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Predictive value of lung ultrasound score in weaning from mechanical ventilation in neonatal respiratory distress syndrome



Mengwen Li¹, Maojun Li¹, Jie Feng², Feng Xiao¹ and Qian Yang^{1*}

Abstract

Background To explore the predictive value of lung ultrasound score (LUS) in weaning from mechanical ventilation in neonatal respiratory distress syndrome (RDS).

Methods A total of 111 neonates with RDS who received mechanical ventilation in the neonatal intensive care unit (NICU) of Sichuan Provincial People's Hospital were selected as the subjects. Before weaning, the LUS was performed by the 12-region ultrasound score of the lungs. Those neonates were divided into the weaning success group (n = 95) and weaning failure group (n = 16) according to whether they received mechanical ventilation again 48 h after weaning. Oxygenation index (OI) before weaning and arterial blood gas indexes after weaning were collected. The correlation of LUS with OI or arterial blood gas was analyzed, and the difference in LUS between the two groups was compared. The receiver operating characteristic (ROC) curve of LUS in predicting the weaning outcome of mechanical ventilation in neonatal RDS was drawn and its predictive value was verified.

Results LUS of all neonates before weaning was significantly correlated with OI and arterial blood gas indexes, which was positively correlated with OI value (r=0.671, p < 0.001) and arterial partial pressure of carbon dioxide (r=0.461, p < 0.001), and negatively correlated with arterial partial pressure of oxygen (r=-0.531, p < 0.001). The LUS in the weaning success group was significantly lower than that in the weaning failure group (5(3,8) points vs. 12.5(10,16.75) points, p < 0.001). The ROC curve showed that the AUC was 0.898. The optimal cut-off value of LUS was 9.5 as the predictive value of successful weaning, with a sensitivity of 0.875 and a specificity of 0.811.

Conclusion LUS is a convenient, sensitive, and accurate predictor of successful weaning of mechanical ventilation in NRDS, and can be used as an important tool for clinical guidance of weaning.

Keywords Newborn, Lung ultrasound score, Respiratory distress syndrome, Weaning, Mechanical ventilation

*Correspondence: Qian Yang

YangQian910kk@163.com

¹Department of Pediatrics, Sichuan Provincial People's Hospital, University

of Electronic Science and Technology of China, 32 West 2nd Section, 1st

Ring Road, Qingyang District, Chengdu 610000, China

²Department of Pediatrics, Longquanyi District of Chengdu Maternity and

Child Health Care Hospital, Chengdu 610100, China



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Introduction

With the development of perinatal medicine, the survival rate of premature infants is increasing. Neonatal respiratory distress syndrome (RDS) is one of the most common causes of neonatal respiratory failure and neonatal death, especially in premature infants [1]. It is reported that the incidence of neonatal RDS is about 57% in preterm infants with a gestational age of 30-31 weeks, about 80% in those with a gestational age of 28 weeks, and up to 92% in those with a gestational age of 24-25 weeks [2]. Neonatal RDS is due to pulmonary surfactant (PS) deficiency and immature lung development caused by neonatal ventilatory dysfunction, progressive exacerbation of inspiratory dyspnea, or respiratory failure [3]. Neonates with severe RDS need mechanical ventilation (MV) treatment to improve lung ventilation and ventilation function [4]. However, prolonged mechanical ventilation may cause hypocapnia, resulting in intracranial hemorrhage and white matter damage, which is related to the short-term and long-term poor prognosis of neonatal neurological development disorders and pulmonary complications [5]. When the neonatal condition is stable, the machine should be withdrawn as soon as possible to reduce the occurrence of complications. However, premature withdrawal increases the risk of extubation failure (EF) and may lead to repeated intubation, thereby increasing the incidence of airway injury and stenosis in neonates [6]. RDS usually occurs in premature infants because their lung structure and function are immature. Improper weaning may aggravate lung damage and even systemic organ damage, lead to adverse events, and increase hospitalization time and cost. Therefore, it is of great clinical significance to accurately predict the weaning outcome and select the best weaning time to improve the prognosis.

At present, the clinical manifestations, blood gas analysis, chest X-ray examination, and ventilator parameters of the neonates are used to comprehensively determine whether there are conditions for weaning. However, these methods are subjective, time-consuming, and invasive, and the relevant parameters are controversial in predicting the weaning outcome, which cannot accurately predict the respiratory prognosis [7]. It is urgent to further optimize the weaning evaluation criteria in combination with other indicators, improve the success rate of weaning, and provide guidance for clinical work.

Bedside ultrasonography can quickly diagnose and timely evaluate the patient's condition and guide the treatment with the characteristics of convenient, noninvasive, and repeatable. It is an important auxiliary tool in the diagnosis and treatment of patients in the intensive care unit (ICU) [8]. In recent years, lung ultrasound has been increasingly used in the diagnosis of neonatal respiratory diseases such as RDS, meconium aspiration syndrome, and pneumothorax [9]. Unlike chest X-rays, lung ultrasound can dynamically assess changes in lung ventilation [10]. Lung ultrasound score (LUS) is based on the detection of gas-liquid interface-related artifacts, which can quantify lung ultrasound signs. The classification and scoring of bilateral lung ultrasound by LUS can intuitively evaluate the lesions in each area of the lung, which is convenient for clinicians to operate and interpret bedside. Its application in neonatal respiratory diseases has gradually attracted attention. Studies have shown that LUS has practical value in guiding whether RDS neonates need mechanical ventilation or alveolar surfactant therapy [11]. However, there is still a lack of its application in the withdrawal of mechanical ventilation in neonatal RDS.

Therefore, we aimed to explore the predictive value of LUS in weaning from mechanical ventilation in neonatal RDS. Our results could be helpful in accurately predicting the high-risk neonates with weaning failure in the early stage, guide the evaluation and intervention of mechanical ventilation weaning, provide an important reference for clinicians to grasp the timing of weaning as accurately as possible, and improve the success rate of weaning in NRDS.

Subjects and methods Subjects

A total of 111 RDS neonates who were admitted to the neonatal intensive care unit (NICU) of the Sichuan Provincial People's Hospital within 2 h of birth from January 2022 to April 2023 were included. All neonates were treated with invasive mechanical ventilation. There were 56 males and 55 females. There were 82 cases of cesarean section and 29 cases of spontaneous delivery. The gestational age was 26-37 weeks, with an average of (31.1 ± 2.5) weeks. The birth weight was 0.69–3.60 kg, with an average of (1.78 ± 0.69) kg. This study was approved by the Ethical Committee of the Sichuan Provincial People's Hospital(Ethical approval Number: No. 243, 2023). The informed consent was obtained from the family members of all neonates. Inclusion criteria: (1) neonates with gestational age ≥ 26 weeks, regardless of gender; (2) singleton; (3) in line with the diagnostic criteria of NRDS [12]; (4) received invasive mechanical ventilation treatment ≥ 24 h; (5) the informed consent of the legal guardian of the newborn. Exclusion criteria: (1) neonatal congenital abnormalities, respiratory or chest malformations, congenital heart disease; (2) cardiac pulmonary edema, meconium aspiration syndrome, air leak syndrome, pulmonary hemorrhage or central respiratory failure; (3) combined chromosomal abnormalities; (4) serious infection.

Grouping

Those neonates were divided into the weaning success group (n = 95) and weaning failure group (n = 16) according to whether they received mechanical ventilation again 48 h after weaning. Weaning failure was defined as tracheal intubation or mechanical ventilation should be performed again within 48 h of weaning. The timing of weaning and getting on mechanical ventilation was determined by the attending physician of the neonates according to their actual clinical manifestations and the 2022 European NRDS prevention and treatment guidelines [13]. The attending physician of the neonates did not participate in this study.

Data collection

(1) General information: gender, gestational age, birth weight, mode of delivery, history of asphyxia, mother's history and maternal history; (2) main clinical observation indexes: vital signs of neonates, bedside chest X-ray examination before weaning, respiratory support mode and ventilator parameters (positive end-expiratory pressure, peak inspiratory pressure, mean airway pressure, inhaled oxygen concentration), oxygenation index (OI, $OI = FiO_2 \times mean airway pressure \times 100/PaO_2$), and arterial blood gas index.

Lung ultrasound

All neonates underwent lung ultrasound examination using Mindray7 bedside ultrasound diagnostic instrument (linear array probe 8–12 MHz) within 4 h before weaning. In a quiet state, the neonates were taken to supine, lateral, and prone positions. According to the parasternal line, anterior axillary line, posterior axillary line, posterior median line, and double nipple line, the lungs on both sides were divided into 6 regions. These 12 regions were scanned from top to bottom, from left to right, and from front to back, and the sonograms were saved. The main observation indexes included pleural line abnormalities, lung parenchyma, A-line, B-line, and diffuse pulmonary edema. To avoid the system error of the machine, the same preset instrument setting was adopted. To ensure a comprehensive assessment of lung function, video images of each lung region were recorded. All neonates were examined and scored by a professional clinician trained in bedside ultrasound. The lung ultrasound examination results were quality-controlled by two professional ultrasound doctors who were not aware of the diagnosis and clinical conditions of the neonates. The whole operation process was controlled within 10 min.

LUS

According to the 12-region ultrasound score of lungs described by Rouby et al. [14], each lung was divided

into six regions (anterior-superior-inferior, posteriorsuperior-inferior, lateral-superior-inferior), with a total of 12 regions in both lungs score. Each region scored 0 to 3 points, and the total score ranged from 0 to 36 points. The higher the score, the more severe the lung condition. The most severe ultrasound findings in each region were scored. Specific ultrasound scoring criteria: 0 was normal lung ventilation, only A-line, or a few B lines (less than 3); 1 was divided into moderate reduction of pulmonary ventilation, increased B-line, mutual fusion (fusion B-line < 50% of the intercostal space during cross-section scanning), pulmonary interstitial syndrome, localized pulmonary edema or subpleural consolidation; 2 was divided into severe reduction of pulmonary ventilation function, fusion B line to form a waterfall sign to occupy the entire intercostal space; 3 was divided into severe loss of pulmonary ventilation function, lung consolidation signs.

Statistical analysis

SPSS 27.0 statistical software was used for data analysis. The measurement data with normal distribution were expressed as means ± standard deviation (SD), and the difference between the two groups was compared by independent sample t-test. The measurement data that did not conform to the normal distribution were expressed as M (Q1, Q3), and the difference between the two groups was compared by Mann Whitney U test. The count data were expressed as numbers (%), and the difference between the two groups was compared by χ^2 test. Spearman correlation analysis was used to analyze the correlation of LUS with OI value before weaning or arterial blood gas analysis after weaning. The receiver operator characteristic (ROC) curve was used to evaluate the value of LUS in predicting the weaning success in NRDS. The optimal cut-off value of LUS was further defined according to the maximum Youden index, and the sensitivity and specificity were calculated. p < 0.05 was considered statistically significant.

Results

Comparison of basic clinical data between the two groups

In NICU, a total of 152 neonates were diagnosed with NRDS and treated with invasive mechanical ventilation within 2 h after birth. 17 cases of pulmonary diseases caused by non-PS deficiency such as pneumonia, pneumothorax, and pulmonary hemorrhage were excluded. 8 cases of complex malformations, congenital lung disease, and congenital heart disease were excluded. 14 cases of severe infection were excluded. Treatment was abandoned in 2 cases. Finally, 111 cases were included in this study. There were 95 cases in the weaning success group, with a successful rate of 85.59%. There were 16 cases in the weaning failure group, with a failure rate of 14.41%.

There were no significant differences in gender, gestational age, birth weight, and delivery mode between the two groups (p > 0.05). Compared with the weaning success group, the OI value (p < 0.01) and PCO₂ (p < 0.001) before weaning in the weaning failure group were significantly higher, and PO₂ (p < 0.001) was significantly lower. The LUS in the weaning success group was significantly lower than that in the weaning failure group (5(3,8) points vs. 12.5(10,16.75) points, p < 0.001). There was no lung consolidation in the weaning success group. The results are shown in Table 1.

Correlation of LUS with OI value and arterial blood gas index

Spearman correlation analysis showed that LUS of all neonates before weaning was positively correlated with OI value (r=0.671, p<0.001) and arterial partial pressure of carbon dioxide (r=0.461, p<0.001), and negatively correlated with arterial partial pressure of oxygen (r = -0.531, p<0.001, Fig. 1).

Value of LUS in predicting the successful weaning of mechanical ventilation

The area under the ROC curve (AUC) of LUS before weaning was 0.898 (95%CI: 0.952-1.000, p < 0.001), and the AUC of OI value was 0.749 (95%CI: 0.596–0.903, p < 0.001), which was statistically significant (p = 0.017). With an AUC of LUS of 9.5 as the optimal cut-off value, the sensitivity was 87.5% and the specificity was 81.1% (Fig. 2).

Discussion

NRDS is an important neonatal disease mainly in premature infants, and can also occur in neonates of cesarean section and neonates with diabetic mothers. The goal of its prevention and treatment is to improve the survival rate of neonates as much as possible while minimizing potential adverse reactions. As an important means of NRDS treatment, mechanical ventilation can rapidly improve lung ventilation function and relieve respiratory distress. However, inappropriate extension of mechanical ventilation time or premature weaning may cause adverse outcomes for neonates. Although it is a skill that every neonatal physician needs to master to comprehensively judge whether the newborn has weaning conditions through clinical manifestations, blood gas analysis, and chest X-ray examination, the clinical failure to accurately predict the respiratory prognosis of the neonates occurs from time to time. Bedside ultrasound is an important non-invasive auxiliary tool that NICU can pick up the first time, which has been increasingly applied to the diagnosis and treatment of neonatal diseases [15, 16]. The purpose of this study was to find a more economical and effective method to evaluate the weaning time of RDS neonates with mechanical ventilation by bedside lung ultrasound, to improve the success rate of weaning and reduce the occurrence of related complications.

The main lung ultrasound signs of RDS neonates include pulmonary consolidation with air bronchogram, abnormal pleural line and disappearance of A-line, and alveolar-interstitial syndrome (AIS) sign in non-consolidated area. It is worth noting that the nature and severity of different lung field lesions may be different even on the same side of the lung [17]. In this study, 4 neonates with weaning failure had pulmonary consolidation only in a certain area of the posterior lung, and 12 neonates with severe pulmonary ventilation reduction had neonatal lesions confined to the unilateral lung. Therefore, to facilitate a comprehensive and accurate assessment of lung status, in recent years, LUS has been introduced to quantify lung ultrasound signs. LUS is a semi-quantitative score of alveolar ventilation. The better the alveolar ventilation status, the lower the score. At present, there are many LUS methods, such as 6-region ultrasound score of lungs, 12-region ultrasound score of lungs, and prone position scoring method, all of which have their advantages and limitations [18]. In this study, we used the 12-region ultrasound score of lungs, which is commonly used in clinical practice. On the premise of proficiency and gentleness, the accurate evaluation of the various regions of the lung is carried out as comprehensively as possible. Each area was recorded with the most serious lung ultrasound signs, and the total score of 12 areas was analyzed. We found that the LUS in the weaning success group was significantly lower than that in the warning failure group. Of the 16 failed neonates, only 3 had no

 Table 1
 Comparison of basic clinical data between the two groups

Items	Weaning success group (n=95)	Weaning failure group ($n = 16$)	Z/χ²	р
Gender (male: female)	49:46	7:9	0.336	0.562
Gestational age (week)	31.1 ± 2.5	30.8±2.7	0.011	0.918
Birth weight (kg)	1.7(1.32,2.13)	1.75(1.125,1.875)	-0.551	0.582
Mode of delivery (cesarean section: natural childbirth)	71:24	11:5	0.039	0.844
LUS (points)	5(3,8)	12.5(10,16.75)	-5.096	< 0.001
OI	3(2.3,3.6)	4.45(3.05,6.85)	-3.185	< 0.01
PO ₂ (mmHg)	71(65,80)	59.5(55.25,64.75)	-4.218	< 0.001
PCO ₂ (mmHg)	38(31,44)	47.5(41.25,54.25)	-4.073	< 0.001



Fig. 1 Correlation of LUS with OI value and arterial blood gas index. (A) correction between LUS and OI; (B) correction between LUS and PO₂; (C) correction between LUS and PCO₂

lung consolidation. Interestingly, chest X-ray examination of all neonates before weaning showed no obvious abnormal manifestations such as pulmonary consolidation, which confirmed that lung ultrasound can find hidden lung changes that chest X-ray cannot show [19]. Further research found that the accuracy of weaning success was higher when the LUS before weaning was less than 9.5 as the prediction boundary value. In addition, this study also showed that the OI value before weaning was an effective predictor of weaning from mechanical ventilation in RDS neonates. The higher the OI value, the greater the possibility of weaning failure. However, the predictive value of the LUS was better than the OI value.

The OI value is an important indicator of the severity of respiratory diseases [20]. It takes into account the significant influence of the pressure value during respiratory support on the setting of oxygen concentration and arterial oxygen partial pressure in blood gas analysis. It has been reported that OI is an independent predictor of mortality in acute RDS [21]. In the 'Montreux criteria' of neonatal acute RDS, OI is used to assess the severity of oxygenation disorders and the severity of the disease, but OI cannot be used as a basis for whether RDS neonates need invasive ventilation and extubation [22]. In this study, we found that compared with the weaning success group, the OI value and PCO₂ before weaning in the weaning failure group were significantly increased, and the PO2 was significantly decreased. LUS was significantly correlated with the OI value, PO₂ and PCO₂, indicating that the LUS score can be used to describe the oxygenation state. The higher the LUS, the worse the oxygenation function. The lung oxygenation function is affected by multiple factors, such as ventilation-blood perfusion ratio, intrapulmonary shunt, inhaled oxygen



Fig. 2 ROC curve of LUS and OI in predicting weaning from mechanical ventilation

ratio, and lung ventilation status, and these factors are the key to determining whether the RDS neonates can withdraw successfully. It also explains from the side that LUS is a good tool to accurately and reliably predict the clinical weaning of mechanical ventilation. Based on this, LUS combined with OI value can be used to predict the weaning time of mechanical ventilation in further research.

This study also has certain limitations. Because LUS relies on the examiner's judgment and evaluation of the lung ultrasound morphology, there is a certain degree of subjectivity. Although all operations are performed skillfully by professional clinicians trained in bedside ultrasound, we still lack systematic and structured training courses and assessment systems. This needs to be further summarized and improved. In addition, LUS has some limitations because it does not include pleural sliding and the size of lung consolidation. Therefore, to more accurately reflect the actual lung status, it still needs to be explored. This study is a single-center study with a small

and limited sample size. Future studies are expected to include multi-center validation.

Conclusion

In conclusion, LUS can be used as an important indicator to predict the successful weaning of mechanical ventilation in RDS neonates. It is a reliable tool to guide weaning and provides an effective reference for us to explore a more reasonable and effective prediction scheme for mechanical ventilation weaning in NRDS.

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Author contributions

Conceptualization, Writing paper: MwL and FX. Supervision and modification: MjL and QY. Project administration: JF. All authors have read and agreed to the published version of the manuscript.

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Data availability

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

Declarations

Ethics approval and consent to participate

This study was approved by the Ethical Committee of the Sichuan Provincial People's Hospital (Ethical approval Number: No. 243, 2023). All methods were performed in accordance with the ethical standards as laid down in the Declaration of Helsinki and its later amendments or comparable ethical standards. Written informed consent was provided by a parent and/or legal guardian for all participants because they were under 16 years of age.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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