

Development and internal validation of a clinical nomogram for predicting bronchopulmonary dysplasia in preterm infants

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Received June 24, 2025; Accepted November 20, 2025

DOI: 10.3892/etm.2025.13045

Abstract. Bronchopulmonary dysplasia (BPD) is a major morbidity in preterm infants, necessitating early risk assessment to guide interventions. The present study aimed to develop and internally validate a clinical prediction model for BPD. A total 120 preterm infants (<32 gestation weeks) admitted to a neonatal intensive care unit from January 2020 to December 2022 were retrospectively analyzed. Infants were retrospectively classified into BPD (n=34) and non-BPD (n=86) groups based on the 2018 National Institute of Child Health and Human Development criteria. Clinical variables, including maternal, neonatal, respiratory and comorbid factors, were assessed. Univariate and multivariate logistic regression identified independent predictors, which were used to construct a nomogram. Model performance was evaluated using the area under the curve (AUC) of a receiver operating characteristic curve, a calibration curve and Hosmer-Lemeshow test. Internal validation was performed via bootstrapping. The results demonstrated that gestational age, birth weight, sepsis, patent ductus arteriosus and intraventricular hemorrhage were independent predictors of BPD. The model demonstrated good discrimination (AUC=0.918; 95% confidence interval, 0.866-0.971) and good calibration. The nomogram enabled individualized risk estimation, and internal validation confirmed model robustness. In conclusion, the proposed nomogram demonstrated strong discriminative power and clinical applicability for early BPD risk assessment. Future multicenter validation will help extend its generalizability across diverse neonatal populations.

Introduction

Bronchopulmonary dysplasia (BPD) is a chronic lung disease that remains a notable cause of morbidity in preterm infants, particularly those born at low gestational ages (<28 weeks) or with very low birth weight (<1,000 g). Globally, among infants born at <28 weeks' gestation, reported incidence of BPD ranges from 10 to 89% depending on region and definition, with population-based rates in recent meta-analyses of very low birth weight (<1,500 g) or very low gestational age (<32 weeks) neonates estimated at approximately 21% (95% CI 19-24%) (1). Despite advances in neonatal intensive care, the incidence of BPD has not markedly declined, largely due to the increased survival of extremely preterm infants who remain at the highest risk (2-4). BPD is characterized by abnormal alveolar and vascular development, resulting from a complex interplay of antenatal, perinatal and postnatal factors, including inflammation, oxygen toxicity, mechanical ventilation and sepsis (5).

Early identification of infants at high risk for BPD is crucial for optimizing management strategies and minimizing long-term complications such as recurrent wheezing, reduced pulmonary function, asthma-like symptoms, feeding difficulties, growth failure, and neurodevelopmental impairments including cognitive delays, motor dysfunction, and increased risk of cerebral palsy (6,7). However, the current diagnostic criteria for BPD, as updated by the National Institute of Child Health and Human Development (NICHD) in 2018, rely on the need for respiratory support or supplemental oxygen at 36 weeks postmenstrual age, which is defined as gestational age at birth plus the infant's postnatal age. Because this assessment point occurs after birth, it limits the usefulness of the criteria for early risk stratification (8,9). This highlights the need for early-stage predictive tools to identify high-risk infants before BPD diagnosis is clinically confirmed.

Previous studies have explored risk factors for BPD, such as gestational age, birth weight and exposure to invasive ventilation. However, to the best of our knowledge, few studies have integrated these variables into a comprehensive, clinically applicable prediction model (10-12). Furthermore, the utility of advanced statistical tools such as nomograms in quantifying individualized risk has been underexplored in neonatal populations. Nomograms provide a graphical representation of complex statistical models, and are particularly valuable in clinical practice for their simplicity and interpretability (13).

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Key words: bronchopulmonary dysplasia, preterm infants, risk prediction model, nomogram, neonatal outcome

The present study aimed to develop and validate a robust risk prediction model for BPD in preterm infants, incorporating readily available clinical and demographic variables. Using a retrospective cohort of 120 preterm infants, a nomogram was constructed to estimate individualized risk, and its performance was evaluated in terms of discrimination, calibration and internal validation. The present model aimed to provide an early and accurate assessment of BPD risk, thereby supporting clinical decision-making and improving outcomes for preterm infants.

Patients and methods

Study design and population. The present retrospective cohort study was conducted to develop and validate a prediction model for BPD in preterm infants. Data were collected from 120 preterm infants admitted to the neonatal intensive care unit (NICU) of The Affiliated Hospital of Southwest Medical University, Luzhou, Sichuan, China, between January 2020 and December 2022. Infants were stratified into two groups based on their BPD status, defined according to the 2018 diagnostic criteria published by the NICHD: A BPD group (n=34) and a non-BPD group (n=86).

Inclusion criteria included preterm infants with gestational ages <32 weeks and birth weights $\leq 2,500$ g who were admitted to the NICU within the first week of life. Exclusion criteria included i) major congenital anomalies or chromosomal abnormalities; ii) severe congenital heart defects; iii) genetic or metabolic disorders; iv) mortality or discharge before 14 days of life; and v) transfer to another hospital within 7 days of birth. During the study period (January 2020–December 2022), a total of 156 preterm infants with gestational age <32 weeks were admitted to the NICU of The Affiliated Hospital, Southwest Medical University (Luzhou, China). Of these, 36 patients were excluded for the following reasons: Major congenital anomalies or chromosomal abnormalities (n=5), severe congenital heart defects (n=4), genetic or metabolic disorder (n=2), early mortality or discharge before 14 days of life (n=15) and transfer to another hospital within 7 days of birth (n=10). The final analysis therefore included 120 infants, representing an inclusion rate of 76.9%. Ethical approval for the study was obtained from the Institutional Review Board of The Affiliated Hospital, Southwest Medical University (approval no. KY2025055), and informed consent was waived due to the retrospective nature of the study.

Data collection. Clinical and demographic data were collected from electronic medical records. Maternal factors included maternal age (years), parity, pre-pregnancy body mass index (BMI, kg/m²) and the presence of chronic medical conditions such as hypertension, diabetes or thyroid disease. Antenatal corticosteroid administration was recorded in detail, including whether any course was received, the specific agent used (betamethasone or dexamethasone) and whether the course was complete or partial according to the standardized institutional protocol. Chorioamnionitis was diagnosed through clinical or histopathological findings. The mode of delivery (vaginal or cesarean section) was also documented. Neonatal characteristics encompassed gestational age measured in completed weeks, birth weight in grams, sex,

and Apgar scores at 1 and 5 min, which were documented to assess immediate postnatal adaptation (14). Detailed respiratory support data were obtained, including the duration (in days) and type of support provided, such as continuous positive airway pressure (CPAP), non-invasive positive pressure ventilation (NIPPV) and high-frequency oscillatory ventilation (HFOV). Additionally, neonatal comorbidities were recorded, including the occurrence of sepsis confirmed by positive blood cultures or clinical diagnosis, patent ductus arteriosus (PDA) diagnosed via echocardiography, intraventricular hemorrhage (IVH, graded using Papile's classification) and necrotizing enterocolitis (NEC, identified based on modified Bell's criteria) (15). For the purposes of the prediction model, these comorbidities were defined as events occurring within the first 14 days of life, ensuring that only early-onset cases were included to maintain the model's utility for early risk stratification of BPD. Although the formal definitions for sepsis, PDA, IVH and NEC in the present dataset were restricted to events occurring within the first 14 days of life, in clinical practice, the majority of these conditions in the present cohort were either diagnosed or strongly suspected within the first 72 h after birth, based on early clinical signs, laboratory findings, and echocardiographic or cranial ultrasound assessments. Therefore, these variables retain practical utility for early postnatal risk stratification. Finally, key outcome measures included the length of hospital stay (in days) and the presence or absence of BPD, defined according to the 2018 NICHD criteria. This comprehensive dataset provided a robust foundation for analyzing factors contributing to BPD in preterm infants.

During the study period, respiratory management in the NICU followed a standardized protocol based on gestational age, respiratory distress severity and oxygen requirements. Initial support typically involved CPAP for infants with mild-to-moderate respiratory distress. NIPPV was applied when CPAP was insufficient, or in cases of apnea or moderate respiratory acidosis. HFOV was typically initiated in cases of severe respiratory failure or persistent hypercapnia despite conventional support. Intubation and mechanical ventilation were considered in cases of refractory hypoxemia, recurrent apnea unresponsive to non-invasive support or clinical deterioration. Decisions regarding escalation or de-escalation of support were made collaboratively by the attending neonatologist and the respiratory team based on ongoing clinical assessments.

Statistical analysis. Statistical analyses were conducted to summarize baseline characteristics, develop a predictive model and evaluate its performance. Baseline characteristics were described using the mean \pm standard deviation for normally distributed continuous variables, median (interquartile range) for non-normally distributed continuous variables and frequencies (percentages) for categorical variables. Comparisons between groups were performed using independent Student's t-tests for normally distributed continuous variables, the Mann-Whitney U test for non-normally distributed variables, and χ^2 or Fisher's exact tests for categorical variables. $P < 0.05$ was considered to indicate a statistically significant difference. Univariate logistic regression analyses were used to assess the association between each predictor variable and the risk

Table I. Baseline characteristics of the study population stratified by BPD status.

Characteristic	Non-BPD (n=86)	BPD (n=34)	P-value
Maternal characteristics			
Maternal age, years (mean ± SD)	29.7±4.8	30.1±5.1	0.642
Primiparity (%)	49 (57.0)	18 (52.9)	0.683
Chronic hypertension, n (%)	6 (7.0)	4 (11.8)	0.462
Diabetes mellitus, n (%)	8 (9.3)	3 (8.8)	>0.999
Pre-pregnancy BMI, kg/m ² (mean ± SD)	22.9±3.4	23.4±3.6	0.514
Antenatal corticosteroids use			
Any, n (%)	64 (81.7)	27 (79.4)	0.565
Betamethasone, n (%)	39 (45.3)	16 (47.1)	0.859
Dexamethasone, n (%)	25 (29.1)	11 (32.4)	0.815
Complete course, n (%)	58 (67.4)	24 (70.6)	0.753
Neonatal characteristics			
Gestational age, weeks (mean ± SD)	29.29±1.70	28.02±1.05	<0.001
Birth weight, g [median (IQR)]	1,244.7 (989.9-1,354.0)	1,036.3 (890.2-1,123.2)	<0.001
Male sex, n (%)	45 (52.3)	22 (64.7)	0.218
Respiratory support use			
CPAP, n (%)	51 (59.3)	12 (35.3)	0.018
NIPPV, n (%)	37 (43.0)	21 (61.8)	0.064
HFOV, n (%)	15 (17.4)	12 (35.3)	0.035
Comorbidities			
Sepsis, n (%)	7 (8.1)	20 (58.8)	<0.001
PDA, n (%)	25 (29.1)	19 (55.9)	0.006
IVH, n (%)	10 (11.6)	10 (29.4)	0.018
NEC, n (%)	5 (5.8)	8 (23.5)	0.013
Length of stay, days [median (IQR)]	34.0 (31.0-37.0)	69.5 (67.0-72.8)	<0.001

Values are expressed as mean ± SD, median (IQR) or n (%). Comparisons between groups were performed using independent Student's t-test for normally distributed continuous variables, the Mann-Whitney U test for non-normally distributed continuous variables and the χ^2 or Fisher's exact test for categorical variables. P<0.05 was considered to indicate a statistically significant difference. BPD, bronchopulmonary dysplasia; BMI, body mass index; IQR, interquartile range; CPAP, continuous positive airway pressure; NIPPV, non-invasive positive pressure ventilation; HFOV, high-frequency oscillatory ventilation; PDA, patent ductus arteriosus; IVH, intraventricular hemorrhage; NEC, necrotizing enterocolitis; SD, standard deviation.

of BPD. Prior to multivariate modeling, collinearity among candidate predictors (particularly gestational age and birth weight) was assessed using variance inflation factors (VIFs). All VIF values were <2, indicating no significant multicollinearity. Variables with P<0.1 in univariate analysis were included in a multivariate logistic regression model, where a stepwise backward elimination approach was applied to identify independent predictors. The results were expressed as odds ratios (ORs) with 95% confidence intervals (CIs). To evaluate model performance, discrimination was assessed using a receiver operating characteristic (ROC) curve, with calculation of the area under the curve (AUC), while calibration was evaluated using a calibration curve comparing predicted and observed probabilities. The Hosmer-Lemeshow test was used to assess goodness-of-fit. Based on the multivariate logistic regression model, a nomogram was constructed to visually represent the BPD risk prediction tool. Points were assigned to each predictor based on the magnitude of regression coefficients in the multivariable logistic regression model,

with the predictor contributing the largest coefficient scaled to 100 points and other predictors allocated proportionally. The total points were then mapped onto the corresponding predicted probability of BPD. Internal validation of the nomogram was performed using bootstrapping with 1,000 resamples to ensure robustness. All analyses were conducted using R software (version 4.2.2; Posit Software, PBC), with the 'rms' and 'pROC' packages utilized for nomogram construction and ROC curve analysis (16,17). There were no missing data for the variables included in the analysis; therefore, no imputation or exclusion due to missingness was required.

Results

Baseline characteristics. A total of 120 preterm infants were included in the analysis, of whom 34 (28.3%) developed BPD. The baseline characteristics of the study population stratified by BPD status are summarized in Table I. There were no significant differences between the two groups in terms of

Table II. Univariate and multivariate logistic regression analyses of risk factors for bronchopulmonary dysplasia.

Characteristic	Univariate OR (95% CI)	P-value	Multivariate OR (95% CI)	P-value
Gestational age, weeks	0.570 (0.419-0.777)	<0.001	0.625 (0.420-0.932)	0.021
Birth weight, g	0.997 (0.994-0.999)	<0.001	0.997 (0.994-1.000)	0.059
Male sex	1.670 (0.735-3.796)	0.221	-	-
Antenatal steroids	1.326 (0.507-3.470)	0.566	-	-
CPAP use	2.671 (1.171-6.093)	0.020	2.158 (0.656-7.098)	0.205
NIPPV use	2.139 (0.949-4.822)	0.067	2.458 (0.731-8.271)	0.146
HFOV use	2.582 (1.053-6.332)	0.038	1.725 (0.440-6.758)	0.434
Sepsis	16.122 (5.748-45.225)	<0.001	12.847 (3.187-51.789)	<0.001
PDA	3.091 (1.359-7.028)	0.007	4.514 (1.324-15.389)	0.016
IVH	3.167 (1.177-8.517)	0.022	5.926 (1.217-28.845)	0.028
NEC	4.985 (1.499-16.575)	0.009	3.663 (0.718-18.698)	0.119

Univariate analysis was performed for all variables, and multivariate analysis included variables with $P < 0.1$ in the univariate analysis. Gestational age and birth weight were analyzed as continuous variables. $P < 0.05$ was considered to indicate a statistically significant difference. The dash (-) indicates that the variable was not included in the final multivariate model due to lack of significance in univariate analysis. CPAP, continuous positive airway pressure; NIPPV, non-invasive positive pressure ventilation; HFOV, high-frequency oscillatory ventilation; PDA, patent ductus arteriosus; IVH, intraventricular hemorrhage; NEC, necrotizing enterocolitis; OR, odds ratio; CI, confidence interval.

maternal characteristics, including age, primiparity, pre-pregnancy BMI or prevalence of chronic medical conditions such as hypertension or diabetes. Antenatal corticosteroid exposure was also comparable between groups, with similar proportions receiving any corticosteroid, similar distributions of specific agents (betamethasone or dexamethasone) and no difference in the proportion of patients completing the full treatment course. Infants in the BPD group had significantly lower gestational age (28.02 ± 1.05 vs. 29.29 ± 1.70 weeks; $P < 0.001$) and lower median birth weight ($1,036.3$ vs. $1,244.7$ g; $P < 0.001$) compared with those in the non-BPD group. CPAP use was significantly less frequent in the BPD group (35.3 vs. 59.3% ; $P = 0.018$) than in the non-BPD group, whereas HFOV use was more common (35.3 vs. 17.4% ; $P = 0.035$). Comorbidities, including sepsis (58.8 vs. 8.1% ; $P < 0.001$), PDA (55.9 vs. 29.1% ; $P = 0.006$), IVH (29.4 vs. 11.6% ; $P = 0.018$) and NEC (23.5 vs. 5.8% ; $P = 0.013$), were significantly more prevalent in the BPD group than in the non-BPD group. The median length of hospital stay was significantly longer among infants with BPD (69.5 vs. 34 days; $P < 0.001$).

Univariate and multivariate analyses. The results of univariate and multivariate logistic regression analyses for predictors of BPD are presented in Table II. In the univariate analysis, lower gestational age, lower birth weight, absence of CPAP, use of HFOV, and presence of sepsis, PDA, IVH and NEC were significantly associated with an increased risk of BPD ($P < 0.05$ for all). In the multivariate model, lower gestational age (OR=0.625; 95% CI, 0.420-0.932; $P = 0.021$), sepsis (OR=12.847; 95% CI, 3.187-51.789; $P < 0.001$), PDA (OR=4.514; 95% CI, 1.324-15.389; $P = 0.016$) and IVH (OR=5.926; 95% CI, 1.217-28.845; $P = 0.028$) remained independent predictors of BPD. Although birth weight did not reach statistical significance in the multivariate model (OR=0.997; $P = 0.059$), it was retained due to its established clinical importance in neonatal outcome prediction (18).

Model performance and validation. The predictive performance of the multivariate model was evaluated through discrimination and calibration analyses. The nomogram demonstrated excellent discrimination, with an apparent AUC of 0.918 (95% CI, 0.866-0.971) in the derivation dataset (Fig. 1). This result indicates indicating only minimal optimism and confirms the robustness of the model after adjustment for potential overfitting. The calibration performance of the internally validated model is shown in Fig. 2, which demonstrates strong agreement between observed and predicted probabilities. The Hosmer-Lemeshow test yielded a non-significant result ($P > 0.05$), indicating a good overall model fit.

Nomogram construction. Based on the final multivariate model, a clinical nomogram was constructed to estimate the individualized risk of BPD in preterm infants (Fig. 3). The predictors included in the nomogram were gestational age, birth weight, sex, antenatal steroid use, respiratory support modalities (CPAP, NIPPV and HFOV), and comorbidities (sepsis, PDA, IVH and NEC). Although certain predictors did not reach statistical significance in the multivariate model, they were retained in the nomogram because of their established clinical relevance and routine use in neonatal risk assessment, consistent with accepted nomogram-building practices. Each factor contributed a weighted score to the total, which corresponded to the predicted probability of BPD. This nomogram offered a practical and interpretable tool for bedside application in neonatal intensive care settings.

Discussion

The present study provides a comprehensive analysis of risk factors for BPD and presents a validated predictive model for early identification of at-risk preterm infants. The present model demonstrated high discriminatory power, with an

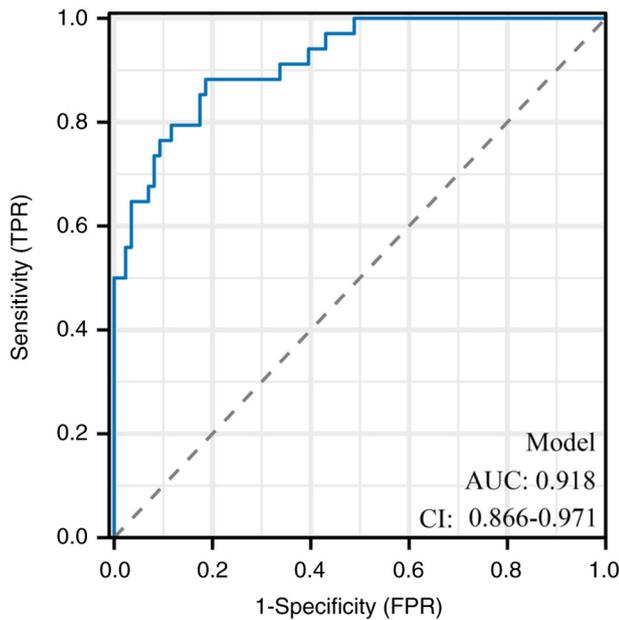


Figure 1. ROC curve for the BPD risk prediction model. The ROC curve illustrates the diagnostic performance of the prediction model for BPD. AUC=0.918 (95% CI, 0.866-0.971) indicated the excellent discriminative ability of the model. BPD, bronchopulmonary dysplasia; AUC, area under the curve; CI, confidence interval; ROC, receiver operating characteristic; TPR, true positive rate; FPR, false positive rate.

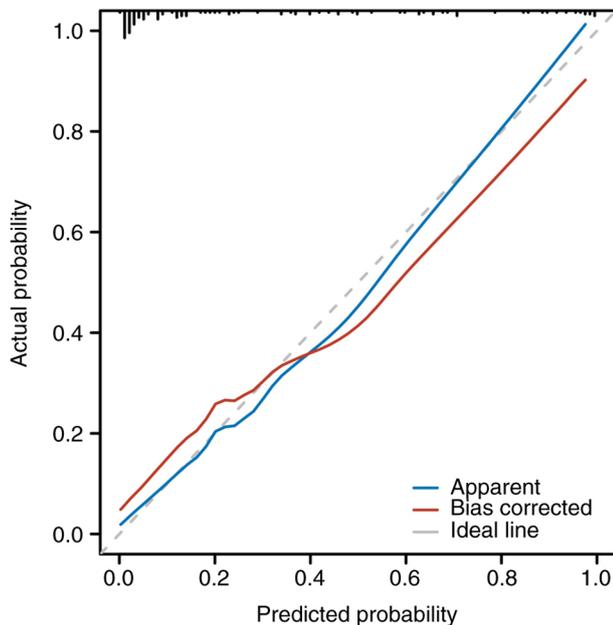


Figure 2. Calibration curve for the BPD risk prediction model. The calibration curve compares the predicted probabilities of BPD occurrence against the observed probabilities. The apparent (blue) and bias-corrected (red) curves align closely with the ideal line (gray dash), indicating a good calibration of the model. BPD, bronchopulmonary dysplasia.

area under the ROC curve of 0.918, and robust calibration, highlighting its potential clinical utility.

Here, gestational age and birth weight emerged as critical predictors of BPD, which is consistent with prior research highlighting the heightened vulnerability of extremely preterm

infants and those with impaired early growth (19-21). Lower gestational age (OR=0.625; P=0.021) reflects the immaturity of the lung parenchyma, surfactant deficiency, and susceptibility to barotrauma and oxygen toxicity (5). Similarly, reduced birth weight (P=0.059 in multivariate analysis) underscores the importance of intrauterine growth and its association with postnatal outcomes (22). These findings reinforce the need for strategies targeting antenatal interventions, such as corticosteroids and optimal timing of delivery, to reduce prematurity-related risks.

In the present study, sepsis showed the strongest independent association with BPD in the multivariate model (OR=12.847; P<0.001), with an effect size notably greater than that of the other significant predictors. This increased risk aligns with prior studies linking systemic inflammation to disrupted alveolarization and pulmonary vascular remodeling (23,24). Pro-inflammatory cytokines and reactive oxygen species released during sepsis amplify lung injury, perpetuating the cycle of inflammation and impaired repair mechanisms (25,26). This underscores the importance of stringent infection control measures in the NICU, including early recognition and management of sepsis.

Notably, the OR value for sepsis in the multivariate analysis conducted in the present study was markedly high (OR=12.847). This magnitude likely reflects both the strong biological plausibility of the association and the relatively concentrated distribution of severe early-onset sepsis in the present BPD cohort. All cases of sepsis included in the present analysis were diagnosed within the first 14 days of life, a critical period for lung development, during which systemic inflammation can exert disproportionate and irreversible effects on alveolarization and microvascular maturation (27). Early-onset sepsis in preterm infants has been shown to trigger release of cytokines (including IL-6, TNF- α and IL-1 β), oxidative stress and endothelial dysfunction, which collectively disrupt pulmonary angiogenesis and promote interstitial fibrosis (23,24,26). Furthermore, severe infection frequently necessitates prolonged invasive ventilation and higher oxygen exposure, compounding the risk of ventilator-induced lung injury and oxygen toxicity (25).

Clinically, this finding underscores the imperative for early sepsis prevention and prompt antimicrobial treatment in the NICU, particularly during the first 2 postnatal weeks. Stringent infection control protocols, rapid pathogen identification and optimized empiric antibiotic strategies may therefore represent critical interventions to mitigate BPD risk in high-risk preterm populations.

PDA (OR=4.514; P=0.016) was a significant predictor identified in the present study, in agreement with previous studies suggesting that prolonged ductal patency exacerbates pulmonary overcirculation, increasing the risk of pulmonary edema and ventilator dependency (28,29). The role of PDA treatment in mitigating BPD remains controversial; however, the present findings suggest that early closure, whether pharmacological or surgical, may reduce the burden of ventilator-associated lung injury in high-risk infants.

IVH (OR=5.926; P=0.028) was strongly associated with BPD, reflecting shared mechanisms of systemic inflammation, oxidative stress and vascular fragility (30,31). The interplay between brain and lung injury highlights the importance of

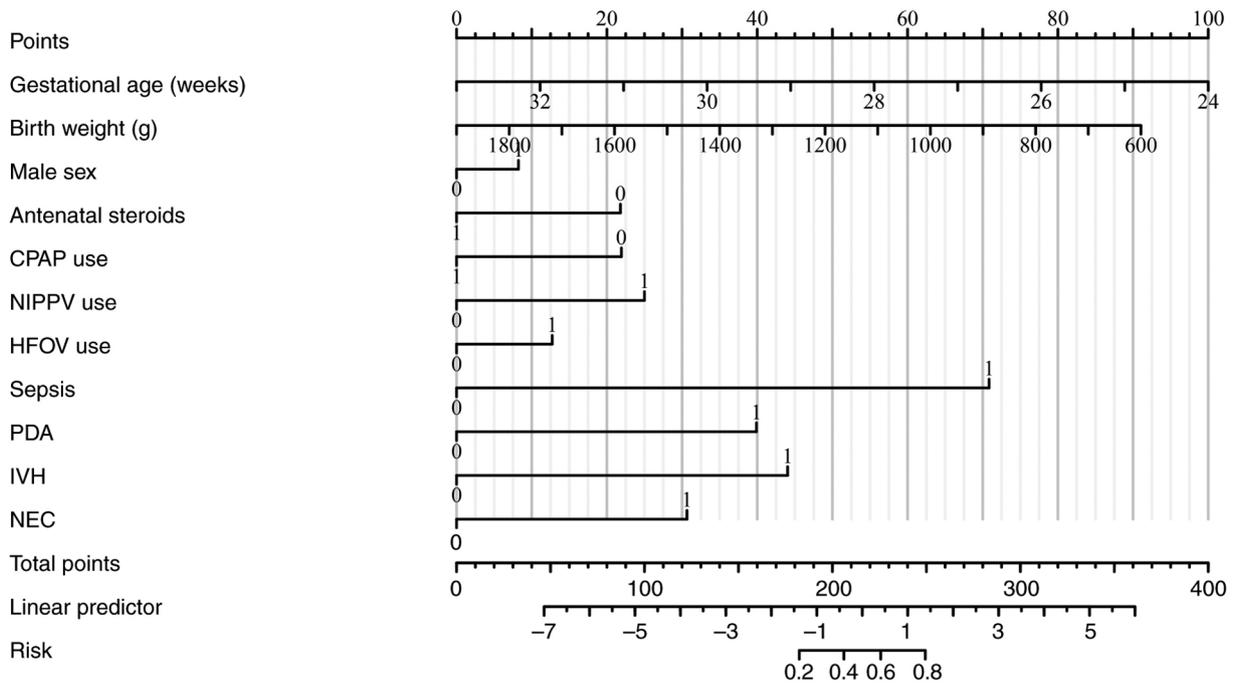


Figure 3. Nomogram for BPD risk prediction. The nomogram visualizes the contribution of multiple predictors to the risk of BPD. Predictors include gestational age, birth weight, sex, antenatal steroids, respiratory support modes, sepsis, PDA, IVH and NEC. The total points correspond to the predicted probability of BPD. BPD, bronchopulmonary dysplasia CPAP, continuous positive airway pressure; NIPPV, non-invasive positive pressure ventilation; HFOV, high-frequency oscillatory ventilation; PDA, patent ductus arteriosus; IVH, intraventricular hemorrhage; NEC, necrotizing enterocolitis.

a multidisciplinary approach to managing extremely preterm infants, focusing on neuroprotection and minimizing invasive procedures that increase hemodynamic instability.

While CPAP and high-frequency oscillatory ventilation (HFOV) were significant in univariate analysis, their effects did not remain significant in multivariate models. This may indicate that respiratory support modalities reflect underlying disease severity, rather than acting as direct predictors of BPD. Nonetheless, the judicious use of non-invasive ventilation and minimizing oxygen toxicity remain cornerstones of BPD prevention (32,33). CPAP is generally regarded as a protective modality that reduces ventilator-associated lung injury (34). In the present cohort, CPAP use was lower among infants who ultimately developed BPD, whereas escalation to HFOV was more frequent. This pattern most likely reflects baseline illness severity rather than a detrimental effect of CPAP: Infants with more severe initial respiratory compromise were less able to tolerate CPAP and required earlier escalation to invasive ventilation or HFOV. Thus, the observed group difference in respiratory support should be interpreted as a marker of underlying disease severity, consistent with prior reports showing that the choice of respiratory support modality typically reflects the infant's clinical acuity rather than functioning as an independent predictor of BPD (35,36).

NEC, a systemic inflammatory condition, was significant in the present univariate analysis, but lost significance in multivariate modeling. This result may reflect collinearity with sepsis and other variables. Nevertheless, the present findings align with previous research highlighting NEC as a driver of systemic inflammation and impaired lung development (15). Preventative measures, such as human milk feeding and probiotics, could have dual benefits for gut and lung health in preterm infants (37).

The nomogram constructed in the present study provides a user-friendly tool for bedside application. While some predictors in the final model, such as sepsis or HFOV use, were formally coded as occurring within the first 14 days, in the majority of cases, these events were clinically apparent or could be anticipated within the first 72 h after birth. For example, early-onset sepsis in preterm infants often manifests within the first 48 h, and the need for HFOV is typically determined during initial respiratory stabilization (38). As such, the model maintains its intended role for early risk stratification and timely intervention in clinical practice. By integrating gestational age, birth weight, sepsis, PDA and IVH, the model facilitates individualized risk stratification and enables timely interventions. Compared with earlier models that primarily relied on gestational age and birth weight (39,40), the present approach incorporates comorbidities, thus enhancing predictive accuracy. Importantly, the present study introduces several novel aspects: Unlike prior models that typically focused on gestational age and birth weight alone, the present nomogram integrates comorbidities such as sepsis, PDA and IVH, variables with high clinical relevance yet often excluded from earlier predictive tools. The development of a visually intuitive nomogram enhances practical usability, making the model more accessible for bedside application by clinicians. Moreover, to the best of our knowledge, this is one of the few studies conducted in Southwest China that has systematically developed and internally validated a BPD risk prediction model, thereby addressing a regional gap in neonatal research and contributing valuable insights to the global literature. Although birth weight and sex were not statistically significant in the present multivariate model, they were retained in the nomogram due to their strong clinical relevance and prior validation as BPD risk factors (41). Including such variables ensures

clinical interpretability and aligns with accepted practices in predictive model development (42).

The present model's high AUC (0.918) surpasses benchmarks reported in similar studies (11), underscoring its robustness. Moreover, the calibration curve in the present study demonstrated excellent agreement between predicted and observed probabilities, thus ensuring reliability across various clinical settings. These strengths make the model particularly valuable for guiding early interventions, such as caffeine therapy, optimization of ventilation strategies and nutritional support (43).

The inclusion of these parameters significantly enhances predictive accuracy while maintaining applicability within the first 72 h of life in most cases. The comprehensive collection of maternal, neonatal and comorbid factors allowed for a thorough exploration of BPD risk determinants, while multivariate logistic regression ensured the identification of independent predictors. Furthermore, the application of bootstrapping for internal validation enhanced the reliability of the model and reduced the risk of overfitting. The visually intuitive nomogram bridges the gap between complex statistical models and bedside decision-making, facilitating rapid individualized risk estimation by clinicians.

However, certain limitations exhibited by the current study should be acknowledged. First, the model underwent only internal validation using bootstrapping without any external validation, which restricts its generalizability and positions it as a preliminary exploratory tool; external validation in diverse cohorts is necessary to confirm its applicability across different clinical environments. Furthermore, the ratio of BPD events ($n=34$) to the 11 candidate predictors initially entered into the multivariate model resulted in an events-per-variable ratio of $\sim 3.1:1$, which is below the commonly recommended threshold of $10:1$ (44). To minimize this risk, a stepwise backward elimination process was applied to retain only the most stable predictors and performed bootstrap internal validation to assess and adjust for optimism. This yielded a bias-corrected AUC of 0.902, which was only slightly lower than the apparent AUC, supporting the relative stability of the model. Nevertheless, external validation in larger, multi-center cohorts is essential to confirm the generalizability of the present findings. The retrospective design of the present study, despite meticulous data collection, is inherently prone to selection and information biases. Additionally, the current study was conducted in a single center with a relatively small sample size ($n=120$; BPD cases= 34), which may limit statistical power and precluded more granular subgroup analyses by gestational age and birth weight categories. The relatively small number of events also means that some clinically important variables, such as birth weight and infant sex, did not reach statistical significance in multivariable analysis.

Future research should focus on addressing the limitations of the present study and further advancing the field of BPD risk prediction. Conducting multicenter, prospective studies with larger and more diverse populations will be essential to validate the current model externally and ensure its generalizability. Incorporating biomarkers such as peripheral blood cytokines (e.g., IL-6, IL-8) or molecular signatures identified through transcriptomic approaches may enhance the precision of the model and provide insights into the underlying mechanisms of BPD (45). Additionally, integrating advanced imaging

techniques, such as lung ultrasound or magnetic resonance imaging, may offer novel perspectives on disease progression and early risk stratification. Long-term follow-up studies are crucial to evaluate the predictive impact of the model on neurodevelopmental and respiratory outcomes, ensuring that early identification translates into improved quality of life for preterm infants. Finally, assessing the real-world clinical utility of the model, including its integration into electronic health records and decision-support systems, will determine its potential to optimize neonatal care and resource allocation.

Since only internal validation was performed, the present study should be regarded as a preliminary exploratory effort requiring future external validation to confirm its broader applicability. In the current study, a clinically meaningful preliminary risk prediction model for BPD in preterm infants was constructed. The inclusion criteria were intentionally broad (gestational age <32 weeks and birth weight $\leq 2,500$ g) to ensure the applicability of the model to a wider range of preterm infants in routine clinical practice. Although this approach may include infants at relatively lower risk for BPD, it enhances the generalizability and relevance of the model in diverse neonatal care settings. While the model demonstrates strong discrimination and calibration, the relatively small sample size ($n=120$) and single-center design aspect of the current study may limit the generalizability of the present findings. Nevertheless, the use of readily accessible clinical predictors and the application of 1,000 bootstrap resamples for internal validation provide a reliable foundation for further model development. This exploratory analysis offers an important first step toward establishing a practical risk stratification tool. Although internal validation using 1,000 bootstrap resamples indicates strong model stability and reduces overfitting risk, the absence of external validation remains a key limitation of the present study. Without testing it on an independent cohort, the generalizability of the model across different populations and clinical practices cannot be fully ensured. Future research should therefore prioritize external validation through large-scale, multicenter, prospective studies to confirm the performance of the nomogram in broader settings. Establishing external credibility through future validation is essential for integrating this model into routine clinical practice and reinforcing its predictive value.

Acknowledgements

Not applicable.

Funding

No funding was received.

Availability of data and materials

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

Authors' contributions

YSP conceived and designed the study, and participated in data collection, statistical analysis and manuscript drafting. LX

participated in data acquisition, interpretation of results and critical revision of the manuscript. WBD was responsible for data management, literature review and assisting in statistical analysis. JWD conceived and designed the study and critically revised the manuscript. All authors have read and approved the final manuscript. YSP and LX confirm the authenticity of all the raw data.

Ethics approval and consent to participate

The present study was conducted in accordance with The Declaration of Helsinki and was approved by the Institutional Review Board of The Affiliated Hospital, Southwest Medical University (approval no. KY2025055). Due to the retrospective nature of the present study, the requirement for informed consent was waived by the ethics committee. All patient data were fully anonymized and utilized exclusively for research purposes.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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