Research article

Diagnostic value of lung ultrasound in evaluating the severity of neonatal respiratory distress syndrome

Houqing Pang[a,1], Bo Zhang[a,1], Jing Shi[b], Jing Zang[b], Li Qiu[c,*]

[a] Department of Ultrasound, West China Second Hospital of Sichuan University, Chengdu 610041, Sichuan Province, China
[b] Department of Neonatology, West China Second Hospital of Sichuan University, Chengdu 610041, Sichuan Province, China
[c] Department of Ultrasound, West China Hospital of Sichuan University, No. 37 Guo Xue Xiang, Chengdu 610041, Sichuan Province, China

ABSTRACT

Background: It is still unclear whether lung ultrasound (LUS) can be used to evaluate the severity of neonatal respiratory distress syndrome (NRDS).
Objective: To evaluate the role of LUS in assessing NRDS.
Methods: From January 2017 to January 2018, newborns with suspected NRDS were enrolled. The LUS score and lung consolidation areas were determined. The receiver operative curve (ROC) was used to analyze the LUS score and lung consolidation to predict NRDS severity.
Results: Neonates with NRDS had higher LUS scores than those with non-NRDS (23.6 ± 3.6 vs. 16.2 ± 1.8, $P < 0.05$). Among neonates with NRDS, the LUS scores increased with NRDS severity (18.0 ± 2.7 vs. 24.0 ± 1.7 vs. 27.0 ± 1.7, all $P < 0.05$). There were almost no consolidation areas in non-NRDS, while 1.9 ± 1.7 consolidation areas were observed in the NRDS group ($P < 0.05$). The number of consolidation areas also increased with NRDS severity (0 vs. 1.5 ± 0.8 vs. 4.1 ± 1.3, all $P < 0.05$). The LUS score for NRDS vs. non-NRDS showed 80.2% sensitivity and 100% specificity using a cut-off of 21.5 (Area under the ROC curve, AUC = 0.938; $P < 0.001$). The LUS score for severe vs. mild/moderate NRDS showed 73.1% sensitivity and 95.7% specificity using a cut-off of 25.5 (AUC = 0.944; $P < 0.001$). The LUS score for predicting mechanical ventilation showed 81.3% sensitivity and 88.8% specificity using a cut-off of 25.5 (AUC = 0.912; $P < 0.001$). The AUCs of consolidation areas were similar to those of LUS score (all $P > 0.05$).
Conclusion: The LUS score and consolidation areas can discriminate NRDS from non-NRDS and the different grades of NRDS, and predict the application of mechanical ventilation.

1. Introduction

Neonatal respiratory distress syndrome (NRDS) is one of the most common causes of neonatal respiratory failure and neonatal mortality, especially in premature infants, who tend to have very low birth weight [1]. NRDS is a pulmonary insufficiency caused by structural and functional immaturity of the lungs [2]. The incidence of NRDS depends upon gestational age and varies from 92% for infants born at 24–25 weeks to 57% got those born at 30–31 weeks [2]. Mortality from NRDS varies according to the infants' weight, from 50% for infants of < 1.0 kg to 0% for those of > 4.0 kg [3]. Infants affected by NRDS usually require pulmonary surfactant and continuous positive airway pressure (invasive ventilation or mechanical ventilation) [4,5]. Transient tachypnea of the newborn (TTN) is another very common neonatal respiratory condition [6] and can be very difficult to differentiate from NRDS.

Lung ultrasound (LUS) is a valuable non-invasive technique for the diagnosis of neonatal respiratory conditions such as NRDS, TTN, neonatal pneumonia, meconium aspiration syndrome, pneumothorax, and pediatric pneumonia [7–9]. In addition, LUS is easily accessible, inexpensive, radiation-free, and portable [10]. Compared to conventional chest X-ray, LUS offers a more accurate and specific diagnostic approach, especially for NRDS [8]. The LUS score is strongly associated with lung aeration in adults [11]. To determine the LUS score, the 12 intercostal regions are evaluated and scored (0 = normal aeration; 1 = moderate loss of lung aeration; 2 = severe loss of lung aeration; and 3 = complete loss of lung aeration) and the LUS score is the sum of all 12 regions [11]. The LUS score can evaluate the severity of the adult respiratory distress syndrome (ARDS) [12] and predict postextubation distress [13]. Furthermore, it has been suggested that the LUS score can

---

* Corresponding author.
  E-mail address: wsqiuli@126.com (L. Qiu).
[1] These authors contributed equally to this work.

predict surfactant administration in preterm babies under continuous positive airway pressure [14]. Lung consolidation is of extreme importance for NRDS ultrasound appearance [8]. Nonetheless, more data are needed to verify the correlation between the LUS score and the extent and scope of lung consolidation with the severity of RDS, to evaluate the severity of NRDS by LUS, and to monitor the treatment of the NRDS by LUS.

We hypothesized that the LUS score and the area of lung consolidation are correlated with NRDS severity and could accurately predict the grade of NRDS and the application of mechanical ventilation. The aim of the present study was to determine the LUS score and lung consolidation area of each grade of NRDS and TTN, and to evaluate the correlation between the LUS score and the grade of NRDS. A secondary aim was to assess the possibility of using the LUS score and lung consolidation to predict the application of mechanical ventilation.

2. Materials and methods

2.1. Study design and patients

This study was approved by the ethics institutional review board of our institution and was conducted according to the principles of the Declaration of Helsinki. Oral informed consent was obtained from the children's parents.

From January 2017 to January 2018, newborns from the obstetrics department of our institution with suspected NRDS were consecutively enrolled. Those who had clinical manifestations included progressive respiratory distress occurring shortly after birth, tachypnea, expiratory grunting, nasal flaring, subcostal retractions, cyanosis, reduced or absent breath sounds would be suspected of NRDS [2]. Those patients with congenital malformations and those intubated prior to the ultrasound examination were excluded.

2.2. Lung ultrasound

A high-resolution linear probe (Voluson S8, GE Healthcare, Waukesha, WI, USA) with a frequency of > 7.5 MHz (generally 10 MHz) was used in this study. LUS was performed in the incubator by the same experienced radiologist (with 5 years of experience) and assisted by the NICU nurse within 2 h after admission and before the clinician's diagnosis. The patients were examined in both the dorsal decubitus and prone position. If the lung US image is unclear, the patient would be in the lateral position. The video images of each lung area were recorded by the initial operator and were reanalyzed by a senior radiologist specialized in ultrasound who was blind to the clinical conditions and diagnosis.

The LUS score used in the present study was modified from an index proposed for adult patients [14]. Basically, each lung was divided into six areas (upper and lower areas of anterior, posterior, and lateral sections) (Fig. 1), for a total of 12 areas. For each lung area, a 0- to 3-point score was given (total score ranging from 0 to 36): 0 indicates A-
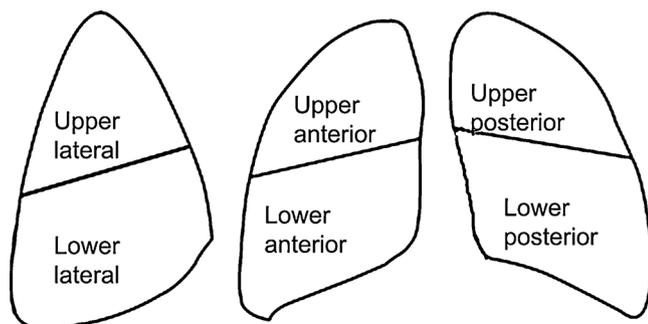

Fig. 1. The diagram of the six parts of the right lung.

pattern (defined by the presence of A-lines only or the presence of < 3 B-lines, Fig. 2a); 1, B-pattern (defined as the presence of ≥3 well-spaced B-lines, Fig. 2b); 2, severe B-pattern (defined as the presence of crowded and coalescent B lines, with or without consolidations limited to the subpleural space (alveolar-interstitial syndrome), Fig. 2c); and 3, extended consolidations. Some lung consolidations without presence of air bronchograms were dotted and looked like a beach (Fig. 2d). Some lung consolidations showed the presence of air bronchograms or fluid bronchograms (Fig. 2e). The presence of pleural effusion and lung pulse (a sign of complete atelectasis and is a manifestation of the vibrations of the heart transmitting through a motionless lung [15]) is scored 3 points. A-lines represent reflection of the pleura due to ultrasound diffusing through an air-filled lung. B-lines represent fluid filling the interstitium and the alveolar space if they become confluent. For each lung area, if extended consolidation was observed using US, it accounts for one consolidation area.

2.3. Diagnosis of NRDS and treatment

The clinical data were collected by a neonatologist. The data included clinical manifestations, chest X-ray examination, and arterial blood gas analysis. The neonatologist was blind to the LUS results and made the diagnosis of NRDS based on clinical signs and symptoms, chest X-ray (evaluated by a radiologist that did not perform US or evaluate LUS), and arterial blood gas, i.e. based on the non-LUS data. The clinical criteria were: 1) respiratory rate > 60/min; and 2) dyspnea characterized by intercostal, subcostal, or suprasternal retraction, grunting, or cyanosis. The laboratory criteria were: 1) blood pH < 7.25; 2) $PaCO_2$ > 60 mmHg; and 3) PaO_2 < 50 mmHg. The X-ray grading included: grade I: mild ground glass veiling; grade II: bilateral well-evident reticulonodular pattern; grade III: air bronchogram; and grade IV: bilateral white lung [16]. The newborns with NRDS were classified into three grades, i.e. mild, moderate, and severe. The clinicians treated the patients according to the local neonatal intensive care unit (NICU) protocols. The mode of respiratory support was also recorded. There were three modes: nasal continuous positive airway pressure (NCPAP), synchronous intermittent mandatory ventilation (SIMV), and high frequency oscillatory ventilation (HFOV). NCPAP is noninvasive. SIMV and HFOV are invasive mechanical ventilation.

2.4. Statistical analysis

All statistical analyses were performed using SPSS v20.0 (IBM Corp., Armonk, NY, USA). Quantitative data were expressed as means ± standard deviation and analyzed using the Student's t-test or Mann-Whitney U test. Categorical data were expressed as numbers (percentage) and analyzed using the chi-square test. Correlations between LUS score, consolidation area, and the severity of the NRDS were analyzed using Spearman's correlation. Receiver operating characteristic (ROC) curve analysis was used to evaluate the ability of the LUS score and the consolidation area to diagnose and grade NRDS and predict mechanic ventilation. Area under the curves (AUC), cut-off values, sensitivity, and specificity when Youden index was maximum were reported. The AUCs were compared using the Z test. P < 0.05 was considered statistically significant.

3. Results

3.1. Characteristics of the subjects

One hundred and forty-six premature newborn infants were enrolled. Ninety-six were suffered from NRDS and 50 had other disease (All of them were with transient tachypnea of newborn (TTN)). The mean gestational age was 29.0 ± 3.4 weeks in NRDS patients and 35.1 ± 2.9 weeks in TTN group (P = 0.001). The mean birth weight was 950 ± 253 g in RDS neonates and 2297 ± 411 g in TTN neonates
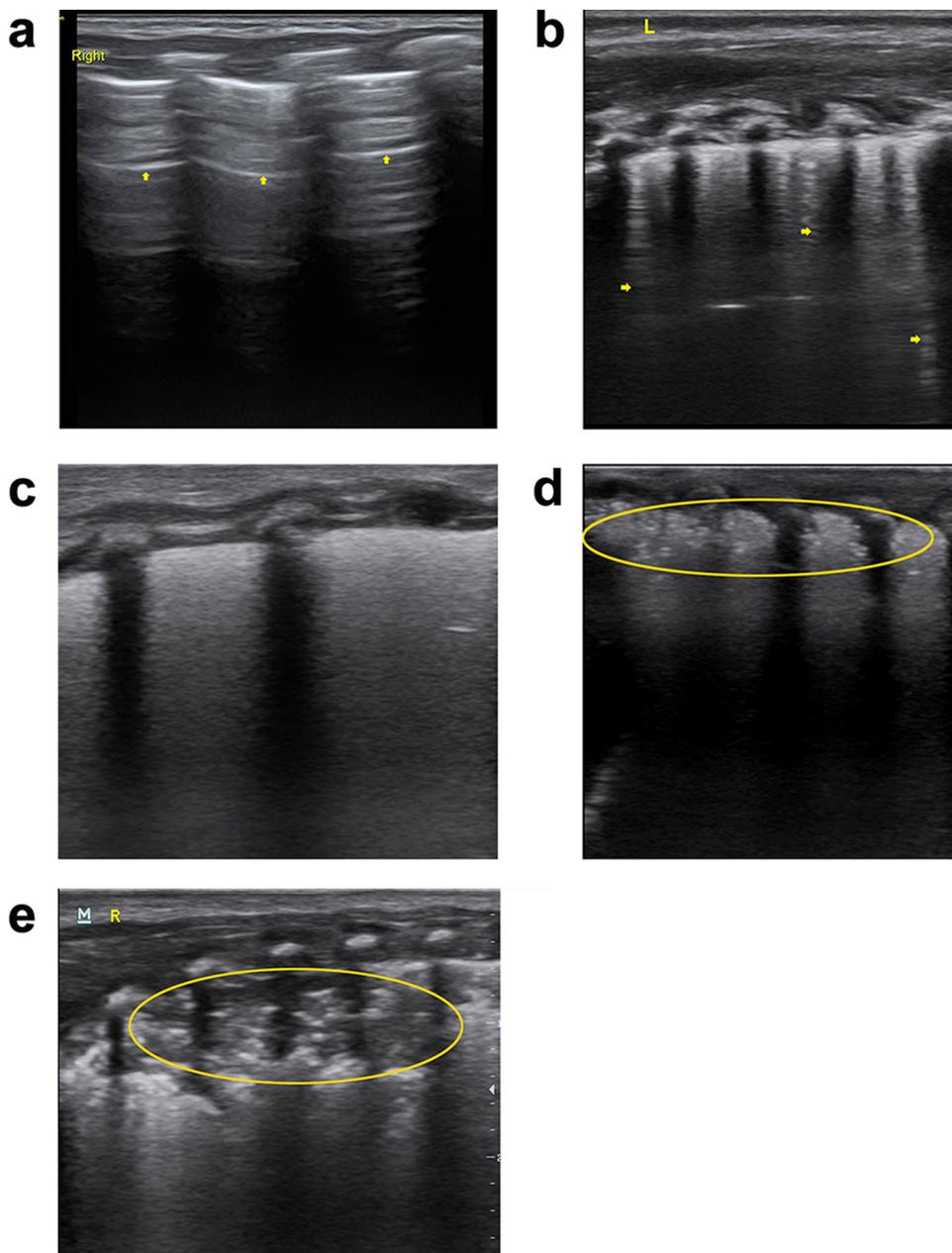
Fig. 2. Representative images of lung ultrasound (LUS). For each area, a score of 0–3 ha s been assigned. Score values correspond to 4 different patterns as shown in the ultrasonograms. (a) Score 0 indicates A-pattern (defined by the presence of only A-lines or < 3 B-lines). A-lines were indicated by arrows. (b) Score 1, B-pattern (defined as the presence of ≥ 3 well-spaced B-lines). B-lines were indicated by arrows. (c) Score 2, severe B-pattern (defined as the presence of crowded and coalescent B lines with or without consolidations limited to the subpleural space (alveolar-interstitial syndrome)). (d) Score 3, extended consolidations without presence of air bronchograms were dotted and looked like a beach. Sand-like consolidation was indicated by oval. (e) Score 3, extended consolidations with presence of air bronchograms (indicated by oval).

Table 1
Characteristics of the patients.

Characteristic	NRDS (n = 96)	TTN (n = 50)	P value
Gender, n (%)			
Male	50 (52.1%)	26 (52.0%)	0.992
Female	46 (47.9%)	24 (48.0%)	
Gestational age (range)	29 ± 3.4	35.1 ± 2.9	0.001
(weeks)	(26–41)	(32–40)	
Birth weight (g)	950 ± 253	2297 ± 411	0.001
NRDS grade, n (%)			
Mild	20 (20.8%)	–	–
Moderate	50 (52.1%)	–	
Severe	26 (27.1%)	–	
Ventilation mode, n (%)			
Mechanical ventilation	16 (16.7%)	0	0.001
NCPAP	80 (83.3%)	50 (100%)	

NRDS: neonatal respiratory distress syndrome; TTN: Transient tachypnea of the newborn; NCPAP: nasal continuous positive airway pressure.

(P = 0.001). The average age of infants at the time of LUS was 3.0 ± 1.3 h. There were 20 mild NRDS cases (20.8%), 50 moderate NRDS cases (52.1%), and 26 severe NRDS cases (27.1%). Eighty neonates (83.3%) with NRDS were treated with NCPAP, and 16 (16.7%) with intubation mechanical ventilation. All TTN babies were treated with NCPAP (P = 0.001) (Table 1).

3.2. Lung ultrasound appearance

The ultrasound appearance of TTN lung was coalescent B-lines, bilateral white lung (or alveolar-interstitial syndrome, which is caused by the presence of a large amounts of lung fluid (including pulmonary interstitial and alveolar fluid [17]), and an abnormal pleural line (thickened or blurred). There was no lung consolidation in the TTN group. Pleural line abnormalities, bilateral white lung, and lung consolidation were shown in NRDS infants. Lung consolidation with air bronchograms was seen in most NRDS infants. The consolidation was rare and mainly located in the subpleural area in mild NRDS. Air bronchograms sometimes were not visible. In severe NRDS, the area of

Table 2

LUS score and consolidation areas of each group.

Group	LUS score	Consolidation areas
NRDS (n = 96)	23.57 ± 3.63[*]	1.88 ± 1.70[**]
Mild NRDS (n = 20)	17.95 ± 2.70[a]	0[a]
Moderate NRDS (n = 50)	24.00 ± 1.69[b]	1.50 ± 0.76[b]
Severe NRDS (n = 26)	27.03 ± 1.73[c]	4.07 ± 1.32[c]
TTN (n = 50)	16.2 ± 1.83[*]	0[**]
Ventilation mode		
Mechanical ventilation (n = 16)	27.5 ± 1.57[†]	4.33 ± 1.3[‡]
NCPAP (n = 130)	22.53 ± 3.30[†]	1.2 ± 1.0[‡]

LUS: lung ultrasound; NRDS: neonatal respiratory distress syndrome; TTN: transient tachypnea of the newborn; NCPAP: nasal continuous positive airway pressure.

Note: The differences between mild NRDS and TTN were not statistically significant (P > 0.05).

[*] indicate P < 0.05.

[**] indicate P < 0.05.

[†] indicate P < 0.05.

[‡] indicate P < 0.05.

[a] Different letters indicate P < 0.05.

[b] Different letters indicate P < 0.05.

[c] Different letters indicate P < 0.05.

lung consolidation was observed expanding into other areas and even involving deep lung tissue. In addition, the air bronchograms became more evident in patients with severe NRDS. Pleural effusion and lung pulse were only seen in severe cases.

Significant correlation was found between LUS score and the severity of NRDS (r = 0.844, P < 0.001). The consolidation area was also well correlated with the severity of NRDS (r = 0.859, P < 0.001). Table 2 presents the LUS scores and consolidation areas. Globally, neonates with NRDS had higher LUS scores than those with TTN (23.6 ± 3.6 vs. 16.2 ± 1.8, P < 0.05). Among neonates with NRDS, the LUS scores increased with NRDS severity (18.0 ± 2.7 vs. 24.0 ± 1.7 vs. 27.0 ± 1.7, all P < 0.05). There were almost no consolidation areas in TTN, while 1.9 ± 1.7 consolidation areas were observed in the NRDS group (P < 0.05). The number of consolidation areas also increased with NRDS severity (0 vs. 1.5 ± 0.8 vs. 4.1 ± 1.3, all P < 0.05). The differences between mild NRDS and TTN were not statistically significant (P > 0.05). The LUS scores and consolidation areas were higher in neonates on mechanical ventilation compared with those on NCPAP (LUS score: 27.5 ± 1.6 vs. 22.5 ± 3.3, P < 0.05; consolidation areas: 4.3 ± 1.3 vs. 1.2 ± 1.0, P < 0.05).

3.3. LUS score for diagnosis and grading NRDS

The ROC analysis of the LUS score for the diagnosis of NRDS vs. TTN showed that sensitivity was 80.2% and specificity was 100% when using a cut-off of 21.5 (AUC-ROC: 0.938; 95% confidence interval (CI): 0.900-0.976). The ROC analysis of lung consolidation areas for the diagnosis of NRDS showed that sensitivity was 82.3% and specificity was 100% when using a cut-off of 0.5 (AUC-ROC: 0.896; 95%CI: 0.844-0.947, Table 3 and Fig. 3a). There was no difference in diagnostic value between the two scores (Z test, P = 0.184).

The ROC analysis of the LUS score for the diagnosis of severe NRDS vs. mild and moderate NRDS showed that sensitivity was 73.1% and specificity was 95.7% when using a cut-off of 25.5 (AUC-ROC: 0.944; 95%CI: 0.897-0.990). The ROC analysis of lung consolidation areas for the diagnosis of severe NRDS showed that sensitivity was 92.3% and specificity was 88.6% when using a cut-off of 2.5 (AUC-ROC: 0.948; 95%CI: 0.901-0.996, Table 3 and Fig. 3b). There was no difference in diagnostic value between the two scores (Z test, P = 0.497).

3.4. ROC analysis for predicting the application of mechanical ventilation in NRDS

Regarding the need for mechanical ventilation in NRDS, the sensitivity of the LUS score was 81.3% and specificity was 88.8% using a cut-off of 25.5 (AUC-ROC: 0.912; 95%CI: 0.851-0.973). The sensitivity and specificity of lung consolidation areas were 93.8% and 81.2%, respectively, for predicting the application of mechanical ventilation using a cut-off of 2.5 (AUC-ROC: 0.919; 95%CI: 0.845-0.993) (Table 4 and Fig. 3c). There was no difference in diagnostic value between the two scores (Z test, P = 0.839).

4. Discussion

It is still unclear whether LUS can be used to evaluate the severity of NRDS. Therefore, this study aimed to evaluate the role of LUS score in assessing the severity of NRDS. The results suggest that the LUS score can discriminate NRDS from TTN and the different grades of NRDS, and predict the application of mechanical ventilation.

For a long time, ultrasound was considered a less ideal tool for checking the normal aerated lung because ultrasounds do not travel well in air. Over recent years, the evaluation of the lung became possible due to advances in technology [7–9]. A change in the balance between air and fluids in the lung parenchyma determines a significant and corresponding change in the acoustic patterns that can be easily detected and measured [10]. The B-lines are vertical echoic comet-tail artifacts that can be detected by LUS [18] and they are typically correlated with the loss of pulmonary aeration and an increase in lung water [19]. If there is more lung water and less pulmonary aeration, the B-lines will increase accordingly. Accordingly, we are now able to evaluate the extravascular lung water and the change of the pulmonary aeration area by counting the number of B-lines [20]. Anile et al. [21] showed that the presence of > 3 positive lung quadrants with B-lines had a good performance in identifying extravascular lung water.

NRDS is characterized by diffuse lesions of the pulmonary capillaries and increased permeability [2]. Its primary pathological changes include pulmonary edema, atelectasis, and the formation of a transparent membrane [2], which suggest that there is more extravascular lung water and less gas compared to the lungs of normal babies. LUS has already been used for quantitative diagnosis in the NICU. A study by Brat et al. [14] reported that the LUS score may be used to describe oxygenation independently from the type of respiratory condition or gestation age, and that the LUS score can be used to predict the need for surfactant in NRDS infants. Nonetheless, few studies examined how to predict the severity of NRDS using LUS [8].

The present study is in line with a recently published study [8]. The main lung ultrasound features of NRDS include lung consolidation with or without air bronchograms, pleural line abnormalities, and bilateral white lung. LUS has a very high sensitivity and specificity for the diagnosis of neonatal RDS. Except for lung consolidation, the other abnormalities can also be identified in TTN babies [22,23]. Consequently, the most important and specific feature of NRDS is lung consolidation.

A more complex LUS score based on 12 lung areas has been suggested in adult patients with ARDS undergoing lung recruitment [13,24]. The present study adapted the adult score to neonates in order to predict the grade of RDS and the use of mechanical ventilation. In the present study, the LUS score in mild NRDS was not significantly different from the LUS score in TTN. Furthermore, there was no lung consolidation in these two groups. This finding is in line with the existing literature and that LUS cannot distinguish mild RDS from TTN [22]. On the other hand, the LUS scores in moderate and severe RDS were significantly higher compared to mild RDS.

We found that the lung consolidation area was small in mild NRDS and that it was limited to the subpleural area. The area expanded in moderate and severe NRDS, whereas the other lung areas without consolidation were "white" lung or with alveolar interstitial syndrome.

Table 3

LUS scores and consolidation areas for the diagnosis and grading of NRDS.

	Cut-off	Sensitivity	Specificity	AUC (95% CI)	P value
NRDS vs. TTN					
LUS score	21.5	80.2%	100%	0.938 (0.900–0.976)[*]	< 0.001
Consolidation areas	0.5	82.3%	100%	0.896 (0.844–0.947)[*]	< 0.001
Severe vs. mild and moderate NRDS					
LUS score	25.5	73.1%	95.7%	0.944 (0.897–0.990)[**]	< 0.001
Consolidation areas	2.5	92.3%	88.6%	0.948 (0.901–0.996)[**]	< 0.001

LUS: lung ultrasound; CI: confidence interval; NRDS: neonatal respiratory distress syndrome; TTN: transient tachypnea of the newborn.

　* The differences between AUCs of LUS score and lung consolidation for NRDS vs. TTN and severe vs. mild & moderate NRDS were not statistically significant (P = 0.184, P = 0.497, using the Z test).

　** The differences between AUCs of LUS score and lung consolidation for NRDS vs. TTN and severe vs. mild & moderate NRDS were not statistically significant (P = 0.184, P = 0.497, using the Z test).

The main difference between each grade of RDS was the lung consolidation area and the differences were significant. These results are supported by studies in other patient populations. Indeed, LUS integrated with chest X-ray is a first-line diagnostic technique to identify small pneumonic consolidations in pediatric pneumonia [25]. LUS is not only able to evaluate the severity of ARDS but also to predict the progression and the outcome of ARDS in blunt trauma patients [24].

In the present study, both the LUS score and consolidation areas could predict the use of mechanical ventilation. This is supported by Rodriguez-Fanjul et al. [26], although they used a different LUS evaluation method than in the present study. Tenza-Lozano et al. [27] showed that LUS can be used to predict the success of mechanical ventilation weaning.

Nevertheless, the AUC-ROC of LUS score and consolidation areas showed no significant difference. Due to the progresses in obstetrics, the number of preterm babies is dramatically increasing and since NRDS incidence is correlated with the gestation week, the number of infants with NRDS should also increase [1,2]. Since diagnosing and managing NRDS in a timely manner is extremely important for prognosis, using the most direct and rapid approach could be more clinically advisable, but this will have to be further studied.

The present study has some limitations. The time of US image analysis and the consistency between operators were not evaluated. The number of enrolled infants was relatively small. In addition, the gestational age and birth weight of the TTN group were higher compared to the RDS group. More studies with a larger sample size are required to overcome these limitations.

5. Conclusion

The present study revealed a strong correlation between the LUS score, the number of lung consolidation areas, and the grade of NRDS. The LUS score and consolidation areas can discriminate NRDS from TTN and the different grades of NRDS, and predict the application of mechanical ventilation. Using the more simplified method for counting the lung consolidation areas can be more beneficial than the more complex LUS score.
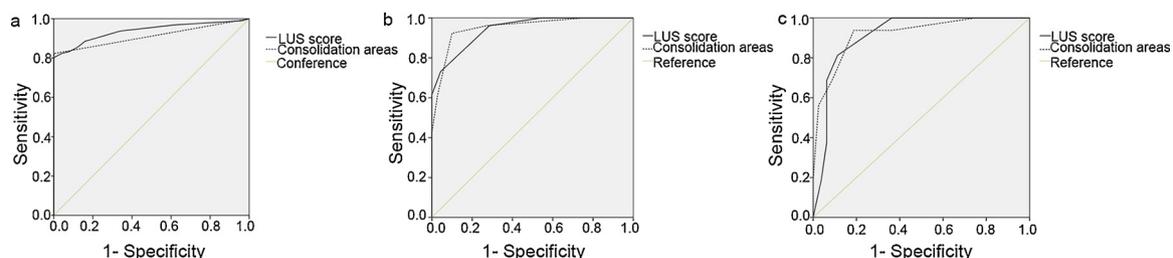
Table 4

LUS score and consolidation areas for predicting mechanical ventilation in neonatal respiratory distress syndrome patients.

Test	Cut-off	Sensitivity	Specificity	AUC (95%CI)	P value
LUS score	25.5	81.3%	88.8%	0.912 (0.851–0.973)[*]	< 0.001
Consolidation areas	2.5	93.8%	81.2%	0.919 (0.845–0.993)[*]	< 0.001

LUS: lung ultrasound; CI: confidence interval.

　* The difference between AUCs of LUS score and lung consolidation on predicting mechanical ventilation was not statistically significant (P = 0.839, using Z test).

Funding

Competing interests

All authors declare that they have no competing interests.

Authors' contributions

Li Qiu and Houqing Pang conceived and supervised the study; Houqing Pang, Bo Zhang and Jing Shi designaed experiments; Houqing Pang, Jing Shi, Bo Zhang performed experiments; Houqing Pang provided new tools and reagents; Houqing Pang and Jing Zang analysed data; Houqing Pang, Bo Zhang and Jing Shi wrote the manuscript; Li Qiu made manuscript revisions. All authors reviewed the results and approved the final version of the manuscript.

Transparency document

The Transparency document associated with this article can be found in the online version.

Fig. 3. Receiver operating characteristic (ROC) analysis of the lung ultrasound (LUS) score and consolidation areas for: (a) diagnosis of neonatal respiratory distress syndrome (NRDS) (NRDS vs. transient tachypnea of the newborn); (b) diagnosis of severe NRDS (severe vs. mild and moderate NRDS); (c) predicting the application of mechanic ventilation in NRDS.

Acknowledgments

References

[1] M. Koivisto, R. Marttila, M. Kurkinen-Raty, T. Saarela, M.L. Pokela, P. Jouppila, et al., Changing incidence and outcome of infants with respiratory distress syndrome in the 1990s: a population-based survey, Acta Paediatr. 93 (2004) 177–184.

[2] D.G. Sweet, V. Carnielli, G. Greisen, M. Hallman, E. Ozek, R. Plavka, et al., European consensus guidelines on the management of neonatal respiratory distress syndrome in preterm infants–2013 update, Neonatology 103 (2013) 353–368.

[3] L.L. Qian, C.Q. Liu, Y.X. Guo, Y.J. Jiang, L.M. Ni, S.W. Xia, et al., Current status of neonatal acute respiratory disorders: a one-year prospective survey from a Chinese neonatal network, Chin. Med. J. (Engl.) 123 (2010) 2769–2775.

[4] C.L. Roberts, T. Badgery-Parker, C.S. Algert, J.R. Bowen, N. Nassar, Trends in use of neonatal CPAP: a population-based study, BMC Pediatr. 11 (2011) 89.

[5] G.M. Schmolzer, M. Kumar, G. Pichler, K. Aziz, M. O'Reilly, P.Y. Cheung, Non-invasive versus invasive respiratory support in preterm infants at birth: systematic review and meta-analysis, BMJ 347 (2013) f5980.

[6] L.U. Machado, H.H. Fiori, M. Baldisserotto, P.C. Ramos Garcia, A.C. Vieira, R.M. Fiori, Surfactant deficiency in transient tachypnea of the newborn, J. Pediatr. 159 (2011) 750–754.

[7] J. Liu, H.Y. Cao, W. Fu, Lung ultrasonography to diagnose meconium aspiration syndrome of the newborn, J. Int. Med. Res. 44 (2016) 1534–1542.

[8] J. Liu, H.Y. Cao, H.W. Wang, X.Y. Kong, The role of lung ultrasound in diagnosis of respiratory distress syndrome in newborn infants, Iran. J. Pediatr. 25 (2015) e323.

[9] J. Liu, F. Liu, Y. Liu, H.W. Wang, Z.C. Feng, Lung ultrasonography for the diagnosis of severe neonatal pneumonia, Chest 146 (2014) 383–388.

[10] S.W. Chen, M.Y. Zhang, J. Liu, Application of lung ultrasonography in the diagnosis of childhood lung diseases, Chin. Med. J. (Engl.) 128 (2015) 2672–2678.

[11] F. Caltabeloti, A. Monsel, C. Arbelot, H. Brisson, Q. Lu, W.J. Gu, et al., Early fluid loading in acute respiratory distress syndrome with septic shock deteriorates lung aeration without impairing arterial oxygenation: a lung ultrasound observational study, Crit Care 18 (2014) R91.

[12] B. Bataille, G. Rao, P. Cocquet, M. Mora, B. Masson, J. Ginot, et al., Accuracy of ultrasound B-lines score and E/Ea ratio to estimate extravascular lung water and its variations in patients with acute respiratory distress syndrome, J. Clin. Monit. Comput. 29 (2015) 169–176.

[13] A. Soummer, S. Perbet, H. Brisson, C. Arbelot, J.M. Constantin, Q. Lu, et al., Ultrasound assessment of lung aeration loss during a successful weaning trial predicts postextubation distress, Crit. Care Med. 40 (2012) 2064–2072.

[14] R. Brat, N. Yousef, R. Klifa, S. Reynaud, S. Shankar Aguilera, D. De Luca, Lung ultrasonography score to evaluate oxygenation and surfactant need in neonates treated with continuous positive airway pressure, JAMA Pediatr. 169 (2015) e151797.

[15] D.A. Lichtenstein, N. Lascols, S. Prin, G. Meziere, The "lung pulse": an early ultrasound sign of complete atelectasis, Intensive Care Med. 29 (2003) 2187–2192.

[16] H.K. Sawires, E.A. Abdel Ghany, N.F. Hussein, H.M. Seif, Use of lung ultrasound in detection of complications of respiratory distress syndrome, Ultrasound Med. Biol. 41 (2015) 2319–2325.

[17] J. Liu, X.X. Chen, X.W. Li, S.W. Chen, Y. Wang, W. Fu, Lung ultrasonography to diagnose transient tachypnea of the newborn, Chest 149 (2016) 1269–1275.

[18] G. Volpicelli, M. Elbarbary, M. Blaivas, D.A. Lichtenstein, G. Mathis, A.W. Kirkpatrick, et al., International evidence-based recommendations for point-of-care lung ultrasound, Intensive Care Med. 38 (2012) 577–591.

[19] D.A. Lichtenstein, Ultrasound in the management of thoracic disease, Crit. Care Med. 35 (2007) S250–261.

[20] B. Bouhemad, H. Brisson, M. Le-Guen, C. Arbelot, Q. Lu, J.J. Rouby, Bedside ultrasound assessment of positive end-expiratory pressure-induced lung recruitment, Am. J. Respir. Crit. Care Med. 183 (2011) 341–347.

[21] A. Anile, J. Russo, G. Castiglione, G. Volpicelli, A simplified lung ultrasound approach to detect increased extravascular lung water in critically ill patients, Crit. Ultrasound J. 9 (2017) 13.

[22] J. Liu, Lung ultrasonography for the diagnosis of neonatal lung disease, J. Matern. Fetal Neonatal Med. 27 (2014) 856–861.

[23] R. Copetti, L. Cattarossi, F. Macagno, M. Violino, R. Furlan, Lung ultrasound in respiratory distress syndrome: a useful tool for early diagnosis, Neonatology 94 (2008) 52–59.

[24] D. Leblanc, C. Bouvet, F. Degiovanni, C. Nedelcu, G. Bouhours, E. Rineau, et al., Early lung ultrasonography predicts the occurrence of acute respiratory distress syndrome in blunt trauma patients, Intensive Care Med. 40 (2014) 1468–1474.

[25] S. Ianniello, C.L. Piccolo, G.L. Buquicchio, M. Trinci, V. Miele, First-line diagnosis of paediatric pneumonia in emergency: lung ultrasound (LUS) in addition to chest-X-ray (CXR) and its role in follow-up, Br. J. Radiol. 89 (2016) 20150998.

[26] J. Rodriguez-Fanjul, C. Balcells, V. Aldecoa-Bilbao, J. Moreno, M. Iriondo, Lung ultrasound as a predictor of mechanical ventilation in neonates older than 32 weeks, Neonatology 110 (2016) 198–203.

[27] E. Tenza-Lozano, A. Llamas-Alvarez, E. Jaimez-Navarro, J. Fernandez-Sanchez, Lung and diaphragm ultrasound as predictors of success in weaning from mechanical ventilation, Crit. Ultrasound J. 10 (2018) 12.