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ORIGINAL RESEARCH

Development and Validation of a Nomogram for Predicting Bronchiolitis Obliterans in Children with Severe Adenovirus Pneumonia: Identification of Key Risk Factors

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Objective: This study aimed to identify the risk factors for bronchiolitis obliterans (BO) development in children with severe adenovirus pneumonia (SAP) and to construct and validate a nomogram prediction model.

Methods: This retrospective study included 152 pediatric patients with SAP between January 2019 and December 2023. We categorized these patients as having developed BO (n=36) and non-BO (n=116) based on long-term follow-up outcomes. Key clinical features were optimized using the least absolute shrinkage and selection operator (LASSO) regression and a nomogram was developed using logistic regression. Model performance was assessed and validated through receiver operating characteristic (ROC) curve analysis, calibration curves, and decision curve analysis (DCA).

Results: The LASSO regression analysis initially identified nine potential clinical predictors. Subsequent univariable and multivariable logistic regression revealed four independent risk factors significantly associated with BO development, namely, younger age, Odds ratio (OR) =0.94, 95% CI, 0.90–0.99, p=0.010; longer duration of fever, OR=2.27, 95% CI, 1.52–3.39, p<0.001; requirement for tracheoscopy, OR=5.25, 95% CI, 1.06–26.09, p=0.040; and extended oxygen therapy, OR=1.64, 95% CI, 1.10–2.43, p=0.010. The final prediction model incorporated three key predictors (months of age, fever duration, and oxygen therapy duration) into a clinically practical nomogram. The model demonstrated excellent discrimination, with an area under the curve (AUC) of 0.95, 95% CI, 0.91–0.98, a sensitivity of 0.83, and a specificity of 0.93. The Hosmer-Lemeshow test, $\chi 2$=5.24, p=0.732 indicated good calibration, and the DCA demonstrated positive clinical benefits.

Conclusion: We developed and validated a clinically practical nomogram, incorporating three key predictors mainly, months of age, fever duration, and oxygen therapy duration in predicting BO in children with SAP.The model demonstrates strong discriminatory power, reliable calibration, and clinical utility. This tool enables early risk stratification, facilitating timely intervention for high-risk pediatric SAP patients.

Keywords: severe adenovirus pneumonia, bronchiolitis obliterans, risk factors, nomogram, children

Introduction

Adenovirus, a non-enveloped double-stranded DNA virus, represents a leading etiological agent of pediatric respiratory infections.[1–3] Among hospitalized adenovirus-positive children, approximately 70% develop radiologically confirmed adenovirus pneumonia,[4,5] which typically presents with fever, cough, wheezing, and shortness of breath, with disease severity ranging from mild to severe. Notably, 35% of adenovirus infections progress to severe adenovirus pneumonia (SAP),[6,7] which is associated with rapid progression and numerous pulmonary and extrapulmonary complications.[8] One of the most concerning sequelae of SAP is bronchiolitis obliterans (BO).

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Bronchiolitis obliterans (BO), is a chronic, irreversible fibrotic disorder that leads to progressive small airway damage and persistent airway obstruction, manifesting as recurrent wheezing, exercise intolerance, and chronic respiratory insufficiency that profoundly impacts pediatric quality of life.[9,10] While BO pathogenesis in children may involve post-transplant complications or other etiologies, post-infectious BO (PIBO) constitutes the predominant form in pediatric populations.[11] The clinical presentation of PIBO is highly variable, ranging from mild respiratory disturbances to severe and persistent airway obstruction.[12] Mounting evidence implicates adenovirus as the principal causative agent of PIBO,[13–15] with epidemiological studies demonstrating striking disease burden: A 5-year longitudinal study revealed 50% of children with adenovirus pneumonia developed PIBO,[16] and Chinese cohort studies report PIBO incidence of 24% in SAP cases.[17,18] The mechanisms underlying adenovirus-associated PIBO remain incompletely understood, though current evidence suggests complex interactions between viral cytopathology, host immune response, and genetic susceptibility factors.[11] This strong epidemiological association, coupled with the condition's irreversible progression, underscores the critical need for early prediction and intervention strategies in high-risk SAP patients.

The diagnosis of PIBO remains clinically challenging, frequently leading to diagnostic delays and suboptimal outcomes. Current diagnostic approaches rely on composite clinical criteria incorporating medical history, pulmonary function tests, and imaging findings, often without histological confirmation.[11] These challenges are particularly pronounced in young children, as nonspecific symptomatology and difficulties in performing reliable pulmonary function tests in infants, frequently result in diagnostic delays of months to years.[19] Population data demonstrated a 10.3-month median gap between initial pulmonary injury (median age: 7.2 months) and definitive PIBO diagnosis (median age: 17.5 months) in children.[20] Such diagnostic delays have significant clinical consequences: postponement of comprehensive management strategies, progressive small airway dysfunction and irreversible lung function impairment.[21,22] Longitudinal data underscore these concerns, with a 12-year follow-up study demonstrating that PIBO patients develop severe, persistent obstructive lung defects, experience recurrent hospitalization for respiratory infections, ultimately leading to poor long-term outcomes.[23] Longitudinal pulmonary function assessments in PIBO patients demonstrated significant and persistent obstructive deficits, with mean Forced Expiratory Volume in 1 second (FEV1) declining by 1.07% annually over an 8-year follow-up period.[24] These findings highlight the critical need for early PIBO identification to improve outcomes and reduce disease burden. However, studies exploration of risk factors for the development of BO in children with SAP are still limited.

In this study, we primarily aimed to identify the risk factors for BO development in children with SAP, and to construct and validate a nomogram-based prediction model. The prediction model enables early risk stratification, facilitating timely intervention for high-risk pediatric SAP patients.

Methods

Study Population

This retrospective observational study was conducted at a tertiary specialized pediatric hospital in Zhejiang Province, China, from January 2019 to December 2023. Hospitalized children aged under 14 years old diagnosed with SAP were collected. The study was approved by the Ethics Committee of the Institutional Review Board of Hangzhou Children's Hospital (Approval No.2024–27). The informed consent was waived by the committee in compliance with the national regulations "Ethical Review Measures for Biomedical Research Involving Human Subjects" in China, as the retrospective studies utilized fully anonymized data that could not be linked back to individual participants.

Inclusion Criteria

1) Aged 28 days to 14 years old, male or female; 2) confirmed diagnosed with adenovirus pneumonia by pediatric specialists in accordance with the "Guideline for diagnosis and treatment of adenovirus pneumonia in children (2019 Edition)",[25] with positive adenovirus test through direct immunofluorescence and/or polymerase chain reaction; 3) had any of the manifestations of severe pneumonia, and 4) successful completion at least 6 months follow-up.

Severe Pneumonia Criteria

Severe pneumonia was defined by meeting at least one of the following clinical criteria: 1) compromised general condition; 2) feeding refusal or clinical signs of dehydration; 3) impaired consciousness; 4) hypoxemia manifestations, including cyanosis, dyspnea, tachypnea (respiratory rate >70 breaths/min in infants or >50 breaths/min in older children), or pulse oxygen saturation ≤92%; 5) hyperpyrexia or persistent fever exceeding 5 days; 6) radiographic evidence of pulmonary infiltration involving multiple lobes or ≥2/3 of lung volume; 7) intrapulmonary complications (pleural effusion, pneumothorax, atelectasis, pulmonary necrosis, or pulmonary abscess); and 8) extrapulmonary complications. Patients fulfilling any of these criteria were classified as severe pneumonia cases.

Exclusion Criteria

The exclusion criteria were as follows: 1) had been diagnosed with BO before; 2) comorbidity with other chronic diseases and conditions, such as bronchopulmonary dysplasia, immune deficiency, connective tissue diseases, bone marrow transplantation, and organ transplantation; 3) absence of clinical data, such as loss of follow-up, death or unknown diagnosis.

Grouping Criteria

Based on the children's clinical presentation and lung imaging in the last 6 months, we categorized the children into BO group according to the following criteria:[11] 1) had a history of severe respiratory tract infection in a previously healthy patient, 2) evidence of persistent or recurrent airway obstruction not responding to systemic corticosteroids and bronchodilators based on clinical symptoms and/or by lung function tests, 3) mosaic pattern and/or air trapping on chest tomography, 4) exclusion of other chronic lung diseases.

Figure 1 summarizes the patient enrollment process. Among 163 children with SAP initially enrolled, we excluded 11 cases (1 with pre-existing BO, 3 with chronic comorbidities, 3 with incomplete clinical data, and 4 lost to follow-up), resulting in 152 participants for final analysis.

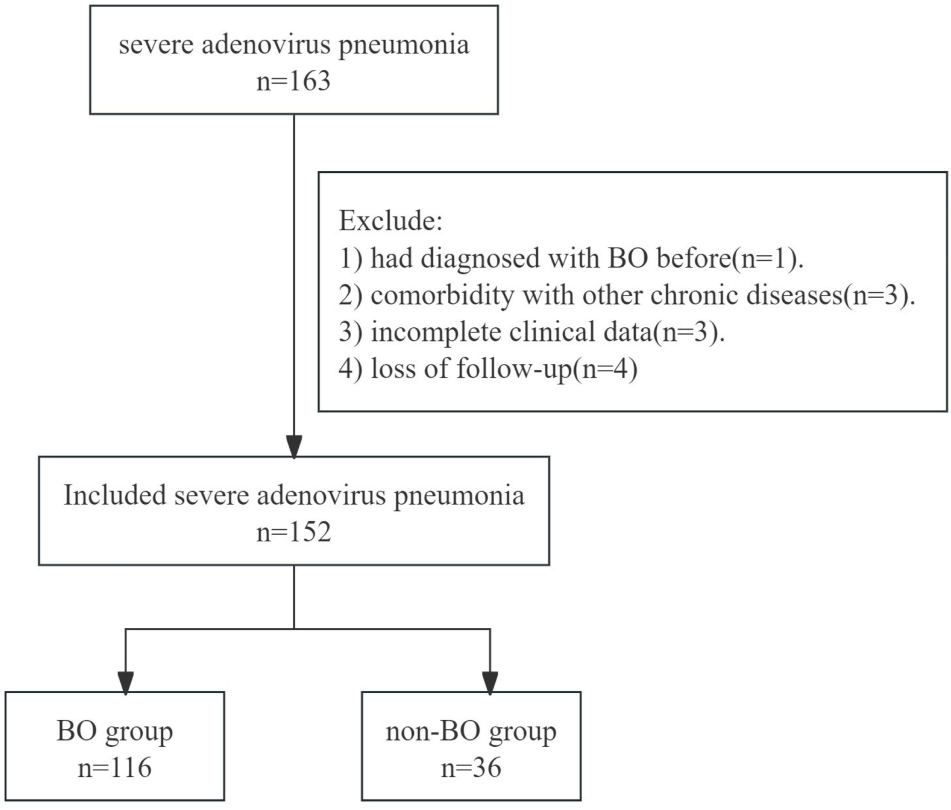

Figure 1 Patients included in the study analysis.

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Pathogenetic Testing

All participants underwent nasopharyngeal aspiration to obtain nasopharyngeal secretion specimens and sputum specimens within 24 hours of admission. Direct immunofluorescence and/or Polymerase chain reaction (Applied Biological Technologies CO., Ltd., Beijing, China) was conducted to test common respiratory pathogens, such as adenovirus, influenza A virus, influenza B virus, human parainfluenza virus, respiratory syncytial virus, rhinovirus, bocavirus, metapneumovirus, coronavirus, *Mycoplasma pneumoniae* (MP), *Chlamydia*. Additionally, bacterial infections were identified through sputum cultures, bronchoalveolar lavage, or blood cultures.

Clinical Data Collection

Comprehensive clinical data were systematically extracted from the electronic medical records system for all enrolled patients. The following medical data were collected: demographic characteristics (gender and age), history of prematurity, past medical history, hospitalization duration, clinical manifestations, laboratory parameters, pulmonary imaging findings, therapeutic interventions and prognosis.

Statistical Analysis

All statistical analyses were conducted using R statistical software (version 4.2.2) and GraphPad Prism 9.0. Shapiro–Wilk test was used to check for normality in all variables. Continuous variables were presented as either mean ± standard deviation (SD) for parametric data or median (25th Percentile, 75th Percentile) for non-parametric distributions. Parametric between-group comparisons were analyzed using Student's *t*-test, while non-parametric comparisons were evaluated through Mann–Whitney *U*-test. Categorical variables were expressed as frequency (percentage), with between-group differences analyzed by χ^2-test or Fisher's exact test when applicable. To optimize the selection of clinical features, the least absolute shrinkage and selection operator (LASSO) regression was applied. Subsequent univariable and multivariable logistic regression were performed to identify potential risk factors. A nomogram prediction model was developed using the stepwise Akaike information criterion (step-AIC) method. The discriminatory ability of the model was assessed by calculating the area under the receiver operating characteristic curve (AUROC). Calibration was evaluated using a calibration curve and the Hosmer-Lemeshow (HL) test. Additionally, decision curve analysis (DCA) was employed to assess the model's clinical efficacy. A p-value of < 0.05 was considered statistically significant.

Results

Demographic and Clinical Characteristics of the Study Population

After excluding 11 cases (1 with pre-existing BO, 3 with chronic comorbidities, 3 with incomplete clinical data, and 4 lost to follow-up), 152 children with SAP were included in the final analysis with a median age of 30 months. The cohort consisted of 89 males (58.6%) and 63 females (41.4%), with 68 patients (44.7%) under 2 years of age. After a follow-up period of at least 6 months, the participants were stratified into two groups: the non-BO group (n = 116) and the BO group (n = 36) (Figure 1). Comparative analysis of demographic and clinical characteristics between the groups is presented in Table 1. Notably, children in the BO group exhibited significantly younger age ($p < 0.001$), prolonged hospitalization ($p < 0.001$), extended duration of fever ($p < 0.001$), and higher prevalence of dyspnea ($p = 0.001$) compared to the non-BO group. Laboratory findings demonstrated marked differences, with the BO group showing elevated platelet counts (PLT), erythrocyte sedimentation rate (ESR), lactate dehydrogenase (LDH), and D-dimer levels, alongside reduced serum albumin concentrations (all $p < 0.05$). Regarding intrapulmonary complications, the BO group displayed significantly higher rates of pulmonary consolidation, atelectasis, and bilateral lung infections. Therapeutic interventions also differed substantially between groups, with the BO group receiving more frequent glucocorticoid therapy, intravenous immunoglobulin administration, bronchoscopic procedures, and intensive care unit (ICU) admissions. 55 children (36.2%) required supplemental oxygen therapy, typically administered via nasal cannula, face mask, or high-flow oxygen, with none requiring mechanical ventilation. Both the frequency and duration of oxygen therapy were significantly greater in the BO group compared to the non-BO group ($p < 0.001$).

Table 1 Comparison of Clinical Characteristics Between Non-BO and BO Groups

Clinical Variables	Non-BO (n = 116)	BO (n = 36)	*p*-Value
Gender, male/female	71/45	18/18	0.233
Age(month), M (P25, P75)	37.0 (20.0, 63.8)	20.0 (14.0, 33.8)	<0.001
<24months, n (%)	43 (37.1)	25 (69.4)	0.001
Premature birth, n (%)	9 (7.8)	5 (13.9)	0.435
Underlying diseases, n (%)	34 (29.3)	12 (33.3)	0.646
Hospital stay(days), M (P25, P75)	6.0 (5.0, 8.0)	8.0 (7.0, 11.0)	<0.001
Duration of fever(days), M (P25, P75)	6.0 (5.0, 7.0)	9.0 (7.0, 11.0)	<0.001
Wheezing, n (%)	57 (49.1)	14 (38.9)	0.281
Tachypnoea, n (%)	35 (30.2)	22 (61.1)	0.001
White blood cells (× 10^9/L), M (P25, P75)	10.0 (7.8, 14.0)	9.8 (6.8, 15.5)	0.938
Neutrophil proportion (%),M (P25, P75)	64.3 (49.3, 76.7)	67.3 (54.4, 80.9)	0.224
Lymphocytes proportion (%),M (P25, P75)	25.4 (16.7, 41.0)	22.4 (13.4, 36.2)	0.265
Hemoglobin (g/L), mean ± SD	122.5 ± 9.1	125.4 ± 9.0	0.088
PLT (× 10^9/L), M (P25, P75)	261.0 (225.0, 331.0)	312.0 (251.8, 376.8)	0.018
C-reactive protein (mg/L), M (P25, P75)	13.6 (3.2, 29.6)	14.3 (4.6, 22.9)	0.922
ESR (mm/h), M (P25, P75)	27.5 (16.0, 42.8)	45.0 (27.0, 60.0)	0.001
PCT (ng/mL), M (P25, P75)	0.2 (0.1, 0.4)	0.3 (0.1, 0.4)	0.402
ALT(U/L), M (P25, P75)	15.0 (12.0, 22.0)	14.5 (11.0, 19.8)	0.773
AST(U/L), M (P25, P75)	35.0 (29.0, 45.8)	34.5 (29.0, 38.8)	0.573
Albuminous protein(g/L), M (P25, P75)	41.1 (38.5,43.9)	37.8 (35.0, 39.6)	<0.001
LDH (U/L), M (P25, P75)	346.5 (298.0, 421.8)	393.5 (342.0, 500.3)	0.010
CKMB(U/L), M (P25, P75)	25.0 (20.1,37.8)	26.0 (22.0,35.8)	0.306
IL-6(pg/mL), M (P25, P75)	31.5 (12.0,60.6)	44.8 (18.7,59.8)	0.323
Fib(g/L), M (P25, P75)	3.3 (3.1,4.0)	3.4 (3.0,4.5)	0.554
D-dimer(mg/L), M (P25, P75)	0.4 (0.3,0.6)	0.6 (0.4,1.1)	<0.001
IgA(g/L), M (P25, P75)	0.7 (0.4,1.3)	0.8 (0.6,1.2)	0.363
IgG(g/L), M (P25, P75)	8.1 (6.7,10.1)	8.5 (6.4,9.8)	0.611
IgM(g/L), M (P25, P75)	1.2 (0.8,1.5)	1.2(0.8,1.8)	0.530
Co-infection, n (%)	81 (69.8)	23 (63.9)	0.503
Coinfection with other viruses, n (%)	39 (33.6)	9 (25.0)	0.331
Coinfection with MP, n (%)	34 (29.3)	11 (30.6)	0.886
Coinfection with bacteria, n (%)	17 (14.7)	5 (13.9)	0.909
Pulmonary consolidation, n (%)	61 (52.6)	26 (72.2)	0.037
Atelectasis, n (%)	18 (15.5)	13 (36.1)	0.007
Bilateral lung infection, n (%)	76 (65.5)	32 (88.9)	0.007
Pleural effusion, n (%)	19 (16.4)	9(25.0)	0.244
Extrapulmonary complications, n (%)	22 (19.0)	17 (47.2)	0.001
Use of glucocorticoids, n (%)	65 (56.0)	32 (88.9)	<0.001
Use of immunoglobulin, n (%)	49 (42.2)	26 (72.2)	0.002
Tracheoscopy therapy, n (%)	15 (12.9)	20 (55.6)	<0.001
Oxygen requirement, n (%)	31 (26.7)	24 (66.7)	<0.001
Oxygen requirement (days), M (P25, P75)	0.0 (0.0, 2.0)	4.0 (0.0, 5.0)	<0.001
Transfer to ICU, n (%)	6 (5.2)	12 (33.3)	<0.001
ICU stay(days), M (P25, P75)	0.0 (0.0, 0.0)	0.0 (0.0, 2.0)	<0.001

Notes: All data were collected from the children at baseline.

Abbreviations: M (P25, P75), median (25th Percentile, 75th Percentile); BO, bronchiolitis obliterans; PLT, platelets; ESR, erythrocyte sedimentation rate; PCT, procalcitonin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; LDH, lactate dehydrogenase; CKMB, creatine kinase-MB; MP, *Mycoplasma pneumoniae*; ICU, intensive care unit.

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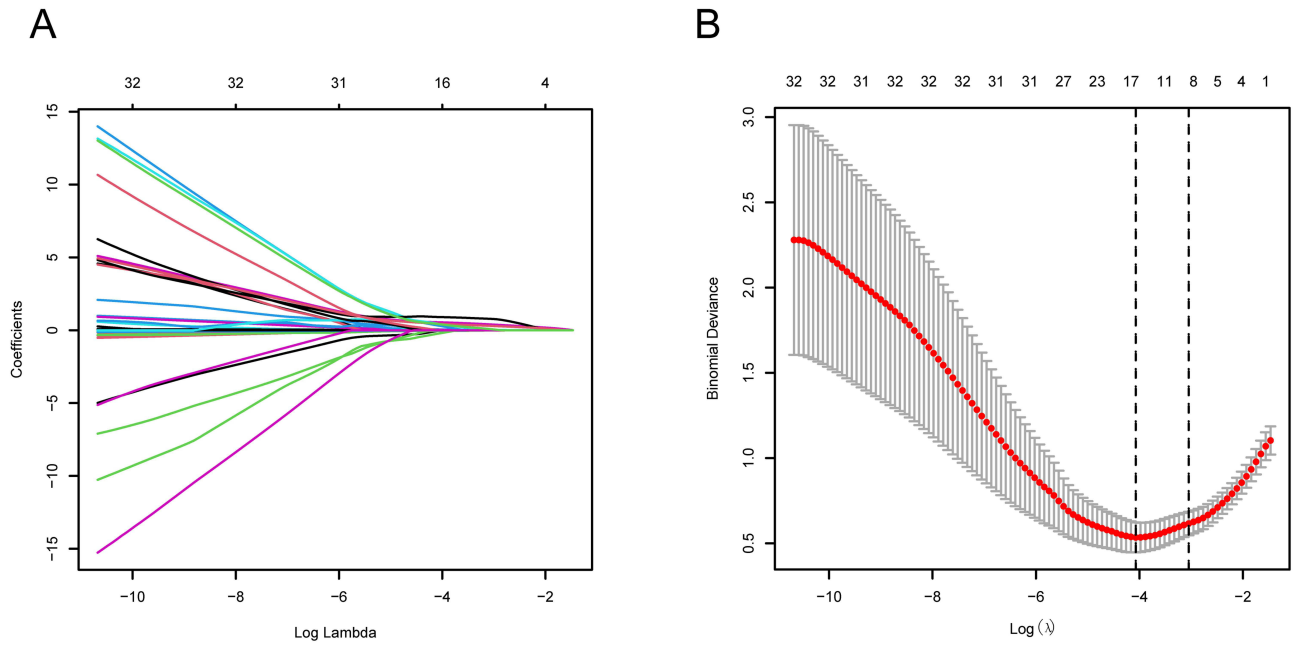

Figure 2 The appropriate clinical characteristics between non-BO and BO groups were selected by LASSO. (**A**) LASSO coefficient profiles of 44 variables. (**B**) Tuning parameter (λ) selection using 10-fold cross-validation via minimum criteria to select the best penalty parameter lambda. LASSO, least absolute shrinkage and selection operator.

Risk Factors and Prediction Model of BO Following SAP

Initially, 44 clinical variables were evaluated in this study. To address multicollinearity among predictors, we performed LASSO regression analysis, which identified 9 key clinical features for subsequent univariable and multivariable logistic regression analyses (Figure 2 and Table 2). Multivariable analysis revealed four independent risk factors significantly associated with BO development in SAP patients, namely, younger age, Odds ratio (OR) =0.94, 95% CI, 0.90–0.99, p=0.010; longer duration of fever, OR=2.27, 95% CI, 1.52–3.39, p<0.001; requirement for tracheoscopy, OR=5.25, 95% CI, 1.06–26.09, p=0.040; and extended oxygen therapy, OR=1.64, 95% CI, 1.10–2.43, p=0.010. Using the stepwise AIC method in R software, we developed a clinically practical nomogram prediction model, incorporating months of age, fever duration, and oxygen therapy duration as predictive factors (Figure 3).

Table 2 Univariable and Multivariable Regression Analysis of Risk Factors for BO

Factors	Univariable Analysis			Multivariable Analysis		
	p-Value	OR	95% CI	*p*-Value	OR	95% CI
Months of age	<0.001	0.96	0.94–0.98	0.010	0.94	0.90–0.99
Days of hospital stay	<0.001	1.69	1.37–2.10	0.340	1.19	0.84–1.68
Days of fever	<0.001	1.88	1.49–2.36	<0.001	2.27	1.53–3.39
Hemoglobin	0.090	1.04	0.99–1.08	-	-	-
Albuminous protein	<0.001	0.80	0.72–0.89	0.210	0.89	0.75–1.07
CKMB	0.310	0.99	0.96–1.01	-	-	-
Tracheoscopy therapy	<0.001	8.42	3.59–19.74	0.040	5.25	1.06–26.09
Days of oxygen requirement	<0.001	1.64	1.35–1.98	0.010	1.64	1.10–2.43
Transfer to ICU	<0.001	9.17	3.13–26.86	0.380	2.78	0.28–27.85

Abbreviations: CKMB, creatine kinase-MB; ICU, intensive care unit; OR, odds ratio; 95% CI, 95% confidence interval.

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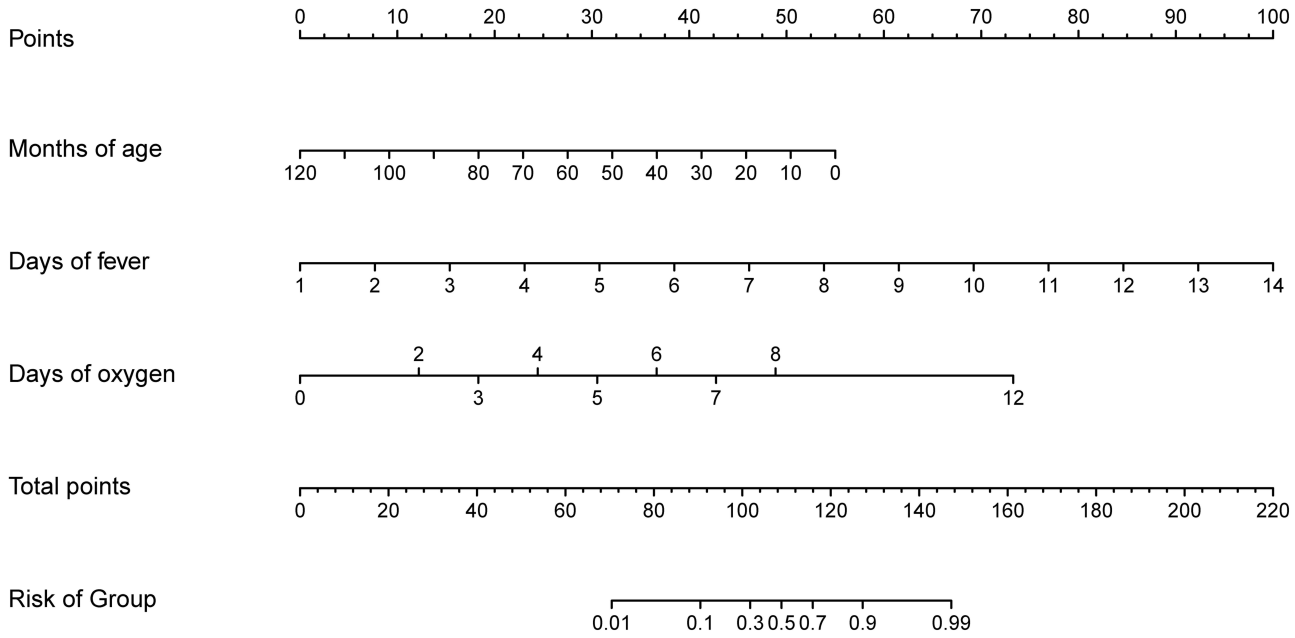

Figure 3 The nomogram for predicting the risk of BO following SAP. Locate patient's value on each predictor axis; Draw vertical lines to the "Points" axis to obtain the corresponding score for each variable; Sum all individual points and locate on "Total Points" axis; Draw a vertical line to the "Risk of group" axis to obtain the final risk percentage.

Validation of the Prediction Model

The predictive performance of the nomogram was rigorously evaluated through multiple validation approaches. ROC analysis demonstrated excellent discriminative ability, with an area under the curve (AUC) of 0.95, 95% CI, 0.91–0.98 (Table 3, Figure 4A). At the optimal cutoff value, the model achieved a sensitivity of 83% and specificity of 93%, outperforming all individual predictors in diagnostic accuracy. The Hosmer-Lemeshow goodness-of-fit test showed no significant deviation ($\chi^2 = 5.238$, $p = 0.732$). Visual inspection of the calibration curve revealed close agreement between predicted probabilities and observed outcomes across all risk strata (Figure 4B), indicating good calibration. DCA was performed to evaluate clinical utility (Figure 4C), which demonstrated favorable clinical benefits, supporting its potential for clinical implementation.

Discussion

In this retrospective cohort study of 152 pediatric patients with SAP, we developed and validated a clinically practical nomogram prediction model incorporating three key parameters: months of age, fever duration, and oxygen therapy duration. The model demonstrated robust predictive performance, with excellent discrimination (AUC 0.95), good calibration (Hosmer-Lemeshow $p = 0.732$), and meaningful clinical utility as evidenced by DCA. These findings suggest this tool may enable clinicians to identify high-risk patients for BO development at an early stage, potentially facilitating timely intervention and improved outcomes.

Table 3 The ROC Curves of Different Variables and the Prediction Model

Variables	Cut-off	AUC (95% CI)	Sensitivity	Specificity
Model	-	0.95(0.91–0.98)	0.83	0.93
Months of age	42.5	0.72(0.62–0.81)	0.86	0.47
Days of fever	7.5	0.84(0.76–0.92)	0.69	0.85
Days of oxygen requirement	3.5	0.75(0.66–0.85)	0.58	0.91

Abbreviations: AUC, area under curve; ROC, receiver operating characteristic; 95% CI, 95% confidence interval.

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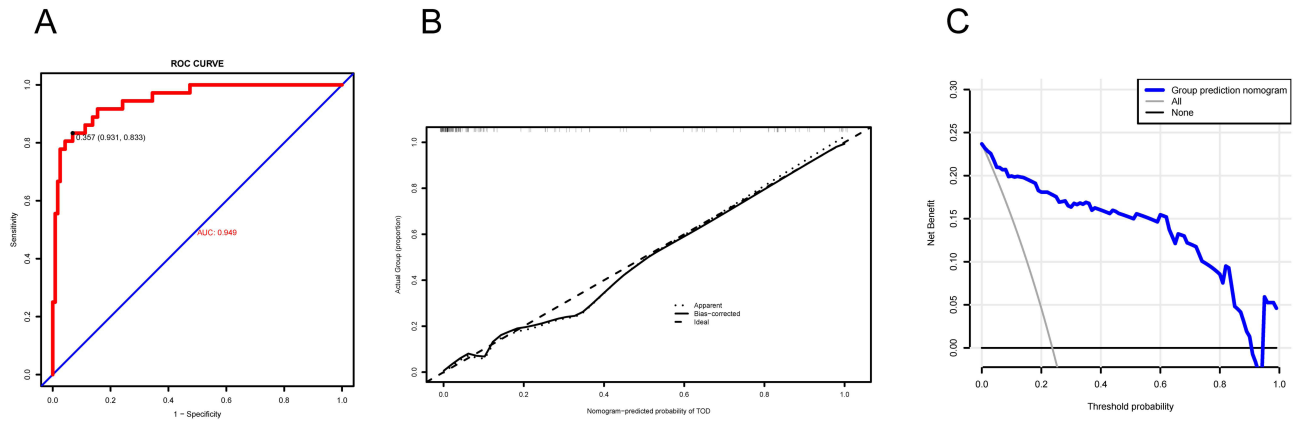

Figure 4 Validation of the prediction model. (**A**) ROC curve of the prediction model. (**B**) Calibration curve of the prediction model. (**C**) Decision curve analysis of the prediction model (blue line).

Our study revealed that 23.7% (36/152) of pediatric SAP cases progressed to BO, a complication rate consistent with previous Chinese cohort studies.[17,18] Comparative analysis demonstrated that BO patients presented with distinct clinical profiles, including: younger age, extended hospitalization duration, prolonged febrile episodes, more frequent respiratory distress, markedly elevated inflammatory markers (PLT, ESR, LDH, D-dimer; all $p<0.05$), higher rates of intrapulmonary complications, greater requirement for intensive interventions and treatments such as glucocorticoids, immunoglobulins, bronchoscopy, and oxygen therapy. These findings collectively suggest that BO development reflects more severe initial pulmonary damage during SAP hospitalization, consistent with the established pathogenesis of post-infectious small airway fibrosis.[16,26] The observed treatment patterns (glucocorticoids, IVIG, bronchoscopy) likely represent clinical responses to this heightened disease severity rather than causative factors. BO is associated with small airway fibrosis following severe pneumonia, and the severity of the initial pneumonia appears to correlate with a higher risk of developing BO.[11]

Through rigorous multivariate analysis employing the stepwise AIC method, we identified three key independent predictors: months of age, fever duration, and oxygen therapy duration. In this study, nearly half of the children with SAP were younger than two years old, and younger age was identified as an independent risk factor for BO. These findings align with existing literature demonstrating increased BO susceptibility in infants under 1 year,[18] while providing novel quantitative risk estimates. The clearance of adenovirus primarily depends on cell-mediated immunity, which develops with age.[27] In younger children, especially those between 6 and 24 months, the level of neutralizing antibodies against adenovirus is low, increasing susceptibility to severe infections.[28]

Recent trends indicate that the incidence of adenovirus pneumonia is increasingly affecting younger children. One study reported that the peak incidence of SAP occurs in children aged 6 to 36 months, with the highest frequency in those aged 12 to 36 months. The incidence significantly decreases in children older than 36 months.[29] This pattern may be linked to the decline of maternal antibodies after six months of age and the immature development of the immune system in younger children. Over two-thirds of children hospitalized with adenovirus type 7 pneumonia were under two years old, and approximately 40% of patients with severe pneumonia and respiratory failure were under 12 months.[30] Furthermore, age below 12 months has been identified as an independent mortality risk factor for children with SAP.[31] These findings highlight the need for great clinical attention to children younger than two years in the management of SAP. In this study, fever duration was found to be an independent risk factor, with an AUC of 0.84, and sensitivity and specificity of 0.69 and 0.85 at a cut-off value of 7.5 days. Fever duration has also been reported to be a risk factor for the development of BO in SAP.[17] There was a linear correlation between fever duration and the risk of BO, with a predictive threshold of 10.5 days and sensitivity and specificity of 0.73 and 0.79, respectively. These children with fever longer than 10.5 days had higher rate of developing BO, longer hospital stay, higher peak temperature, higher incidence of dyspnea and extrapulmonary complications.[17] Additionally, prolonged fever was also found to be an independent risk factor for PIBO in children with SAP following invasive mechanical ventilation.[32] On the other hand, in our cohort, children who developed BO were more likely to present with shortness of breath and required

oxygen therapy, with the duration of oxygen requirement identified as another independent predictor. This can be attributed to the rapid progression of SAP, which frequently results in hypoxemia and necessitates respiratory support, including mechanical ventilation.[33] Several studies have highlighted that children requiring respiratory support are at greater risk of developing BO.[34] A meta-analysis confirmed that hypoxemia was the most significant risk factor for PIBO, followed by mechanical ventilation, shortness of breath, and wheezing.[35]

Prolonged fever and oxygen therapy may indicate a persistent inflammatory response. Although elevated inflammatory markers such as ESR and LDH were noted in the BO group, they were not independent risk factors. Inflammatory mediators can further activate the immune system, causing multi-organ damage and potentially contributing to the development of BO.[10] Moreover, children with PIBO have been shown to exhibit markedly increased oxidative stress in their lungs.[36] High pretreatment LDH levels have been associated with greater disease severity, increased risk of PIBO, and higher mortality rates in children with SAP.[37] Other studies have also reported elevated levels of inflammatory markers, including LDH, interleukin-8, and interferon-gamma, in patients with PIBO.[38] Furthermore, increased levels of Caspase-1 in these patients suggested that inflammasome activation might play a role in fibrosis.[39]

Prediction models, particularly those using nomograms, are increasingly employed in clinical settings to visually quantify risk factors and assist clinicians in early risk identification. In this study, we developed a nomogram prediction model that incorporated months of age, days of fever, and days of oxygen requirement, showing excellent calibration and positive clinical benefits. The model demonstrated strong predictive performance, with an AUC of 0.95 (95% CI 0.91–0.98), a sensitivity of 0.83, and a specificity of 0.93. Currently, only a limited number of nomogram prediction models exist for BO in children with SAP. One nomogram, incorporating admission to the PICU, fever duration, bilateral lung infection, and age under one year old, demonstrated an AUC of 0.85 (95% CI 0.78–0.92).[18] Another model, which included gender, fever duration, adenovirus load, and fungal co-infection, achieved an AUC of 0.86 (95% CI 0.74–0.93) for predicting PIBO in children with SAP after invasive mechanical ventilation.[32] Several other studies have also constructed nomograms for predicting BO in children with severe pneumonia.[15,40] Our findings suggest that nomogram prediction models hold promise as effective tools for pediatricians in predicting BO.

However, our study has several limitations. As a single-center, retrospective study, the sample size was limited, particularly in the BO group. Additionally, while adenovirus typing is known to influence prognosis, and adenovirus type 7 has been associated with more severe outcomes,[41] our study did not include adenovirus typing. Further multicenter studies with larger sample sizes and adenovirus typing are needed to optimize and validate the prediction model.

Conclusions

We developed a prediction model for BO in children with SAP based on three key risk factors: months of age, fever duration, and oxygen therapy duration. The model demonstrated strong discriminatory ability, good calibration, and practical clinical utility. This tool can aid clinicians in early quantitative risk assessment of BO, potentially improving prognosis and enhancing long-term survival outcomes for affected children. Future research should focus on expanding the sample size and conducting multicenter studies to further refine and validate the model.

Ethics Approval

This study was in compliance with the Declaration of Helsinki, and approved by the Ethical Committees of Hangzhou children's Hospital. The informed consent was waived by the committee in compliance with the national regulations "Ethical Review Measures for Biomedical Research Involving Human Subjects" in China, as the retrospective studies utilized fully anonymized data that could not be linked back to individual participants.

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.

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Disclosure

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