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Advances in the Application of Lung Ultrasound in the Diagnosis of Neonatal Respiratory Distress Syndrome

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Abstract

Neonatal respiratory distress syndrome (NRDS) is a prevalent and critical condition in the neonatal period, where early and accurate diagnosis is crucial for timely intervention and improved prognosis. In recent years, lung ultrasound (LUS) has emerged as a non-invasive, portable, repeatable, and radiation-free imaging modality, demonstrating significant advantages in the diagnosis and assessment of NRDS. LUS enables bedside, real-time monitoring of pulmonary lesion changes. By identifying characteristic sonographic findings—including absence of lung sliding, disappearance of A-lines, increased B-lines, and irregular pleural lines, LUS facilitates visual assessment of pulmonary ventilation disorders. Studies have shown that LUS offers high sensitivity and specificity in diagnosing NRDS, with diagnostic accuracy comparable to or exceeding that of chest X-ray. Additionally, LUS effectively evaluates disease severity, informs clinical decision-making, and assists in prognosis prediction. This review summarizes recent advances in the application of lung ultrasound for the diagnosis of neonatal respiratory distress syndrome.

Keywords

Neonatal Respiratory Distress Syndrome, Lung Ultrasound, Diagnosis, Application Progress

1. Introduction

Neonatal Respiratory Distress Syndrome (NRDS), also known as neonatal hyaline membrane disease, is among the most common critical conditions during the neonatal period. Studies indicate that the global incidence of NRDS in preterm in-

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fants reaches 50% - 80%, particularly in those with a gestational age of less than 32 weeks [1]. NRDS primarily results from immature pulmonary development and inadequate synthesis and secretion of pulmonary surfactant in newborns, causing progressive alveolar collapse, reduced lung compliance, impaired gas exchange, and consequently severe respiratory failure, along with a spectrum of long-term complications that place a heavy burden on both families and society [2]. Accordingly, early and accurate diagnosis of NRDS is essential for timely initiation of effective treatment measures and improving the prognosis of affected infants. Conventional diagnostic approaches mainly include clinical assessment, blood gas analysis, and chest X-ray examination; however, these techniques have certain limitations. For instance, traditional chest X-rays carry risks of ionizing radiation and patient transportation, particularly exhibiting inherent limitations in their applicability to sensitive populations, critically ill patients, and special scenarios. In recent years, lung ultrasound (LUS) has emerged as a safer and more efficient modality for evaluating neonatal lung conditions, owing to its lack of radiation, high portability, and real-time imaging capabilities [3]. This has driven its evolution from an adjunctive tool to a preferred diagnostic method. LUS enables real-time visualization of structural and functional changes in neonatal lungs, enhancing diagnostic reproducibility while minimizing subjectivity [4]. Furthermore, LUS holds potential value in guiding treatment decisions and assessing long-term prognosis [5], such as determining the optimal timing for exogenous surfactant administration and predicting failure of non-invasive respiratory support in neonates. As a rapid and non-invasive bedside diagnostic tool, LUS offers substantial advantages in clinical practice; however, its limitations must not be overlooked. For example, it is highly dependent on the operator's skill level, with diagnostic accuracy directly influenced by the clinician's experience, technical proficiency, and anatomical knowledge. Additionally, LUS may struggle to clearly differentiate over-ventilated regions from normally ventilated areas, potentially leading to overestimation of lung re-expansion effects. This review summarizes recent advances in the use of lung ultrasound for diagnosing neonatal respiratory distress syndrome, aiming to provide a reference for clinical practice and future research.

2. Pulmonary Ultrasound Features of Neonatal Respiratory Distress Syndrome

2.1. Typical Imaging Features of Lung Ultrasound in NRDS

In the pulmonary ultrasound examination of NRDS, various characteristic ultrasound signs possess significant diagnostic value. These signs are closely associated with the pathophysiological changes of NRDS. Accurate interpretation of these ultrasound features can offer critical information for both the diagnosis and assessment of disease severity in NRDS.

The typical lung ultrasound features of NRDS primarily include the following: First, there is attenuation or disappearance of the lung sliding sign. In healthy lungs, pleural sliding is visualized on ultrasound during respiration, whereas in NRDS infants, increased pulmonary surface tension and alveolar collapse lead to a significant reduction or absence of the lung sliding sign [6]. Second, there is a decrease or loss of A-lines. A-lines, which are horizontal artifacts formed by pleural reflection in normal lung tissue, become less apparent in NRDS due to alveolar collapse and resulting changes in the air-fluid interface. Third, there is a marked increase and fusion of B-lines. B-lines, observed as vertical artifacts originating from the pleura, are considerably increased in NRDS as a result of pulmonary interstitial edema, and their density is positively correlated with disease severity. More distinctively, the "white lung sign" is present, characterized by densely confluent B-lines that render the entire lung field as a highly echogenic region, resembling a solid organ. Additionally, pleural line thickening, irregularity, and lung consolidation are common ultrasound manifestations in NRDS. Multicenter studies have indicated [7] that approximately 87.5% of infants with NRDS display a significant increase in B-lines, and 93.2% exhibit various degrees of the "white lung sign." These characteristic findings contribute to the sensitivity and specificity of lung ultrasound for NRDS diagnosis, which reach 96.2% and 88.7%, respectively.

It is noteworthy that lung ultrasound can also be used to grade NRDS based on sonographic image characteristics. Mild NRDS is indicated by a localized increase in B-lines, moderate NRDS by a widespread increase in B-lines with partial fusion, and severe NRDS by extensive "white lung sign" accompanied by areas of lung consolidation [8]. This grading correlates well with clinical severity and blood gas analysis results, thus providing important references for the development of clinical treatment strategies [9]. Ultrasound examination further enables dynamic monitoring of treatment efficacy; research demonstrates that, within 24 - 48 hours after effective therapy, approximately 65% of affected neonates exhibit a clear reduction in B-line numbers and gradual restoration of lung sliding sign [10]. Recent data from the field of neonatal intensive care show [11] that lung ultrasound-guided therapeutic intervention can reduce the mean duration of mechanical ventilation by 1.8 days and shorten hospital stay by 2.3 days for infants with NRDS, highlighting the significant clinical value of lung ultrasound in NRDS management.

2.2. Dynamic Ultrasound Feature Changes of NRDS at Different Stages

The progression of LUS findings in neonatal NRDS exhibits considerable variability. With clinical improvement, observable features include reduction in the extent of lung consolidation, fewer bronchial air signs, alleviated pulmonary edema, normalization of the pleural line, and reappearance of A-lines. In addition, due to the lack of pulmonary surfactant, the alveolar surface tension increases, leading to alveolar collapse, alveolar structural destruction, interstitial lesions or abnormal distribution of fine particulate matter (liquid/gas/calcification). Therefore, under ultrasound, subpleural consolidation areas with diffuse fine granular echoes (snowflake sign) and combined bronchial inflation signs can be seen. Additionally, lung ultrasound is a valuable tool for detecting NRDS-related complications, such as atelectasis, consolidation, and microabscesses. In recent years, novel lung ultrasound markers—including the ground-glass sign and snowflake sign, have been introduced for NRDS diagnosis. Ground-glass opacities commonly appear in the early stages of NRDS and may be mistaken for dense B-lines. The snowflake sign, characterized by spotted, patchy, or fine linear bronchial air signs within consolidated regions, is indicative of a more advanced stage of NRDS. The snowflake pattern is considered highly specific for NRDS and serves as a significant diagnostic indicator in ultrasound imaging [12].

Based on the stages of disease progression, the ultrasound features of NRDS can be categorized into three primary phases: early, progressive, and recovery stages. In the early stage (0 - 6 hours postnatally), lung ultrasound typically shows a gradual disappearance of A-lines and the initial appearance of B-lines with low density, primarily as single or few B-lines. The pleural line may appear slightly irregular at this time, but the lung sliding sign is largely preserved. The progressive stage (6 - 48 hours after birth) represents the period with the most pronounced sonographic changes in NRDS, characterized by dense (coalescent) B-lines throughout the entire lung field, resulting in a "white lung" appearance. The pleural line becomes markedly irregular and thickened, while the lung sliding sign is significantly reduced or absent. In some infants, areas of lung consolidation with "hepatization" may be observed, and small punctate hyperechoic foci can appear at the lung-pleura interface. Notably, ultrasound findings vary according to disease severity; severe cases present with a more extensive distribution of "white lung" and more prominent areas of consolidation.

In the recovery phase—typically after 48 hours of treatment, the therapeutic effects become evident and lung ultrasound findings gradually improve: confluent B-lines decrease and separate into discrete B-lines, A-lines begin to reappear, the pleural line progressively returns to a regular pattern, lung sliding is gradually restored, and areas of consolidation diminish and eventually resolve. Notably, clinical studies indicate that changes observed on lung ultrasound often precede the improvement of clinical symptoms, establishing ultrasound as a sensitive indicator for assessing treatment efficacy. A recent study demonstrated [13] that ultrasound improvement occurred on average 12.6 hours (95% CI: 9.8 - 15.4 hours) earlier than clinical symptom improvement, providing valuable guidance for clinical decision-making. Furthermore, the rate of change in ultrasound findings varies among different treatment modalities, such as lung surfactant therapy and mechanical ventilation, offering new perspectives for the development of individualized treatment strategies.

3. Analysis of Lung Ultrasound Scores in Neonatal Respiratory Distress Syndrome

3.1. Establishment and Standardization of Lung Ultrasound Scoring System

To enable objective, quantitative, and dynamic evaluation of neonatal respiratory distress syndrome (NRDS) severity, several research teams have recently developed a variety of lung ultrasound (LUS)-based scoring systems utilizing characteristic LUS findings. These systems convert ultrasound image features into quantifiable values, thereby enhancing diagnostic reproducibility and providing a visual foundation for clinical decision-making. Currently, commonly used scoring systems include the Lung Ultrasound Severity Score (LUS-S), Neonatal Respiratory Distress Ultrasound Score (NRDUSS), and the e-POCUS score. All three methods are based on ultrasound and address the limitations of traditional imaging modalities (such as X-ray and CT) through quantitative scoring, thereby advancing the application of LUS in neonatal respiratory distress syndrome. Typically, these systems partition the lungs into multiple regions (e.g., the six-region method: anterior superior, anterior inferior, lateral superior, lateral inferior, posterior superior, and posterior inferior), with severity of specific ultrasound features assessed and assigned a numerical score in each region. The scores are then summed to generate a total score reflecting the extent of lung involvement. Brat *et al.* [14] introduced the LUS-S scoring system, which divides each lung into three regions, for a total of six. Each region is scored from 0 to 3 based on B-line density, pleural line abnormalities, lung consolidation, and the presence or absence of A-lines (0: normal; 1: a few B-lines; 2: multiple B-lines or reduced "lung sliding"; 3: lung consolidation or "white lung"), yielding a total possible score of 0 to 18. In a study of 120 preterm infants, the LUS-S score demonstrated a significant negative correlation with chest X-ray scores and blood gas parameters (such as PaO_2/FiO_2) ($r = -0.78$, $P < 0.01$), indicating strong validity and clinical relevance. The NRDUSS system, developed by Liu *et al.* [15], places greater emphasis on NRDS-specific features, including pleural line abnormalities (0 - 2 points), absence of A-lines (0 - 2 points), bilateral "white lung" (0 - 3 points), and lung consolidation (0 - 3 points), for a total score of 10 points. Studies report that when NRDUSS ≥ 7, both the sensitivity and specificity for diagnosing NRDS reach 100%, with an AUC (area under the Receiver Operating Characteristic curve) of 0.99, significantly outperforming traditional clinical scores. Owing to its simplicity, efficiency, and high specificity, NRDUSS has been widely adopted in multiple neonatal intensive care units (NICUs). Additionally, research by Srinivasan *et al.* [16] further confirmed that the presence of "lung consolidation with air or fluid bronchograms, bilateral lung whitening, and the absence of normal lung tissue regions (no spared areas)" on ultrasound images yields both sensitivity and specificity of 100% for NRDS diagnosis, indicating that this combination of features possesses extremely high diagnostic value. This finding provides critical evidence supporting the development of highly specific scoring systems.

3.2. Study on the Correlation between Lung Ultrasound Score and Disease Severity

In clinical practice, lung ultrasound scoring systems have demonstrated significant clinical utility. In a prospective cohort study involving 50 preterm infants with suspected NRDS, the LUS-S scoring system was utilized for assessment and compared against clinical symptoms, blood gas analyses, and chest X-ray findings. Results indicated a strong positive correlation between the LUS-S score and clinical severity grading (such as the Silverman score) ($r = 0.82$, $P < 0.001$). Furthermore, a LUS-S score of ≥12 exhibited a positive predictive value of 94.7% for the need for exogenous pulmonary surfactant replacement therapy [17]. Importantly, dynamic monitoring of LUS scores can effectively inform the adjustment of mechanical ventilation strategies. For instance, when the LUS score continues to decrease, A-lines reappear, and B-lines are reduced, it is safe to gradually decrease positive end-expiratory pressure (PEEP) and fraction of inspired oxygen (FiO_2), thereby lowering the risk of ventilator-associated lung injury.

Additionally, the lung ultrasound scoring system can be utilized to evaluate treatment response and prognosis. Raimondi *et al.* [18] reported that among infants whose LUS score decreased by ≥3 points within two hours after PS therapy, the failure rate of non-invasive ventilation was significantly lower compared to those with a score decrease of <3 points (12% vs. 45%, $P = 0.01$). This finding indicates that the LUS score may serve as an early biomarker for predicting treatment response. Thus, the lung ultrasound scoring system not only enables accurate identification of NRDS, but also quantifies disease severity, guides individualized therapy, predicts treatment response, and assesses prognosis, providing an important complement to conventional imaging and clinical evaluations. With the incorporation of artificial intelligence-based image recognition technologies, lung ultrasound scoring is expected to achieve greater automation and standardization in the future, thereby further enhancing its application prospects in neonatal intensive care.

4. Application of Bedside Point-of-Care Lung Ultrasound in Neonatal Respiratory Distress Syndrome

4.1. Operational Standards and Key Techniques of Bedside Point-of-Care Ultrasound

With regard to operational standards, a high-frequency linear array probe (10 - 15 MHz) should be selected to provide superior resolution for evaluating superficial lung tissues. Prior to the examination, the probe must be disinfected and a sterile coupling agent applied. During the scan, it is essential to maintain the neonate's body temperature and adopt an appropriate position, typically supine or slightly lateral. According to the International Lung Ultrasound Consensus (2020) [19], the standard scanning regions encompass the anterior chest wall (within the anterior axillary line), lateral chest wall (between the anterior and posterior axillary lines), and posterior chest wall (outside the posterior axillary line) on each lung, with each side subdivided into upper, middle, and lower zones, yielding a total of 12 regions. For each region, dynamic images of at least 3 seconds should be acquired, capturing dynamic features such as lung sliding and B-lines. The entire examination should be completed within 5 - 10 minutes to minimize unnecessary disturbance to critically ill neonates. Notably, recent research indicates [20] that for infants with NRDS, concentrating on six regions (anterior and lateral chest walls) achieves high diagnostic efficacy, enabling a streamlined scanning protocol. Examination outcomes should undergo semi-quantitative assessment using a standardized scoring system (e.g., modified lung ultrasound score), and a standardized reporting template should be established to ensure result comparability and consistency.

From a technical standpoint, it is essential to master the correct orientation of probe placement: during intercostal scanning, the probe indicator should be positioned perpendicular to the rib direction to achieve an optimal intercostal acoustic window, while for longitudinal scanning, the probe indicator should be aligned parallel to the body's long axis. Image acquisition should concurrently display two adjacent ribs and the intervening pleural line; this so-called "bat sign" serves as a reference point for image interpretation. Scanning depth is generally set at 3 - 4 cm, with the focal point located at the pleural line. Differentiation between B-lines and artifacts requires appropriate adjustment of gain and frequency, as well as observation of the dynamic changes of B-lines with respiration. In diagnosing NRDS, particular attention should be given to the extent and distribution of lung consolidation, as well as the thickness and regularity of the pleural line. To minimize subjective bias, the use of dual independent assessment or AI-assisted analysis systems is recommended; recent studies indicate that [21] this can increase diagnostic consistency by 18.5%.

4.2. The Role of Real-Time Ultrasound in the Early Diagnosis of NRDS

Bedside point-of-care lung ultrasound offers distinct advantages for the early diagnosis of neonatal respiratory distress syndrome (NRDS). Conventional diagnostic approaches, such as chest X-ray, necessitate transferring infants to the radiology department, thereby increasing their exposure to ionizing radiation and prolonging the time to diagnosis. In contrast, bedside point-of-care lung ultrasound is both non-invasive and free from radiation, allowing the examination to be completed directly within the NICU in an average of 3 - 5 minutes, which is significantly faster than chest X-ray (which has an average delay of 30 - 60 minutes) [22]. Studies have shown [23] that point-of-care lung ultrasound achieves a sensitivity of 93.7%, specificity of 92.5%, positive predictive value of 94.2%, and negative predictive value of 91.8% for the early diagnosis of NRDS, rates that are comparable to or exceed those of chest X-ray.

The early diagnostic value of bedside real-time lung ultrasound for NRDS is further evidenced by its capacity to detect specific sonographic alterations. According to data from a multicenter study by Sartorius *et al.* [24], the characteristic ultrasound findings in neonates with NRDS include reduced or absent lung sliding (95.7%), irregular pleural lines (92.3%), disappearance of A-lines (98.1%), densely coalescent B-lines resulting in a "white lung" appearance (96.8%), and regions of lung consolidation (76.4%). Several studies have confirmed [25] that the "bilateral white lung" sign is strongly associated with surfactant deficiency, facilitating differential diagnosis from other respiratory disorders. Furthermore, point-of-care ultrasound allows for semi-quantitative assessment using a lung ultrasound scoring system, which divides each lung into three regions and assigns a score of 0 - 3 based on the number and distribution of B-lines, for a total range of 0 - 18 points. A total score of ≥10 demonstrates a diagnostic sensitivity of 94.1% for NRDS, and higher scores correlate positively with disease severity. In clinical practice, this immediate assessment enables clinicians to quickly identify high-risk infants, guide timely interventions, and thereby improve patient outcomes.

4.3. Personalized Treatment Strategies under Real-Time Ultrasound Guidance

Lung ultrasound serves not only as a critical tool in the diagnosis of neonatal respiratory distress syndrome (RDS), but also empowers clinicians to devise individualized treatment plans. Bedside real-time lung ultrasound enables continuous assessment of disease progression, thereby facilitating greater precision and personalization in therapeutic strategies. Research presented in the 2022 European Consensus Guidelines [26] on the Management of Respiratory Distress Syndrome confirms that neonates with RDS treated using ultrasound-guided personalized regimens experienced an 18.7% reduction in overall mortality compared to traditional approaches, along with an average shortening of 2.3 days in mechanical ventilation duration and a 3.5-day decrease in hospital stay. Real-time ultrasound can guide multiple aspects of clinical decision-making. Real-time ultrasound supports a wide range of clinical decision-making. Firstly, in surfactant replacement therapy, ultrasound allows for the evaluation of ventilation status across different pulmonary regions, identification of areas requiring selective administration, and optimization of both dosage and frequency. Evidence suggests [27] that selective administration protocols adjusted according to ultrasound scores reduce drug consumption by 26.4% compared to conventional dosing regimens, while also decreasing the incidence of adverse reactions. Secondly, in respiratory support, ultrasound enables dynamic monitoring of lung recruitment efficacy and detection of potential complications, permitting timely adjustment of ventilator settings (such as PEEP and tidal volume) to avoid lung injury. A study conducted in neonatal intensive care units demonstrated [28] that precision ventilator parameter adjustments under ultrasound guidance reduced the incidence of atelectasis by 31.2% and decreased complications such as pneumothorax by 22.8%. Additionally, ultrasound assists in fluid management, correction of electrolyte imbalances, and assessment of cardiopulmonary function, thereby achieving comprehensive care for infants with RDS. Ultrasound-guided precision fluid resuscitation protocols led to a 15.6% reduction in pulmonary edema incidence and improved cardiac output. The implementation of individualized treatment strategies necessitates standardized ultrasound assessment workflows and treatment response scoring systems. Regular bedside ultrasound monitoring (recommended every 4 - 6 hours for critically ill infants) and multidisciplinary team discussions enable dynamic adjustment of therapeutic regimens according to the disease stage. Recent research is exploring the integration of artificial intelligence with bedside ultrasound, leveraging intelligent image recognition and data analytics to deliver increasingly precise treatment recommendations, thereby further enhancing the accuracy and convenience of personalized care.

5. Outlook

A review of current literature demonstrates that lung ultrasound has proven to be an effective tool for diagnosing neonatal respiratory distress syndrome (NRDS), offering a non-invasive, portable, and radiation-free alternative for clinical practice. Multiple studies have indicated that the sensitivity and specificity of lung ultrasound in NRDS diagnosis exceed 90%, showing diagnostic performance comparable to, or even surpassing, that of conventional chest X-rays. Through identification of characteristic sonographic features—such as the disappearance of lung sliding, absence of A-lines, increased dense B-lines, and irregular pleural lines, lung ultrasound allows for accurate differentiation between NRDS and other neonatal pulmonary diseases. Furthermore, the development of ultrasound scoring systems has provided a reliable means for evaluating disease severity, monitoring therapeutic efficacy, and predicting prognosis. Despite limitations related to operator dependency and insufficient visualization of deep lesions, the clinical value of lung ultrasound remains significant. With advancements in technology and accumulation of clinical experience, in the future, the combination of AI and ultrasound will be valuable in lowering operational barriers, improving diagnostic consistency, promoting resource transfer, and further helping clinicians make medical decisions during diagnosis and treatment through image optimization, intelligent diagnosis, equipment innovation, and remote collaboration.

Future efforts should focus on establishing standardized diagnostic criteria, conducting large-scale multicenter studies, and exploring integration with other imaging modalities to further enhance the accuracy and effectiveness of NRDS diagnosis, ultimately improving outcomes for affected infants.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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