Am J Transl Res 2025;17(12):9968-9981
www.ajtr.org /ISSN:1943-8141/AJTR0168364

Original Article

Development and validation of a nomogram to predict bronchopulmonary dysplasia in very preterm, very low birth weight infants

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Received August 26, 2025; Accepted December 11, 2025; Epub December 15, 2025; Published December 30, 2025

Abstract: Objectives: This study aimed to identify early predictors of bronchopulmonary dysplasia (BPD) in very preterm, very low birth weight infants and to construct and externally validate a nomogram that quantifies individual BPD risk shortly after birth to guide proactive clinical management. Methods: We retrospectively analyzed 304 preterm infants admitted to our hospital between 2019-2024. The cohort comprised 113 infants diagnosed with BPD and 191 non-BPD controls. Clinical data, including maternal characteristics, neonatal parameters, and hematological indices measured at 14 days of postnatal age, were collected. Significant predictors of BPD were identified using logistic regression analysis and incorporated into a nomogram model for BPD risk assessment. The model's performance was externally validated using an independent cohort of 30 preterm infants admitted between January and June 2025. Results: Factor analysis identified nine key BPD predictors (gestational age, birth weight, hypertensive disorders, neonatal respiratory distress syndrome, patent ductus arteriosus, blood transfusion, duration of nasal continuous positive airway pressure therapy, mean platelet volume, and white blood cell count), which were used to develop a BPD risk nomogram. The model demonstrated robust predictive performance, with area under the curve (AUC) values of 0.946 (95% CI: 0.927-0.966) for internal validation and 0.883 (95% CI: 0.750-0.989) for external validation, indicating a high discriminative ability. Conclusion: The results of this study provide an important basis for the early identification and management of BPD in premature infants and have potential clinical application value, which is helpful in improving the prognosis of children and optimizing the allocation of medical resources.

Keywords: Bronchopulmonary dysplasia, premature infants, risk factors, nomogram, prediction model

Introduction

Bronchopulmonary dysplasia (BPD) represents one of the most prevalent and severe complications in premature infants and is a leading cause of chronic respiratory disease during infancy [1]. The incidence of BPD increases inversely with gestational age and birth weight, affecting approximately 30% of preterm infants with a gestational age < 32 weeks [2]. Although survival rates among premature infants with BPD - particularly those with very low birth weight (birth weight < 1500 g) - have significantly improved due to advances in neonatal care, the overall incidence of BPD remains high, and effective therapeutic interventions are still lacking. This poses a substantial challenge to the long-term quality of life in affected infants [3]. Throughout childhood, children with BPD frequently experience recurrent lower respiratory tract infections, wheezing, cardiovascular disorders, and delays in physical growth and neurodevelopment. These comorbidities not only impair individual health outcomes but also

https://doi.org/10.62347/ZDPG3250

impose a considerable burden on families and healthcare systems [4]. Therefore, identifying modifiable risk factors and implementing early preventive strategies are crucial to mitigating adverse impacts on patients and their caregivers.

The development and progression of BPD are influenced by multiple interacting factors. A review of existing literature indicates that several neonatal characteristics are associated with BPD onset, including low birth weight, early gestational age, intrauterine distress, neonatal respiratory distress syndrome, acute necrotizing enterocolitis, intracranial hemorrhage, late-onset sepsis, and prolonged mechanical ventilation - all established as independent risk factors [5]. Additionally, prenatal maternal exposures such as infection and smoking further elevate the risk of BPD [6, 7]. Despite this knowledge, few studies have specifically examined these risk factors in preterm infants with a gestational age < 32 weeks, and those that exist often involve limited sample sizes [8, 9]. Furthermore, investigations extending beyond identification to predictive modeling remain insufficient. Existing prediction models for BPD are sparse and demonstrate suboptimal predictive performance, limiting their clinical utility.

Against this backdrop, our study analyzes the general characteristics, neonatal complications, laboratory parameters, and maternal factors in newborns with a gestational age < 32 weeks and birth weight < 1,500 g, aiming to identify significant risk factors for BPD. Concurrently, we employ machine learning techniques to develop a comprehensive prediction model designed to enhance the accuracy of early BPD risk assessment in preterm infants. By leveraging this integrated approach, we aim to provide a more reliable tool for early identification of at-risk individuals, enabling timely intervention and ultimately improving treatment outcomes and long-term quality of life for this vulnerable population.

Methods

Case selection

This study enrolled premature infants admitted to the Neonatal Intensive Care Unit (NICU) of the Eighth Affiliated Hospital of Guangxi Medical University between January 2019 and June 2025. Participants were stratified into two groups based on the 2018 National Institute of Child Health and Human Development (NICHD) diagnostic criteria [10]: those diagnosed with BPD comprised the BPD group, while the remaining infants were assigned to the non-BPD group. The study protocol received approval from the Institutional Ethics Committee of the Eighth Affiliated Hospital of Guangxi Medical University (NO: LWE-2023-010-01).

Inclusion criteria: Participants must meet the BPD diagnostic criteria published by the NICHD in 2018 [10]; have a gestational age of < 32 weeks and birthweight < 1,500 g; be admitted to the neonatal department within 24 hours of birth; and have been hospitalized in the NICU for at least 14 days.

Exclusion criteria: Premature infants were excluded from the study if they met any of the following conditions: those who experienced critical illness or death within the first postnatal week; infants presenting with severe congenital malformations of the digestive or urinary tract; cases diagnosed with genetic metabolic disorders or chromosomal abnormalities; patients with severe congenital heart disease including pulmonary atresia or tetralogy of Fallot (with the exception of isolated patent ductus arteriosus); subjects whose families requested treatment discontinuation; or participants with incomplete clinical data.

Data collection

Two neonatologists systematically extracted comprehensive clinical data from the electronic medical record system. The collected parameters are included as follows.

Primary indicators: Baseline neonatal characteristics: These are crucial pieces of information reflecting the characteristics of the neonates, including gender, gestational age, birthweight, and 5-minute Apgar scores (used to assess the physical condition of the neonate 5 minutes after birth, with a scoring range of 0-10).

Respiratory support modalities and treatment durations: These indicators evaluate neonatal

respiratory status and treatment needs. They include the duration of invasive mechanical ventilation, nasal continuous positive airway pressure (nCPAP), non-invasive positive pressure ventilation (nIPPV), and nasal high-frequency oscillatory ventilation (nHFOV) with respective treatment durations.

Pharmacological Interventions: Refer to the drug treatment measures taken within 3 days after the neonate's birth, including the use of caffeine citrate and the administration of pulmonary surfactant.

Secondary indicators: Clinical outcomes were ascertained through standardized chart review, identifying complications including neonatal respiratory distress syndrome (NRDS), neonatal infections, echocardiogram-diagnosed patent ductus arteriosus (PDA), documented apnea episodes, transfusion records, radiologically confirmed intracranial hemorrhage (ICH), necrotizing enterocolitis (NEC) meeting Bell's criteria, ophthalmologist-diagnosed retinopathy of prematurity (ROP), and reintubation events.

Hematological parameters on postnatal day 14: Collected from laboratory reports, these parameters reflect the neonate's blood status.

Maternal Variables: Extracted from obstetric records, including mother's age, gestational diabetes mellitus (GDM), pregnancy-induced hypertension (HDP), placenta previa, antenatal steroid administration, delivery mode, premature rupture of membranes, and placental abruption. All data were independently verified by both clinicians to ensure accuracy.

Statistical methods

Data analysis was performed using SPSS version 27.0. Normally distributed continuous variables are expressed as mean ± SD and were compared using t-tests. Non-normally distributed variables are presented as median (25th, 75th percentiles) and compared using the Mann-Whitney U test. Count data were expressed as frequencies (%) and analyzed using Fisher's exact test or the chi-square test. Key BPD predictors were identified using least absolute shrinkage and selection operator (LASSO) and multivariate logistic regression. The R (4.2.1) package "rms" was used to construct a Nomogram model, and its accuracy was evaluated using Receiver Operating Characteristic (ROC) curve, and calculate the Area Under the Curve (AUC). Calibration was assessed using the Hosmer-Lemeshow test and calibration curves. All tests were two-sided with $P < 0.05$.

Results

Participant characteristics

The study initially recruited 3,444 preterm infants. Among them, 2,741 infants had a gestational age of ≥ 32 weeks, 115 had a birth weight of ≥ 1,500 g, 179 resided in the NICU for less than 14 days after birth, 50 had incomplete prenatal information, and 25 had missing maternal characteristics, leading to their exclusion. Ultimately, 334 premature infants were included in this study. They were allocated to the training (n=304) and validation (n=30) set based on their admission time (**Figure 1**). **Table 1** shows the basic characteristics, complications, blood test indicators, and maternal characteristics of the two groups of premature infants in the training set. Among the 301 premature infants, 113 (37.2%) had BPD, and the remaining 191 had no BPD.

Compared with non-BPD infants, BPD-affected infants had significantly lower gestational age, birth weight, and Apgar-5 min scores, as well as longer durations of invasive mechanical ventilation and nCPAP (all $P < 0.001$). Compared to premature infants without BPD, those with BPD had significantly higher incidence rates of NRDS, pulmonary surfactant use, caffeine administration within the first 3 days after birth, infections, PDA, apnea episodes, blood transfusion requirements, intracranial hemorrhage, necrotizing enterocolitis, retinopathy of prematurity, and greater need for invasive mechanical ventilation, nCPAP, nIPPV, nHFOV, and reintubation procedures (all $P < 0.05$). Blood tests on day 14 of life showed significantly higher HCT, HGB, LMPH#, MONO#, MPV, NEUT#, and WBC in infants with BPD compared to those without, mothers of BPD infants had a lower incidence of pregnancy-induced hypertension than mothers of non-BPD infants (all $P < 0.05$).

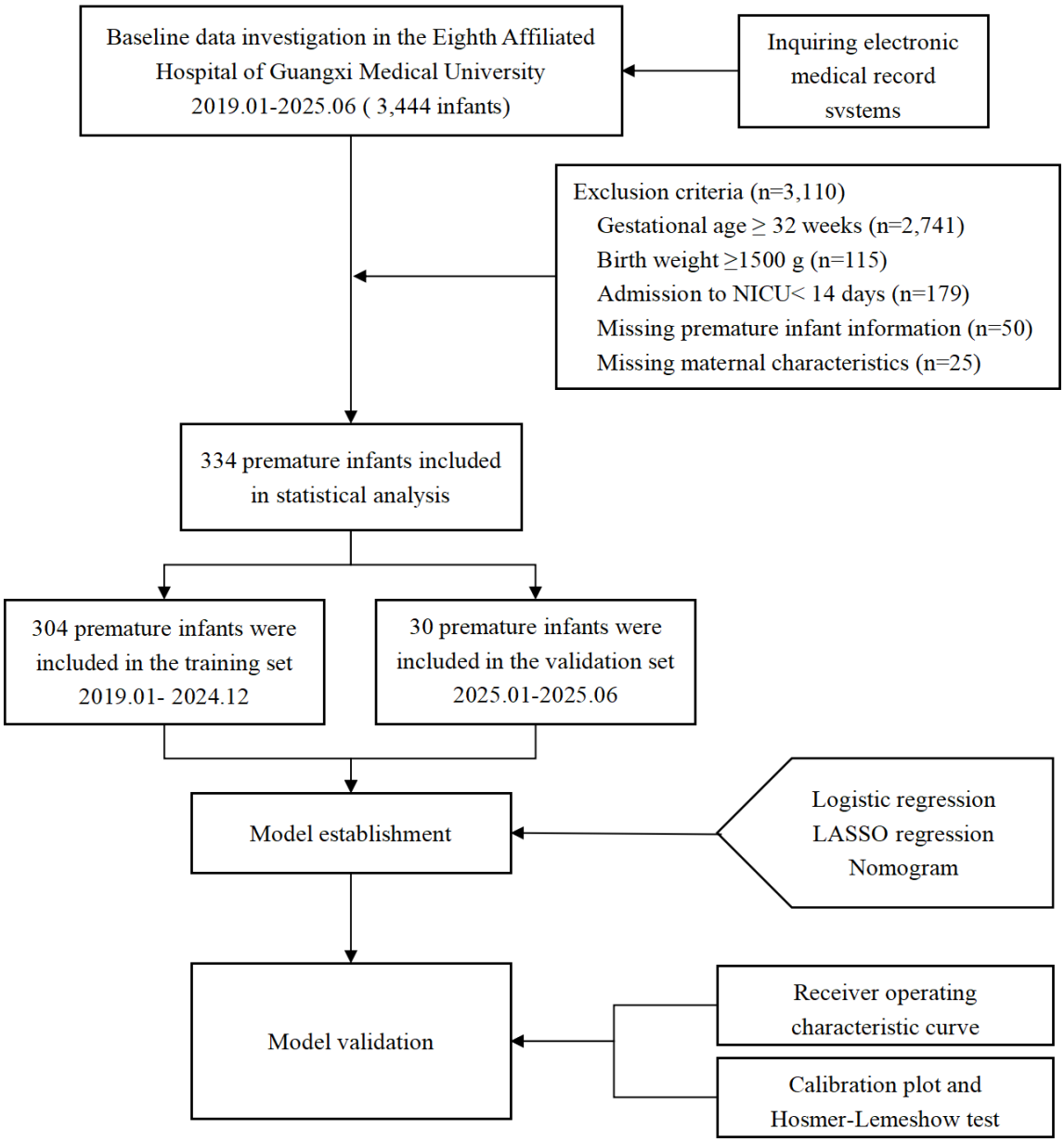

Figure 1. Flow diagram of study design. LASSO, least absolute shrinkage and selection operator.

LASSO regression analysis and screening of predictive variables

The LASSO regression represents a refined approach to linear regression analysis. This method incorporates L1 regularization, which effectively shrinks the coefficients of non-contributory variables to zero, thereby facilitating automatic feature selection of the most influential predictors [11]. In the present study, we employed Lasso regression to examine the significant differential characteristics between the BPD and non-BPD groups. The analytical results demonstrated null coefficients for reintubation incidence, MONO#, and NEUT#.

The LASSO regression analysis identified multiple clinically significant variables with non-zero coefficients. These predictive variables included maternal factors (hypertensive disorders of pregnancy), neonatal characteristics (gestational age, birthweight, Apgar scores), respiratory conditions (NRDS, pulmonary surfactant use, PDA), therapeutic interventions

Table 1. Comparison of general data between the two groups of premature infants

Variables	Non-BPD (*n*=191)	BPD (*n*=113)	$t/\chi^2/Z$	*P*
Maternal factors				
Age, year	30.71 ± 5.79	31.42 ± 5.26	1.068	0.286
GDM	36 (18.8)	22 (19.5)	0.018	0.894
HDP	51 (26.7)	14 (12.4)	8.651	0.003
Placenta previa	9 (4.7)	10 (8.8)	2.074	0.150
Antenatal steroid	136 (71.2)	85 (75.2)	0.577	0.447
Caesarian	148 (77.5)	80 (70.8)	1.695	0.193
Premature rupture of membranes	50 (26.2)	38 (33.6)	1.916	0.166
Placental abruption	17 (8.9)	12 (10.6)	0.243	0.622
Neonatal factors				
Gender (male/female)	109/82	68/45	0.282	0.595
Gestational age, week	30.53 ± 1.21	28.81 ± 1.49	10.975	< 0.001
Birthweight, g	1317.84 ± 136.89	1165.64 ± 201.53	7.826	< 0.001
Apgar 5-min	7.43 ± 1.33	6.33 ± 1.29	7.110	< 0.001
NRDS	116 (60.7)	108 (95.6)	44.449	< 0.001
PS	50 (26.2)	68 (60.2)	34.556	< 0.001
Caffeine citrate	85 (44.5)	76 (67.3)	14.755	< 0.001
Infections	110 (57.6)	98 (86.7)	27.890	< 0.001
PDA	33 (17.3)	65 (57.5)	52.639	< 0.001
Apnea syndrome	90 (47.1)	87 (77.0)	26.044	< 0.001
Blood transfusion	130 (68.1)	106 (93.8)	27.094	< 0.001
ICH	21 (11.0)	26 (23.0)	7.840	0.005
NEC	6 (3.1)	13 (11.5)	8.475	0.004
ROP	4 (2.1)	31 (27.4)	44.746	< 0.001
IMV	59 (30.9)	79 (69.9)	43.612	< 0.001
IMV time, hour	0 (0, 17)	37 (0,136)	7.939	< 0.001
nCPAP	123 (64.4)	94 (83.2)	12.628	< 0.001
nCPAP time, day	1.29 (0, 2.92)	4.00 (1.02, 8.69)	6.306	< 0.001
nIPPV	49 (25.7)	68 (60.2)	35.741	< 0.001
nHFOV	2 (1.0)	7 (6.2)	6.548	0.010
Reintubation	6 (3.1)	16 (14.2)	12.838	< 0.001
HCT, %	37.77 ± 5.35	39.64 ± 5.36	2.946	0.003
HGB, g/L	126.08 ± 18.42	133.86 ± 15.95	3.736	< 0.001
LMPH#, $\times10^9$/L	4.29 ± 1.27	4.67 ± 1.07	2.645	0.009
LMPH%, %	39.73 ± 11.49	38.95 ± 9.64	0.609	0.543
MCH, pg	33.45 ± 2.82	33.16 ± 3.21	0.818	0.414
MCV, fL	101.02 ± 8.29	99.10 ± 8.20	1.958	0.051
MONO#, $\times10^9$/L	1.76 ± 0.85	1.98 ± 0.65	2.361	0.019
MONO%, %	15.40 ± 5.12	14.95 ± 4.60	0.782	0.435
MPV, fL	11.78 ± 1.11	12.51 ± 1.41	4.992	< 0.001
NEUT#, $\times10^9$/L	4.11 (2.77, 5.47)	4.96 (3.54, 6.40)	3.139	0.002
NEUT%, %	39.74 ± 10.93	39.92 ± 10.73	0.142	0.679
PCT, %	0.40 (0.34, 0.48)	0.41 (0.35, 0.51)	0.725	0.469
PDW, fL	15.39 ± 3.66	16.13 ± 3.93	1.648	0.100
PLT, $\times10^9$/L	284 (225, 363)	278 (201, 391)	0.308	0.758
RDW-CV, $\times10^9$/L	17.81 ± 2.67	17.52 ± 2.83	0.591	0.555
RDW-SD, %	63.87 ± 9.85	62.43 ± 8.76	1.286	0.199

WBC, $\times 10^9$/L	10.51 ± 3.01	12.56 ± 3.73	5.239	< 0.001

The *P* values of BPD and non-BPD in premature infants were compared. For continuous variables with normal distribution, they were expressed as mean ± standard deviation. For continuous variables with non-normal distribution, they were expressed as medians (25 percentiles, 75 percentiles). Count data were expressed as frequency (%). BPD, Bronchopulmonary dysplasia; GDM, Gestational diabetes mellitus; HDP, Hypertensive disorders of pregnancy; NRDS, Neonatal Respiratory Distress Syndrome; PS, Pulmonary Surfactant; PDA, Patent ductus arteriosus; ICH, Intracranial hemorrhage; NEC, necrotizing enterocolitis; ROP, retinopathy of prematurity; IMV, Invasive mechanical ventilation; nCPAP, Nasal Continuous Positive Airway Pressure; nIPPV, Non-invasive Positive Pressure Ventilation; nHFOV, Nasal High-Frequency Oscillatory Ventilation; HCT, Hematocrit; HGB, Hemoglobin; LMPH#, Lymphocyte Count; LMPH%, Lymphocyte Percentage; MCH, Mean Corpuscular Hemoglobin; MCV, Mean Corpuscular Volume; MONO#, Monocyte Count; MONO%, Monocyte Percentage; MPV, Mean Platelet Volume; NEUT#, Neutrophil Count; NEUT%, Neutrophil Percentage; PCT, Plateletcrit; PDW, Platelet Distribution Width; PLT, Platelet Count; RDW-CV, Red Cell Distribution Width - Coefficient of Variation; RDW-SD, Red Cell Distribution Width - Standard Deviation; WBC, White Blood Cell Count.

(caffeine citrate on day 3, blood transfusion, IMV, nCPAP, nIPPV, nHFOV, duration of IMV and nCPAP therapy), neonatal complications (infections, ICH, retinopathy, NEC), and hematological parameters (HCT, HGB, LMPH#, MPV, WBC at 14 days postnatal age) (**Figure 2**).

Following multivariate logistic regression analysis, nine variables were identified as independent predictors of BPD in preterm infants: hypertensive disorders of pregnancy, gestational age, birth weight, NRDS, PDA, blood transfusion requirements, nCPAP time, MPV, WBC count measured at 14 days postnatal age (**Table 2**). The "visreg" package of R software was used to analyze the interactions between various factors. The results showed no significant interaction between them ($P > 0.05$, **Figure 3**).

Construction and verification of nomogram model

A nomogram prediction model was established using multivariate logistic regression analysis to assess the risk of BPD in preterm infants. As shown in **Figure 4**, the nomogram incorporates multiple functional components. The initial scoring scale assigns point values according to the different states or values of the predictive factors. Subsequent scales represent nine clinical parameters: gestational age, birth weight, HDP, NRDS, PDA, blood transfusion, nCPAP time, MPV, and WBC. The cumulative score scale (range: 0-400 points) combines individual factor scores, whereas the final probability scale estimates the risk of BPD based on the total score. For clinical application, vertical projections are drawn from each parameter's axis value to determine the corresponding points on the scoring scale. These values were summed to obtain a total score, which was then plotted on a cumulative scale. The corresponding BPD probability can be directly derived from the final probability scale, facilitating individualized risk assessment in preterm infants.

The nomogram model was externally validated using an independent cohort of 30 preterm infants (**Table 3**). Receiver operating characteristic analysis demonstrated excellent predictive performance, with an internal AUC of 0.946 (95% CI: 0.927-0.966) and an external AUC of 0.883 (95% CI: 0.750-0.989) for BPD risk prediction. Model calibration was assessed using calibration curve analysis and the Hosmer-Lemeshow test, which showed good agreement between the predicted and observed outcomes (χ^2=7.056, P=0.531; χ^2=3.667, P=0.886), indicating robust model performance (**Figure 5**).

Discussion

In our study, we found that the incidence of pulmonary surfactant and caffeine use within 3 days of birth was higher in preterm infants in the BPD group. However, in multivariate logistic regression analysis, these factors were not included in the final BPD predictor. A study showed that early selective surfactant use within two hours after birth reduces the risk of acute lung injury in premature infants with NRDS needing ventilation, lowering the rates of pneumothorax, pulmonary interstitial emphysema, neonatal death, and chronic lung disease [12]. Additionally, a randomized, double-blind, placebo-controlled clinical trial revealed that early caffeine use did not reduce BPD incidence [13]. However, another study indicated that high doses of caffeine (40-80 mg/kg loading dose + 20 mg/kg maintenance dose) can

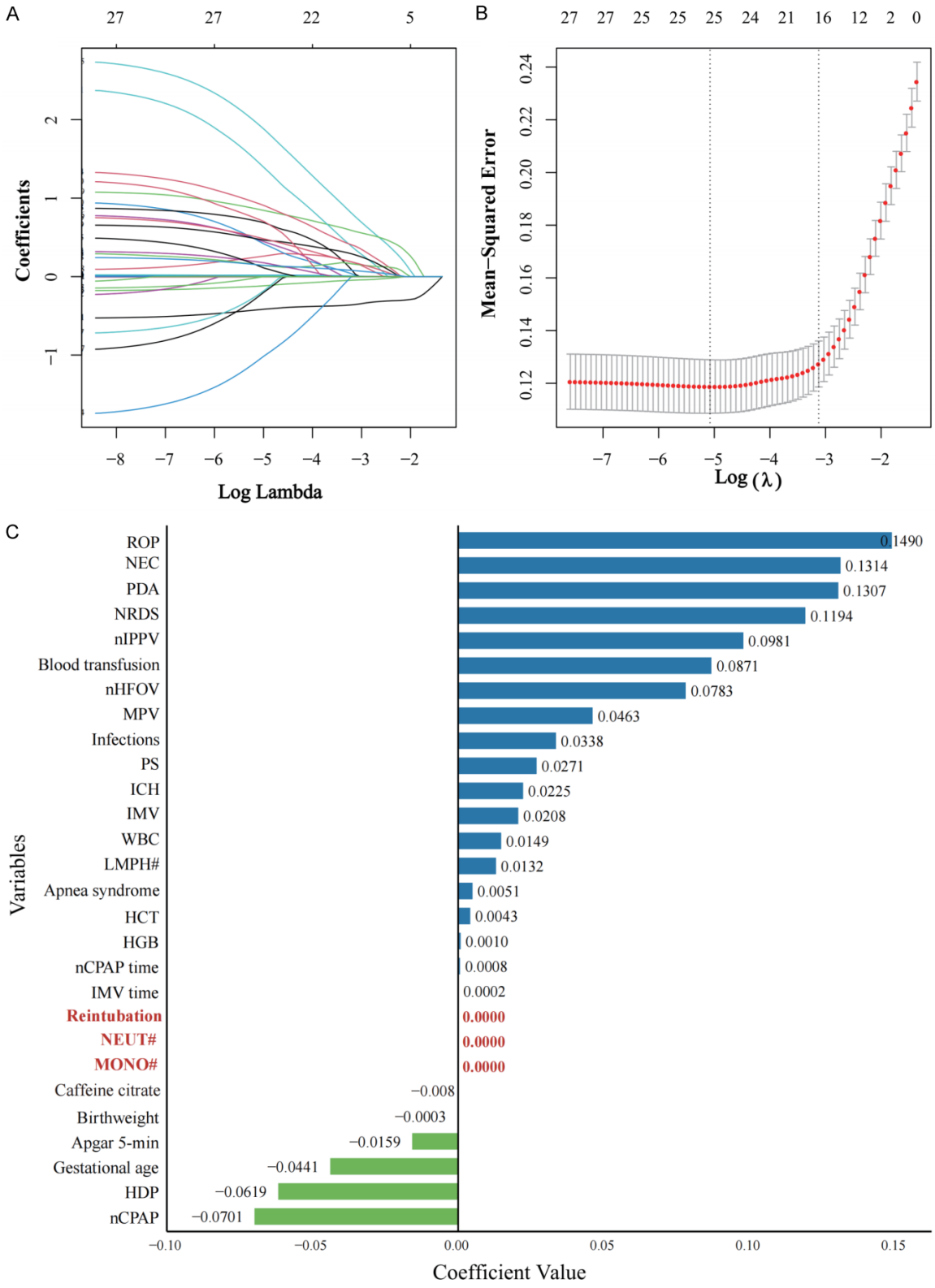

Figure 2. Least absolute shrinkage and selection operator regression screening bronchopulmonary dysplasia predictors. A. When λ=0.0062, the vertical line is drawn, and 25 variable relationship diagrams are selected. B. The relationship between characteristic variables and log (λ) after adjusting λ. C. The least absolute shrinkage and selection operator regression coefficient of each variable. ROP, retinopathy of prematurity; NEC, necrotizing entero-

colitis; PDA, Patent ductus arteriosus; NRDS, Neonatal Respiratory Distress Syndrome; nIPPV, Non-invasive Positive Pressure Ventilation; MPV, Mean Platelet Volume; PS, Pulmonary Surfactant; ICH, Intracranial hemorrhage; IMV, Invasive mechanical ventilation; WBC, White Blood Cell Count; LMPH#, Lymphocyte Count; HCT, Hematocrit, median; HGB, Hemoglobin; nCPAP, Nasal Continuous Positive Airway Pressure; NEUT#, Neutrophil Count; MONO#, Monocyte Count; HDP, Hypertensive disorders of pregnancy; nHFOV, Nasal High-Frequency Oscillatory Ventilation.

Table 2. Logistic regression analysis of multiple factors affecting the incidence of bronchopulmonary dysplasia in premature infants

Variables	*β*	*SE*	Wald χ^2	*P*	*OR (95% CI)*
HDP	-1.661	0.744	4.982	0.026	0.190 (0.044-0.817)
Gestational age	-0.497	0.206	5.819	0.016	0.608 (0.406-0.911)
Birthweight	-0.006	0.002	12.219	< 0.001	0.994 (0.991-0.997)
Apgar 5-min	-0.182	0.207	0.775	0.379	0.834 (0.556-1.25)
NRDS	2.759	0.875	9.945	0.002	15.779 (2.841-87.641)
PS	0.769	0.674	1.303	0.254	2.158 (0.576-8.077)
Caffeine citrate	-0.757	0.526	2.069	0.150	0.469 (0.167-1.316)
Infections	0.107	0.551	0.038	0.846	1.113 (0.378-3.277)
PDA	1.080	0.519	4.335	0.037	2.945 (1.065-8.139)
Apnea syndrome	0.655	0.527	1.540	0.215	1.924 (0.684-5.41)
Blood transfusion	2.219	0.805	7.591	0.006	9.197 (1.897-44.583)
ICH	-0.264	0.623	0.180	0.671	0.768 (0.227-2.601)
NEC	1.040	0.894	1.351	0.245	2.828 (0.490-16.323)
ROP	1.280	0.898	2.032	0.154	3.596 (0.619-20.888)
IMV	0.140	0.697	0.040	0.841	1.150 (0.293-4.512)
IMV time	-0.0001	0.003	0.002	0.968	1.000 (0.994-1.006)
nCPAP	-0.738	0.638	1.338	0.247	0.478 (0.137-1.670)
nCPAP time	0.264	0.072	13.432	< 0.001	1.303 (1.131-1.500)
nIPPV	0.552	0.489	1.275	0.259	1.736 (0.666-4.524)
nHFOV	1.296	1.507	0.740	0.390	3.655 (0.191-70.019)
HCT	0.021	0.065	0.101	0.750	1.021 (0.898-1.161)
HGB	0.020	0.021	0.911	0.340	1.020 (0.979-1.062)
LMPH#	0.309	0.221	1.962	0.161	1.363 (0.884-2.101)
MPV	0.722	0.218	10.981	0.001	2.059 (1.343-3.156)
WBC	0.219	0.078	7.833	0.005	1.245 (1.068-1.452)

HDP, Hypertensive disorders of pregnancy; NRDS, Neonatal Respiratory Distress Syndrome; PS, Pulmonary Surfactant; PDA, Patent ductus arteriosus; ICH, Intracranial hemorrhage; NEC, necrotizing enterocolitis; ROP, retinopathy of prematurity; IMV, Invasive mechanical ventilation; nCPAP, Nasal Continuous Positive Airway Pressure; nIPPV, Non-invasive Positive Pressure Ventilation; nHFOV, Nasal High-Frequency Oscillatory Ventilation; HCT, Hematocrit, median; HGB, Hemoglobin; LMPH#, Lymphocyte Count; MPV, Mean Platelet Volume; WBC, White Blood Cell Count.

diminish the incidence of BPD and mortality [14, 15]. Fehrholz et al. [16] demonstrated that caffeine is closely associated with lung compliance and enhances lung function by augmenting respiratory system compliance. Moreover, physiological caffeine levels can augment the role of glucocorticoids in facilitating the production, maturation, and release of surfactant protein B in premature infants, both in vivo and in vitro. Although previous studies have shown various effects of surfactant and caffeine use on lung - related conditions in premature infants, our results diverge from those reported in the literature. This divergence may be attributable to the dosage of caffeine administered and the potential bias in the selected patient population.

In this study, nine key predictors were identified using statistical methods: gestational age, birth weight, hypertensive disorders of pregnancy, neonatal respiratory distress syndrome, patent

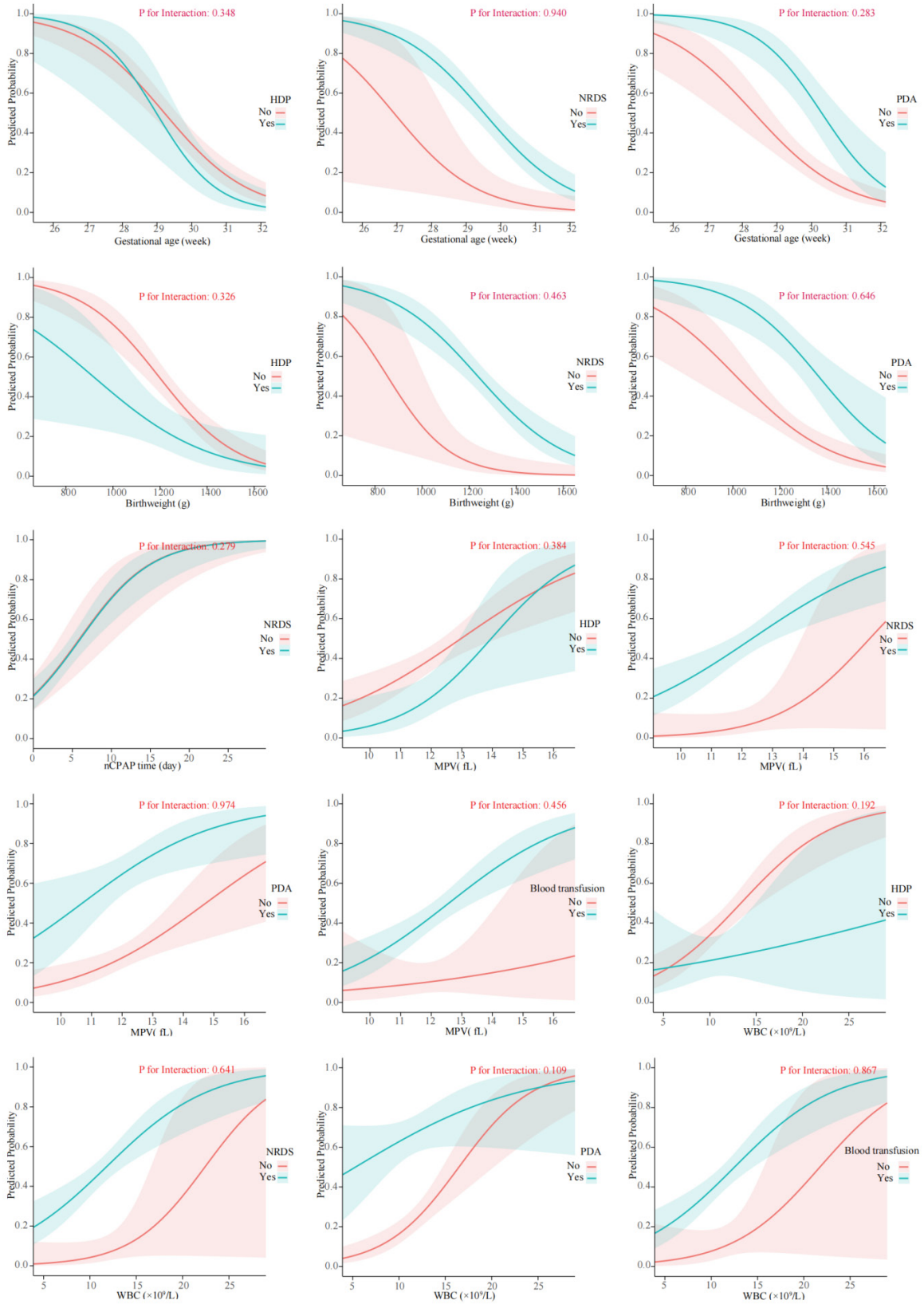

Figure 3. Interaction analysis between bronchopulmonary dysplasia related risk factors. HDP, Hypertensive disorders of pregnancy; NRDS, Neonatal Respiratory Distress Syndrome; PDA, Patent ductus arteriosus; nCPAP, Nasal Continuous Positive Airway Pressure; MPV, Mean Platelet Volume; WBC, White Blood Cell Count.

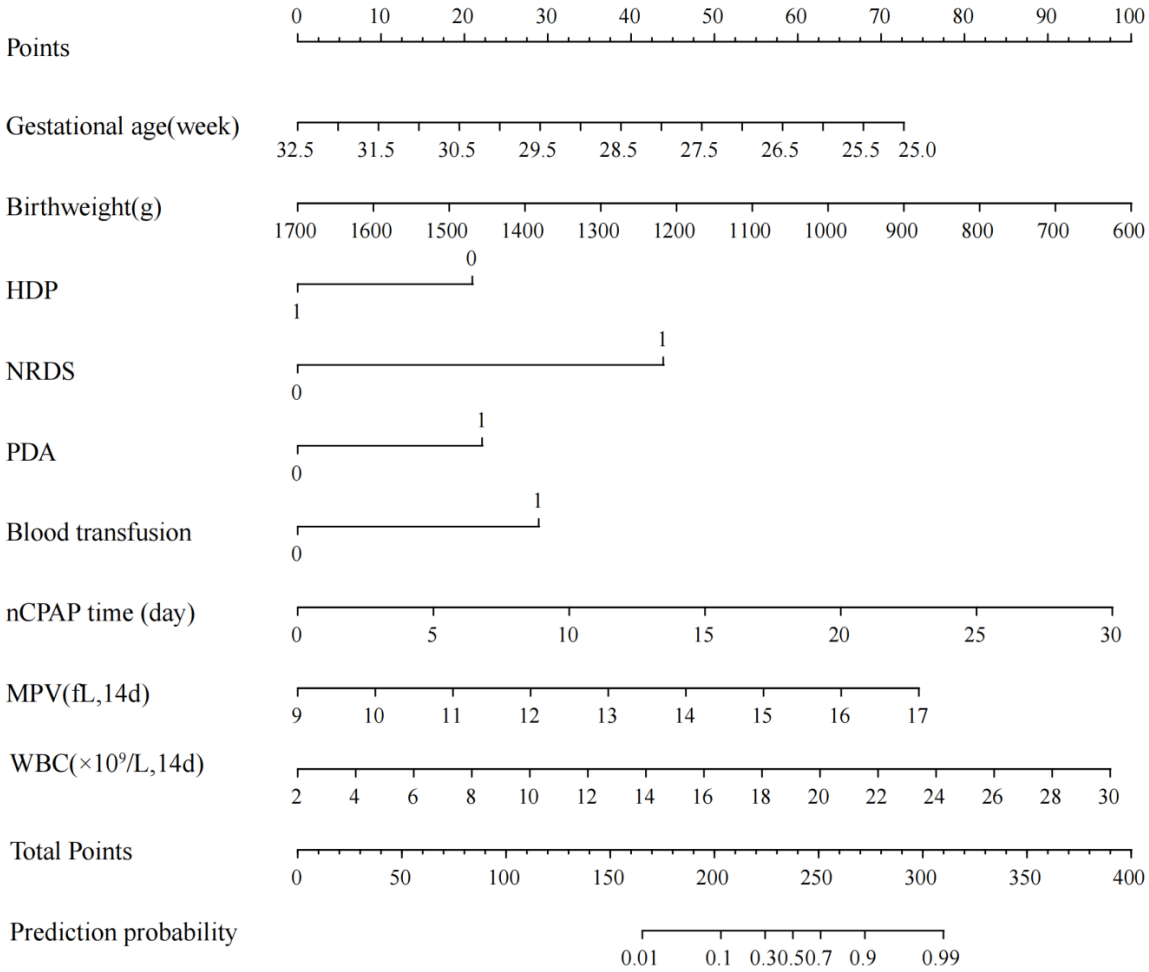

Figure 4. Nomogram model for predicting bronchopulmonary dysplasia in premature infants. HDP, Hypertensive disorders of pregnancy; NRDS, Neonatal Respiratory Distress Syndrome; PDA, Patent ductus arteriosus; nCPAP, Nasal Continuous Positive Airway Pressure; MPV, Mean Platelet Volume; WBC, White Blood Cell Count.

Table 3. Basic information of 30 preterm infants included in the external validation set

Variables	Non-BPD (*n*=20)	BPD (*n*=10)	χ^2/Z	*P*
HDP	3 (15.0)	0	1.611	0.204
Gestational age, week	31.4 (39.7, 32.1)	28.7 (27.1, 30.0)	3.194	< 0.001
Birthweight, g	1325 (1250, 1400)	1200 (938, 1400)	1.955	0.055
NRDS	9 (45.0)	8 (80.0)	3.215	0.073
PDA	9 (45.0)	8 (80.0)	3.215	0.073
Blood transfusion	11 (55.0)	10 (10.0)	6.214	0.013
nCPAP time, day	1.63 (0, 2.80)	6.85 (3.56, 19.86)	3.313	<0.001
MPV, fL	11.25 (10.73, 12.18)	12.30 (11.25, 12.65)	1.726	0.085
WBC, $\times 10^9$/L	12.59 (8.71, 15.83)	11.92 (10.06, 18.28)	0.542	0.594

The *P* values of BPD and non-BPD in premature infants were compared. For continuous variables with normal distribution, they were expressed as mean ± standard deviation. For continuous variables with non-normal distribution, they were expressed as medians (25 percentiles, 75 percentiles). Count data were expressed as frequency (%). BPD, Bronchopulmonary dysplasia; HDP, Hypertensive disorders of pregnancy; NRDS, Neonatal Respiratory Distress Syndrome; PDA, Patent ductus arteriosus; nCPAP, Nasal Continuous Positive Airway Pressure; MPV, Mean Platelet Volume; WBC, White Blood Cell Count.

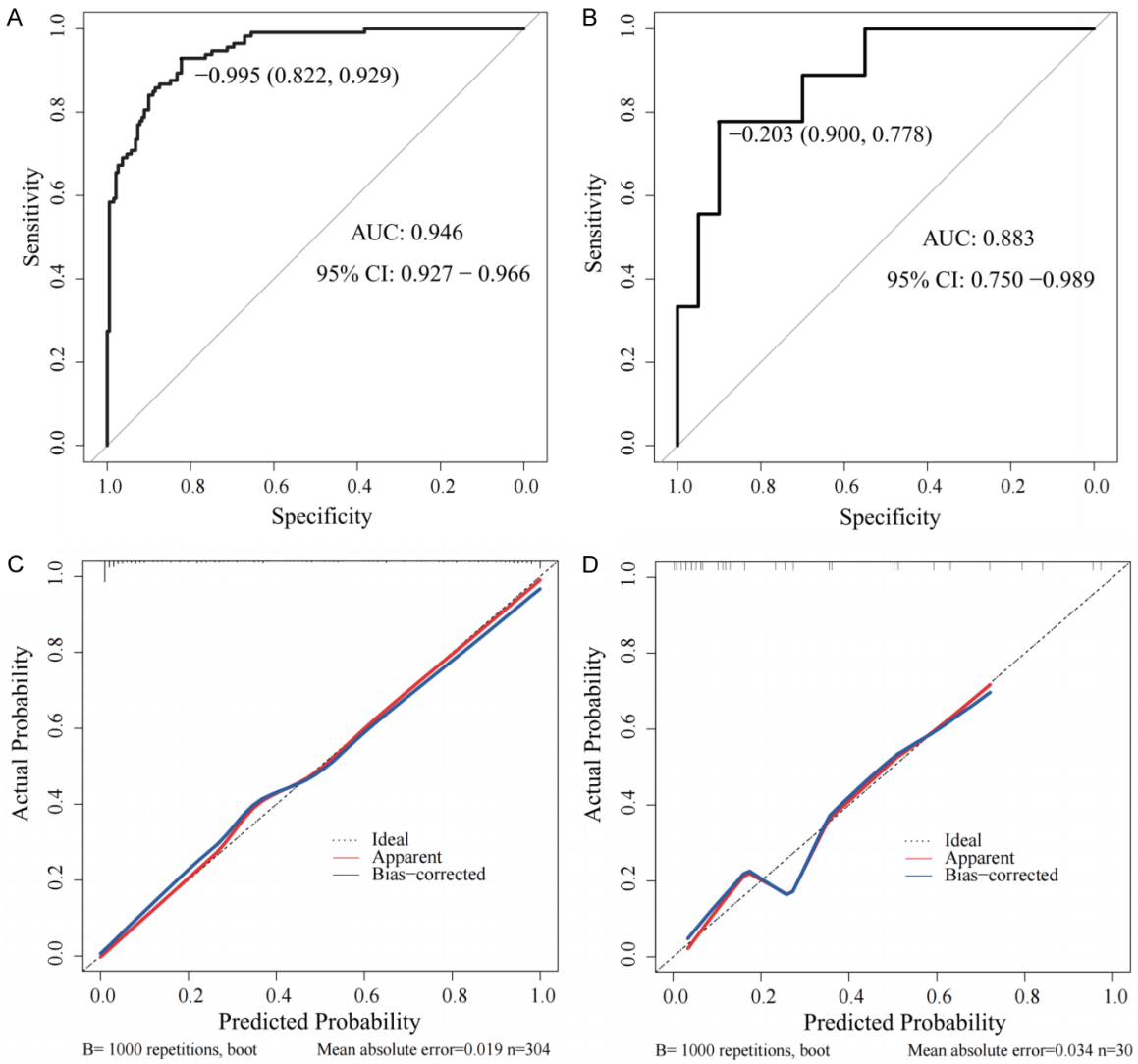

Figure 5. Receiver operating characteristic and calibration curves for the internal and external validation sets of the nomogram model. A. The receiver operating characteristic curve for internal verification; B. The receiver operating characteristic curve for external validation; C. The calibration curves for internal verification; D. The calibration curves for external validation. AUC, Area Under the Curve.

ductus arteriosus, blood transfusion, duration of nasal continuous positive airway pressure therapy, mean platelet volume, and white blood cell count. The identification of these predictors enables clinicians to identify high-risk preterm infants earlier and promptly implement individualized interventions.

The meta-analysis conducted by Romijn et al. [17] identified gestational age and birth weight as the most critical predictors of BPD, a finding consistent with the results of this study. Lung development in full-term infants is generally mature at birth; however, premature infants with gestational ages under 32 weeks are more prone to lung injury and abnormal repair due to interrupted development at the vesicle and alveolar stages, leading to significant impairment in lung development [18]. Consequently, the lower the gestational age, the less growth and development of the fetal heart, lung, and other organs, corresponding to a higher risk of BPD. Of 304 preterm infants ≤ 32 weeks of gestation, 37.2% (113/304) developed BPD, which was higher than the 30% rate in the previous study [2]. This discrepancy is likely attributable to the birth weights of the premature infants included in the study. This study primar-

ily included newborns with birth weights < 1,500 g. Birth weight is a significant influencing factor of BPD; the lower the birth weight, the higher the risk of BPD [3]. Thus, gestational age and birth weight remain the cornerstone variables for any BPD risk algorithm, and their combined use in our nomogram offers clinicians an immediate visual estimate of baseline vulnerability.

The results of this study indicated that NRDS, PDA, and blood transfusion elevated the risk of BPD, a finding consistent with that of Huang et al. [19]. PDA increases pulmonary blood flow and vessel hydrostatic pressure, leading to pulmonary edema and decreased lung compliance [20]. A study involving infants under 28 weeks of age revealed that the presence of a large PDA triples the risk of BPD [21]. NRDS is the main disorder threatening the life and health of premature infants, with a mortality rate of up to 30% [22]. The prevalence of BPD among neonates with NRDS ranges from 14% to 29% [23]. The progression from NRDS to BPD is gradual. NRDS can induce inflammation and exudation in the lungs, and if the intervention is delayed, the lung injury will intensify, culminating in alveolar wall rupture and resultant BPD symptoms [24]. Additionally, blood transfusion is associated with an elevated risk of BPD development. This may be due to the augmentation of free iron and oxygen-free radicals in premature infants, exacerbating oxidative stress and lung injury, thereby impacting lung development [25]. In addition, long-term use of nCPAP is an important factor in promoting BPD in premature infants. During long-term NCPAP treatment, continuous positive airway pressure may increase BPD in premature infants through various mechanisms. On the one hand, excessive alveolar expansion can lead to alveolar wall rupture, interstitial emphysema and even pneumothorax, and damage the lung structure. However, the accompanying hyperoxia exposure can damage lung cells and promote fibrosis through oxidative stress, which aggravates the pathological process of bronchopulmonary dysplasia [26]. NRDS, PDA, transfusion, and prolonged nCPAP are more than correlates of BPD; they are modifiable risk factors. Identifying and addressing them early through optimized respiratory support, timely management of hemodynamically significant PDA, and judicious transfusion practices can reduce the severity of lung injury and lower the risk or incidence of BPD.

The results of routine blood work from premature infants has significant implications for clinical practice. This study identified that elevated MPV on the 14th day post-birth serves as a risk factor for BPD in preterm infants, which is consistent with the findings of Dani et al. [27]. In previous animal studies, an increased MPV was observed in rats subjected to oxygen exposure. Furthermore, in infants with BPD, platelet counts were diminished and MPV was elevated at two weeks post-birth, suggesting heightened activation of platelets in these infants [28]. It is hypothesized that platelet parameters in the initial days post-birth are susceptible to neonatal transition and pharmacological treatments. Cekmez et al. [29] found that elevated MPV early post-birth correlated with BPD in preterm infants, supporting our hypothesis. We also noted higher white blood cell counts on day 14 in BPD cases, which was confirmed as an independent risk factor by multivariate analysis. The role of inflammation in BPD pathogenesis has garnered widespread attention [30]. Under the influence of stress or pharmacological agents, preterm infants produce certain inflammatory factors in the bloodstream, which subsequently promote the proliferation of vascular endothelial elements and stimulate monocytes and macrophages to generate granulocyte colony-stimulating factors, culminating in an elevation of white blood cells and thereby mitigating the inflammatory response [31, 32]. Consequently, the combination of MPV and WBC on day 14 provides a readily available, minimally invasive inflammatory signature that can be incorporated into routine rounds to refine BPD risk stratification.

Integrating the predictive model derived from this study into a clinical decision support system can aid clinicians in making data-informed medical decisions. For instance, in a neonatal intensive care unit, real-time monitoring of factors such as gestational age and birth weight, coupled with dynamic risk assessments via machine learning algorithms, enables doctors to rapidly determine treatment options tailored to the child's condition at each time point. This includes adjustments to respiratory support measures and decisions to initiate or continue specific pharmacological treatments of

patients. This integration not only enhances the precision of individualized treatment but also optimizes the overall efficacy of neonatal intensive care [33]. Additionally, given the high incidence of BPD and associated consumption of medical resources, our study offers a crucial foundation for formulating public health policies. Implementing this model can not only promote scientifically grounded and standardized health decision-making but also positively impact the reduction of medical costs in the long run.

Limitations of the study

The present study was a single-center study with a small sample size; therefore, the representativeness of the research sample was relatively insufficient. A multicenter study with a larger sample size should be conducted to further enhance the results.

Acknowledgements

This work was supported by the following grants: Guangxi Clinical Research Center for Pediatric disease (NO: GUI KE AD22035219); Guangxi Natural Science Foundation (2017-GXNSFDA198008); The Guangxi Medical High-level Backbone Talent "139" Plan.

Disclosure of conflict of interest

None.

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