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Clinical value of bedside ultrasound in different degrees of neonatal chest imaging

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► ***Original article***

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ABSTRACT

Background: This research aimed to investigate imaging features of bedside ultrasound in different degrees of neonatal respiratory distress syndrome (NRDS). ***Materials and Methods:*** Eighty premature children admitted to neonatal intensive care unit (NICU) of Zhongda Hospital Affiliated to Southeast University within 6-12 hours after birth and diagnosed with NRDS by clinical and chest X-ray between January 2019 and December 2019 were selected. The children were divided into pulmonary surfactant (PS) treatment group (22 cases) and non-PS treatment group (58 cases). The lung ultrasound (LUS) score and total score of 12 regions was calculated, and score was compared with different degrees of NRDS in clinical neonates to compare ultrasound characteristics of different degrees of NRDS. ***Results:*** There was a positive correlation between 12 zone ultrasound score of double lung and grade of chest X-ray impact (r=0.872, P<0.001). The ultrasound scores were positively correlated with degree of respiratory distress (r=0.905, P<0.001). In PS administration group, the degree of respiratory distress improved from severe to mild (10 cases) and non-mild (12 cases) 2 hours after administration. ***Conclusion:*** Ultrasonography can be used as a non-invasive imaging method to diagnose condition of children with NRDS and dynamically predict prognosis of NRDS, which may offer a preliminary basis for ultrasonic-assisted clinical diagnosis and therapy.

INTRODUCTION

Recently, the incidence of preterm infants has gradually increased [1], and the incidence of preterm infants in China is also on the rise. At present, about 1.2 to 1.5 million preterm infants are born every year [2]. With the increase of premature births, the prevention and reasonable diagnosis and treatment of neonatal respiratory distress syndrome (NRDS) are attracting increasing attention. NRDS, also known as hyaline membrane-disease, is a serious respiratory disease caused by insufficient pulmonary surfactant (PS) secreted by type II epithelial cells. It is often found in premature infants, manifested as progressive dyspnea, hypoxemia, and respiratory failure a few hours after survival, with high mortality and disability rates [3]. Over the past 20 years, the application of exogenous PS in treatment of NRDS has been studied at home and abroad for many years, and both pharmacokinetic and clinical studies have confirmed that exogenous PS can effectively and rapidly improve lung dilation and gas exchange in children with NRDS, improve pulmonary oxygenation function, and significantly reduce inhaled oxygen concentration [4]. Many clinical practices have also proved [5-9] that the application of PS can improve the survival rate of children with NRDS and shorten time of oxygen and mechanical ventilation. Other studies have shown [10, 11] that the treatment of NRDS with large doses of PS can improve respiratory function of children to the greatest extent in a short period, reduce incidence of related complications, and thus shorten course of treatment and length of hospital stay, and improve outcome of children.

However, after years of clinical practice, perinatal medicine community has gradually realized that not all preterm infants need early prevention and treatment of PS, and the methods of endotracheal administration of PS are also insufficient, and some children receiving high-dose PS treatment may have complications such as pulmonary edema, which limits clinical application of PS in clinical practice. Because of this, the 2016 updated European Guidelines for the Management of Respiratory Distress Syndrome in Preterm infants [12] also put forward reasonable choice of PS application more cautiously, and since Göpel *et al.* [13] published a method of administering alveolar surfactant to preterm infants with a thinner catheter in the Lancet in 2011, more and more people have paid attention to application of less invasive surfactant administration (LISA) technology in premature infant NRDS [14-16]. Based on above situation, more studies are urgently needed to provide relevant evidence to guide clinical practice.

The traditional diagnosis of NRDS in preterm infants mainly relies on history, clinical presentations, arterial blood gas analysis, along with

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chest X-ray examination. For critically ill children, continuous and dynamic X-ray examination is not only difficult to achieve, but also has great side effects. Recently, with advancement of technology and improvement of understanding, ultrasound has been extensively applied in diagnosis of lung diseases. Moreover, relative to chest X-ray examination, ultrasound has higher sensitivity and specificity and has been gradually accepted and applied in clinical practice [17-19]. Therefore, this study aimed to investigate classical medical history, clinical manifestations and appropriate chest radiography of children diagnosed with different degrees of NRDS, and dynamically monitor their lung changes through real-time color ultrasound at the bedside, which was the first time to study characteristics of each method and response of severe NRDS children to different doses of PS, so as to provide clinical clues.

MATERIALS AND METHODS

General data

Eighty premature children who were admitted to the neonatalintensive care unit (NICU) within 6-12 hours after birth from January 2019 to December 2019, were diagnosed with NRDS by clinical and chest X-ray. All the children met the diagnostic criteria of the fifth edition of Practical Neonatology, including 54 males and 26 females, with an average gestational age of 32.61±1.40 weeks. The birth weight was 150-3000 g, and the average weight was (2078.13±419.17) g. The Apgar score was 8.2±2.2 points in 1 min and 9.0±1.9 points in 5 min (table 1). There were 63 cesarean section births, 17 vaginal births, 76 single births and 14 twin births. There were 21 cases of unnatural conception, including artificial insemination, test-tube baby, and fresh embryo transfer. This study met the standards of medical ethics and was approved by the Ethics Committee. All enrolled children obtained informed consent from their families and signed informed consent. According to respiratory distress score, 80 children with NRDS were separated into mild group, moderate group as well as severe group, of which 29 cases were mild group, 25 cases were moderate group, and 26 cases were severe group. Based on chest X-ray, 80 children with NRDS were divided into grade I-IV, including 27 cases of grade I, 25 cases of grade II, 17 cases of grade III, along with 11 cases of grade IV.

Table 1. Descriptive statistics. SE=standard error; SD=Standard deviation.

	N	Range	Minimum value	Maximum value	Average ± SE (SD)	Variance
Birth weight	80	1500	1500	3000	2078.125± 46.8644 (419.1676)	175701.503
Gestational age	80	5.14	29.71	34.86	32.6143± 0.15607 (1.3959)	1.949
Apgar 1	80	10	0	10	8.24±0.226 (2.020)	4.082
Apgar 5	80	10	0	10	8.97±0.215 (1.922)	3.696
Effective N (listwise)	80					

Inclusion and exclusion criterion

Inclusion criterion: (1) Gestational age: 28 weeks ≤34 weeks; (2) Weight: 1500 g≤ weight < 4000 g; (3) The time of admission was within 6 hours after birth; (4) Met the diagnostic criteria of neonatal respiratory distress syndrome; (5) No obvious heart or brain malformations were observed; (6) Children's families sign informed consent.

Exclusion criterion: (1) Any one did not meet the inclusion criteria; (2) Patients who had been treated with pulmonary surfactant before admission; (3) There were any factors that endanger the safety of the subject; (4) Children with respiratory distress caused by meconium aspiration syndrome.

X-ray diagnostic criteria and grading

The X-ray diagnostic criteria and grading were as follows [20]: Grade I: The opacity of the lung field was reduced, only extensive granular shadows were seen in the lung, and the heart shadow and transverse septum outline were clearly visible. Grade II: The opacity of the lung field was further reduced, extensive mesh and granular shadows were seen in the lung, and air bronchial signs appeared, and the heart shadow and transverse septum outline were still clear. Grade III: The opacity of the lung field was significantly reduced, the mesh and granular shadows in the lung were significantly increased and enlarged, the boundary was blurred, extensive fusion could be seen, the air bronchial sign was more extensive, and the heart shadow and the transverse septum were blurred. Grade IV: The lung field presented a dense shadow (white lung), and the heart shadow and transverse septal contour edges were difficult to distinguish.

Neonatal respiratory distress score

Neonatal respiratory distress score [21] included the score of respiratory rate, inhaled oxygen concentration, groan, trisfovea sign, pulmonary breathing sound and gestational age, each of which was assigned three grades of 0, 1 and 2, with a total of 12 points. <5 was classified as mild; 5 to 8 was moderate, which required further respiratory support, containing nasal continuous positive airway pressure, or even mechanical ventilation, and > 8 was severe, which required immediate tracheal intubation and mechanical ventilation.

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Brief introduction of pulmonary ultrasound scoring criteria

The lung ultrasound scoring system was based on dividing the lung into 12 regions, and then scanning each lung region. According to the scanning results, each partition was scored separately, and the final score was obtained by adding the scores of the 12 partitions. The lowest score was 0 and the highest score was 36. 0 point was classified as normal, otherwise it may be abnormal, and the higher the score, the more serious the condition. The specific criteria were as follows: 0 point: normal lung volume (i.e. normal lung); 1 point: moderate reduction in lung volume, and the specific criteria were: 1 point: The presence of pulmonary interstitial syndrome (multiple isolated B-lines) or focal pulmonary edema (fusion of B-lines < 50% of intercostal space on vertical scan) or subpleural consolidation; 2 points: Severe reduction of lung volume (presence of alveolar edema, that is, diffuse fusion line B, occupying the entire intercostal space); 3 points: Complete loss of lung volume (presence of lung consolidation, i.e., hepatoid changes in lung tissue with or without air bronchogram) [22, 23].

Lung ultrasonography

A total of 80 preterm infants with gestational age and weight that met the inclusion criteria and were clearly diagnosed with NRDS were selected and six areas on both sides of the children (the upper chest, lower anterior, upper axillary, lower armpit, upper posterior and lower posterior) were detected respectively by Philips d70 color Doppler ultrasound high-frequency linear array probe (Philips, Amsterdam, Netherlands) 2 h after pulmonary alveolar surfactant (PS; Poractant Alfa, Curosurf®, Italy) and assisted ventilation therapy. The front and back chest walls were connected by the anterior axillary line, the posterior axillary line and the double nipple line were divided into lung B-ultrasound. At the same time, according to the clinical manifestations, arterial blood gas analysis and 12 regions of the upper chest, anterior inferior, axillary, axillary, posterior upper and posterior inferior, the lung ultrasound (LUS) score (each region was calculated based on the most severe ultrasound score), the total score of the 12 regions was calculated, and the score was compared with the clinical neonates with different degrees of NRDS of different gestational ages to grasp the ultrasound characteristics of different degrees of NRDS. Blood gas and chest X-ray examination were completed, and NRDS classification (grade I-IV) was determined, which was divided into 4 groups according to the classification. Combined with the degree of respiratory distress (severe) and chest X-ray (grade III-IV), children with severe RDS (22 cases) were selected. At the same time, changes in skin color, heart rate, and blood oxygen saturation of the children were observed and recorded. B-ultrasound examination was performed 2 h after medication, and respiratory distress score was given, and severe improvement was defined as mild as effective.

Statistical methods

SPSS 22.0 statistical analysis software (IBM Corp., NY, USA) was adopted to analyze the data, and the measurement data were exhibited as (x±s). The correlation analysis between ultrasound score and X-ray grading in 12 areas of double lungs was analyzed, and the correlation analysis between ultrasound score and respiratory distress score was analyzed by Spearman analysis. ANOVA was adopted for comparison of ultrasound scores between different groups, and Dunnett test was adopted for comparison between groups. The rank sum test is used for non-normally distributed data. Paired sample t test was used to compare the mean ultrasound scores before and after the use of PS. $P<0.05$ was considered statistically significant.

RESULTS

Comparison of ultrasound score and chest X-ray grading

The contrast-enhanced X-ray solography of varying degrees of respiratory distress were displayed in figure 1. The average ultrasound score in 12 areas of both lungs was (14.36±7.21) points. X-ray grading and ultrasound scores among each group were shown in the following table 2.

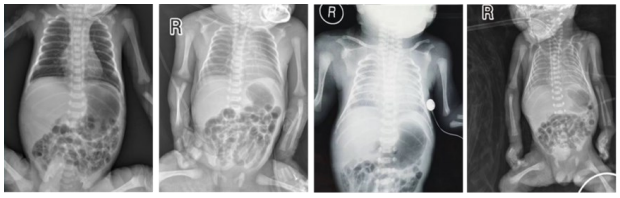

Figure 1. X-ray solography of varying degrees of respiratory distress.

Grade I: Small particle shadows were found in the lung field, and the shadows in the lower lung lobes were more severe. Grade II: Decreased lung field transparency, accompanied by bronchial inflation sign and significant consolidation of both lungs; small reticular granule shadows, especially in the lower lung lobes, were more severe. Grade III: A large shadow area in the lung field, with a significant decrease in lung transparency and bronchial inflation sign, manifested as ground glass-like changes. Grade IV: Significant increase in lung field density, white lung in both lungs, and disappearance of heart shadow.

Correlation analysis of ultrasound score and chest X-ray grading

There was a positive correlation between the

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ultrasound scores in 12 areas of double lung and X-ray grading (r=0.872, P<0.001). There were statistically significant differences in ultrasound scores among different groups (P<0.001) and statistically significant differences in ultrasound scores among different groups (P<0.001). The higher the grade of chest film, the higher the ultrasound score was (tables 3-5).

Table 2. Comparison of ultrasound score and chest X-ray grading. SD= standard deviation.

X	Average ± SD	Minimum value	Maximum value	N
1	8±2.386	1	13	27
2	11.88±3.308	6	20	25
3	20.47±3.300	15	26	17
4	26.18±3.125	18	30	11
Total	14.36±7.205	1	30	80

Table 3. Correlation analysis of ultrasound score and chest X-ray grading.

		X	Ultrasound score
X	Correlation coefficient	1.000	0.872**
	P (double tail)		0.000
	N	80	80
Ultrasound score	Correlation coefficient	0.872**	1.000
	P (double tail)	0.000	
	N	80	80

Note: **The correlation was significant at layer 0.01 (double tail).

Table 4. Variance analysis.

	Quadratic sum	df	Mean square	F	P
Between groups	3417.976	3	1139.325	126.868	0.000
In group	682.512	76	9.980		
Total	4100.488	79			

Table 5. Multiple comparisons.

	(I) X	(J) X	Average variance (I-J)	Standard error	P	95% confidence interval	
						Lower limit	Upper limit
Bonferroni method	1	2	-3.880*	0.832	0.000	-6.13	-1.63
		3	-12.471*	0.928	0.000	-14.98	-9.96
		4	-18.182*	1.072	0.000	-21.09	-15.28
	2	1	3.880*	0.832	0.000	1.63	6.13
		3	-8.591*	0.942	0.000	-11.14	-6.04
		4	-14.302*	1.084	0.000	-17.24	-11.36
	3	1	12.471*	0.928	0.000	9.96	14.98
		2	8.591*	0.942	0.000	6.04	11.14
		4	-5.711*	1.160	0.000	-8.85	-2.57
	4	1	18.182*	1.072	0.000	15.28	21.09
		2	14.302*	1.084	0.000	11.36	17.24
		3	5.711*	1.160	0.000	2.57	8.85
Dunnett t (bilateral) [b]	2	1	3.880*	0.832	0.000	1.87	5.89
	3	1	12.471*	0.928	0.000	10.23	14.71
	4	1	18.182*	1.072	0.000	15.59	20.77

Note: *The mean difference was significant at 0.05 level. b: Dunnett t test treated one group as a control and compared all other groups to it.

Comparison of ultrasound score and respiratory distress degree

The ultrasound scores analysis of respiratory distress group among all groups showed that the ultrasound score of lung increased with the severity of respiratory distress (table 6). There were statistically significant differences in ultrasound scores between different groups (P<0.001), and pairwise comparison of rank sum test between groups had statistically significant differences in ultrasound scores (P<0.001, table 7).

Table 6. Ultrasonographic score analysis of respiratory distress group among all groups. SD= standard deviation.

Respiratory distress degree	Average±SD	Minimum value	Maximum value	N
Mild	7.76±2.166	1	13	29
Moderate	12.84±2.764	8	18	25
Severe	23.19±4.176	12	30	26
Total	14.36±7.205	1	30	80

Table 7. Ultrasound scores between different groups.

Respiratory distress degree	N	Average grade
Mild	29	16.57
Moderate	25	40.88
Severe	26	66.83
Total	80	
Chi-square		64.739
df		2
P		0.000***

Note: ***P<0.001.

Correlation analysis between ultrasound score and respiratory distress degree

Ultrasound score was positively correlated with the degree of respiratory distress (r=0.905, P<0.001), as shown in the table 8.

Table 8. Correlation analysis between ultrasound score and respiratory distress degree.

		Ultrasound score	Respiratory distress degree
Ultrasound score	Correlation coefficient	1.000	0.905**
	P (double tail)		0.000
	N	80	80
Respiratory distress degree	Correlation coefficient	0.905**	1.000
	P (double tail)	0.000	
	N	80	80

Note: **The correlation was significant at layer 0.01 (double tail).

Comparison of respiratory distress relief after 2 hours of administration of PS

In PS administration group, the degree of respiratory distress improved from severe to mild (10 cases) and non-mild (12 cases) 2 hours after administration, with an effective rate of 100%.

DISCUSSION

Recently, with the improvement of people's understanding of pulmonary ultrasound and the increasing maturity of ultrasound technology, pulmonary ultrasound has been widely applied in the diagnosis of neonatal lung diseases [24, 25], providing more medical information, and has formed domestic or international guidelines [26, 27]. Due to its high accuracy and reliability, continuous dynamic observation and reduced radiation effects, providing more safety [28], pulmonary ultrasound has gradually replaced X-ray examination and been routinely applied in neonatal units and NICU [29, 30].

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The exploration of 12 different areas of the double lung can visually observe the lesions in each area of the lung and help to find focal lesions. In our study, there was a positive correlation between the 12-zone pulmonary ultrasound scoring method used and the currently recognized X-ray grading to judge the severity of NRDS in children (r=0.872, P<0.001), which was consistent with previous studies. Our findings suggest that the higher the X-ray grade, the higher the pulmonary ultrasound score. Neonatal respiratory distress score is a simple and objective evaluation criterion, which can quickly and effectively judge the respiratory condition of children. The higher the respiratory distress score, the more serious the respiratory distress degree and the more serious the condition. Our results displayed that the ultrasound score was positively correlated with the degree of respiratory distress (r=0.905, P<0.001), that is, the more severe the degree of respiratory distress, the higher the ultrasound score and the more serious the disease. According to the respiratory distress score, they were divided into three groups: mild, moderate and severe, and pairwise comparison among the three groups showed statistically significant differences (P<0.001). These results indicated that pulmonary ultrasound score and respiratory distress score were consistent in predicting the severity of NRDS. An ultrasound score of >12.8 points can indicate moderate respiratory distress, and an ultrasound score of >23.2 points can indicate severe respiratory distress. Our findings indicate that clinicians can quickly understand the degree of respiratory distress of children according to the ultrasound score, and timely take appropriate respiratory support, containing nasal continuous positive airway pressure ventilation, or even tracheal intubation mechanical ventilation.

In this study, comparison and observation of the effect of PS before and after use, we conducted a control observation of 22 cases of children using PS. Ultrasound indicated that the respiratory distress received great relief 2 hours after PS treatment, indicating that the condition of the children was significantly improved after 2 hours after PS treatment, which was consistent with the results of ultrasound score. Our findings indicate that ultrasound score was consistent with the clinical treatment effect, and further indicate that ultrasound score was credible and feasible, with high clinical value in dynamic monitoring of children's condition. Furthermore, our findings indicate that lung ultrasound score can more intuitively describe lung lesions by means of ultrasonic quantification. If the lung ultrasound score is lower than before within 2 hours of medication, it can indicate that clinical treatment is effective. If the change of 2-hour ultrasound score is not obvious or increased, it can also prompt clinicians to adjust the treatment plan in time. With the development of perinatal medicine technology and the improvement of neonatal resuscitation level, some NRDS children are given PS injection in the delivery room or the local hospital at birth to control the condition, so the number of cases can be included less. Meanwhile, more clinical evidence is needed to accurately assess the condition of children. In addition, we are concerned that new research suggests that lung ultrasound images may be confounded by other factors, such as heart disease, patient fluid management, and diaphragm function, which are not included in the LUS score [31, 32]. As a result, pulmonary ultrasound skills require more extensive training and guidance to ensure that the necessary support is provided for physicians to identify children with non-critical and critical NRDS.

CONCLUSION

Ultrasonography can be used as a non-invasive imaging method to diagnose condition of children with NRDS and dynamically predict prognosis of NRDS, which may offer a preliminary basis for ultrasonic-assisted clinical diagnosis and therapy.

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***Ethical consideration*:** All patients signed a documented, voluntarily informed consent form. All methods were carried out in compliance with the Helsinki Declaration criteria, and this study was authorized by the ethics committee of School of Medicine, Zhongda Hospital, Southeast University with the approval No. ZD2019-002A (January 2019).

***Author contribution*:** X.W.; conceived and designed experiments. X.W., M.Y. and Y.Z.; contributed markedly to experiments and arranging data. W.J. and L.Q.; conducted data analysis. M.Y.; wrote a draft manuscript. X.W.; revised the manuscript. All authors read and approved of the final manuscript.

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