MV) requirement among the six predictors in contributing to PICS occurrence within the framework of predictive model construction. RDW-CV is formulated as the ratio of standard deviation of erythrocyte volume to mean erythrocyte volume, expressed as a percentage. This metric encapsulates the heterogeneity of red blood cell sizes. An elevated RDW-CV signifies a greater degree of variability in red blood cell size. Although red blood cells are not conventionally considered key players in sepsis, they exhibit heightened sensitivity to sepsis-induced injury.[17] They serve as early indicators of sepsis, signifying microvascular dysfunction associated with organ malfunction. Augmented Red Cell Distribution Width (RDW) can act as a harbinger of inflammation.[18] Despite limited research on RDW-CV in sepsis, our unpublished data indicated that RDW-CV foretold sepsis-related mortality with an AUC of 0.65. Additionally, amalgamating RDW-CV with other indicators of organ severity status enhanced AUC for outcome prediction. The cytokine milieu during infection or tissue damage triggers myeloid cell proliferation, at the expense of erythropoiesis and lymphocyte production. Iron-restricted anaemia regulated by iron-modulating hepcidin remains somewhat refractory to exogenous iron and erythropoietin supplementation. Consequently, this leads to diminished Red Blood Cell (RBC) survival, prevalence of anaemia, and variations in erythrocyte size.[19] This elucidates the anaemia and escalated RDW (including RDW-CV) observed in sepsis. Aberrant RBC production translates to a reduction in oxygen-carrying capacity, and judicious blood transfusion offers a potential remedy.[20] On the contrary, excessive blood transfusions and mechanical ventilation can exacerbate lung injury, culminating in a prolonged course of sepsis.[21] Lung injury is notably associated with an adverse long-term prognosis in the context of sepsis.[22] Extended reliance on

ventilator support, coupled with delayed ventilator weaning due to severe trauma and infection, can potentiate the emergence of PICS, consequently heightening the risk of chronic sepsis.[23] Notably, Ventilator-Associated Pneumonia (VAP) stands as a prevalent nosocomial infection encountered within ICU.[24] Studies have identified that individuals with persistent critical illness are predisposed to protracted mechanical ventilation and display an elevated incidence of VAP. Mechanical ventilation's influence on the prognosis of two-thirds of individuals with persistent critical illness is also noteworthy.[25] This protracted mechanical ventilation exposure may additionally trigger other ventilator-associated events, collectively exerting an adverse influence on patients' clinical prognosis.[26] Prolonged ICU stays, coupled with exceedingly protracted mechanical ventilation, harbor significant implications in terms of drug-resistant bacterial infections. Among these, Gram-negative bacteria present a notable global challenge, encompassing ultra-broad-spectrum β-lactamase-producing Enterobacteriaceae, de-repressed AmpC bacteria, carbapenemase-producing *Enterobacteriaceae* (CPE), and carbapenem-resistant *Acinetobacter baumannii* (CRAB). Furthermore, Gram-positive challenges encompass methicillin-resistant *Staphylococcus aureus* (MRSA) and glycopeptide-resistant *Enterococcus* (GRE).[27,28] The administration of empiric antibiotic treatments has the potential to foster the emergence of hospital-acquired infections characterized by resistant organisms, thereby contributing to prolonged ICU stays.[29] The utilization of norepinephrine points towards microcirculatory dysfunction, while elevated lactate levels tend to signify microcirculatory dysfunction.[30] Notably, the administration of high doses of norepinephrine in cases of infectious shock is linked with elevated case fatality rates.[31] In a reciprocal manner, research has indicated that the 28-day mortality in individuals with infectious shock correlates with mean lactate levels and the clearance of lactate at the 3-hour and 6-hour marks. Of note, lactate levels at the 6-hour juncture exhibit the most robust predictive value (lactate area under the curve at 6 hours: 0.845).[32] Therefore, these two indicators signify the contribution of circulatory function to the incidence of PICS. Haemodialysis predominantly finds its application as renal replacement therapy among patients experiencing late-stage Acute Kidney Injury (AKI). The need for haemodialysis also hints at compromised perfusion not only within the kidneys but across various other organs as well. Despite the development of a predictive model for PICS in this study, several notable limitations warrant consideration. The nature of this study being retrospective in design restricts the analysis to the available deposited data, consequently influencing the credibility of the drawn conclusions.

Therefore, the findings of this study should be interpreted as informative insights rather than definitive outcomes. The findings of this research also indicate that the prediction model consisting of six crucial variables plays a significant role in forecasting the progression from sepsis to septic shock, and possesses considerable clinical utility. These results can be utilized to develop static or dynamic nomograms, mobile application interfaces, etc., for predicting the potential advancement of the condition. Additionally, the findings assist healthcare professionals in managing pivotal variables, thereby enhancing disease trajectory and clinical outcomes.

Conclusion

RDW-CV, HF requirement, MV requirement, NE requirement, lactic acidosis, and MDR identified through LASSO regression at the time of ICU admission emerge as pivotal factors for predicting the manifestation of PICS in sepsis patients. The predictive model constructed using these factors may provide commendable clinical significance, characterized by elevated accuracy and specificity in prognosticating the occurrence of PICS.

Data Sharing Statement

The data and materials used in this study are available upon request. Researchers interested in accessing the dataset or related materials for academic and non-commercial purposes can contact the corresponding author for further information.

Ethics Approval

Present study approved from the Medical Research Ethics Committee, Shenzhen People's Hospital communicated through letter no LL-KY-2019508

Consent for Publication

Due to the retrospective nature of this study, the Institutional Ethics Committee determined that explicit written consent from patients was not required. The study adhered to the guidelines of the Declaration of Helsinki and international ethical standards.

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.

Funding

This project is funded by Natural Science Foundation of Guangdong Province (Grant No. 2024A1515012909), Guangzhou Municipal Science and Technology Bureau (Grant No. 2014A03J0643).

Disclosure

The authors report no conflicts of interest in this work.

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