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Application of Lung Ultrasound in Evaluating the Response to Surfactant Therapy in Neonates with Acute Respiratory Distress Syndrome

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Abstract

Background: Neonatal acute respiratory distress syndrome (nARDS) is a common critical condition in the NICU, characterized by rapid progression, which increases the risk of severe respiratory failure and neonatal mortality. Early diagnosis and effective management are essential for better outcomes, yet challenges remain with timely diagnosis using the 2017 Montreux criteria. Lung ultrasound, providing radiation-free, real-time imaging, has become critical for diagnosing and assessing neonatal lung disease severity in nARDS cases. Pulmonary surfactant (PS) therapy, effective for neonatal respiratory distress syndrome (nRDS), also shows potential for nARDS treatment, though optimal timing and efficacy require further research.

Objective: This study aims to evaluate the role of lung ultrasound in the early diagnosis of neonatal ARDS and assess the response to PS therapy.

Methods: This prospective cohort study included 97 neonates (≥35 weeks' gestation) with respiratory distress admitted to the NICU of The First Affiliated Hospital of Guilin Medical University from January 2023 to June 2025, categorized based on the Montreux criteria into ARDS and non-ARDS groups, with an additional control group of 65 neonates without lung disease. nARDS cases were further divided by Oxygenation Index (OI) threshold:(4≤OI≤16 for mild/moderate nARDS; OI≥16 for severe nARDS). Lung ultrasound was performed at various intervals—24 hours post-diagnosis, pre-PS, and at 1, 6–12, and 24–48 hours post-PS, 3 days post-PS, and post-symptom resolution—to monitor A-lines, B-lines, pleural lines, pulmonary edema, consolidation, and alveolar-interstitial syndrome (AIS). The non-ARDS and control groups underwent lung ultrasound only at 24 hours, 3 days, and 7 days after birth or the onset of respiratory distress, with baseline data recorded. Statistical analysis utilized SPSS 25.0 software, employing χ^2 tests, Mann-Whitney U tests for skewed data, and Kruskal-Wallis H tests for group comparisons, with post-hoc Wilcoxon rank-sum tests. A p-value <0.05 indicated significance. **Results**: (1) ARDS neonates exhibited more pronounced lung ultrasound abnormalities (e.g., A-line loss, marked B-lines, pleural line distortion, pulmonary edema, consolidation with bronchograms, AIS) compared to non-ARDS and control groups, with severe nARDS cases showing more severe features. (2) The mild/moderate nARDS group demonstrated significant ultrasound and clinical improvement 6–12 hours post-PS ($p < 0.05$), whereas some severe ARDS neonates abnormalities persisted at both 6–12 and 24–48 hours post-PS.

Conclusion: Lung ultrasound effectively reflects nARDS-related pulmonary abnormalities in neonates, facilitating early diagnosis and monitoring for disease progression. It also serves as a valuable tool for evaluating PS therapy efficacy, supporting timely interventions to alleviate respiratory distress.

1. Introduction

Neonatal acute respiratory distress syndrome (nARDS) is a frequent and life-threatening critical condition encountered in the neonatal intensive care unit (NICU)[1, 17]. Unlike respiratory distress syndrome (RDS) primarily caused by surfactant deficiency in preterm infants, nARDS in late preterm and term neonates is characterized by heterogeneous lung pathology stemming from various direct or indirect insults. The clinical course of nARDS is often rapid and fulminant, leading to severe respiratory failure and a significant

risk of neonatal mortality. Consequently, early accurate diagnosis and timely, effective management are paramount for improving clinical outcomes and reducing the burden of this disease.

The diagnosis of nARDS has historically relied on clinical criteria, most notably the Montreux definition established in 2017[1]. While these standardized criteria—encompassing acute onset, oxygenation defects, and origin of edema—have improved diagnostic consistency, challenges remain in their timely application at the bedside. Traditional diagnostic modalities, such as chest radiography, are limited by radiation exposure, transportation risks, and relative insensitivity to early pathological changes[10, 15]. Furthermore, the reliance on oxygenation indices alone may delay the recognition of structural lung injury. In this context, Lung Ultrasound (LUS) has emerged as a revolutionary tool in neonatology[2, 4]. Offering the advantages of being radiation-free, non-invasive, bedside-accessible, and real-time, LUS allows for the dynamic visualization of lung aeration and pathology. It has proven highly sensitive in detecting pulmonary edema, atelectasis, and consolidation, making it invaluable for the early diagnosis and severity assessment of neonatal lung diseases.

Regarding management, Pulmonary Surfactant (PS) therapy remains the gold standard for treating neonatal RDS. Recent evidence suggests that PS therapy may also confer benefits in nARDS by improving lung compliance and oxygenation, even though the underlying pathophysiology differs from primary surfactant deficiency. However, the response to PS in nARDS is variable; while some neonates show rapid improvement, others exhibit persistent respiratory failure[7, 17]. Currently, the evaluation of therapeutic efficacy largely depends on clinical parameters and blood gas analysis, which provide physiological data but lack direct visualization of lung recruitment. There is a growing need to explore objective imaging markers that can not only facilitate the early identification of nARDS but also monitor the real-time morphological changes in the lung following surfactant administration.

Despite the established utility of LUS in diagnosing lung disease, data regarding its specific role in monitoring the dynamic response to PS therapy in nARDS—particularly across different severity stratifications—remain limited. Therefore, this prospective cohort study was designed to evaluate the diagnostic value of LUS in neonates with nARDS based on the Montreux criteria and to assess its efficacy in monitoring the response to PS therapy. We aimed to correlate specific ultrasound findings, such as the persistence of B-lines and consolidation, with clinical recovery in mild, moderate, and severe cases, thereby providing a basis for more precise clinical interventions.

2. Methods

2.1 Study design and setting

This prospective cohort study was conducted in the Neonatal Intensive Care Unit (NICU) of The First Affiliated Hospital of Guilin Medical University. The study period ranged from January 2023 to June 2025. The protocol was approved by the Institutional Ethics Committee of The First Affiliated Hospital of Guilin Medical University (Approval No.[2022XYSYJSLL-07]), and written informed consent was obtained from the

parents or legal guardians of all participating neonates. The study adhered to the principles of the Declaration of Helsinki.

2.2 Study participants

A total of 97 neonates (gestational age ≥ 35 weeks) admitted to the NICU with signs of respiratory distress were enrolled as the study cohort. Additionally, 65 neonates without lung disease, matched for gestational age and admitted during the same period, were recruited as a control group.

2.3 Diagnostic criteria and grouping

Participants were categorized based on the 2017 Montreux criteria for neonatal Acute Respiratory Distress Syndrome (nARDS). The study cohort was divided into two primary groups: the nARDS group and the non-ARDS group. Furthermore, the nARDS group was stratified according to disease severity using the Oxygenation Index (OI). Neonates with $4 \leq OI < 16$ were classified as having mild to moderate nARDS, while those with $OI \geq 16$ were classified as having severe nARDS.

2.4 Lung ultrasound protocol

The lung ultrasound (LUS) examination is conducted using a portable ultrasound system equipped with a high-frequency linear probe. The scans are performed by trained neonatologists, and the interpretation of the ultrasound images is reviewed by an experienced ultrasound specialist who is unaware of the clinical details to minimize bias[18].

2.4.1 The timing of the LUS examinations differed between the groups

1)nARDS group: Examinations were performed at the following time points: 24 hours post-diagnosis, immediately prior to Pulmonary Surfactant (PS) administration (pre-PS), and at 1 hour, 6–12 hours, 24–48 hours, and 3 days post-PS. A final scan was conducted post-symptom resolution.

2) Non-ARDS and control groups: LUS was performed at 24 hours, 3 days, and 7 days after birth or the onset of respiratory distress. Baseline data were recorded for all participants.

2.4.2 The LUS images were analyzed for specific pathological features including

1)Presence or absence of A-lines;

2)Presence and quantity of B-lines;

3)Integrity and characteristics of the pleural line;

4)Signs of pulmonary edema;

5)Presence of consolidation, particularly with air bronchograms;

6)Alveolar-interstitial syndrome (AIS).

2.5 Statistical analysis

All statistical analyses were performed using SPSS version 27.0 software. Continuous data are presented as medians (interquartile range) or means ± standard deviations as appropriate, while categorical data are expressed as frequencies and percentages. The normality of data distribution was assessed using the Shapiro-Wilk test. For comparisons between groups, the X^2 test was used for categorical variables. For continuous variables with skewed distributions, the Mann-Whitney U test was employed for comparisons between two groups, while the Kruskal-Wallis H test was used for comparisons among multiple groups. Post-hoc analysis was performed using the Wilcoxon rank-sum test with Bonferroni correction if necessary. A p-value < 0.05 was considered statistically significant.

3. Results

3.1 Demographics and baseline characteristics

A total of 162 neonates were enrolled in this study, comprising 97 in the respiratory distress cohort and 65 in the healthy control group. There were no significant differences in gestational age, birth weight, or sex ratio among the groups at baseline (Data shown in [Table 1]). Among the respiratory distress cohort, patients were stratified into ARDS and non-ARDS groups according to the Montreux criteria, with the ARDS group further subdivided by severity based on the Oxygenation Index (OI).

Table 1. Baseline Characteristics of the Study Population

Variables	Respiratory Distress Cohort (n = 97)	Healthy Control Group (n = 65)	p-value
Gestational age (weeks)	37.97 ± 1.84	37.73 ± 1.41	0.380
Birth weight (g)	2822.16 ± 533.05	2868.15 ± 558.03	0.598
Sex, n (%)			0.096
Male	66 (68.0%)	35 (53.8%)	
Female	31 (32.0%)	30 (46.2%)	
Mode of delivery, n (%)			0.516
Cesarean section	57 (58.8%)	34 (52.3%)	
Vaginal delivery	40 (41.2%)	31 (47.7%)	

3.2 Diagnostic performance of Lung Ultrasound in nARDS

Lung ultrasound examination revealed distinct pathological patterns across the study groups. Neonates in the control group predominantly presented with normal lung aeration, characterized by the presence of A-lines and continuous, smooth pleural lines[8,9]. In stark contrast, neonates with nARDS exhibited

significantly more pronounced LUS abnormalities compared to both the non-ARDS and control groups ($p<0.05$)[6].

Specifically, the nARDS cohort was characterized by a loss of A-lines and the appearance of marked B-lines, indicative of interstitial edema and alveolar-interstitial syndrome (AIS). Furthermore, we observed significant pleural line abnormality, pulmonary edema, and consolidation with air bronchograms. Notably, a severity dependent gradient was evident: severe nARDS cases presented with more extensive consolidation and denser B-line profiles compared to mild/moderate cases (See [Table 2]). Representative ultrasound images illustrating the progression severe nARDS features are shown in [Figure 1].

Table 2. Comparison of Lung Ultrasound Findings Across Groups [Cases (%)]

Group	Cases (n)	A-line loss	B-lines	Pulmonary Edema	Lung Consolidation	Pleural Line Abnormality	AIS
Study Group	97	85 (87.6%)	97 (100.0%)	73 (75.3%)	83 (85.6%)	76 (78.4%)	73 (75.2%)
- mild/moderate nARDS Subgroup	28	21 (75.0%)	28 (100.0%)	14 (50.0%)	26 (92.8%)	22 (78.5%)	25 (89.2%)
- severe nARDS Subgroup	15	15 (100.0%)	15 (100.0%)	13 (86.7%)	15 (100.0%)	15 (100.0%)	14 (93.3%)
- Non-nARDS Group	54	49 (90.7%)	54 (100.0%)	46 (85.2%)	42 (77.8%)	39 (72.2%)	34 (63.0%)
Control Group	65	0 (0%)	5 (7.6%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
X^2 -Value		122.82	142.02	99.24	117.20	99.81	96.73
P -Value		< 0.001	<0.001	< 0.001	<0.001	< 0.001	< 0.001

3.3 Dynamic evaluation of response to Pulmonary Surfactant therapy

Serial LUS examinations provided critical insights into the therapeutic efficacy of Pulmonary Surfactant (PS)[17]. The response trajectory varied significantly depending on the baseline severity of the nARDS.

In the mild to moderate nARDS group ($4 \leq OI < 16$), LUS monitoring demonstrated a rapid positive response to PS therapy. Significant improvement in both ultrasound features and clinical parameters was observed as early as 6–12 hours post-administration ($p<0.05$)[5,12]. This improvement was sonographically marked by the regression of diffuse B-lines, the restoration of A-lines, and the resolution of consolidation, indicating effective lung recruitment (See [Figure 2 and Figure 3]).

Conversely, in the severe nARDS group (OI ≥ 16), the response to PS was delayed and incomplete. Abnormalities on lung ultrasound, including persistent consolidation and pleural Line Abnormality, remained evident at both the 6–12 hour and 24–48 hour intervals post-PS. This persistence of pathological sonographic signs suggested ongoing alveolar collapse or injury despite surfactant administration, distinguishing this group from the more responsive mild/moderate cohort. The temporal trends of LUS scores for each group are detailed in [Figure 4]. (Using the 12-zone scoring method.)[3,11,16]

Therefore, for children diagnosed with nARDS, dynamic monitoring of lung ultrasound—by observing characteristic changes including the disappearance of A-lines, presence of significant B-lines, blurring or disappearance of pleural lines, pulmonary edema, lung consolidation with bronchial air signs, and alveolar-interstitial syndrome(AIS)—can better guide the timing of pulmonary surfactant administration. Particularly, the presence of pulmonary consolidation with bronchial air signs and alveolar-interstitial syndrome shows good sensitivity for identifying nARDS (See [Figure 5]).

4. Discussion

4.1 Interpretation of Findings

The present study demonstrates the significant role of lung ultrasound (LUS) in the diagnosis and assessment of neonatal acute respiratory distress syndrome (nARDS). Our findings indicate that dynamic monitoring of characteristic lung ultrasound changes—including A-line loss, prominent B-lines, pulmonary edema, lung consolidation with bronchial air signs, and alveolar-interstitial syndrome—provides valuable insights for guiding the timing of pulmonary surfactant (PS) administration[2, 5]. Notably, the identification of pulmonary consolidation with bronchial air signs and alveolar-interstitial syndrome exhibited high sensitivity for nARDS diagnosis (Fig. 5), consistent with previous research in this field.

4.2 Comparison with Existing Literature

Our results align with contemporary studies investigating the application of lung ultrasound in neonatal respiratory distress. As a non-invasive, bedside imaging modality, LUS offers real-time assessment of pulmonary pathology, providing crucial information for clinical decision-making. Compared to traditional chest radiography, lung ultrasound demonstrates superior sensitivity and specificity, particularly in the early detection of lung parenchymal abnormalities[10]. The trend analysis of LUS scores over time (Fig. 4) revealed that severe nARDS patients maintained higher scores compared to mild/moderate cases, supporting the utility of LUS in disease stratification.

4.3 Clinical Implications

The dynamic monitoring of lung ultrasound carries several important clinical implications: (1)Early nARDS identification: Detection of early changes such as A-line disappearance and increased B-lines enables timely recognition of disease progression; (2)Disease severity assessment: The temporal trend of LUS scores (Fig. 4) demonstrates that severe nARDS patients consistently show higher scores than mild/moderate cases, providing an objective basis for disease classification; (3)Treatment guidance: Lung

ultrasound characteristics serve as important reference indicators for PS administration timing, particularly when pulmonary consolidation with bronchial air signs is identified, suggesting the need for timely intervention.

4.4 Study Limitations

Several limitations should be acknowledged: (1)Sample size constraints: Although 162 neonates were included, the severe nARDS subgroup had relatively fewer cases; (2)Single-center design: Results may be influenced by the specific practices of our medical center; (3)Limited follow-up period: Long-term outcomes were not assessed; (4)Operator dependency: Lung ultrasound findings may be influenced by operator experience.

4.5 Future Research Directions

Future investigations should focus on several key areas to advance our understanding of lung ultrasound in neonatal acute respiratory distress syndrome. Firstly, researchers should expand the sample size, with particular emphasis on increasing the number of severe nARDS cases to provide more robust statistical power. Secondly, conducting multi-center studies would be essential to validate the generalizability of our findings across different clinical settings and populations. Thirdly, extending follow-up periods would allow for the evaluation of lung ultrasound's predictive value for long-term outcomes, which remains an important gap in current knowledge. Additionally, standardizing operational procedures is crucial to minimize inter-operator variability and ensure consistent, reliable results across different practitioners[18]. Finally, exploring the combined use of lung ultrasound with other biomarkers represents a promising direction to enhance diagnostic accuracy and provide a more comprehensive assessment of neonatal respiratory conditions[13, 14].

5. Conclusions

Lung ultrasound serves as a non-invasive, real-time assessment tool with significant value in the diagnosis, disease assessment, and treatment monitoring of nARDS. Through dynamic monitoring of characteristic lung ultrasound changes—particularly lung consolidation with bronchial air signs and alveolar-interstitial syndrome—clinicians can better guide the timing of PS administration and improve patient outcomes. Further high-quality research is needed to validate the clinical utility of lung ultrasound in neonatal respiratory diseases.

Declarations

Conflict of Interest Statement

1. **Author Contributions**: Author **Yuan Tan** conceived the study and designed the experiments. Author **Xiaojun Wei** and Author **Zenghong Huang, Shuchun Lü**, **XiangYü Liao** performed the experiments and collected the data. Author **Yuan Tan** and Author **Sifeng Yue** conducted the statistical analysis and created the figures. Author **Xiaojun Wei** and Author **Sifeng Yue** provided critical technical expertise. The initial manuscript was drafted by Author **Xiaojun Wei** and Author **Yuan Tan**. All authors (Xiaojun Wei, Yuan Tan,

Zenghong Huang, Shuchun Lü, Sifeng Yue, XiangYü Liao) critically reviewed, edited the manuscript, and approved the final version for submission.

2. Consent for publication: All authors of this manuscript have read and approved the final version to be submitted. We certify that this work is original, has not been published elsewhere, and is not under consideration for publication by any other journal. We give our consent for the manuscript to be published in [Journal Name] upon acceptance.

3. **Competing interests**：The authors declare that they have no competing interests.

4. **Availability of data and material:** The datasets generated and/or analyzed during the current study are not publicly available due to privacy restrictions and institutional policy but are available from the corresponding author on reasonable request.

5. **Ethics approval and consent to participate**: This study involves human participants or patient data. The study was approved by the Institutional Ethics Committee of The First Affiliated Hospital of Guilin Medical University (Approval No. [2022XYSYJSLL-07]); All the subjects included in the study have been informed and have signed the consent form.

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Figures

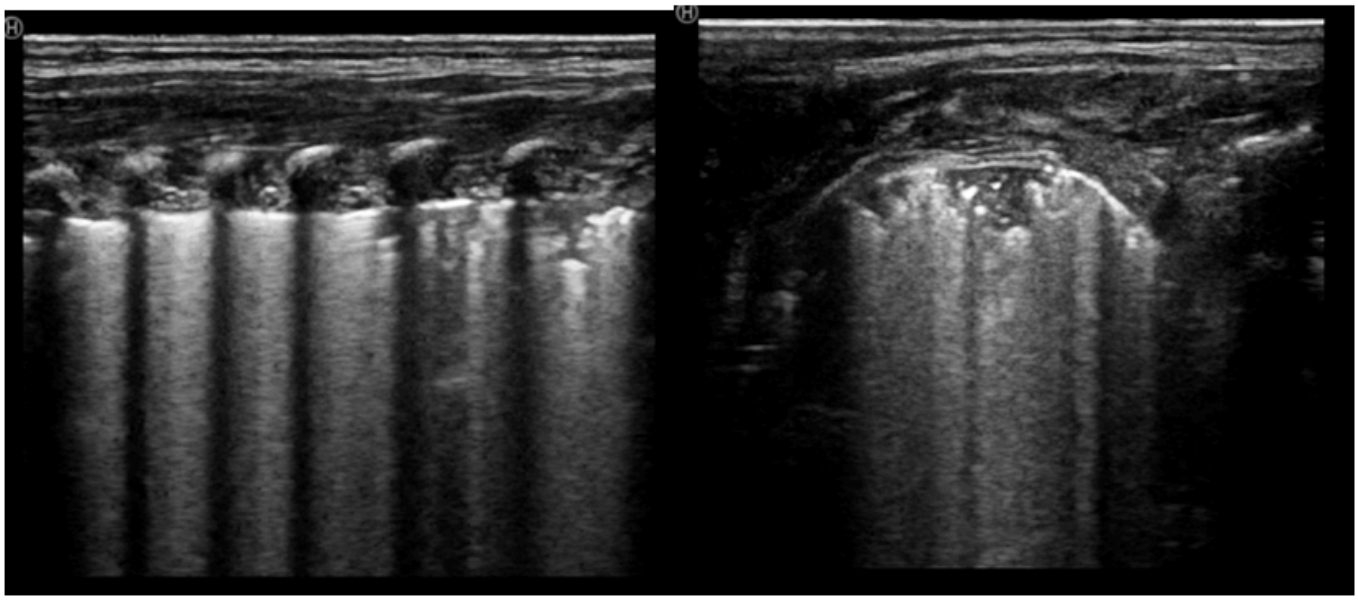


Figure 1

The figure illustrates the changes observed in lung ultrasound diagnosis for pediatric patients with severe nARDS, prior to the administration of PS.

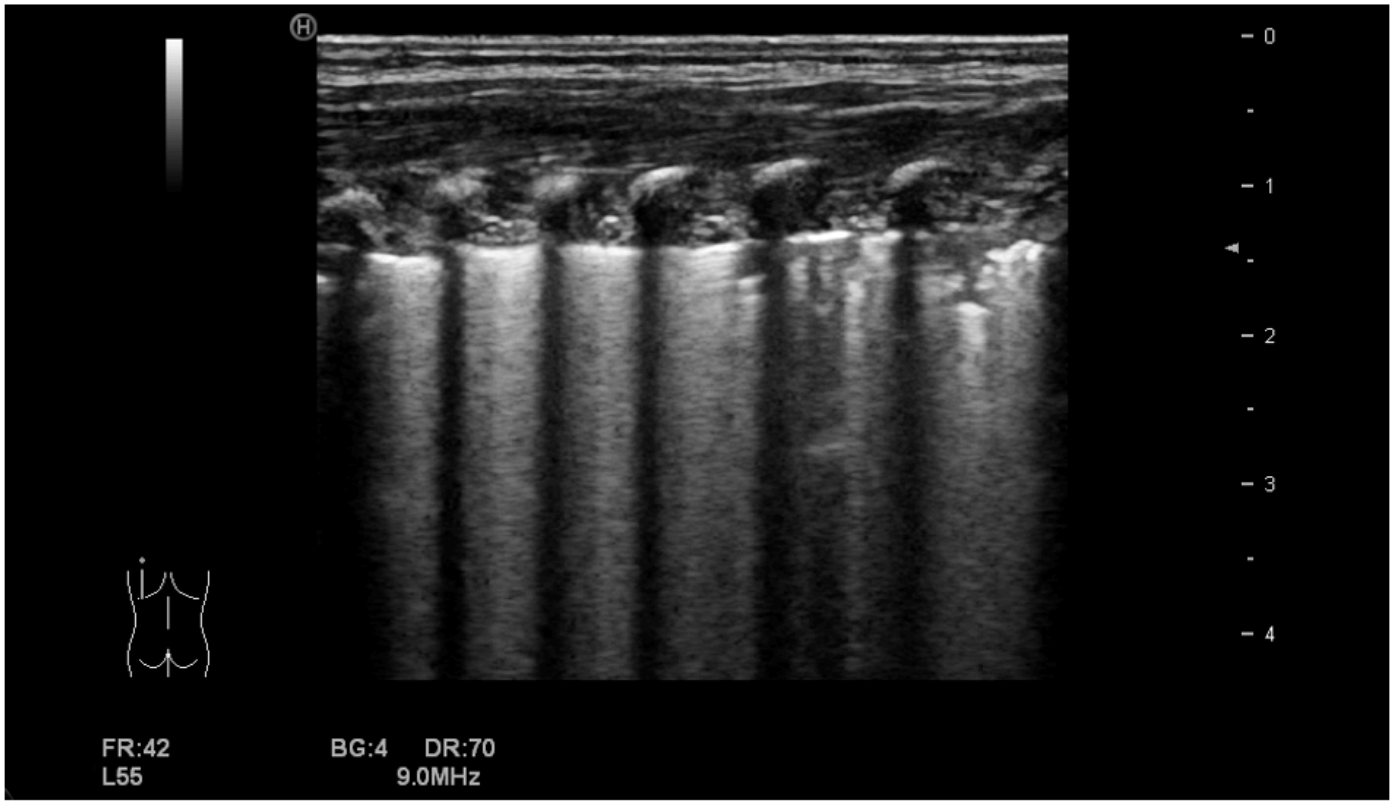


Figure 2

The figure illustrates the changes in lung ultrasound observed within 24 hours of diagnosis with nARDS, before the administration of PS.

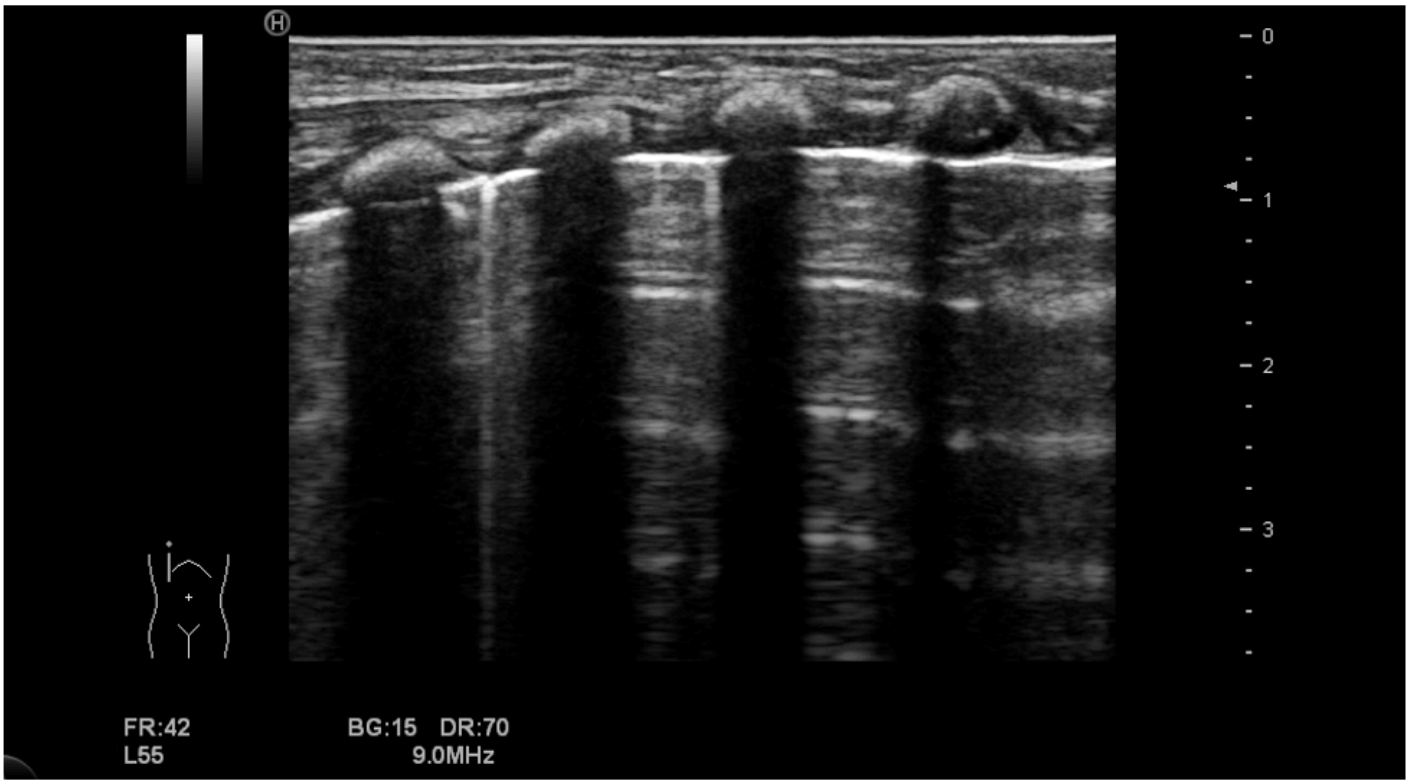


Figure 3

The figure illustrates the changes in lung ultrasound observed diagnosis in pediatric patients with nARDS, 1 hour after the administration of PS.

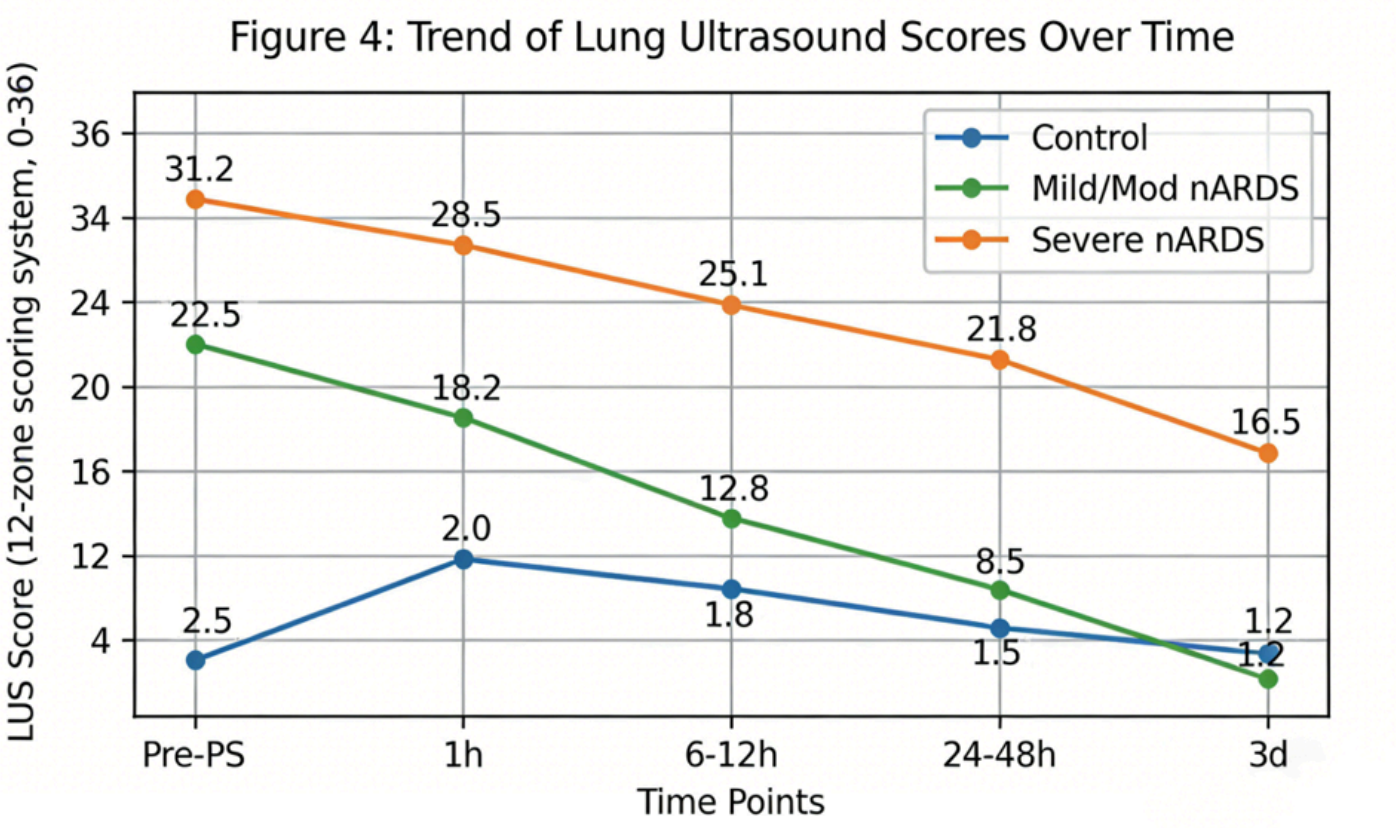


Figure 4

See image above for figure legend.

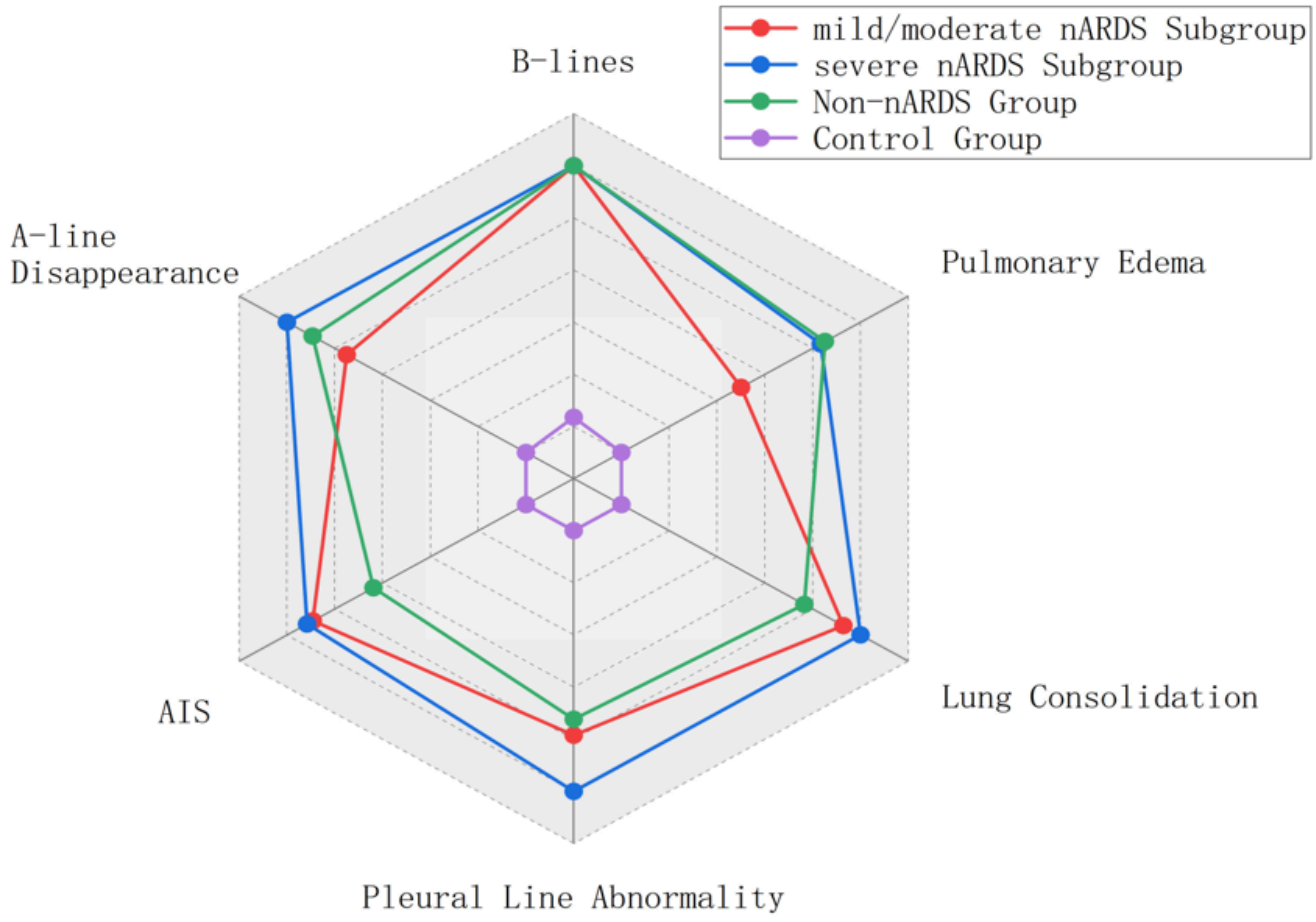


Figure 5

This radar chart presents the characteristic changes in lung ultrasound of different subgroups (including disappearance of the A line, significant thickening of the B line, pleural line abnormality, pulmonary edema, lungconsolidation with bronchial inflation sign, and alveolar-interstitial syndrome(AIS)).