Original Article

Construction of a predictive model of respiratory endoscopic intervention in children with lobar pneumonia caused by *Mycoplasma pneumoniae* infection

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Background: This study aimed to analyze the clinical features of children with lobar pneumonia caused by *Mycoplasma pneumoniae* (MP) infection, to explore the independent risk factors for bronchoscopic intervention in children with lobar pneumonia caused by MP infection. There is a lack of objective assessment tools to guide the use of bronchoscopy in clinical practice. For children with lobar pneumonia caused by MP infection, whether line shall be actively bronchoscope intervention therapy remains to be further defined. We also aimed to construct an early warning model of bronchoscopic intervention to provide an objective evaluation tool for clinicians.

Methods: We collected the clinical data of 533 children with lobar pneumonia caused by MP infection. The patients were divided into three groups according to the interventional indications for bronchoscopy and whether they were treated with bronchoscopic intervention, and the clinical features and prognosis of the three groups were compared. A binary logistic regression analysis was performed on the indicators with a significance value of $P<0.05$, which we retrieved from the comparative analysis between the first two groups to uncover the independent risk factors and regression equations concerning bronchoscopic intervention. The regression coefficient (β) of our regression model was then used to score related values in the model to construct a predictive scoring model of bronchoscopic intervention for the treatment of children with lobar pneumonia caused by MP infection.

Results: Children with lobar pneumonia caused by MP infection who demonstrated absolute indications for bronchoscopy exhibited more severe clinical manifestations, and children without absolute indications for bronchoscopy had a better prognosis even without bronchoscopic intervention. To establish our early warning model of bronchoscopic intervention for children with lobar pneumonia caused by MP infection, we used the following indices: C-reactive protein ≥20.94 mg/L (β_1=2.253) received 3 points, while a fever duration before bronchoscopy ≥6.5 d (β_2=1.424), lactate dehydrogenase ≥461.5 U/L (β_3=1.246), or fever (β_4=1.223) each received 2 points, and the complication of pleural effusion (β_5=0.841) received 1 point, for a total possible score of 10 points.

Conclusions: When the score for the children with lobar pneumonia caused by MP infection was ≥6, the possibility of bronchoscopic intervention for treatment was >80%. The higher the score, the greater the possibility of bronchoscopic intervention.

Keywords: Lobar pneumonia; *Mycoplasma pneumoniae* (MP); prognosis; risk factors; predictive model

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Introduction

Mycoplasma pneumoniae (MP) is the smallest prokaryotic pathogenic microorganism known. It is transmitted through droplets and direct contact and can cause disease in any season of the year. The incidence of mycoplasma pneumoniae pneumonia (MPP) has gradually increased annually, and macrolide anti-bacterial agents have been used widely as a treatment. However, the incidence of macrolide-resistant mycoplasma pneumoniae (MRMP) is increasing worldwide, severely limiting the treatment options for children with MPP (1,2).

The chest imaging findings in MPP vary, and the worse radiological finding of consolidative lesions and pleural effusion in children with MPP were associated with more severe clinical course and poor treatment response (3). Respiratory endoscopy equipment and technology have led to progressive improvements in recent years, and endoscopy has gradually become an important treatment modality in treating various respiratory diseases in pediatrics (4). For example, respiratory endoscopy can be used to clear sputum plugs in the trachea, flush inflammatory secretions, and even resolve foreign bodies in the trachea.

Highlight box

Key findings

- Our results showed that the fever duration before bronchoscopy ≥6.5 d, C-reactive protein ≥20.94 mg/L, lactate dehydrogenase ≥461.5 U/L, fever, and complication with pleural effusion were the risk factors for bronchoscopic intervention in children with *Mycoplasma pneumoniae* (MP)-infected lobar pneumonia.

What is known and what is new?

- Children with lobar pneumonia caused by MP infection whether should be actively treated with bronchoscopy requires further investigation.
- We construct an early warning model of bronchoscopic intervention to provide an objective evaluation tool for clinicians.

What is the implication, and what should change now?

- Respiratory endoscopic intervention clinical decision is a big difficulty. A better early warning model is needed to standardize diagnosis and treatment.

However, the clinical symptoms and signs of lobar pneumonia caused by MP infection in children are often atypical, which is different from that in adults, and the question of whether they should be actively treated with bronchoscopy requires further investigation. The bronchoscopy treatment process itself can cause a certain degree of airway obstruction and may induce airway spasms, exacerbating hypoxia. Additionally, excessive suction during respiratory endoscopy can lead to alveolar collapse, worsening respiratory failure. As a result, respiratory endoscopic intervention clinical decision is a big difficulty. To better grasp the indications and contraindications of respiratory endoscopic intervention and to avoid over- or under-treatment, we must acknowledge that there is an urgent need for corresponding early warning models to standardize the indications of bronchoscopic intervention and to provide clinicians with objective assessment tools. We present this article in accordance with the TRIPOD reporting checklist (available at https://tp.amegroups.com/article/view/10.21037/tp-24-245/rc).

Methods

Patients and data collection

Children with lobar pneumonia due to MP infection from December 2017 to December 2019 were selected as the research subjects of the study. All the children were hospitalized at the Children's Hospital of Soochow University. To be eligible for inclusion in this study, the patients had to meet the following inclusion criteria: (I) have a diagnosis of MP infection, with serum MP-immunoglobulin M (IgM) ≥1.1 cut off index (COI), and/or nasopharyngeal aspirates (NPAs), and/or bronchoalveolar lavage fluid (BALF) MP-DNA, determined by fluorescence quantitative polymerase chain reaction, $>10^4$ copies/ml; and (II) manifest respiratory symptoms with or without fever, consistent with the chest imaging diagnosis of lobar pneumonia (5); that is, a chest radiograph or chest computer tomography (CT) examination showing uniform consolidation of one or more segments/lobes of the lung. Patients were excluded from the study if they met any of

the following exclusion criteria: (I) had contraindications to fiberoptic bronchoscopy; (II) exhibited bronchopulmonary dysplasia or malformations, repeated respiratory infections, aspiration pneumonia, or exogenous foreign bodies in the bronchus; and/or (III) had incomplete medical history data; (IV) respiratory syncytial virus, influenza virus A, influenza virus B, parainfluenza virus type 1–3, adenovirus, human metapneumovirus, human rhinovirus, human bocavirus and coronavirus disease 2019 (COVID-19) were excluded.

The clinical data collected included sex, age, date of hospitalization, pre-hospitalization course and pre-endoscopic heat course, number of hospitalization days, bronchoscopy time, clinical manifestations and signs, laboratory examinations, and lung imaging examinations. No external validation samples were used in this study, and our research group plans to collect data in the next few years for verification of this study.

The study protocol was approved by the Ethical Review Committee of the Children's Hospital of Soochow University (reference number: 2020CS078). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Informed consent was obtained from all the children's legal guardian(s) before data collection.

Definitions

Classification criteria and establishment of groups

Our criteria reflected the "Experts Consensus on Diagnosis and Treatment of Respiratory Endoscopy in Children with Refractory Pneumonia in China" Respiratory Endoscopy Intervention Indications (6) and were as follows: (I) slow absorption of pneumonia: the symptoms and signs of the patient improved after treatment with anti-infective drugs, but chest X-ray and CT lesion absorption was less than 50% after 2 weeks; (II) pneumonia that persisted for a lengthy period: The course of the disease was prolonged (>2 weeks), and the condition was not alleviated after active treatment but deteriorated and persisted; (III) extensive erosion of airway mucosa, necrotic epithelial shedding, mucus plugs blocking the airways, and even bronchial shaping that could be observed under respiratory endoscopy; and (IV) imaging showing unilateral emphysema, mediastinal emphysema, disappearance of bronchial inflation signs in unilateral or bilateral lung consolidation, tree-bud signs, or other small airway diseases. For the bronchoscopy absolute indication group (Group A), children with lobar pneumonia caused by MP infection who met any of the four bronchoscopic intervention indications underwent bronchoscopy and lavage during hospitalization. For the bronchoscopy relative indication group (Group B), children with lobar pneumonia caused by MP infection underwent bronchoscopy during their hospitalization on the basis of routine anti-infective and anti-inflammatory, cough and phlegm, and atomized inhalation treatments. Thin or flocculent secretions were noted under the bronchoscope, but there were no signs of airway mucosal erosion, necrotic epithelial shedding, mucus plugs blocking the airway, or bronchial shaping. If none of the four indications for bronchoscopic intervention were met, children with lobar pneumonia caused by MP infection were treated with routine anti-infective and anti-inflammatory, cough and phlegm, and atomized inhalation treatments, and bronchoscopic intervention was not implemented during hospitalization (Group C). The three groups comprised 229, 166, and 138 children, respectively.

Prognostic evaluation criteria for the three groups of children

Evaluation

The evaluation standards were as follows (7): (I) a normal body temperature: a body temperature <37.4 ℃ within 72 hours; (II) the degree of coughing, which was classified as follows: no cough (0 point); mild cough (i.e., an occasional or intermittent cough that did not affect the study or quality of life of the patient) (1 point); moderate cough (i.e., a cough between a mild and severe cough) (2 points); severe cough (i.e., frequent or paroxysmal coughing day and night that affected sleep, study, or quality of life) (3 points); (III) the degree of rales in the lungs, which was assessed as follows: no rales in either lung (0 point); a small amount of rales heard in both lungs (1 point); rales that were audible and moderate in both lungs (2 points); and abundant rales (3 points); and (IV) the degree of absorption of lung lesions on chest X-ray or CT, which was designated as follows: complete absorption of lesions (0 point); lesion absorption ≥1/2 (1 point); lesion absorption <1/2 (2 points); and no absorption or aggravation of lesions (3 points).

Prognostic evaluation criteria (7)

The children were re-examined using chest radiography or chest CT 1 week after admission to the hospital, and their clinical symptoms, signs, and chest radiographic or chest CT changes were then used as the criteria. For a child to be classified as: (I) "cured"—the child's body temperature had to have reverted to normal, the child had to have no cough or only a mild cough, the lung signs had to have disappeared, and chest X-ray or CT had to show that the lung lesions had been basically absorbed;

(II) "markedly effective"—the child's body temperature had to have reverted to normal, the degree of coughing had to be moderate or lower, the lung signs had to have disappeared or be only slightly present, and chest X-ray or CT had to show that the absorption of the lung lesions was ≥1/2; (III) "effective"—the child's body temperature had to have reverted to normal, the degree of coughing had to be moderate, the lung signs had to have alleviated, and a chest radiograph or chest CT had to show that the absorption of lung lesions was <1/2; and (IV) "ineffective"—the child's body temperature had to have not dropped significantly, the degree of coughing had to be moderate or severe, both lungs had to be full of rales or the lung rales had to be worse than before, and the chest X-ray or CT had to show that the lung lesions were not absorbed or had worsened. The total effective rate was calculated as follows: total effective rate = (cured + markedly effective + effective cases)/total number of cases ×100%.

Statistical analyses

Statistical Product and Service Solutions (SPSS) version 25.0 was used as the statistical software for the data analysis. The measurement data that conformed to a normal distribution are expressed as the mean ± standard deviation. Two independent-sample *t*-tests were used for comparisons between two groups, and a one-way analysis of variance was used for comparisons among three groups. After the Bonferroni method corrected the significance level, a pairwise comparison was performed. The measurement data that did not conform to a normal distribution are presented as the median (25^{th} percentile, 75^{th} percentile), and the Mann-Whitney *U* test was used for comparisons between two groups, and the Kruskal-Wallis *H* test was used for comparisons among three groups. The Bonferroni method was then used for comparisons between groups. The counting data are expressed as the percentage (%), and the chi-square (χ^2) test or the Fisher exact-probability method was used for comparisons between groups depending on which conditions were met. The differences between the groups were considered statistically significant at P<0.05. A binary logistic regression analysis (backward-stepwise method) was used to establish a regression equation model to obtain the probability of bronchoscopic intervention for children with lobar pneumonia, and a receiver operating characteristic (ROC) curve was drawn. ROC curve is a composite indicator that reflects the degree of sensitivity and specific. ROC curve with sensitivity (true positive rate) as ordinate, 1 – specificity (false positive rate) as abscissa. Based on the β coefficient in the binary logistic regression model, the factors in the model were weighted to construct a predictive scoring system for children with lobar pneumonia caused by MP infection that required bronchoscopic intervention.

Results

Clinical characteristics

A total of 533 children who met the inclusion criteria were enrolled in the study. There were no significant differences among the three groups of children in terms of either the average age or sex (all P>0.05, *Table 1*). There were also no significant differences among the three groups of children in terms of the incidence rates of a history of wheezing, eczema, allergic rhinitis, or asthma (12.66% *vs.* 15.06% *vs.* 16.67%; 34.50% *vs.* 35.54% *vs.* 36.96%; 14.85% *vs.* 15.06% *vs.* 18.12%; 1.31% *vs.* 4.22% *vs.* 1.45%; respectively; all P>0.05, *Table 1*). The ratio of the disease duration prior to admission, fever duration before bronchoscopy, and fever peak in group A were all higher than those in groups B and C (all P<0.05, *Table 1*).

White blood cell (WBC) count, neutrophil percentage (N%), C-reactive protein (CRP), lactate dehydrogenase (LDH), alanine aminotransferase (ALT), aspartate aminotransferase (AST), total value of immunoglobulin A (IgA), complications with pulmonary atelectasis, and complications with pleural effusion were all higher in group A than groups B and C (all P<0.05, *Table 2*). The MP-DNA copy numbers (medium- and high-load groups) were higher in group A than groups B and C (P<0.05, *Figure 1*), while the percentages of cluster of differentiation (CD)3^+CD4^+ and $CD4^+/CD8^+$ cells in the lymphocyte subpopulations were lower in group A than groups B and C (all P<0.05, *Table 2*). The level of prealbumin (PA) was also significantly lower in group A than group B (after correction, P<0.05, *Table 2*).

Evaluation of the prognosis for the three groups of children 1 week after admission to the hospital

The median hospitalization time for children in group A was 10 days, which was longer than the 8 days of children in group B and 7 days of children in group C (after correction, all P<0.05), and that of group B was longer than that of group C (after correction, P<0.05). The fever subsidence

Table 1 Comparison of the clinical characteristics among the three groups of children

Variables	Group A (n=229)	Group B (n=166)	Group C (n=138)	Statistics	P value
Characteristics					
Sex (male/female)	126/103	82/84	69/69	1.509$^{\triangle}$	0.47
Age (years)	5.92 [3.67, 7.58]	5.67 [3.67, 7.67]	5.83 [3.83, 6.83]	1.192$^{\diamond}$	0.55
Wheezing history	29 (12.66)	25 (15.06)	23 (16.67)	1.190$^{\triangle}$	0.55
Eczema history	79 (34.50)	59 (35.54)	51 (36.96)	0.228$^{\triangle}$	0.89
Allergic rhinitis history	34 (14.85)	25 (15.06)	25 (18.12)	0.782$^{\triangle}$	0.67
Asthma history	3 (1.31)	7 (4.22)	2 (1.45)	4.239$^{\triangle}$	0.12
Disease duration before admission (d)	7 [6, 10][a,b]	7 [5, 10]	7 [5, 9]	9.929$^{\diamond}$	0.007
Fever duration before bronchoscopy (d)	7 [5, 10][a,b]	5 [0, 7]	5 [4, 7]	42.359$^{\diamond}$	0.001
Hot peak (℃)	39.6 (39.0, 40.0)[a,b]	39 (38.5, 39.7)	39 (38.7, 39.5)	45.561$^{\diamond}$	0.001
Signs and symptoms					
Fever	219 (95.6)[a]	143 (86.1)	126 (91.3)	11.225$^{\triangle}$	0.004
Cough	228 (99.6)	166 (100.0)	138 (100.0)	1.330$^{\triangle}$	0.51
Respite	24 (10.48)	14 (8.43)	17 (12.32)	1.240$^{\triangle}$	0.53
Shortness of breath	13 (5.68)	8 (4.82)	5 (3.62)	0.784$^{\triangle}$	0.67
Difficulty breathing	5 (2.18)	3 (1.81)	2 (1.45)	0.258$^{\triangle}$	0.87
Nasal congestion and runny nose	41 (17.90)	34 (20.48)	31 (22.46)	1.177$^{\triangle}$	0.55
Pulmonary rales	102 (44.5)	91 (54.8)	65 (47.1)	4.197$^{\triangle}$	0.12
Decreased breath sounds	64 (27.9)[b]	31 (18.7)	15 (10.9)	15.901$^{\triangle}$	0.001

Data are shown as M (P25–P75) or n (%). Group A, bronchoscopic absolute indication group; Group B, bronchoscopic relative indication group; Group C, bronchoscopic intervention was not provided during hospitalization. $^{\triangle}$, χ^2 value obtained by the Pearson test; $^{\diamond}$, H value obtained by the Kruskal-Wallis *H* test; after the significance level was corrected with the Bonferroni method, pairwise comparisons were performed. [a], P<0.05 after correction compared with groups A and B; [b], P<0.05 after correction compared between groups A and C. M (P25–P75), median (percentile25–percentile75).

Table 2 Comparison of the laboratory indices and imaging characteristics among the three groups of children

Variables	Group A (n=229)	Group B (n=166)	Group C (n=138)	Statistics	P value
WBC count ($\times10^9$ L^{-1})	8.97 (6.78, 12.20)[a,b]	7.59 (6.05, 10.57)	7.00 (5.73, 9.63)	20.253$^{\diamond}$	0.001
N (%)	67.40 (56.85, 76.7)[a,b]	55.05 (44.02, 65.93)[c]	59.00 (44.0, 68.28)	60.368$^{\diamond}$	0.001
EOS ($\times10^9$ L^{-1})	0.20 (0.01, 0.85)	0.40 (0.0, 1.30)	0.50 (0.10, 1.10)	5.473$^{\diamond}$	0.06
CRP (mg·L^{-1})	27.37 (14.55, 49.29)[a,b]	6.63 (1.62, 16.42)	8.13 (3.69, 18.90)	120.547$^{\diamond}$	0.001
PLT ($\times10^9$ L^{-1})	307 (226, 394)	300.50 (239.50, 406.50)	286 (234, 383)	0.772$^{\diamond}$	0.68
LDH (U·L^{-1})	474.80 (366.15, 611.50)[a,b]	357.15 (309.97, 424.30)	333.10 (294.95, 415.45)	85.557$^{\diamond}$	0.001
PA (mg·L^{-1})	132 (108.5, 163.5)[a]	150.5 (121.75, 203.75)[c]	138.00 (122.50, 158.25)	24.492$^{\diamond}$	0.001
ALT (U·L^{-1})	15.30 (11.16, 26.65)[a,b]	13.00 (9.98, 17.08)	12.00 (10.18, 15.53)	25.391$^{\diamond}$	0.001
AST (U·L^{-1})	32.50 (25.95, 43.50)[a,b]	28.55 (23.68, 35.25)	29.15 (24.90, 34.53)	17.235$^{\diamond}$	0.001

Table 2 *(continued)*

Table 2 *(continued)*

Variables	Group A (n=229)	Group B (n=166)	Group C (n=138)	Statistics	P value
Serum MP-IgM (/COI)	2.96 (0.63, 5.99)[b]	2.65 (0.60, 5.86)[c]	1.41 (0.39, 3.86)	15.300[◇]	0.001
Serum MP-IgG (/COI)	20.33 (3.12, 189.31)	6.71 (2.00, 100.80)	15.56 (2.96, 122.18)	4.132[◇]	0.12
Sputum MP-DNA copy number					
Low-load group	37 (16.2)	23 (13.86)	18 (13.04)	0.785[△]	0.67
Medium-load group	25 (10.9)[a,b]	49 (29.52)	44 (31.88)	29.577[△]	0.001
High-load group	167 (72.9)[a,b]	94 (56.62)	76 (55.07)	16.322[△]	0.001
Humoral immunity ($g \cdot L^{-1}$)					
IgG	9.28 (7.80, 11.09)	9.23 (7.40, 10.88)	9.45 (7.57, 10.93)	1.126[◇]	0.57
IgA	1.21 (0.84, 1.63)[a,b]	1.05 (0.64, 1.44)	0.98 (0.57, 1.37)	13.084[◇]	0.001
IgM	1.47 (1.10, 2.17)	1.51 (1.07, 1.89)	1.36 (1.05, 1.80)	6.000[◇]	0.05
Cellular immunity					
$CD3^+T$ (%)	64.4 (55.6, 72.6)	66.85 (60.28, 72.30)	65.85 (60.20, 71.18)	2.970[◇]	0.22
$CD3^+CD4^+T$ (%)	33.22±9.27[a,b]	35.81±8.37	35.44±8.09	5.136[▲]	0.006
$CD3^+CD8^+T$ (%)	27.88±7.94	26.53±7.11	26.06±6.62	3.076[▲]	0.047
$CD4^+/CD8^+T$ (%)	1.20 (0.90, 1.50)[a,b]	1.3 (1.0, 1.8)	1.4 (1.0, 1.8)	14.043[◇]	0.001
$CD3\text{-}CD(15+56)^+T$ (%)	9.70 (5.75, 15.80)	10.2 (6.4, 15.8)	9.40 (7.08, 14.7)	0.777[◇]	0.67
$CD3^-CD19^+T$ (%)	20.80 (14.20, 28.55)	20.20 (13.95, 25.93)	21.45 (16.05, 27.68)	2.260[◇]	0.32
$CD19^+CD23^+T$ (%)	7.3 (5.0, 10.70)[b]	8.00 (5.87, 11.35)	8.85 (5.55, 13.10)	8.024[◇]	0.01
Imaging characteristics					
Left-side pneumonia	60 (26.20)	60 (36.14)	50 (36.23)	5.993[△]	0.05
Right-side pneumonia	101 (44.10)	72 (43.37)	59 (42.75)	0.066[△]	0.96
Inflammation on both sides	68 (29.70)	34 (20.48)	29 (21.01)	5.682[△]	0.05
Pulmonary atelectasis	25 (10.92)[a,b]	5 (3.01)	2 (1.45)	17.501[△]	0.001
Pleural effusion	56 (24.45)[a,b]	16 (9.63)	13 (9.42)	21.678[△]	0.001
Pleural effusion site					
Left side	17 (7.42)[b]	9 (5.42)	3 (2.17)	13.622[△]	0.001
Right side	33 (14.41)[a]	5 (3.01)	10 (7.25)	15.962[△]	0.001
Both sides	6 (2.62)	2 (1.20)	0 (0.00)	4.141[△]	0.12

Data are shown as M (P25–P75) or n (%) or $\bar{x}$±s. Group A, bronchoscopic absolute indication group; Group B, bronchoscopic relative indication group; Group C, bronchoscopic intervention was not provided during hospitalization. [△], χ^2 value obtained from the Pearson test; [◇], H value obtained from the Kruskal-Wallis *H* test; [▲], F value obtained from a one-way analysis of variance, with post-hoc pairwise comparisons made after the Bonferroni method was used to correct the significance level. [a], P<0.05 after correction compared with groups A and B; [b], P<0.05 after correction compared between groups A and C; [c], P<0.05 after correction compared between groups B and C. The copy number was divided into three groups according to the MP-DNA of the child's sputum specimen: low-copy group, MP-DNA copy number ≤10^4/mL; medium-copy group, MP-DNA copy number 10^4–10^6/mL; high-copy group, MP-DNA copy number >10^6/mL. M (P25–P75), median (percentile25–percentile75); WBC, white blood cell; N, neutrophil; EOS, eosinophil count; CRP, C-reactive protein; PLT, platelet; LDH, lactate dehydrogenase; PA, prealbumin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; MP, *Mycoplasma pneumoniae*; IgM, immunoglobulin M; COI, cut off index; IgG, immunoglobulin G; DNA, deoxyribonucleic acid.

time was longer in group A than groups B and C (after correction, all P<0.05). On the 7th day of hospitalization, the scores for the degrees of coughing, moist pulmonary rales, and lesion absorption in group A were 1 [1, 2], 1 [0, 1], and 2 [2, 3], respectively; the scores in group B were 1 [1, 1], 0 [0, 1], and 1 [1, 2], respectively; and the scores in group C were 1 [1, 1], 0 [0, 1], and 1 [1, 2], respectively; with the scores in group A being higher than those in groups B and C. The baseline levels for the children in groups B and C were the same. No differences were observed in terms of the hospitalization time, fever subsidence time, the scores for degrees of coughing, moist pulmonary rales, or lesion absorption 1 week after hospitalization between the two groups (groups B and C) (after correction, all P>0.05).

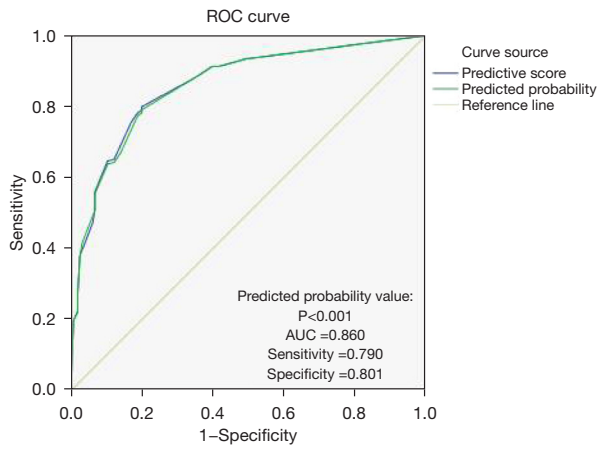

Figure 1 Regression model and ROC curve of the predictive score. ROC, receiver operating characteristic; AUC, area under the curve.

When we compared the total effective rate and cure rate among the three groups after 1 week of hospitalization and treatment, we observed that for group A, the total number of effective cases was 155 (67.69%), including 0 cases (0%) cured, 31 cases (13.54%) markedly effective, 124 cases (54.15%) effective, and 74 cases (32.31%) ineffective. In group B, the total effective cases were 128 (77.11%), including 17 cases cured (10.24%), 66 cases markedly effective (39.76%), 45 cases effective (27.10%), and 38 cases ineffective (22.90%). In group C, the total effective cases were 116 (84.06%), including 17 cases cured (12.32%), 57 cases markedly effective (41.31%), 42 cases effective (30.43%), and 22 cases ineffective (15.94%). There were no significant differences in the total effective rate or cure rate between groups B and C (after correction, all P>0.05).

Independent risk factors for bronchoscopic intervention in children with lobar pneumonia caused by MP infection

The indicators with a P value <0.05 between groups A and B were analyzed by backward-stepwise binary logistic regression analysis, and our results showed that fever duration before bronchoscopy [odds ratio (OR), 1.180; 95% confidence interval (CI): 1.093–1.275], CRP (OR, 1.048; 95% CI: 1.028–1.067), LDH (OR, 1.004; 95% CI: 1.002–1.006), fever (OR, 4.609; 95% CI: 1.533–13.851), and complication with pleural effusion (OR, 3.954; 95% CI: 1.845–8.473) were independent risk factors for bronchoscopic intervention in children with lobar pneumonia caused by MP infection (*Table 3*). The abovementioned five variables were included in the best regression equation, and the regression equation for

Table 3 Logistic regression analysis of the risk factors related to lobar pneumonia caused by MP infection that requires bronchoscopy

Variable	Partial regression coefficient (β)	SE	Wald χ^2 value	P value	OR (95% CI)
Fever duration before bronchoscopy (d)	0.166	0.039	17.745	<0.001	1.180 (1.093–1.275)
CRP (mg/L)	0.047	0.009	24.264	<0.001	1.048 (1.028–1.067)
LDH (U/L)	0.004	0.001	14.074	<0.001	1.004 (1.002–1.006)
Fever	1.528	0.561	7.406	0.007	4.609 (1.533–13.851)
Pleural effusion	1.375	0.389	12.497	<0.001	3.954 (1.845–8.473)
Constant	−7.531	1.206	38.986	<0.001	–

MP, *Mycoplasma pneumoniae*; CRP, C-reactive protein; LDH, lactate dehydrogenase; SE, standard error; OR, odds ratio; 95% CI, 95% confidence interval.

Table 4 Logistic regression analysis after the assignment of each independent risk factor

Variable	Partial regression coefficient (β)	Wald χ^2 value	P value	OR (95% CI)
Fever duration before bronchoscopy (<6.5 d =0; ≥6.5 d =1)	1.424	27.507	<0.001	4.155 (2.440–7.074)
CRP (< 20.94 mg/L =0; ≥20.94 mg/L =1)	2.253	60.055	<0.001	9.513 (5.381–16.816)
LDH (<461.5 U/L =0; ≥461.5 U/L =1)	1.246	18.292	<0.001	3.476 (1.964–6.153)
Fever (no =0; yes =1)	1.223	5.756	0.02	3.397 (1.251–9.228)
Pleural effusion (no =0; yes =1)	0.841	5.325	0.02	2.319 (1.135–4.738)

CRP, C-reactive protein; LDH, lactate dehydrogenase; OR, odds ratio; 95% CI, 95% confidence interval.

predictive probability was logit (P)=−7.532 + 0.166X_1 + 0.047X_2 + 0.004X_3 + 1.528X_4 + 1.375X_5, where X_n was the independent variable; X_1 was the fever duration before bronchoscopy; X_2 was CRP; X_3 was LDH; X_4 was fever; and X_5 was pleural effusion.

The predictive value of independent risk factors in children with lobar pneumonia caused by MP infection who require bronchoscopy

The critical values for the independent factors were used to assign the values for each factor. The fever duration before bronchoscopy ≥6.5 d, CRP ≥20.94 mg/L, LDH ≥461.5 U/L, fever, and complication with pleural effusion were the risk factors for bronchoscopic intervention in children with MP-infected lobar pneumonia; and after assigning values to each risk factor, the logistic regression analysis was statistically significant (P<0.05, *Table 4*). The ROC curve was plotted with the predicted probability value of the regression model, and the area under the curve (AUC) was 0.860 (95% CI: 0.824–0.897; P<0.001), indicating that the predicted probability model had an upper-middle diagnostic accuracy (*Figure 1*).

Establishment of a scoring system for bronchoscopic intervention in children with lobar pneumonia caused by MP infection

According to the β value, each independent risk factor was scored separately. CRP ≥20.94 mg/L (β_1=2.253) received 3 points, fever duration before bronchoscopy ≥6.5 d (β_2=1.424) received 2 points, LDH ≥461.5 U/L (β_3=1.246) received 2 points, fever (β_4=1.223) received 2 points, and complication with pleural effusion (β_5=0.841) received 1 point; such that the total possible score was 10 points (*Table 5*). Using the scores for risk factors to evaluate the risk of bronchoscopic intervention as a treatment for children with lobar pneumonia caused by MP infection, we calculated a predictive AUC score of 0.860 (95% CI: 0.824–0.897; P<0.001) (*Figure 1*).

According to the score, 395 children with lobar pneumonia caused by MP infection who also underwent bronchoscopic intervention (groups A and B) were divided into high-risk (7–10 points), medium-risk (4–6 points), and low-risk groups (0–3 points); there were 129 cases in the high-risk group, 146 cases in the medium-risk group, and 120 cases in the low-risk group; and 117 cases (90.71%) in the high-risk group, 92 cases (63.01%) in the medium-risk group, and 20 cases (16.67%) in the low-risk group with absolute indications for bronchoscopy. When the scores for children with lobar pneumonia caused by MP infection reached 6, 7, 8, 9, or 10 points, the possibilities for bronchoscopic intervention were 83.78%, 87.69%, 88.33%, 97.22%, and 100%, respectively (*Figure 2*).

Discussion

As the principal pathogen causing lobar pneumonia in children, MP has received increasing attention in recent years. When the effect of conventional anti-infective treatment is not favorable, bronchoscopic intervention therapy for lobar pneumonia caused by MP infection has increased clinical application. In this study, we found that children with lobar pneumonia caused by MP infection who demonstrated an absolute indication for bronchoscopy exhibited more severe clinical manifestations and that children without absolute indications for bronchoscopy achieved a better prognosis even without bronchoscopic intervention. Therefore, not all children with lobar pneumonia caused by MP infection should receive a

Table 5 Assignment table of risk factors

Factors	Category	Reference (W_{ij})	Regression coefficients (β_i)	$\beta_i (W_{ij} - W_{iREF})$	$Point_{ij} = \beta_i (W_{ij} - W_{iREF})/B$
Fever duration before bronchoscopy ≥6.5 d	Yes	1	1.424	1.424	2
	No	0= W_{1REF}		0	0
CRP ≥20.94 mg/L	Yes	1	2.253	2.253	3
	No	0= W_{2REF}		0	0
LDH ≥461.5 U/L	Yes	1	1.246	1.246	2
	No	0= W_{3REF}		0	0
Fever	Yes	1	1.223	1.223	2
	No	0= W_{4REF}		0	0
Pleural effusion	Yes	1	0.841	0.841	1
	No	0= W_{5REF}		0	0

'Yes' represents the basic category, and 'No' represents the other categories. Fixed constant B=0.841; βi, regression coefficients of the independent risk factors in the multivariate logistic regression equation; W_{iREF}, risk reference factors; W_{ij}, continuous variables needed to determine their critical value; that is, the value corresponding to the maximal Youden index (sensitivity + specificity – 1) of the risk factor for each continuous variable; we then further transformed the value into a categorical variable and assigned a value (≥ critical value was recorded as 1, < critical value was recorded as 0). i=1, ..., n, where n is the number of risk factors; j=1, ..., m, where m is the number of categories; $\beta_i (W_{i\,j} - W_{i\,REF})$, the distance between the category for each risk factor and the basic category. CRP, C-reactive protein; LDH, lactate dehydrogenase.

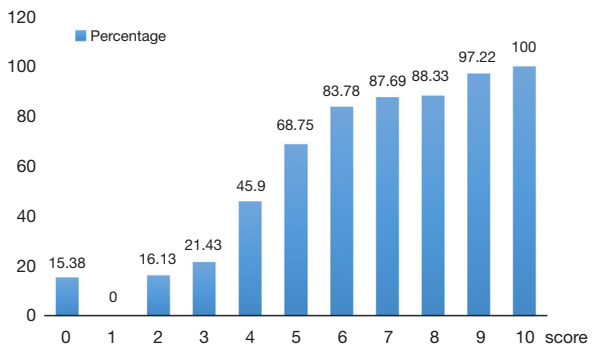

Figure 2 Percentage of the children with lobar pneumonia caused by MP infection in each scoring group who required bronchoscopic intervention. MP, *Mycoplasma pneumoniae*.

bronchoscopic intervention as treatment.

To avoid over- or under-treatment in clinical practice, the indications for the bronchoscopic treatment of lobar pneumonia caused by MP infection need to be rigorously understood. Therefore, we used a binary logistic regression analysis to screen out the independent risk factors for lobar pneumonia caused by MP infection that required respiratory endoscopic intervention and then established an early warning model.

Our results showed that the fever duration before bronchoscopy ≥6.5 d, CRP ≥20.94 mg/L, LDH ≥461.5 U/L, fever, and complication with pleural effusion were the risk factors for bronchoscopic intervention in children with MP-infected lobar pneumonia. MP infection can stimulate the body to produce pyrogenic sources and cause persistent fever. Severe MP infection can cause damage to the mucosal-ciliated columnar epithelium of the airways and can even produce shedding. High secretion of airway mucus then leads to the destruction of mucosal-ciliary system function and impairs airway clearance. Airway secretions provide an excellent culture medium for bacteria and viruses, which can easily lead to mixed infections (8). Mixed infections can then aggravate the systemic inflammatory response, heat-peak height, fever time, and hospital stay in children with lobar pneumonia caused by MP infection (9,10).

CRP is an acute phase, non-specific reactive protein that is significantly augmented during tissue injury or infection, and a study has shown that CRP can be significantly elevated when MP infection is combined with lung consolidation and pleural effusion (11). The levels of CRP and LDH are also positively correlated with the severity of MP infection (12,13), and MP infection is the primary cause of pleural effusion in children (14). After MP infection, specific antibodies induce an autoantibody reaction, pleural disease, and finally fibrinous exudates, which often represent

a stronger immune response.

A study has shown that age, fever duration, CRP, and LDH are independent risk factors for intrabronchial mucus in children with MPP (15); when children with MPP have CRP ≥12.27 mg/L and LDH ≥462.65 U/L, there is a possibility of the formation of mucus plugs in the bronchus (16). In one scoring system for refractory MPP in children undergoing multiple bronchoscopic interventions, CRP >44 mg/L and LDH >480 U/L were assigned 1 point each. In the present study, we established an early warning model of bronchoscopic intervention treatment for children with lobar pneumonia caused by MP infection in which CRP ≥20.94 mg/L received 3 points, fever duration before bronchoscopy ≥6.5 d received 2 points, LDH ≥461.5 U/L received 2 points, fever received 2 points, and complication with pleural effusion received 1 point, for a total possible score of 10 points. When the score was ≥6, the possibility of bronchoscopic intervention was >80%, and the higher the score, the greater the probability of bronchoscopic intervention.

In addition to causing respiratory diseases, extra-pulmonary manifestations of MP infection are not unusual. MP is more than an extra-cellular pathogen colonizing epithelial cells of the respiratory tract. It is able to penetrate the cell membrane of host cells and to invade the respiratory mucosa, leading to pronounced inflammatory responses and also spreading outside the respiratory system, to some extent (17). These extra-pulmonary manifestations resulted to be statistically associated with the infection by macrolide-resistant strains and the delayed appropriate treatment (18). We should incorporate the extrapulmonary manifestations in the process of building to the early warning model, in this respect there is a certain limit (19,20).

This study had some limitations (21,22). First, it was a retrospective study, and the selected research subjects might have shown selection bias. Factors such as the long research timespan, the limitations of the test levels, and the geographical limitations also exerted certain influences on the establishment of the predictive model. Second, the early warning model established by our research is still only in the initial stage, and it needs to be further tested and improved in the clinic to provide clinicians with a simple, convenient, and valuable scoring system, which should then be beneficial in clinical treatment.

Conclusions

In conclusion, our results showed that the fever duration before bronchoscopy ≥6.5 d, CRP ≥20.94 mg/L, LDH ≥461.5 U/L, fever, and complication with pleural effusion were the risk factors for bronchoscopic intervention in children with MP-infected lobar pneumonia. We presented an early warning model of respiratory endoscopic intervention in children with lobar pneumonia caused by MP infection and showed that the evaluative effect of the early warning model was acceptable (with an AUC for the predictive score of 0.860) with suitable accuracy and clinical practicability.

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Conflicts of Interest: All authors have completed the ICMJE

uniform disclosure form (available at https://tp.amegroups.com/article/view/10.21037/tp-24-245/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study protocol was approved by the Ethical Review Committee of the Children's Hospital of Soochow University (reference number: 2020CS078). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Informed consent was obtained from all the children's legal guardian(s) before data collection.

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