Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Exploratory Risk Factor Assessment and Clinical Characterization of Plastic Bronchitis in Severe Pediatric Human Bocavirus 1 Pneumonia: a single-center retrospective case-control study

Jianxing Wei
Fujian Children's Hospital (Fujian Branch of Shanghai Children's Medical Center), Fujian Medical University

Di Lian
Fujian Children's Hospital (Fujian Branch of Shanghai Children's Medical Center), Fujian Medical University

Yan Zheng
Fujian Children's Hospital (Fujian Branch of Shanghai Children's Medical Center), Fujian Medical University

Chenye Lin
Fujian Children's Hospital (Fujian Branch of Shanghai Children's Medical Center), Fujian Medical University

Zhinan Zhang
Fujian Children's Hospital (Fujian Branch of Shanghai Children's Medical Center), Fujian Medical University

Qiuyu Tang
189503561620163.com

Fujian Children's Hospital (Fujian Branch of Shanghai Children's Medical Center), Fujian Medical University

---

Research Article

Keywords: Human bocavirus 1, plastic bronchitis, children, risk factors

Posted Date: October 11th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-10728568/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Abstract

Background

The objective of the research was to assess the exploratory predictors risk factors related to plastic bronchitis (PB) in pediatric patients presenting with severe Human bocavirus 1 (HBoV1) monoinfectious pneumonia.

Methods

Between December 2020 and December 2025, pediatric cases with severe monoinfectious HBoV1 pneumonia hospitalized at Fujian Children's Hospital were enrolled in this study. Pediatric patients who presented with mixed infections, did not undergo bronchoscopy, had severe underlying diseases, or had incomplete clinical data were excluded from the analysis. According to bronchoscopic evaluation, cases were assigned into the non-PB group (n = 35) and the PB group (n = 16). Potential risk factors were determined by first analyzing differences in clinical presentations and laboratory findings across groups. The identification process utilized the least absolute shrinkage and selection operator (LASSO) regression together with Firth's penalized logistic regression. To assess the model's stability, 1,000 bootstrap resamplings were then performed.

Results

Of 484 children initially examined for HBoV1 pneumonia, 51 with severe mono-HBoV1 infection were selected for the final analysis. Serum ferritin (SF), serum amyloid A (SAA), and D-dimer were markedly increased in the PB group. The combination of LASSO feature selection and Firth's penalized logistic regression identified SF (OR = 1.025, 95% CI: 1.010–1.046, P < 0.001), SAA (OR = 1.015, 95% CI: 1.003–1.052, P = 0.014), and D-dimer (OR = 2.247, 95% CI: 1.060–5.994, P = 0.036) as potential predicted factors for PB. Internal validation(1,000 bootstrap resamples) demonstrated good model discrimination, with an AUC of 0.952 (95% CI: 0.882–0.996).

Conclusions

Patients with HBoV1-associated PB have higher levels of SF, SAA, and D-dimer, suggesting tissue damage and hypercoagulative state in PB. These biomarkers may assist in the early identification of PB.

Trial registration

Not applicable.

Introduction

As a respiratory pathogen, it has attracted growing interest for its involvement in pediatric pulmonary infections. According to epidemiological findings, it is responsible for approximately 6.3% of respiratory tract infections, predominantly affecting young children [1]. There are limited comprehensive epidemiological data on pediatric community-acquired pneumonia caused by HBoV1 monoinfection.

Evidence suggests that HBoV1 is associated with a heightened susceptibility to plastic bronchitis (PB) [2–5]. PB is a severe respiratory disease, characterized by sticky, branching bronchial casts that block airways quickly [6]. However, most studies on PB focus on *Mycoplasma pneumoniae* (MP) as the pathogen. Known risk factors for MP-related PB include prolonged fever, high neutrophil counts, elevated lactate dehydrogenase (LDH), and D-dimer levels [6,7]. Compared to that, the role of viral pathogens—particularly HBoV1—in PB pathogenesis is not well understood, and existing studies limited to case reports and case series.

Since there are limited systematic data on HBoV1-associated PB after removing coinfections, our research was conducted to describe the clinical characteristics of HBoV1-associated PB and evaluate potential risk factors for severe disease in pediatric patients. Our findings intend to offer strong evidence in support of timely detection and instant intervention in this high-risk clinical setting.

Methods and Materials

Study design

This study retrospectively analyzed cases admitted to Fujian Children’s Hospital between December 2020 and December 2025. Institutional ethics approval was obtained from Fujian Children's Hospital (No. 2026ETKLRK0104).

Eligible cases met the diagnostic criteria for pediatric severe community-acquired pneumonia, presenting with one of the following standards [8]: (1) compromised systemic status; (2) altered mental status; (3) hypoxemic, including cyanosis, rapid breathing (respiratory rate ≥ 70 per min for infants or ≥ 50 per min for children aged 1 year or older), respiratory struggle such as nasal flaring, grunting, periodic apnea, chest retractions, or peripheral oxygen saturation (SpO_2) < 92%; (4) hyperpyrexia or fever persisting beyond 5 days; (5) severe dehydration or refusal of oral intake; (6) radiological findings on chest CT depicting pneumothorax, multilobar involvement, infiltration involving ≥ 2/3 of a lung, pleural effusion, necrotizing pneumonia, pulmonary abscess or atelectasis; and (7) manifestation of extrapulmonary sequelae. In addition, cases who underwent flexible bronchoscopy upon admission. 3. Targeted next-generation sequencing (tNGS) of bronchoalveolar lavage fluid identified patients with HBoV1 monoinfection.

Cases were excluded if they had any of the following conditions: (1) co-infection with other respiratory pathogens (such as viruses, bacteria, or mycoplasma) confirmed by tNGS or culture; (2) non-severe

cases or failure to undergo flexible bronchoscopy; (3) severe cerebral palsy; (4) congenital immunodeficiency; (5) severe congenital heart disease; (6) iron deficiency anemia or leukemia; or (7) incomplete clinical data.

A total of 484 cases of HBoV1 pneumonia were identified through a search of the hospital case database. 51 cases satisfied the selection requirements and were ultimately enrolled in this study (Fig. 1 shows the detailed study protocol). Group assignment was determined by bronchoscopic visualization of bronchial casts: PB (n = 16) versus non-PB (n = 35).

Data Extraction

Patient electronic medical records provided the source for retrospective clinical and laboratory data collection, which covered: (1) demographic profiles—age, sex, and body weight; (2) clinical manifestations—peak body temperature and peripheral oxygen saturation (SpO_2); (3) laboratory parameters, all measured from the initial blood specimen collected at admission—coagulation parameters (D-dimer), cardiac/tissue enzyme levels [lactate dehydrogenase (LDH)], systemic inflammatory markers [C-reactive protein (CRP) and procalcitonin (PCT)], and hematological indices including count of white blood cell (WBC), the percentage of neutrophils (NEUT%), and other routine tests; (4) chest CT findings (including atelectasis, consolidation, and pleural effusion); and (5) clinical outcomes —length of hospital stay (LOS).

Bronchoscopy

In compliance with standard institutional protocols, all enrolled patients underwent flexible bronchoscopy under sedation or general anesthesia. PB diagnosis was confirmed by the direct observation and extraction of typical bronchial casts throughout the intervention. All bronchoscopic procedures were performed by experienced pediatric pulmonologists.

Statistical methods

Data analysis was conducted using R (version 4.4.2). We assessed the normality of continuous variables using the Shapiro-Wilk test. Data with a normal distribution were reported as mean ± standard deviation (SD) and were compared with the t-test. Non-normally distributed data were expressed as median (IQR) and analyzed using the Mann-Whitney U test. For categorical variables, we presented counts and percentages (n%) and performed comparisons using either the chi-squared test or Fisher's exact test.

Relevant variables were identified through published reports and statistical filter(based on a univariate threshold of $P < 0.05$). Five candidate biomarkers (SF, SAA, D-dimer, CRP, and LDH) were selected. This initial reduction mitigate the risk of overfitting given the limited group size. Then LASSO regression was used to further select variables. The regularization parameter was chosen based on the one-standard-

error rule (λ1se), using 10-fold cross-validation. To test the stability of selected variables, 1,000 bootstrap resamples were performed. Selected factors were then entered into a multivariable Firth's penalized logistic regression.

Due to the small sample size of the PB group, we used Firth's penalized logistic regression to address potential estimation bias associated with sparse data. The selected factors's odds ratios (ORs) with 95% confidence intervals (CIs) were reported. The model's ability to discriminate between groups was evaluated by a receiver operating characteristic (ROC) curve. Robustness was assessed using 1,000 bootstrap resamples, which yielded both calibration plots and corrected area under the curve (AUC) metrics. As this research was exploratory and limited by sample size, a clinical nomogram or point-based scoring system was not developed.

Results

Demographic and clinical profiles

According to bronchoscopic evaluation, 35 cases were categorized into the non-PB group and 16 into the PB group. The two groups were well matched for baseline demographic and clinical parameters (Table 1), including median age (22.0 vs. 28.0 months, P = 0.243) and male proportion (71.43% vs. 56.25%, P = 0.286). Similarly, no significant differences were detected in peak body temperature, SpO_2, or length of hospital stay (LOS).

Table 1
Baseline demographic and clinical parameters

Age(m), IQR	**Non-PB group (n = 35)**	**PB group (n = 16)**	**Statistic**	***P***
	22.0 (13.0, 40.5)	**28.0 (20.8, 42.5)**	**Z= -1.170**	**0.243**
Sex, n%			χ^2= 1.138	0.286
female	10 (28.57)	7 (43.75)		
male	25 (71.43)	9 (56.25)		
BMI, IQR	15.41 (14.09, 17.15)	15.88 (14.76, 17.14)	Z= -0.477	0.633
Peak body temperature, Mean ± SD	38.8 ± 0.8	39.1 ± 0.8	t= -1.135	0.262
SPO2 , IQR	95 (90, 95)	93 (91, 95)	Z= -0.258	0.797
Shortness of Breath, n%			χ^2= 0.638	0.424
no	12 (34.29)	3 (18.75)		
yes	23 (65.71)	13 (81.25)		
LOS, IQR	9.00 (7.00, 11.00)	10.00 (7.75, 12.00)	Z= -0.878	0.380

Note: BMI, body mass index; IQR, interquartile range; LOS, length of stay;SD, standard deviation; SpO_2, peripheral oxygen saturation.

Laboratory and imaging findings

Laboratory indicators and radiological features were compared between the two groups (Table 2). Laboratory analysis revealed markedly higher concentrations of inflammatory and coagulation markers in the PB group than in the non-PB group, including CRP (median: 7.77 vs. 16.41 mg/L, P = 0.003), SF (mean: 90.92 vs. 201.33 ng/mL, P < 0.001), LDH (median: 297.00 vs. 352.40 U/L, P = 0.020), D-dimer (median: 0.35 vs. 1.02 μg/mL, P < 0.001) and SAA (median: 17.50 vs. 94.40 mg/L, P < 0.001). Other baseline laboratory parameters, including WBC, NEUT%, PCT, Apo-B, LDL, and CK-MB, showed no marked variations between groups (P > 0.05). Moreover, the incidence rates of pleural effusion, atelectasis and aerothorax were not notably different between the two patient groups. Notably, all patients included in this study showed varying degrees of pulmonary consolidation on chest imaging. Representative imaging and bronchoscopic findings are displayed in Fig. 2.

Variable selection

Receiver operating characteristic analysis was applied to each factor identified as significant ($P < 0.05$) in univariate analysis (Fig. 3). Table 3 displays the AUCs and optimal cut-off values. LASSO regression was used for variable selection in the final model. In accordance with the $\lambda 1se$ criterion, SF, SAA, and D-dimer were retained as candidate predictors. To evaluate the stability of variable selection, LASSO regression was repeated on 1,000 bootstrap resamples. SF, SAA, and D-dimer had selection frequencies of 99.5%, 91.6%, and 81.2%, respectively, indicating good selection stability. However, CRP and LDH exhibited a relatively low selection frequency of 62.5% and 60.3%, respectively. For SF, SAA, and D-dimer, the variance inflation factors (VIF) were 1.111, 1.199, and 1.206, respectively, which indicated the absence of significant multicollinearity among the predictors. Figure 4 shows the corresponding 10-fold cross-validation curve. Then a multivariable logistic regression with Firth's penalty was applied to these three factors.

Table 2
Comparison of laboratory parameters and imaging findings

WBC(10^9/L), Mean ± SD	**Non-PB group (n = 35)**	**PB group (n = 16)**	**Statistic**	***P***
	11.18 ± 3.90	**10.97 ± 3.97**	**t = 0.178**	**0.860**
NEUT%, IQR	63.70 (53.65, 78.65)	75.15 (64.77, 86.30)	Z= -1.330	0.184
CRP (mg/L), IQR	7.77 (2.01, 13.84)	16.41 (9.64, 34.04)	Z= -3.015	0.003
Apo-B (g/L), Mean ± SD	0.79 ± 0.23	0.87 ± 0.30	t= -0.998	0.323
LDH (U/L), IQR	297.00 (264.50, 334.50)	352.40 (305.25, 379.25)	Z=-2.335	0.020
LDL (mmol/L), Mean ± SD	2.37 ± 0.80	2.40 ± 0.97	t= -0.119	0.905
CK-MB (U/L), IQR	33.00 (23.75, 37.50)	28.50 (24.00, 38.95)	Z= -0.295	0.768
PCT (ng/ml), IQR	0.15 (0.12, 0.23)	0.24 (0.15, 0.33)	Z= -1.890	0.059
SF(ng/ml), Mean ± SD	90.92 ± 38.48	201.33 ± 85.97	t= -4.917	< 0.001
SAA(mg/L), IQR	17.50 (7.15, 32.00)	94.40 (32.40, 320.00)	Z= -3.671	< 0.001
D-dimer(ug/ml), IQR	0.35 (0.24, 0.53)	1.02 (0.62, 1.46)	Z=-4.000	< 0.001
atelectasis			χ^2= 0.735	0.391
no	26 (74.29)	10 (62.50)		
yes	9 (25.71)	6 (37.50)		
aerothorax			-	0.094
no	35 (100.00)	14 (87.50)		
yes	0 (0.00)	2 (12.50)		

Note: WBC, count of white blood cell ; NEUT%, percentage of neutrophile granulocyte; CRP, C-reactive protein; LDH, lactate dehydrogenase; Apo-B, apolipoprotein B; PCT, procalcitonin; LDL, low-density lipoprotein; CK-MB, creatine kinase-MB; SF, serum ferritin; SAA, serum amyloid A.

WBC(10^9/L), Mean ± SD	Non-PB group (n = 35)	PB group (n = 16)	Statistic	*P*
	11.18 ± 3.90	**10.97 ± 3.97**	**t = 0.178**	**0.860**
pleural effusion			χ^2= 0.893	0.345
no	33 (94.29)	13 (81.25)		
yes	2 (5.71)	3 (18.75)		
Note: WBC, count of white blood cell ; NEUT%, percentage of neutrophile granulocyte; CRP, C-reactive protein; LDH, lactate dehydrogenase; Apo-B, apolipoprotein B; PCT, procalcitonin; LDL, low-density lipoprotein; CK-MB, creatine kinase-MB; SF, serum ferritin; SAA, serum amyloid A.				

Table 3
Predictive performance and optimal cut-off values of candidate variables

AUC	CRP (mg/L)	LDH (U/L)	SF(ng/ml)	SAA(mg/L)	D-dimer(ug/ml)
	0.766	**0.706**	**0.863**	**0.823**	**0.853**
Cut-off	19.290	346.400	175.550	33.800	0.575

Model Construction via Firth's Logistic Regression and Bootstrap Validation

Multivariable Firth's penalized logistic regression identified SF, SAA, and D-dimer as the prospective risk factors for PB in children with severe mono-HBoV1 pneumonia (Table 4).

Table 4
Results of multivariable Firth's penalized logistic regression

Variable	β	OR	95%CI	P
(Intercept)	-5.7239	0.003	0.000, 0.041	<0.001
SF	0.0243	1.025	1.010, 1.046	<0.001
SAA	0.0146	1.015	1.003, 1.052	0.014
D_dimer	0.8094	2.247	1.060, 5.994	0.036
Note: OR, odds ratio; 95%CI, 95% confidence interval.				

To assess model stability, we conducted internal validation of the multivariable Firth's penalized regression via 1,000 bootstrap iterations. The model exhibited stable discrimination, with an AUC of 0.952 (95% CI: 0.882–0.996; Fig. 5). Figure 6 presents the calibration curve derived from bootstrap validation. Calibration was satisfactory, as reflected by a Brier score of 0.072 (95% CI: 0.032–0.120), and the Hosmer-Lemeshow test suggested no significant miscalibration (P = 0.556).

Discussion

In this study, after excluding co-infections and severe cardiovascular and cerebrovascular diseases, Firth's penalized regression and bootstrap validation showed that increased SF, SAA, and D-dimer concentrations are exploratory predictors of PB caused by HBoV1. These biomarkers are readily available. They provide a practical way to stratify risk. Furthermore, they may help clarify the pathogenic processes involved in HBoV1-associated PB.

Acute-phase response markers for HBoV1-associated PB: SF and SAA

In this research, SF and SAA were elevated in children with HBoV1-associated PB. SF is an intracellular iron-storage protein that increases sharply during inflammation, infection, or tissue injury [9]. In pneumonia due to MP or COVID-19, SF is an important indicator of severity [10,11]. Although significantly elevated SF levels have also been reported in MP-associated PB vs. non-PB controls, previous studies have not incorporated SF into clinical risk-prediction models [12]. We hypothesize that the significant elevation of SF in HBoV1-associated PB indicates severe airway mucosal damage and a correspondingly robust inflammatory response in the PB group.

Similarly, although SAA is also expressed in extrahepatic tissues during inflammatory cascades, it is a major acute-phase protein primarily synthesized by hepatocytes [13]. Elevated SAA independently correlated with an increased risk of severe pneumonia and served as a potential predictor for sepsis, highlighting its close involvement in systemic inflammatory cascades [14,15]. Our findings showed significantly higher serum SAA levels in children who developed HBoV1-associated PB. This supports the notion that cases in the PB group experience more severe airway damage and stronger inflammatory reactions.

As reported in previous investigations on MP-associated PB, CRP and LDH were significant predictors of PB [16]. Increased CRP and LDH in pediatric HBoV1-associated PB have been described by Liu et al. [17], but their findings lacked a non-PB control group. Although significantly increased in our PB group, CRP and LDH were infrequently selected by bootstrap LASSO. Whether these acute-phase reactants truly predict outcomes in HBoV1-associated PB calls for further evaluation in multicenter settings.

Coagulation dysfunction in HBoV1-associated PB

D-dimer is a marker for cross-linked fibrin degradation. Its rise suggests the activation of coagulation and fibrinolytic pathways [18]. Children with PB showed significantly elevated D-dimer concentrations relative to the non-PB group, suggesting a hypercoagulable state. Given the close interplay among inflammation, coagulation, and fibrinolysis in severe pulmonary infections, the elevated D-dimer levels observed in the PB group may reflect an active coagulation process, indicative of a prothrombotic state driven by airway injury [19].

Previous studies indicate that the levels of D-dimer are increased in MP-related PB, with cut-off values between 0.895 mg/L and 3.68 mg/L [20–22]. Moreover, Liu et al. [17] found that in severe HBoV1-associated PB, the increase in D-dimer was less than that in cases of MP infections. This distinction suggests that a lower threshold for D-dimer might be more appropriate for detecting PB in children with severe mono-HBoV1 pneumonia. Our results are very close to the observations made by Liu et al., in which the median value of D-dimer in the HBoV1-associated PB group was 1.02 mg/L. We found a D-dimer threshold of 0.575 mg/L to predict PB in severe pediatric HBoV1 pneumonia, which is a diagnostic cut-off that has not been previously reported. This is the first diagnostic threshold suggested for this particular setting. Given the limited and single-institution research scope, we should cautiously evaluate this threshold and further test in larger, multi-center groups.

Limited value of radiological features for HBoV1-associated PB

Some studies have reported atelectasis is a key radiographic finding in PB [23,24], but others report no statistical difference in atelectasis occurrence between non-PB and PB patients [25]. Similarly, our results revealed no notable radiological differences between the two groups. Atelectasis, pleural effusion, and pneumothorax were seen at comparable frequencies in both groups. These observations highlight a key limitation: radiological features alone are inadequate for a reliable diagnosis of PB. Quantitative imaging for lesion characterization may, however, prove useful in future work. To date, only one early study has identified lesion volume as an independent risk factor for MP-associated PB [26]. Quantitative evaluation was not feasible in this analysis, because CT slice thicknesses were inconsistent across patients. Standardized imaging protocols in future prospective studies are needed to confirm whether quantitative metrics are reliable PB predictors.

Clinical application of the model

This research is clinically significant. The three biomarkers offer low-cost, rapid results. Combined, they may help guide bronchoscopy decisions. For example, in pediatric patients with severe HBoV1 pneumonia and pulmonary consolidation, elevated biomarker levels could provide early warning of potential PB. This supports clinicians in assessing the need and timing for bronchoscopy. Such a strategy may enable timely intervention for at-risk children and reduce unnecessary invasive procedures. However, these findings are preliminary and require prospective validation in larger, more diverse populations.

Limitations

We acknowledge some limitations in our study. First, because bronchoscopy was in performedall enrolled patients, some degree of selection bias may persist. Most excluded cases that did not undergo bronchoscopy presented with mild pneumonia or showed no pulmonary consolidation. As the absence of consolidation is generally considered a non-indication for bronchoscopy [27], performing the procedure in patients with mild pneumonia may conflict with the ethical principle of non-maleficence. From a pathophysiological perspective, PB typically causes bronchial lumen obstruction, resulting in lung

consolidation or atelectasis. The probability of clinically significant PB occurring without consolidation is extremely low. However, a small subset of children with pulmonary consolidation was excluded because bronchoscopy was not performed for non-medical reasons. Since bronchoscopy is the diagnostic gold standard for PB, treating patients without confirmed results as controls would risk severe false-negative misclassification. Second, because HBoV1-associated PB is uncommon, our sample size was necessarily limited. To reduce overfitting and account for the small sample size, we used bootstrap LASSO regression (1,000 iterations) and Firth's penalized regression, validating the results internally with bootstrapping. In addition, to better understand the specific effects of HBoV1-associated PB, we excluded cases with co-pathogens, since mixed infections are common and can change clinical features. Due to the absence of cytokine and immune-related laboratory parameters, our ability to conduct a more comprehensive analysis of the pathogenesis of HBoV1-associated PB was limited. Future prospective investigations with extensive multicenter cohorts, co-infection subgroups, and comprehensive immune profiling are necessary to support and refine this predictive model.

Conclusion

In conclusion, elevated SF, SAA, and D-dimer levels were observed in children with severe HBoV1 pneumonia who progressed to PB. The findings suggest that virus-induced hypercoagulability and tissue injury may contribute to this process. As these biomarkers are routinely measured, they could support early risk assessment. However, the current evidence remains preliminary, and further studies are needed to determine their clinical relevance.

Declarations

Funding

Funding for this investigation was provided by the Fujian Provincial Health Technology Project (Grant No. 2025QNB026).

Ethics approval

The Institutional Ethics Committee of Fujian Children’s Hospital formally sanctioned this investigation (Approval No. 2026ETKLRK01004). Due to the chart-review nature of the study, written informed consent was exempted. Personal identifiers were completely removed prior to data evaluation.

Competing interests statement

No author has any relevant financial or non-financial interests that might have inappropriately influenced the findings or interpretations presented in this paper.

Author Contribution

Jianxing Wei: Methodology, Data curation, Funding acquisition, Writing–original draft. Di Lian: Software, Visualization. Yan Zheng: Investigation, Resources, Formal analysis, Data curation. Chenye Lin: Formal analysis, Validation. Zhinan Zhang: Resources, Software. Qiuyu Tang: Supervision, Project administration, Writing–review & editin Conceptualization.

Acknowledgement

We extend our gratitude to all the children and their families whose medical records contributed to this study.

Availability of data

Owing to statutory constraints regarding patient privacy, the full dataset is not broadly deposited. Qualified researchers may obtain the necessary data from the corresponding author upon justified request.

References

1. Trapani S, Caporizzi A, Ricci S, Indolfi G. Human Bocavirus in Childhood: A True Respiratory Pathogen or a “Passenger” Virus? A Comprehensive Review. Microorganisms. 2023;11:1243. https://doi.org/10.3390/microorganisms11051243

2. Fei-Zhou Z, Mei-Xia H, Xiaofen T, Lei W, Xuan J, Lan-Fang T. Plastic bronchitis associated with human bocavirus 1 infection in children. Pediatr Pulmonol. 2024;59:2754–60. https://doi.org/10.1002/ppul.27113

3. Zhang X, Zhao J. Plastic bronchitis linked to human bocavirus 1 identified through high-throughput next-generation sequencing: a case report. Medicine (Baltimore). 2024;103:e39361. https://doi.org/10.1097/MD.0000000000039361

4. Rüegger CM, Bär W, Iseli P. Simultaneous atelectasis in human bocavirus infected monozygotic twins: was it plastic bronchitis? BMC Pediatr. 2013;13:209–13. https://doi.org/10.1186/1471-2431-13-209

5. Leon C, Tsukahara K, Boggs K, Phinizy P. Plastic bronchitis secondary to bocavirus in a previously healthy 4-year-old with negative lymphatic evaluation. Pediatr Pulmonol. 2022;57:2276–8. https://doi.org/10.1002/ppul.26024

6. Cai X, Lin M, Zhou L, Sheng W, Jiao W, Bian H, et al. Characteristics of plastic bronchitis in children with infectious pneumonia. Ital J Pediatr. 2025;51:24–34. https://doi.org/10.1186/s13052-025-01873-4

7. Zhai Y, Du Y, Liu Y, Pan Y. Risk factors associated with plastic bronchitis in children with severe mycoplasma pneumoniae pneumonia: a systematic review and meta-analysis. J Thorac Dis. 2026;18:386–386. https://doi.org/10.21037/jtd-2026-1-0052

8. National Health Commission of the People's Republic of China. Guideline for diagnosis and treatment of community-acquired pneumonia in Children (2019 version) (In Chinese). Chin J Clin Infect Dis. Chin J Clin Infect Dis; 2019;12:6-13.

9. Mahroum N, Alghory A, Kiyak Z, Alwani A, Seida R, Alrais M, et al. Ferritin – from iron, through inflammation and autoimmunity, to COVID-19. J Autoimmun. 2022;126:102778. https://doi.org/10.1016/j.jaut.2021.102778

10. Wei D, Zhao Y, Zhang T, Xu Y, Guo W. The role of LDH and ferritin levels as biomarkers for corticosteroid dosage in children with refractory mycoplasma pneumoniae pneumonia. Respir Res. 2024;25:266. https://doi.org/10.1186/s12931-024-02892-1

11. Gao Y, Ding M, Dong X, Zhang J, Kursat Azkur A, Azkur D, et al. Risk factors for severe and critically ill COVID-19 patients: a review. Allergy. 2021;76:428–55. https://doi.org/10.1111/all.14657

12. Yu Y, Wang F, Wang H. Clinical features and risk factors of plastic bronchitis in mycoplasma pneumoniae pneumonia children with pulmonary consolidation: a prospective cohort study. Front Pediatr. 2026;14:1830700. https://doi.org/10.3389/fped.2026.1830700

13. Cheng S, Duan D, Cui H, Lian Y, Jiang F, Chen Q, et al. Serum amyloid a: multifaceted roles in inflammation and cellular interactions. Immunol Res. 2025;73:148. https://doi.org/10.1007/s12026-025-09704-8

14. Zinellu A, Paliogiannis P, Carru C, Mangoni AA. Serum amyloid a concentrations, COVID-19 severity and mortality: an updated systematic review and meta-analysis. Int J Infect Dis. 2021;105:668–74. https://doi.org/10.1016/j.ijid.2021.03.025

15. Xie M, Min Z, Jiang W, He Z, Xia X. Prognostic value of multivariate logistic regression analysis and amyloid a lactate monitoring in patients with severe pneumonia-associated sepsis. BMC Pulm Med. 2025;25:191. https://doi.org/10.1186/s12890-025-03648-3

16. He H, Kuang Z, Zhang Z, Rao G, Xiong C, Lu L, et al. A nomogram prediction model for plastic bronchitis in children with refractory mycoplasma pneumoniae pneumonia. Front Pediatr. 2026;14:1667816. https://doi.org/10.3389/fped.2026.1667816

17. Liu M, Wei D, Zhang T, Xu Y, Guo W. Distinct clinical characteristics of bocavirus and *Mycoplasma pneumoniae* infection in children plastic bronchitis. Immun Inflammation Dis. 2024;12:e1373. https://doi.org/10.1002/iid3.1373

18. Lippi G, Mullier F, Favaloro EJ. D-dimer: old dogmas, new (COVID-19) tricks. Clin Chem Lab Med. 2023;61:841–50. https://doi.org/10.1515/cclm-2022-0633

19. Cerda-Mancillas MC, Santiago-Germán D, Andrade-Bravo B, Pedraza-Olivares F, Valenzo-Hernández F, Leaños-Miranda A, et al. D-dimer as a biomarker of severity and adverse outcomes in patients with community acquired pneumonia. Arch Med Res. 2020;51:429–35. https://doi.org/10.1016/j.arcmed.2020.04.014

20. Zhang X, Sun R, Hou J, Jia W, Li P, Song C, et al. Clinical characteristics and risk factors of pulmonary embolism with mycoplasma pneumoniae pneumonia in children. Sci Rep. 2024;14:24043. https://doi.org/10.1038/s41598-024-74302-x

21. Ma R, Bai T, Yuan B, Zhang L, Li S, Ma L, et al. Risk factor analysis of plastic bronchitis among 126 children with macrolide-resistant mycoplasma pneumoniae pneumonia with mutations at the A2063G site after bronchoscopy examination: a nomogram prediction model. Front Pediatr. 2025;13:1521954. https://doi.org/10.3389/fped.2025.1521954

22. Yue Y, Lian T, Kang L, Liu S, Geng W, Xu M. D-dimer serves as predictor of plastic bronchitis or necrotizing pneumonia in children with mycoplasma pneumoniae pneumonia. Front Pediatr. 2025;13:1604253. https://doi.org/10.3389/fped.2025.1604253

23. Fang X, Lu H. Nomogram for prediction of plastic bronchitis in chinese children with pneumonia. https://doi.org/10.3389/fped.2025.1571479

24. Mu S, Zhai J, Guo Y, Huang B, Zou Y. Prediction of risk factors of plastic bronchitis in children with severe mycoplasma pneumoniae pneumonia. Biomed Eng Online. 2025;24:75. https://doi.org/10.1186/s12938-025-01410-8

25. Dong J-M, Zhou C-Q, Zhen Y-Y. Risk factor analysis of Mycoplasma pneumoniae pneumonia complicated with plastic bronchitis in children: a single-center retrospective study. Clin Respir J. 2025;19:e70142. https://doi.org/10.1111/crj.70142

26. Wu J, Cheng F, Kong X, Chen Q, Shi T, Bian Y, et al. Pulmonary lesion volume ratio and laboratory parameters as risk factors for plastic bronchitis in pediatric refractory mycoplasma pneumoniae pneumonia. BMC Pediatr. 2025;25:963. https://doi.org/10.1186/s12887-025-06381-2

27. Schramm D, Freitag N, Nicolai T, Wiemers A, Hinrichs B, Amrhein P, et al. Pediatric airway endoscopy: recommendations of the society for pediatric pneumology. Respiration. 2021;100:1128–45. https://doi.org/10.1159/000517125

Figures

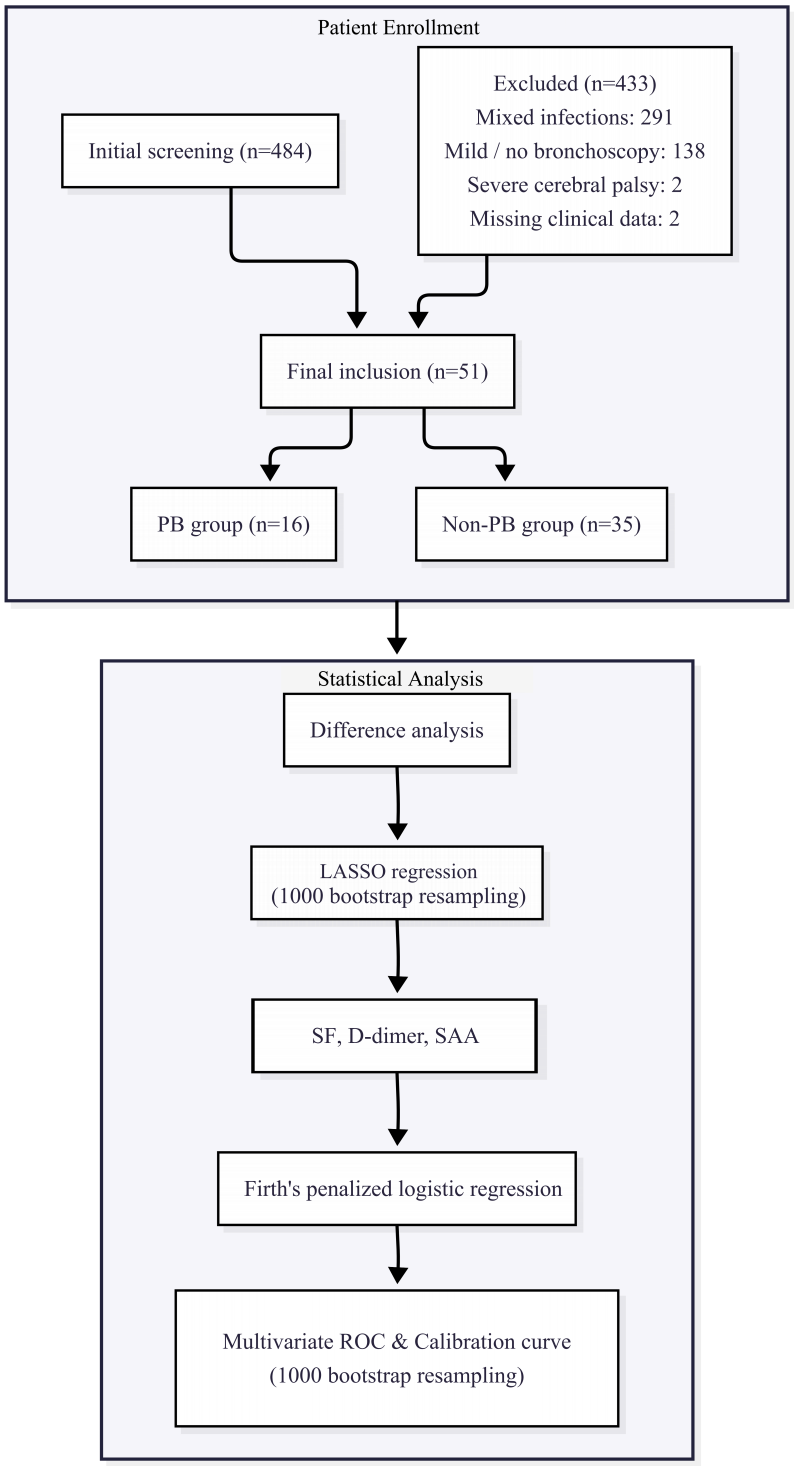


Figure 1

Flowchart of patient enrollment and analysis.

A total of 484 children with HBoV1 pneumonia were initially screened. After excluding 433 cases (mixed infections, n=291; mild or no bronchoscopy, n=138; severe cerebral palsy, n=2; incomplete data, n=2), 51 patients with severe pneumonia resulting from human bocavirus monoinfection were enrolled and divided into PB (n=16) and non-PB (n=35) groups. LASSO regressionidentified three variables for Firth

penalized logistic regression, which yielded D-dimer, LDH, and SAA as independent risk factors. ROC analysis and 1000 bootstrap resamples evaluated model discrimination and calibration.

PB, plastic bronchitis; LASSO: least absolute shrinkage and selection operator; ROC, receiver operating characteristic.

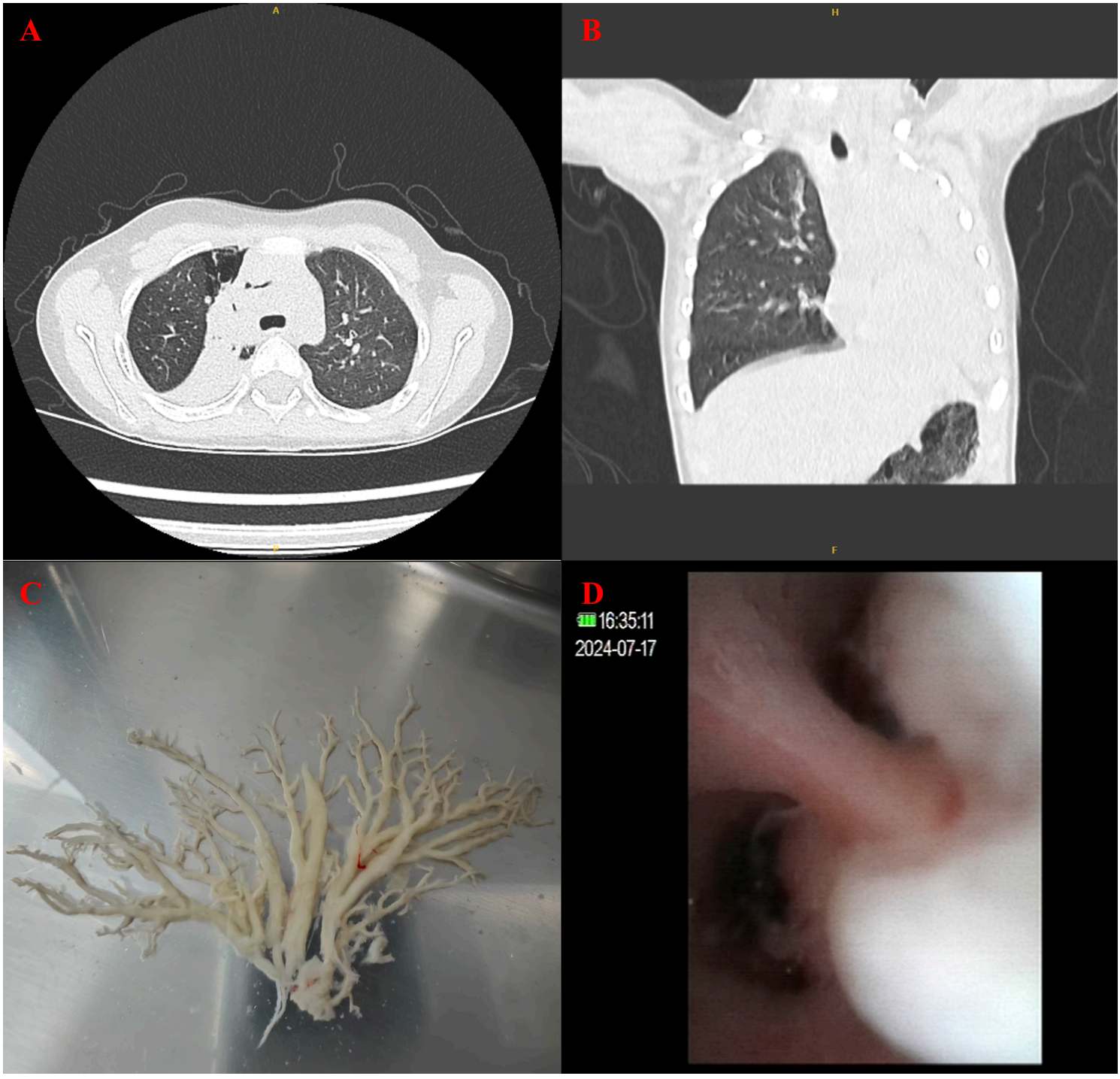


Figure 2

Radiographic and bronchoscopic features in the severe HBoV1 pneumonia.

(A) Chest CT image showing pneumothorax. (B) Chest CT image showing atelectasis. (C) Extracted bronchial cast with tree-like morphology. (D) Bronchoscopic visualization of the bronchial cast.

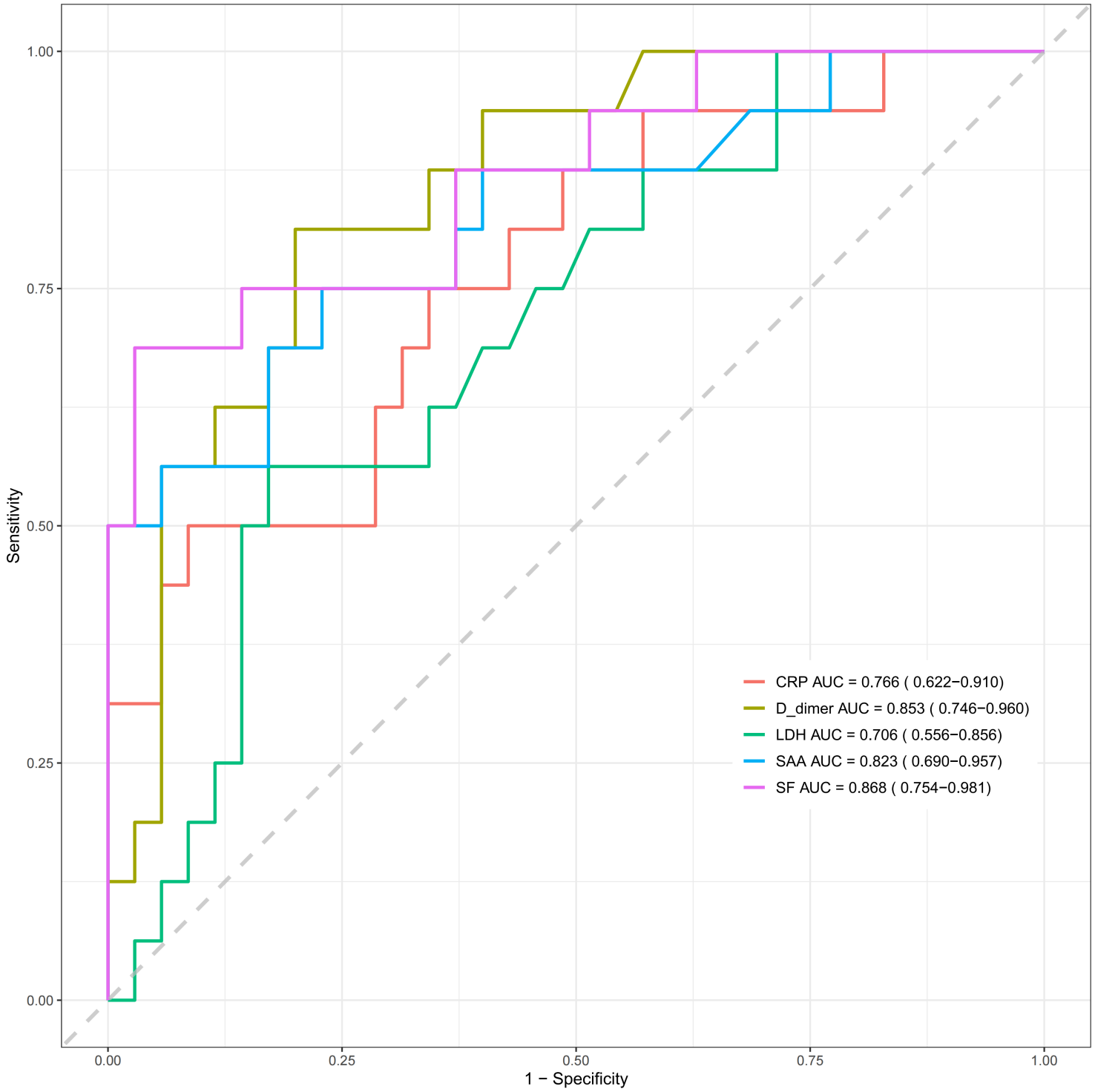


Figure 3

ROC curves of candidate variables for PB.

Receiver operating characteristic curves for C-reactive protein (CRP), D-dimer, lactate dehydrogenase (LDH), serum amyloid A (SAA), and serum ferritin (SF) in predicting plastic bronchitis among children

with severe HBoV1 pneumonia. Area under the curve (AUC) values are shown with 95% confidence intervals.

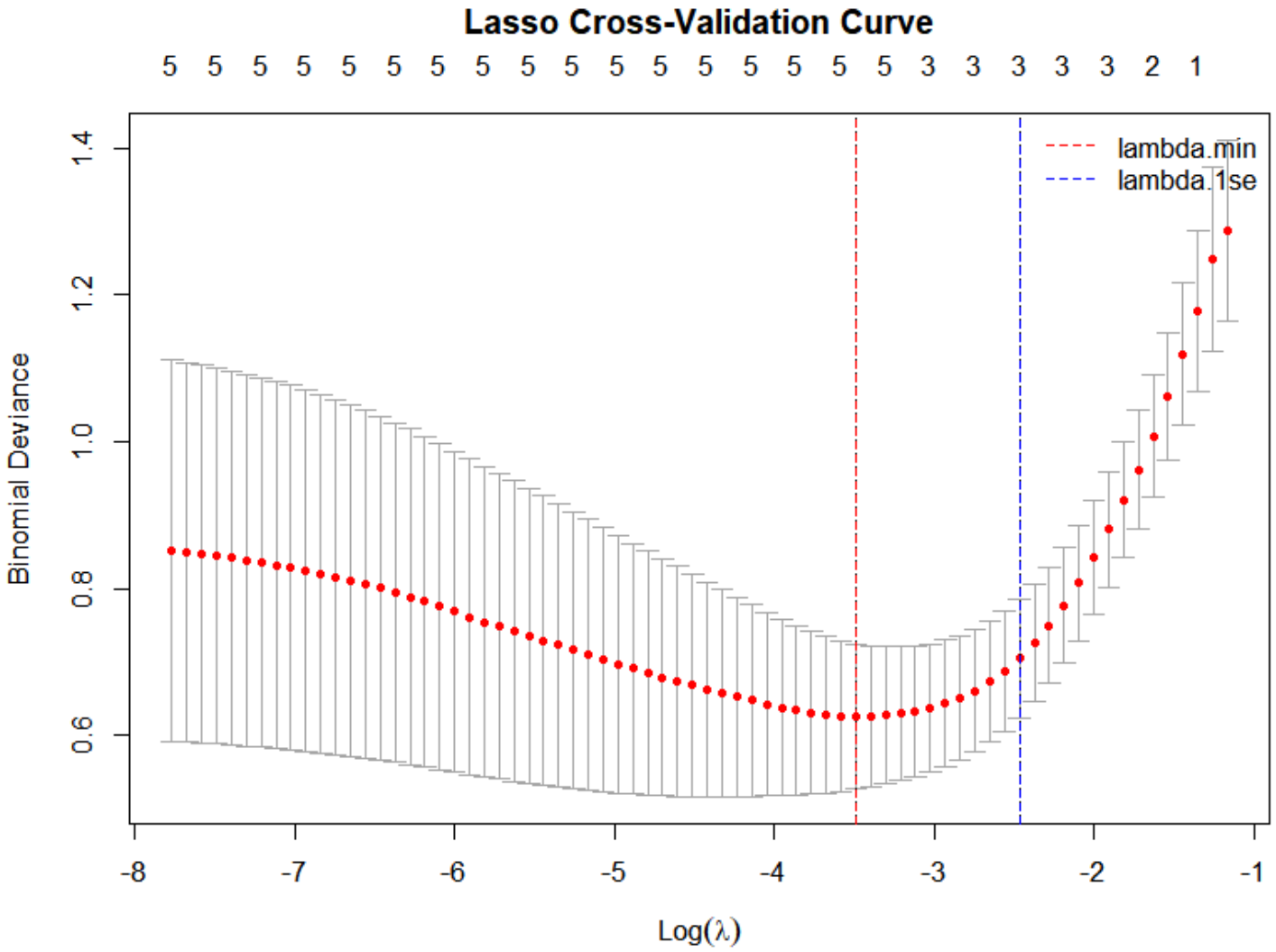


Figure 4

Cross-validation curve of LASSO regression.

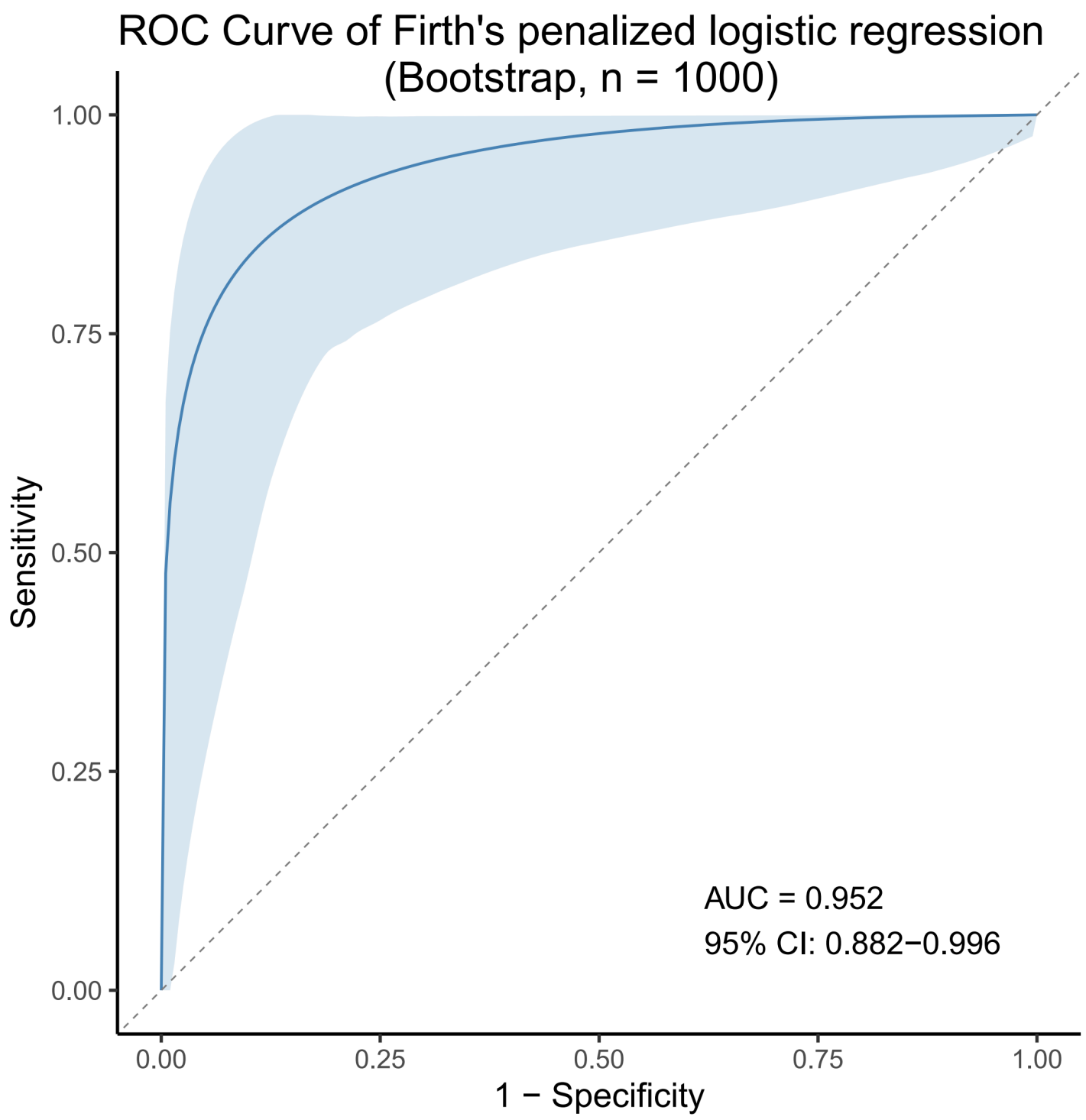


Figure 5

ROC curve of the multivariable Firth's penalized logistic regression model.

The plot illustrates the apparent and optimism-corrected AUCs evaluated via 1000 bootstrap resamples.

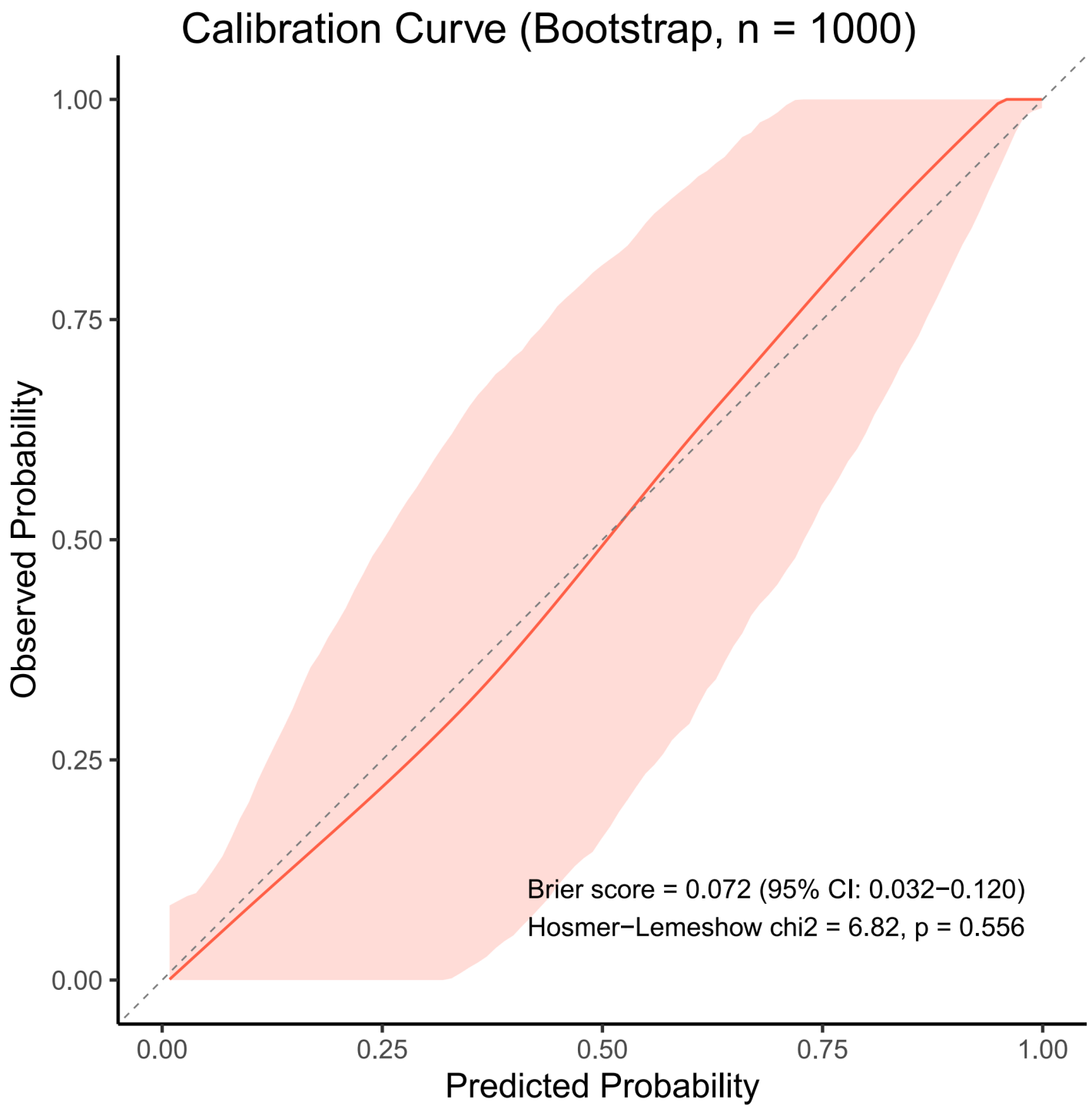


Figure 6

Calibration curve of the multivariable Firth's penalized logistic regression model.

The plot shows the Hosmer-Lemeshow test (P = 0.556) and Brier score (0.072), demonstrating good agreement between predicted probabilities and observed outcomes.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- supplementaryTable1VIF.csv