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Original Article

The value of lung ultrasound in assessing the degree of lesions in children with mycoplasma pneumoniae pneumonia

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Abstract: Objective: To investigate the value of lung ultrasound (LUS) in assessing the degree of lesions in children with mycoplasma pneumoniae pneumonia (MPP). Methods: The clinical data of 100 children with pediatric MPP admitted to Jincheng General Hospital were retrospectively analyzed. Based on the standard of refractory MPP, the enrolled MPP-children were divided into refractory MPP group (n=25) and general MPP group (n=75). The general data were collected and compared between the two groups. The length of parenchymal lung lesions, the area in parenchymal lung lesions, and APACHE II scores were compared between the two groups. Logistic analysis was used to explore the risk factors that influence the extent of lesions in children with MPP. The receiver operating characteristic (ROC) curve was used to evaluate the ability of candidate indicators to predict the extent of lesions in children with MPP. Results: Logistic regression equation analysis revealed that the length and area of parenchymal lung lesions were the factors influencing the extent of lesions in children with MPP ($P<0.05$). ROC curve showed that the AUC value of length of parenchymal lesions was 0.667, and the best sensitivity and specificity were 78.56% and 69.14%, respectively. The AUC value of area of parenchymal lesions was 0.582, and the best sensitivity and specificity were 58.19% and 81.04%, respectively. Conclusion: Lung ultrasound measurement of length and area of parenchymal lung lesions can be used to assess the extent of lesion in children with MPP and provide a basis for clinical treatment planning.

Keywords: Lung ultrasound, parenchymal lung lesions, mycoplasma pneumoniae pneumonia, degree of lesions

Introduction

Mycoplasma pneumoniae (MP) is one of the most general pathogens in pediatric respiratory diseases, and mycoplasma pneumoniae pneumonia (MPP) caused by MP is a very dangerous disease even with mild symptoms [1]. The etiology of pediatric respiratory infections has been thoroughly explored, and the results show that acute pediatric respiratory infections can cause not only lung damage, but also a variety of extrapulmonary symptoms of varying severity, and it correlates with pediatric bronchial asthma. MP is a self-limiting disease, however, its management is difficult, and in some cases fatal [2]. The incubation period of MP infection can reach 2 to 3 weeks, and the onset is slow. About 1/3 of patients feel asymptomatic. After the incubation period, most patients show pharyngitis, rhinitis, tracheitis and bronchiolitis, with symptoms such as fever, headache, chills, cough, sore throat, chest pain, fatigue, muscle soreness, nausea, vomiting and loss of appetite. To avoid the invasion of bacteria, we should pay more attention and take precautions in our daily life, for example, take part in more outdoor sports, pay attention to the hygiene and cleaning of hands, avoid going to crowded public places, and pay attention to ventilation.

In the past, CT and chest radiographs were the main clinical examination methods used for MPP. Lung ultrasound (LUS) has been widely used in the diagnosis of MPP in recent years due to its non-invasive, immediate, safe and convenient advantages [3], and its accuracy and application value have been confirmed by a

large number of clinical studies. However, LUS is less reported clinically in terms of solid length diameter and solid area for early assessment of the severity of MPP [4]. Therefore, if the risk of MPP can be evaluated objectively and accurately before the occurrence of MPP [5], and if the risk group can be accurately identified and treated early, it would be useful to improve the quality of medical treatment and prognosis [6, 7]. The innovation of this study is to collect real patient data and conduct systematic statistical analysis, which is the first time to explore risk factors of the extent of lesions in children with MPP. The purpose of this study is to investigate the correlation between the length and area of solid lesions in LUS pneumonia and the degree of MPP [8-11].

Materials and methods

Object of the study

One hundred children with pediatric MPP admitted to Jincheng General Hospital from January 2020 to January 2022 were retrospectively enrolled, all of whom met the "Expert Consensus on the Diagnosis and Treatment of Mycoplasma pneumoniae Pneumoniae in Children (2015 version)" developed by the Chinese Academy of Medical Pediatrics regarding the diagnosis and treatment criteria for MPP. Based on the standard of refractory MPP, the enrolled MPP-children were divided into refractory MPP group (n=25) and general MPP group (n=75). This study was approved by the Medical Ethics Committee of Jincheng General Hospital.

MMP diagnostic criteria: Upper respiratory tract infection can be diagnosed by nasal congestion, runny nose, sore throat, cough and other symptoms. Lower respiratory tract infection can be diagnosed by fever, chest pain, cough, expectoration, and even hemoptysis. In the clinical setting of respiratory inflammation, lung X-rays shows fibrous tissue thickening, increased density, and speckled or reticulated density of lung tissue, along with positive serum Mycoplasma pneumoniae IgM (MP-IgM).

Definition of refractory MPP: High fever lasts for more than 7 days, lung imaging suggests a large area of high-density uniform consolidation, and CRP is greater than 40 mg/L (reference value is less than 8 mg/L).

Gold standard of refractory MPP diagnosis: a. X-ray of chest: increased lung texture, infiltration shape in lung parenchyma which is more common in the lower lobe, in the form of spotted, patchy or uniform fuzzy shadow; b. Serological examination: serum antibody >1:32, streptococcal mg ≥1:40, serum indirect >1:32, indirect fluorescence >1:66, indirect immunofluorescence against Mycoplasma pneumoniae >1:16, anti-mycoplasma pneumoniae >1:8, positive avidin enzyme immunosorbent assay, or detected mycoplasma pneumoniae antigen within 24 hours.

Inclusion criteria: (1) Meting the diagnostic criteria related to MPP and had accomplished blood and lung CT tests during the treatment. (2) Children who received a complete treatment cycle as planned without arbitrary termination or withdrawal from the treatment process. (3) Children who had not taken antibiotics or antivirals before the treatment.

Exclusion criteria: (1) Children with combined heart, liver, spleen, lung and kidney hereditary or immune diseases. (2) Children with congenital blood disorders or immune deficiencies. (3) Those with other lung diseases such as Mycobacterium tuberculosis infection, lung tumors or lung migratory tumors. (4) Those with immune dysfunction. (5) Those with combined trauma or concurrent surgery and unstable vital signs. (6) Those with pulmonary inflammation caused by large area secondary infection and large area burns caused by traffic accident or burns, etc. (7) Those with a history of new coronary infection.

Ultrasound examination of the lungs

Color ultrasound (LOGIQ E9.GE.USA) with a linear array detector in the range of 6-15 MHz or a convex array probe in the range of 1-6 MHz was used. 12-partition scanning method was applied. With the level of both nipples as the boundary, the chest wall on both sides was divided into upper and lower areas. With the sternum, the anterior axillary line, the posterior axillary line, and the spine as the boundaries, each side of the chest wall was divided into three areas: anterior, lateral, and posterior, with a total of 12 districts. After lung ultrasound examination, length and area of parenchymal lung lesions were recorded, and the APACHE II score was recorded and compared with the

Table 1. Baseline information

Group/Indicator	Number of sample cases	Age	Male/Female (%)	Duration of illness (days)	BMI (kg/m^2)	CRP (mg/L)
Refractory MPP	25	5.98±0.24	15/10	34.71±0.40	14.45±0.17	749.57±29.34
General MPP	75	6.51±0.48	43/32	22.67±0.72	14.07±0.27	152.04±11.46
X^2/t value	-	0.200	0.464	0.930	0.897	0.178
P value	-	0.200	0.902	0.010	0.555	0.382

diagnostic results in clinical treatment to determine their accuracy.

Observation indicators

(1) The general data were collected, including age, duration of illness, BMI, CRP. (2) Length of parenchymal lung lesions and area in parenchymal lung lesions were compared between the two groups. (3) APACHE II scores were compared between the two groups. (4) Logistic regression analysis was used to explore the risk factors that influence the extent of lesions in children with MPP. (5) The value of the length and area of parenchymal lung lesions in children with MPP in assessing the extent of MPP lesions was evaluated by ROC.

Statistical scheme

The statistical software SPSS 22.0 was used to process the data, and the measurement data were described by $\bar{x} \pm sd$, and independent samples t-test was used for comparison between the two groups; the count data were expressed by n (%) and analyzed by χ^2 test. The receiver operating characteristic curve (ROC) was used to analyze the evaluation value of the length and area of pulmonary parenchymal lesions on the degree of MPP lesions, and obtain the area under the curve, confidence interval, sensitivity, specificity and cut-off value. The logistic analysis was used to evaluate the risk factors influencing the extent of lesions in children with MPP. P<0.05 indicated that the difference was statistically significant.

Results

Baseline information table

Comparison of clinical baseline data of 25 cases of refractory MPP and 75 cases of general MPP showed that there were no significant difference in age, gender and BMI between refractory MPP and general MPP groups (all P>0.05); while the disease duration in refractory MPP group was significantly longer than that in general MPP group (t=0.930, P=0.010). See **Table 1**.

Length and area of parenchymal lung lesions in children with MPP

For the comparison of length of parenchymal lung lesions, 28.31±0.24 mm in the refractory MPP group was significantly longer compared to the general MPP group (19.02±0.11 mm, t=4.307, P=0.041; **Figure 1A**). For the comparison of area in parenchymal lung lesions, 151.86±1.83 mm^2 in the refractory MPP group was significantly bigger compared to the general MPP group (105.36±1.00 mm^2, t=3.328, P=0.046; **Figure 1B**). **Figure 1C** and **1D** show the typical pictures of ultrasonic image of the MPP lungs.

APACHE II scores in children with MPP

In the comparison of APACHE II scores, refractory MPP group (48.46±1.60) showed statistically higher score (t=5.377, *P*=0.022) compared to general MPP group (41.20±1.08). See **Figure 2**.

Logistic regression analysis of factors affecting MPP lesion degree

The degree of lesion in children with refractory MPP was set as the dependent variable, and the length of parenchymal lung lesions (mm), area of parenchymal lung lesions (mm^2) and APACHE II score were included in the logistic regression equation as independent variables for analysis, and it was found that the solid lesion length, solid lesion area, and APACHEIIscore were factors influencing the degree of lesion in children with refractory MPP (*P*<0.05), as shown in **Table 2**.

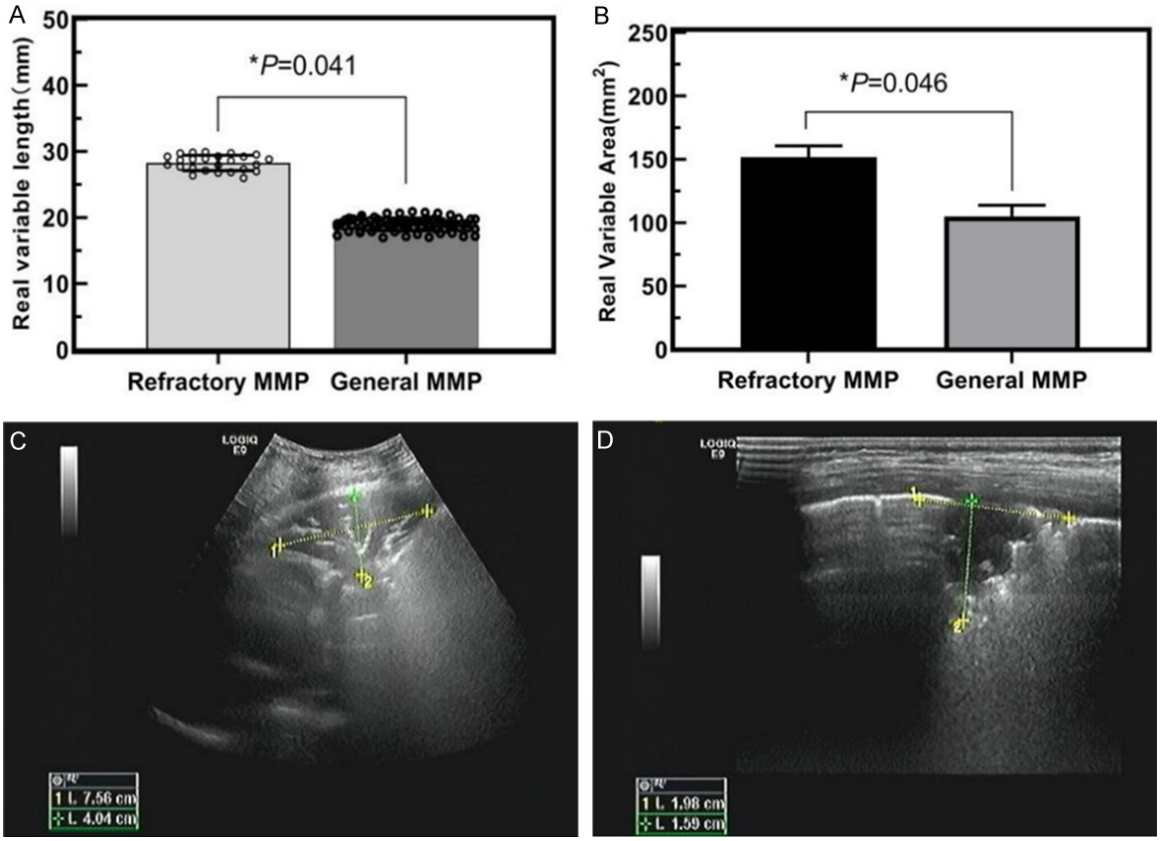

Figure 1. Comparison of length and area of parenchymal lung lesions in children with MPP. Note: A. Comparison of length of parenchymal lung lesions in children with general and refractory mycoplasma pneumoniae pneumonia (MPP); B. Comparison of area of parenchymal lung lesions in children with general and refractory MPP; C. Ultrasonic pictures of the lungs of refractory MPP, length: 75.6 mm, area: 75.6 mm × 40.4 mm; D. Ultrasonic pictures of the lungs of general MPP, length: 19.8 mm, area: 19.8 mm × 15.9 mm.

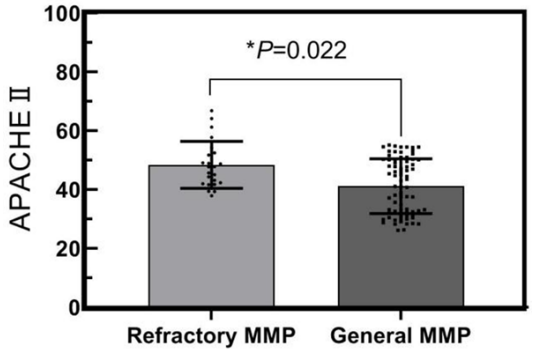

Figure 2. APACHE II scores of children with general and refractory MPP.

The value of the length and area of parenchymal lung lesions in assessing the extent of MPP lesions

The ROC curve for assessing the value of parenchymal lesion length for refractory MPP was plotted with an AUC value of 0.667 and best sensitivity and specificity of 78.56% and 69.14%, respectively. The ROC curve for assessing the value of parenchymal lesion area for refractory MPP was plotted with an AUC value of 0.582 and best sensitivity and specificity of 58.19% and 81.04% **Figure 3**.

Discussion

Severe pneumonia in children is a common disease in ICU, mostly related to infectious pathogens, often dominated by Mycoplasma pneumoniae infection. Patients often have symptoms such as blood in sputum [12], dyspnea, fever, cough and sputum, and in severe cases, respiratory failure, lowered blood pressure, depression and drowsiness, which pose a certain threat to patients' life safety [13]. The incidence of severe pneumonia and the mortality in children are high, and the changes in people's lifestyle and environment have significant-

Table 2. Analysis of factors affecting MPP

Equation Variables	B	Standard Error	Significance	χ^2 Value	OR	Exp (B)
Real variable length	6.107	2757.368	0.020	32.254	3.650	449.027
Real variable area	0.093	474.243	0.001	25.520	5.521	1.098
APACHE II	2.145	152.14	0.018	16.14	4.444	6.025
Constants	-155.795	23732.448	0.995	31.254	5.942	0.000

Note: Acute physiology and chronic health evaluation II (APACHE II).

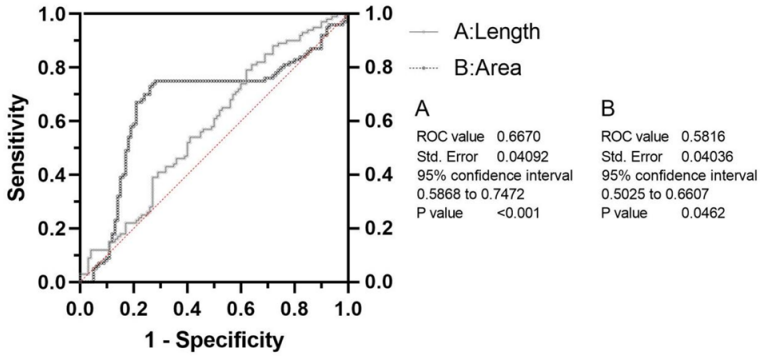

Figure 3. ROC of length and area in assessing the refractory mycoplasma pneumoniae pneumonia (MPP).

ly increased its incidence in recent years [14]. Pediatric patients with severe pneumonia have difficulty coughing because of their increased airway secretions and accumulation in the bronchi, causing airway obstruction, resulting in respiratory distress and, in severe cases, sputum embolism, resulting in bronchial obstruction, respiratory failure, carbon dioxide retention, pulmonary atelectasis, and other complications that endanger the survival of children [15-17]. This may be due to the structural characteristics of children's lungs: weaker development of elastic tissue, large number of blood vessels, high blood content and low air content in the whole lung, vigorous interstitial growth, sparse number of alveoli, and easy occlusion by mucus. Its anatomical characteristics are: narrowing of lung tissue thickness, which facilitates enhanced lung imaging and maintains good image quality [18].

MP has a high affinity for human respiratory epithelial cells, and the mucin P1 protein binds to sialylated glycoproteins in the respiratory epithelium, contributing to MP adhesion and sliding [19]. The invasion and adhesion of MP can cause direct damage to the host respiratory epithelium, which is one of the causes of solid lung changes in children with mycoplasma pneumonia [20].

The pathogenesis of refractory MPP has not been completely clarified and is mostly thought to be related to the cellular immune-mediated inflammatory response. Some studies have pointed out that elevated level of CRP is a high-risk factor for the development of refractory MPP in children, which is consistent with the results of this study [21]. Other authors noted that clinical monitoring of CRP and LDH levels can be used to differentially diagnose refractory MPP from general MPP [22]. This study combined the LUS, at the time of admission, to assess the degree of MPP lesions in children with MPP, and the results showed that the AUC was significantly higher than that of the single assessment, suggesting that the combination of laboratory parameters with imaging parameters to assess the extent of MPP lesions has high clinical value and can be used as a reference for the selection of treatment options for children with MPP [23, 24].

The incidence of MPP has been increasing due to various causes and has attracted extensive attention from medical practitioners. Exudative changes in the lung tissues, such as exudate and inflammatory cells filled in alveoli, are the basis for ultrasonic testing [25, 26]. With the continuous development of ultrasound technology, its superiority in pneumonia is recognized, leading to its greater promotion.

Although CT is recognized as the gold standard for pneumonia diagnosis, it also produces irradiation from radioactive sources which is harmful to sensitive children, pregnant women, and patients who require multiple tests. The weak conduction of ultrasound in the air makes it difficult to ultrasonically image the air-containing

lung tissue. Traditional ultrasonography can only visualize the pleural layer and sliding signs due to breathing, but cannot visualize the internal structure of the lung, and thus the lung was previously considered a contraindication to ultrasound. However, in recent years, it is widely believed that pathological changes in the lungs are an important basis for the pathological manifestations of the lungs and that their pathological features are important for the early identification of lung lesion in children. In recent years, ultrasound has been increasingly used in intrapulmonary lesions [2, 3, 27].

The clinical manifestations of lung ultrasound in mycoplasma pneumonia are hypoechoic with strong signal reflection. Due to the high gas content in the bronchi, a strong gas echo may appear, accompanied by the comet tail sign, which may cause some interference with the posterior wall of the tube, and is often called the "gas-containing bronchial sign". If the bronchi and alveoli are not completely blocked, their location and number may change with breathing, and the location and intensity of strong echoes may also change. If there is inflammatory exudate in the bronchi, a low-frequency echo will appear, which is called "bronchial fluid". Because of its special sonographic features, it is an important tool for clinical diagnosis of Mycoplasma pneumonia. In this study, ultrasound was used to evaluate Mycoplasma pneumonia, and CT examination was the main basis for evaluating its efficacy. It was shown that the length and area of solid lesion of pneumonia can accurately assess refractory mycoplasma pneumonia with a certain combined detection effect [28].

MMP infection increases the expression of mucin in lung epithelial cells by activating Toll-like receptors, resulting in hyperfunction of airway mucin. Increased airway secretions form a natural medium for a variety of pathogenic microorganisms, so children with MPP are prone to co-infection with bacteria and viruses, which is one of the main causes of pulmonary parenchyma lesions [29, 30].

The study still has several shortcomings. On the one hand, this is a retrospective study and needs to be confirmed by more prospective experiments; on the other hand, the level of knowledge we have learned is not sufficient to make an in-depth and detailed analysis of the problem, and thus the accuracy of this study cannot be tested at a deeper level. In addition, further investigation is needed because of the small sample size and the bias of a single study.

Conclusion

Both the length and area of parenchymal lung lesions are closely associated with the development of persistent MPP in children; the lung ultrasound can be repeatedly examined, which can monitor the inflammatory changes in the lungs in real time and evaluate the pathological changes of MPP in children, thus providing a reference for clinical treatment.

Disclosure of conflict of interest

None.

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