Application Value of a New Lung Ultrasound Scoring Method in Neonatal Respiratory Distress Syndrome Treatment

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Abstract

We studied a 14-zone lung ultrasound scoring method to quantify the efficiency of pulmonary surfactant treatment and to determine the timing of mechanical ventilation in neonates with neonatal respiratory distress syndrome. In this prospective study, we identified 88 neonates who received pulmonary surfactant replacement therapy. We measured surfactant efficiency using the 14-zone scoring method pre-treatment and at 12 h, 24 h, 48 h, and 72 h post-treatment. The ultrasound score was inversely associated with pulmonary surfactant treatment. We also identified 67 neonates on mechanical ventilation. We applied the scoring method when the infants met criteria for ventilator withdrawal. A comparison of pre-treatment to 12 h post-treatment showed that scoring method was significantly different ($t = 4.08$, $P < 0.05$); other scoring methods did not differ ($P > 0.05$). Thus, the scoring method performed better on withdrawal time. A score of 41.0 was defined as the threshold for risk of withdrawal failure with 92.36% sensitivity and 93.80% specificity, with an area under the curve of 0.955.

Conclusion: The new 14-zone lung ultrasound scoring method improved scoring on the efficacy of pulmonary surfactant and had good diagnostic efficiency for timing the removal of mechanical ventilation in neonatal respiratory distress syndrome.

Introduction

Neonatal respiratory distress syndrome (NRDS) is the most common critical illness in neonates and has a high mortality [1]. The evaluation of the efficacy of NRDS treatment relies on a chest x-ray (CXR), but this procedure can cause DNA damage and is possibly carcinogenic, which may present a greater risk to premature infants [2]. Many studies [3-5] have shown that lung ultrasound scoring (LUS) is more sensitive and specific than CXR for the diagnosis of NRDS. Currently, the 6-zone, 10-zone, and 12-zone LUS methods are used to evaluate NRDS and have good effects. However, it is not clear which method performs better.

Common LUS methods may not be detailed enough for B-line and lung consolidation scoring, and thus may not reflect the severity of the lung lesions [6]. The lung consolidation method is somewhat subjective as the field is divided into subpleural lung consolidation and lung tissue–liver degeneration, without quantifying the range. Our study divided lung consolidation within a small range (less than 1 cm in depth) and a large range (more than 1 cm in depth). Pulmonary fluid may accumulate in the posterior due to gravity, so the clinical significance of B-line needs to be clarified. However, NRDS often occurs shortly after birth, with clinical symptoms occurring at more than 4–6 h, reaching a disease peak at 12–72 h, the B-line in the posterior chest may still have clinical significance. Therefore, we included the posterior lung into the study scope, and added bilateral lung bases to ensure comprehensive pulmonary scanning. We constructed a new 14-zone LUS method, which may be more accurate to evaluate NRDS.

Exogenous pulmonary surfactant (PS) replacement therapy is an important treatment for NRDS with early administration improving outcomes. Repeated administration may be necessary depending on

disease progression [7]; thus, it is important to assess the effect of PS early to adjust the treatment plan. Perri et al [8] showed that LUS could identify children requiring PS replacement therapy at an early stage, allowing early treatment and radiation reduction. However, none of the studies have shown whether CXR and LUS result in similar improvement in the treatment of NRDS.

Mechanical ventilation (MV) is an important advanced life support method for severe NRDS [9]. Weaning too early requires re-intubation, and repeated MVs significantly increase the incidence of tracheal injury and acquired subglottic stenosis. Late weaning significantly increases the incidence of ventilator-related complications, such as ventilator-associated pneumonia, bronchial pulmonary dysplasia and other complications. In recent years, many studies have used LUS, combined with cardiac function and diaphragm movement, to evaluate the risk of MV and weaning in adult patients, and led to bedside ultrasound becoming an effective tool for ICU evaluation of cardiopulmonary function [10-11]. However, there are currently few reports examining whether LUS can be applied to the weaning of neonates from MV. Therefore, this study aimed to assess the use of a 14-zone LUS method to evaluate the effect of PS treatment and assess the withdrawal time of MV in children with NRDS.

Materials And Methods

Between June 2018 and June 2019, we randomly selected 88 children (53 males and 35 females) with NRDS who required PS replacement therapy. The NRDS diagnostic criteria was based on the European NRDS Guidelines for Prevention and Treatment 2016 [9]. Children with complicated congenital heart disease were excluded. Sixty-seven infants with NRDS were treated with MV. Of these children, 52 were successfully removed from the machine and 15 failed.

We assigned 1-4 points for CXR grades I–IV and the median and quartile of the points at each time point were calculated. Machine withdrawal failure was defined as requiring MV with endotracheal intubation at 48 h after machine withdrawal.

Ultrasonography Method

We used a LOGIQ P6 colour Doppler ultrasound machine (GE Healthcare, Chicago, IL, USA) with an 11-MHz linear array probe and regulated the apparatus depth to 4 cm. Children were scanned in a quiet condition, lying in a supine position, on their side, and in a prone position, from top to bottom, and from left to right. The probe was perpendicular to the ribs, scanning one by one along the intercostal space. Each area was then scored with the most severe ultrasound signs.

LUS Methods

For the new 14-zone LUS method, the chest was divided as follows: the parasternal line, anterior axillary line, posterior axillary line, posterior median line, and double nipple line into 14 regions: anterior superior, anterior inferior, axillary superior, axillary inferior, posterior superior, posterior inferior, basal lung, and there

is a total of 14 regions in both lungs. The total possible score is 70 points, and the lung partition diagram is shown in Fig. 1.

A lung sonogram for each score is shown in Fig. 2, as follows: 0 points, N: the A-line is the main line, but there may be sporadic (fewer than three lines) B lines (Fig. 2a); 1 point, B1: scattered and non-fused B-line (see Fig. 2b); B2: dense, partially fused B-line (see Fig. 2c); 3 points, B3: completely fused B-line (see Fig. 2d); 4 points, C1: abnormal pleural line with a small range (depth of less than 1 cm) of subpleural lung consolidation (see Fig. 2e); 5 points, C2: abnormal pleural line with extensive (depth of greater than 1 cm) lung consolidation (see Fig. 2f).

Currently, there are three LUS methods: a 6-zone, a 10-zone, and a 12-zone, which are detailed in other studies [12-14].

Statistical Analysis

We used SPSS 24.0 statistical analysis software (SPSS Inc., Chicago IL, USA). Measurement data are presented as mean ± standard deviation for normally distributed data, and as median and interquartile range for non-normally distributed data. The Kruskal–Wallis rank-sum test was used to analyse differences in gender, delivery mode, gestational weeks, and birth weight of children. We evaluated the differences in LUS at different time points after PS treatment by repeated-measures analysis of variance (ANOVA). We compared the differences in LUS between the successful weaning group and the failed weaning group by repeated-measures ANOVA. Receiver operating characteristic (ROC) curve analysis was used to evaluate the diagnostic performance of the LUS for predicting weaning timing. $P < 0.05$ was considered statistically significant.

Results

Evaluating PS Replacement Therapy with LUS

The results of the different LUS methods and CXR at each time point after PS are shown in Table 1. With the improvement of PS, LUS score gradually decreased. At 12 h after PS, Compared to before PS, only the 14-zone LUS method was significantly different ($t = 4.08, P < 0.05$), which was consistent with the change of CXR, while the other LUS methods did not differ ($P > 0.05$). We concluded that the 14-zone LUS method was better for measuring the early effect of PS treatment.

Table 1.Comparison of four LUS methods at different time points after PS treatment for NRDS

Scoring						F ^a
method	0h	12h	24h	48h	72h	
6-zone	10.72±2.63	10.09±2.62	9.981±3.02	8.801±3.19	7.141±2.97	39.7
10-zone	28.79±10.32	27.73±10.00	25.13±11.07	20.48±9.60	15.67±8.79	60.4
12-zone	26.13±7.920	25.04±7.80	23.27±8.10	20.17±6.90	17.29±6.84	49.9
14-zone	41.60±13.60	38.50±13.09	36.47±14.27	31.17±13.00	25.78±12.38	58.6
CXR	3(2-4)	2(1.5-3)	2(1.5-2)	2(1-2)	1(1-2)	87.9

Improvement of Pulmonary Lesions after PS Treatment

After PS, the 14-zone LUS showed improvement, and the pulmonary sonogram is shown in Fig. 3. The order of improvement of pulmonary lesions are as follows: a decrease in or disappearance of subpleural consolidation, a decrease in B lines, and the gradual appearance of the A-line. The order of improvement of regions with lung lesions was the anterior chest, followed by the lateral chest, posterior chest, and lung base.

Ultrasonography Results of NRDS on Mechanical Ventilation

In this study, there were 67 NRDS with MV, 52 of whom were successfully weaned from the machine and 15 in whom weaning failed. The characteristics of these children are shown in Table 2. There was no statistically significant difference between the two groups in terms of gender, mode of delivery, gestational week, and birth weight (all $P \geq 0.05$).

Table 2. Basic data of children in the successful group and the failure group

		Successful group (n = 52)	Failure group (n = 15)	<i>H</i>	<i>P</i>
Render	Male	35	6	4.24	0.06
	Female	17	9		
Delivery mode	Eutocia	29	8	0.06	0.84
Caesarean	23	7			
Gestation weeks	31 (27, 36)	29 (27, 33)	2.09	0.16	
Weight(kg)	1560 (1000, 2550)	1350 (1150, 2450)	0.25	0.67	

The withdrawal of ventilator was stratified by LUS as shown in Table 3. The difference in lung scores with the 14-lead LUS between successful extubation group and failure group was statistically significant ($P < 0.05$). Pulmonary oedema (five cases), large posterior pulmonary consolidation (five cases), large

posterior lung consolidation (two cases), large lung atelectasis (two cases), and cardiac insufficiency (one case) were identified by ultrasonography in the failure group. After the second intubation and further treatment, these pulmonary lesions were alleviated, the heart function was improved, and then the patients were successfully weaned. Fig. 4 shows a child who was born at 29 weeks and 4 days and received ventilator treatment for 4 days. Ventilator extubation failed. He was re-intubated, and the scope of lung consolidation was reduced, and then successfully withdrawn.

Table 3. Comparison of LUS by the four methods in the ventilation withdrawal success and failure groups

Scoring method	Successful group	Failure group	W-value	P-value
6-zone	7.33 ± 1.75	9.70 ± 1.33	81.5	< 0.05
10-zone	15.41 ± 5.70	29.49 ± 1.89	21.5	< 0.05
12-zone	16.69 ± 4.90	26.90 ± 1.88	48.0	< 0.05
14-zone	23.86 ± 8.04	42.79 ± 1.80	33.5	< 0.05

Diagnostic Efficiency of Four LUS Systems for Determining Weaning Timing

ROC curves were used to evaluate the diagnostic performance of the four LUS systems for deciding weaning timing, as shown in Table 4. The 14-zone LUS method had the best diagnostic performance for the timing of extubation, with a sensitivity of 92.36%, a specificity of 93.80%, and an area under the curve of 0.955, at a cut-off of 41.0 points. The ROC curve is shown in Fig. 5.

Table 4. Diagnostic efficacy of the four LUS systems for deciding ventilator weaning timing

scoring method	score	AUC	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
6-zone	8.5	0.818	84.60	55.11	33.33	93.11
10-zone	27.5	0.900	84.60	71.44	44.00	94.60
12-zone	25.0	0.931	92.36	81.65	57.15	97.52
14-zone	41.0	0.955	92.36	93.80	80.00	97.88

Discussion

This study showed that the newly developed 14-zone LUS method was more consistent with CXR findings in the early dynamic observation of PS treatment efficacy. The six-zone lung method only includes the

anterior chest and lateral chest, and the B-line score was only divided into a non-fusion mode B and an intensive fusion mode B, without quantifying the range of pulmonary consolidation. Although the B-line score of the 10-zone method was classified into three grades, namely light, medium, and heavy, lung consolidation was not quantified, and the posterior lung was not observed. The B-line score of the 12-zone method was only divided into B1 and B2, and the lung consolidation was not quantified; the lung base was also not observed. In the early stages of PS, the disease gradually improved, the number of B lines in some regions decreased, or there was no fusion, B lines in some regions were still completely or partially fused, and the lung consolidation range gradually narrowed, but did not disappear.

The 14-zone LUS method included all areas of both lungs, and the B-line scores were divided into B1, B2, and B3, and the amount of lung consolidation was increased, including small subpleural lung consolidation (depth less than 1 cm) and large subpleural lung consolidation (depth greater than 1 cm). When B lines or lung consolidation were improved, the scores changed and allowed for better early dynamic observation of PS efficacy. In a previous study, we found that B-line score was positively correlated with pulmonary water volume and pathological severity of lung tissue, which could be used for semi-quantitative evaluation of pulmonary water [15]. Therefore, the B-line score is more detailed, which can better reflect the severity of lung lesions.

The nature and sequence of improvement of pulmonary lesions after PS are demonstrated a certain order. It was first observed that the range of lung consolidation decreased or disappeared, presumably because when PS entered the alveoli, the surface tension of the alveoli decreased rapidly, leading to rapid reversal of alveolar collapse. Pulmonary fluid clearance includes clearance of alveolar fluid and pulmonary interstitial fluid. Therefore, the disappearance of the B-line and the reappearance of the A-line are dependent on pulmonary fluid clearance. The study showed that the order of improvement in pulmonary regions was first the anterior chest, followed by the lateral chest, posterior chest, and lung base. As the child lies supine in the warm incubator, fluid easily accumulates in the posterior chest and lung base due to gravity and the ventilation volume in the posterior chest is relatively small. Therefore, the improvement of lesions in the posterior chest and lung base is relatively slow.

This study shows that the 14-zone LUS method is more effective for determining the timing of weaning. After PS and MV, most of the infants with NRDS could be weaned from the ventilator smoothly. However, one of the main reasons for the failure of weaning was pulmonary oedema, pulmonary consolidation, and atelectasis caused by co-infection. As children lie supine in the incubator, these lesions often occur in the posterior lung and lung base. On the other hand, the 6-zone, 10-zone and 12-zone LUS methods may omit the posterior lung or lung base, and lack more B-line scores, or quantitative scoring of lung consolidation, which may lead to underestimation of lung disease severity and cause an increase in the relative risk of ventilator failure. The newly proposed 14-zone method includes all areas of the lung, the B-line scores and lung consolidation scores are more detailed, allowing more sensitive identification of children at high risk of weaning failure and improve the success rate of weaning. The diagnostic threshold of the 14-zone LUS method was 41.0 points. Therefore, the 14-zone method can dynamically

and individually assess the nature and severity of pulmonary lesions, which is helpful to select the best withdrawal time.

There were some limitations in this study. Due to the small sample size, the results may be biased to some extent. The score for lung consolidation included only the depth and did not include the number of intercostal spaces involved. The LUS assigned depends on the experience of the operator, and the quantitative score can be affected by some subjective factors to a certain extent.

Conclusions

The new 14-zone LUS method can provide a comprehensive and objective assessment of lung disease characteristics. Not only can it be used for dynamic monitoring of the efficacy of PS replacement therapy but is also sensitive enough to identify the children at high risk of failed MV withdrawal. It can greatly reduce the cumulative radiation damage to newborns and medical staff, and can provide a safe, effective, intuitive, and accurate imaging approach for the diagnosis and management of NRDS. We recommend that it should be implemented in clinical practice.

Declarations

Ethics approval and consent to participate

This study was approved by the Quanzhou Women's and Children's Hospital Ethics Committee (Ethics review no. 7 of 2019) and informed consent was obtained from each child's guardian.

Consent for publication

Informed consent was obtained from all individual participants included in the study.

Availability of data and materials

The datasets used during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

SL, HR, and LY performed lung ultrasound examination and image acquisition. LX and CL contributed to clinical data of neonates. SL and LJ performed image modification. LG instructed and supervised this study. The manuscript was drafted by JQ and edited by SL. All authors have read and approved the manuscript.

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Figures

Figure 1

Schematic diagram of the ultrasonic grading method for the 14 lung zones Note: Figure A: front chest Figure B: side chest Figure C: back chest

Figure 2

Pulmonary sonogram after PS replacement therapy: Note: A, 0 h; Figure B, 12h; Figure C, 24h Figure D, 48h; Figure E, 72h

Figure 3

Extensive lung consolidation resulted in withdraw failure, lung consolidation was reduced by intubation and the machine was successfully withdrawn Note: Figure A: Extensive lung consolidation, Figure B: Small range of subpleural lung consolidation

Figure 4

Receiver operating characteristic curves of four LUS systems for predicting weaning timing