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Routine application of lung ultrasonography in the neonatal intensive care unit

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Abstract

The aim of this study was to study the features of lung ultrasonography (LUS) in lung disease and to evaluate the usefulness of LUS in the neonatal intensive care unit (NICU).

All of 3405 neonates included in this study underwent an LUS examination. Diagnoses were based on medical history, clinical manifestation, laboratory examination, and signs on chest radiography (CR) and/or computed tomography (CT). A single expert physician performed all LUS examinations.

There were 2658 cases (78.9%) with lung disease and 747 cases (21.9%) without lung disease. The main signs of neonates with lung disease on LUS were as follows: absence of A-lines, pleural-line abnormalities, interstitial syndrome, lung consolidation, air bronchograms, pulmonary edema, and lung pulse. These abnormal signs were reduced or eliminated on LUS as patient conditions improved. There were 81 cases that could not be diagnosed as lung disease by CR but were discovered as pneumonia, respiratory distress syndrome (RDS), or transient tachypnea of newborn (TTN) on LUS. Likewise, 23 cases misdiagnosed as RDS by CR were diagnosed as TTN on LUS. Among 212 cases of long-term oxygen dependence (LTOD) that failed to yield signs of pulmonary edema and lung consolidation on CR, 103 cases showed abnormal signs on LUS. Among 747 cases without lung disease, B-lines of 713 neonates (95.4%) could be found within 3 days after birth, and 256 neonates (34.3%) could be observed from 3 days to 1 week after birth. B-lines of 19 cases could be detected from 1 to 2 weeks after birth. The longest time at which B-lines could still be observed was 19 days after birth.

LUS has clinical value for the diagnosis of lung disease and the discrimination of causes of LTOP in premature infants, particularly for the diagnosis and identification of RDS and TTN. Moreover, LUS has additional advantages, including its lack of radiation exposure and its ability to noninvasively monitor treatment progress. Therefore, LUS should be routinely used in the NICU.

Abbreviations: BPD = bronchopulmonary dysplasia, CR = chest radiography, CT = computed tomography, LTOD = long-term oxygen dependence, LUS = lung ultrasonography, MAS = meconium aspiration syndrome, NICU = neonatal intensive care unit, RDS = respiratory distress syndrome, TTN = transient tachypnea of newborn.

Keywords: Infant, lung disease, lung ultrasonography, neonatal intensive care unit, newborn

1. Introduction

Pulmonary diseases are not only the most common diseases in neonates but also the most common cause of death in children younger than 5 years.[1] Therefore, timely and accurate diagnosis is extremely important to improve the prognosis for neonates with lung diseases. In the past, the diagnosis of pulmonary disease mainly relied on chest radiography (CR) and/or computed tomography (CT). However, the use of CR or CT especially for neonates is limited because of transportation and inevitable radiation. Increasing the awareness and advancement of lung ultrasonography (LUS) has led to the diagnosis of many lung diseases by LUS in both children and adults,[2–8] and the diagnosis of some lung diseases in new infants,[9–11] but LUS is still not commonly used for diagnosing and monitoring neonatal pulmonary diseases. Therefore, the aim of this study was to find the features of LUS in lung diseases in neonatal intensive care unit (NICU) patients and to promote its application in newborn respiratory diseases.

2. Materials and methods

2.1. Patients

The institutional review board of the General Hospital of Beijing Military Command approved the study protocol (No. 2014-LC-Ped-01). From December 2014 to January 2016, 3405 neonates enrolled in this study were admitted to the Department of Neonatology and the NICU of Bayi Children's Hospital, which had a neonatal ward with 350 beds. A total of 3405 neonates were divided into 2 groups, according to whether or not they had lung disease. The diagnosis of pulmonary disease was based on medical history, clinical manifestations, clinical examination, and

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Table 1

General study group information.

Group	Number	Sex (m/f)	Gestational Age, wk	Birth weight, g	Term (n)	Premature (n)
Newborn without lung diseases	747	401/346	33^{+1}~40^{+4}	1321–5013	631	116
Newborn with lung diseases	2658	1393/1265	25^{+4}~42^{+4}	700–5361	1259	1399
Newborn with lung diseases						
Pneumonia	1016	525/491	26^{+4}~41	830~5361	606	410
RDS	657	364/293	25^{+4}~42^{+4}	700~4131	123	534
TTN	389	188/201	35^{+5}~40^{+4}	2130~4017	303	86
MAS	227	125/102	37^{+3}~41^{+6}	2735~4358	227	0
LTOD	212	114/98	25^{+4}~33^{+5}	845~1718	0	212
Other group	157	77/80	27^{+5}~33^{+4}	936~1732	0	157
Total	3405	1794/1611	25^{+4}~42^{+4}	700–5361	1890	1515

LTOD = long-term oxygen dependence, MAS = meconium aspiration syndrome, RDS = respiratory distress syndrome, TTN = transient tachypnea of newborn.

signs of CR or CT as well as literature reports of lung diseases on LUS.[2–12] The final diagnosis of pulmonary disease was confirmed both by 1 senior neonatal physician proficient in LUS and by 1 radiologist. The group of neonates without pulmonary disease contained 747 cases hospitalized for premature birth, noninfectious jaundice, or nonpulmonary conditions. The group without lung diseases did not undergo the CR examination. All examinations of LUS were performed by a single operator who was blinded to the diagnosis.

2.2. Lung ultrasound

LUS with high-frequency linear 10- to 14-MHz probes (GE Voluson E6 or E8 and Logiq C9 ultrasound equipment; GE Healthcare) was used for patient examinations. The examinations were performed in the supine, lateral, and prone positions for neonates in a quiet state. Findings were recorded from 6 areas of the lung field, which was divided by the anterior and posterior axillary lines. The LUS probe was positioned perpendicular to the ribs in each area, and the scan was made from the apex to the base. The signs on LUS were recorded for this study and included pleura lines, A-lines, B-lines, interstitial syndrome, pulmonary edema, white lung, pleural effusion, lung point, double-lung point, lung consolidation, air bronchograms, and lung pulse, etc.

2.3. Statistical analysis

The data were performed with SPSS for Windows software, version 17.0 (IBM) (SPSS Inc, Chicago, IL). The findings between LUS and CR were compared among the patients with lung diseases using the Fisher exact test. A P value of <0.05 was considered to be statistically significant.

3. Results

3.1. General study group information

Among the 3405 patients enrolled in this study, there were 747 cases without lung disease and 2658 cases with lung disease. The neonates with lung disease were classified as follows: 1016 neonates (29.8%) with pneumonia, 657 neonates (19.3%) with RDS, 389 neonates (11.4%) with TTN, 227 neonates (6.7%) with meconium aspiration syndrome (MAS), 212 neonates (6.2%) with LTOD, and 157 neonates (4.6%) with other group. Table 1 contains general clinical information about the sample. The enrolled criterion of the "other group" referred to cases of lung disease that had been cured for >1 week. There were no abnormal clinical manifestations, laboratory examinations, or signs of CR for cases in the "other group," but these individuals were still hospitalized because of weight loss, feeding problems, etc. (Table 1, Fig. 1). Table 2 contains the informations of neonates who underwent the first examination of LUS after admission.

3.2. Normal neonatal lung ultrasound manifestations

First, normal lung tissue was hypoechoic. Second, the pleural line was a rule, smooth echogenic line <0.5 mm wide. Third, A-lines were echogenic lines parallel to the pleural line and equidistant from one another. Fourth, in this study, B-lines were observed in 713 neonates (95.4%) without lung disease within 3 days after birth, in 256 neonates (34.3%) after 3 days~1 week, in 19 neonates (2.5%) within 1~2 weeks after birth, and in 4 neonates (0.5%) within 2~3 weeks after birth. The longest time of B-lines in this study was 19 days after birth (Table 3). Fifth, there were no abnormal signs in normal neonatal lungs, including interstitial syndrome, pulmonary edema, lung consolidation, lung pulses, and air bronchograms (Fig. 2).

3.3. Lung ultrasound signs of newborn with lung disease

3.3.1. Pneumonia. A-line disappearance, interstitial syndrome, and lung consolidation could be found on LUS in all cases of neonatal pneumonia. As the pneumonia improved, LUS showed the scope of lung consolidation decreasing, the extent of interstitial syndrome alleviating, the pleural line gradually returning to normal, and the A-lines slowly appearing (Table 4, Fig. 3).

3.3.2. RDS. An abnormal pleural line, absence of A-lines, and lung consolidation could be detected in all cases of RDS. Bilateral pulmonary edema or white lung had been found in 88.0% cases with RDS. With improved conditions of RDS, LUS detected the scope of lung consolidation decreasing, the air bronchograms decreasing, the extent of pulmonary edema alleviating, the pleural line gradually returning to normal, and the A-lines appearing (Table 4, Figs. 4 and 5).

3.3.3. TTN. Abnormalities of pleural lines, absence of A-lines, and interstitial syndrome or pulmonary edema could be found on LUS in all cases of TTN, whereas lung consolidation was not detected. A double-lung point was observed in 109 of 320 cases (34.1%) in our sample. The degree of alleviation of pulmonary

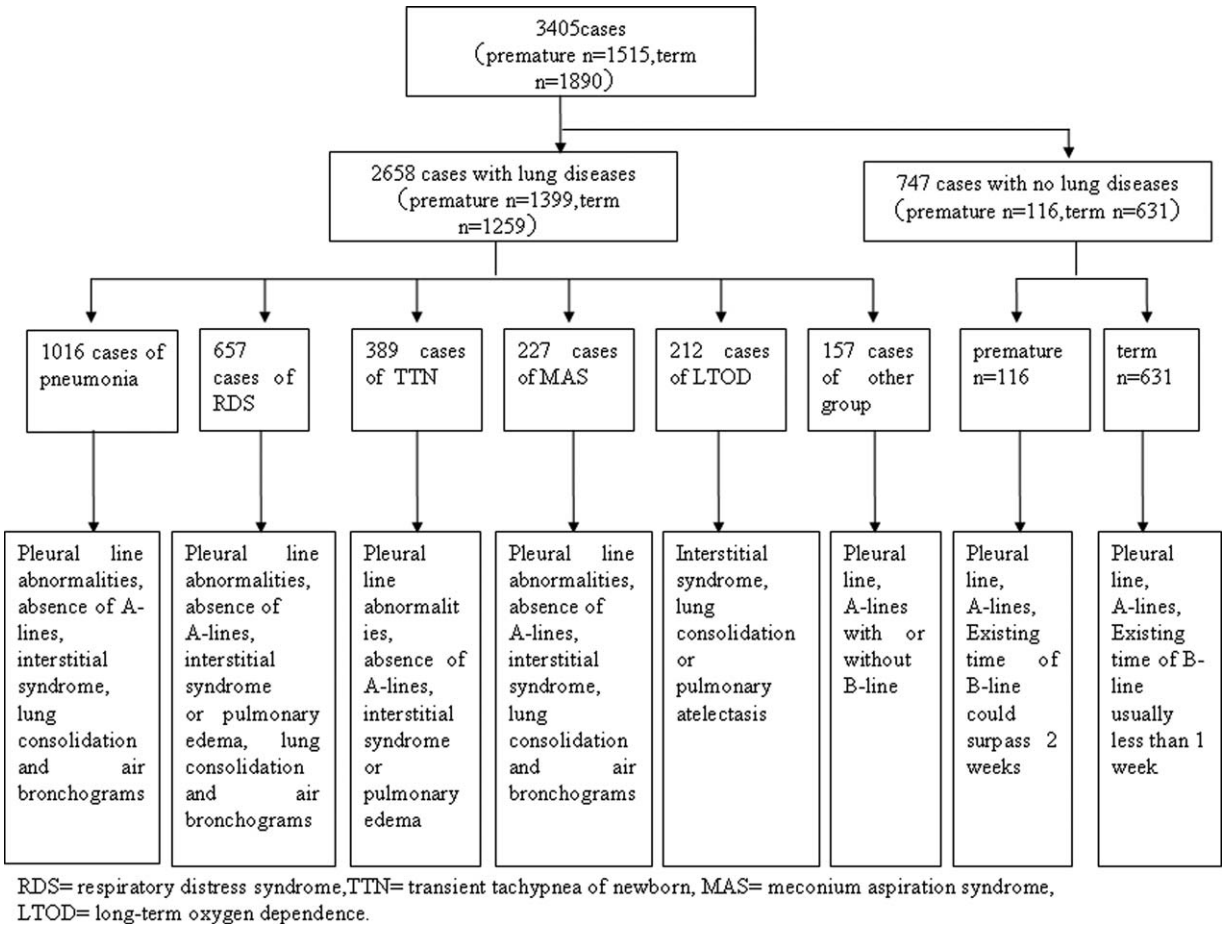

Figure 1. Flow diagram of ultrasonic examination. The features of all children enrolled in this study on lung ultrasonography.

edema or interstitial syndrome represented the better case conditions (Table 4, Fig. 6).

3.3.4. MAS. The absence of A-lines, lung consolidation, and interstitial syndrome could be observed on LUS in all cases of MAS (Table 4, Fig. 7).

3.3.5. LTOD. LUS was able to detect 212 cases of LTOD, including 18 cases with atelectasis, 37 cases with lung consolidation, 32 cases with interstitial syndrome, and 16 cases with both lung consolidation and interstitial syndrome.

3.3.6. Other groups. B-lines were observed in 29 of 91 patients (31.9%) who were hospitalized from 2 to 4 weeks after admission and in 7 of 54 patients (13.0%) who were hospitalized from 4 to 6 weeks after admission. B-lines were observed in 2 cases whose hospitalization time surpassed 6 weeks after admission, and the longest hospital stay was 58 days. All signs of other groups on

Table 2

Informations of neonates with the first examination of lung ultrasonography.

First Examination Time (After Admission) Group	Within 24 hours	24–48 hours	48–72 hours	72 hours–1 wk	>1 wk
Newborn without lung diseases	202	343	202	0	0
Newborn with lung diseases	716	976	393	118	455
Newborn with lung diseases					
Pneumonia	257	468	216	43	32
RDS	229	263	83	42	40
TTN	173	147	59	10	0
MAS	57	98	35	23	14
LTOD	0	0	0	0	212
Other group	0	0	0	0	157
Total	918	1319	595	118	455

LTOD = long-term oxygen dependence, MAS = meconium aspiration syndrome, RDS = respiratory distress syndrome, TTN = transient tachypnea of newborn.

Table 3

B-line of cases with no lung diseases on lung ultrasonography.

Newborn Without Lung Disease*	GA, wk	Delivery Way	The Existing Time of B-line (n)			
			<3 days	3 days≤~<7 days	7 days≤~<14 days	14 days≤~<21 days
GA <35 wk (n=7)	33^{+1}~34^{+2}	Vaginal delivery	7	7	3	1
GA <35 wk (n=9)	33^{+6}~34^{+5}	Cesarean delivery	9	9	6	3
GA ≥35 wk (n=54)	35^{+2}~36^{+3}	Vaginal delivery	54	24	2	0
GA ≥35 wk (n=46)	35^{+1}~36^{+4}	Cesarean delivery	46	31	5	0
GA ≥37 wk (n=309)	37^{+1}~40^{+4}	Vaginal delivery	289	78	0	0
GA ≥37 wk (n=322)	37^{+5}~39^{+1}	Cesarean delivery	308	107	3	0
Total (n=747)	33^{+1}~40^{+4}	Vaginal or Cesarean delivery	713	256	19	4

GA = gestational age.

* The longest time of hospital stays was 19 days.

LUS did not include lung consolidation, air bronchograms, interstitial syndrome, or pulmonary edema.

4. Comparison of the results of LUS with CR

Among the 2658 cases of lung disease, 1692 cases were examined by LUS and CR for the first time within 48 hours after admission. Among 81 cases not diagnosed with lung disease by CR, there were 32 cases of pneumonia, 26 cases of RDS, and 23 cases of TTN by LUS. In addition, 23 cases misdiagnosed as RDS by CR were diagnosed as TTN by LUS. Among the 212 cases of LTOD that failed to show signs of pulmonary edema and lung consolidation on CR, there were 103 cases with abnormal signs of lung atelectasis, lung consolidation, and/or interstitial syndrome on LUS. The above results of LUS were consistent with the patients' clinical data. The results of LUS and CR were input to statistical analysis; LUS more easily found the pulmonary lesions than CR ($P < 0.001$).

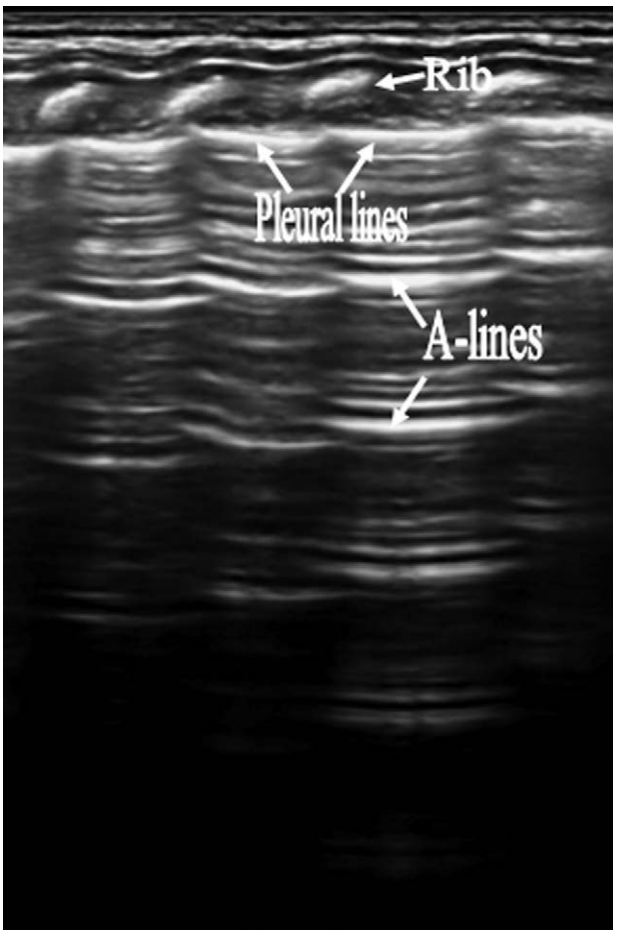

Figure 2. Normal lung on lung ultrasonography (LUS). Smooth and clear pleura lines, parallel A-lines of normal lung on LUS.

5. Discussion

Among the 3405 cases enrolled in this study, there were 2658 cases (78.9%) with lung disease and 747 cases (21.1%) without lung disease, indicating that lung disease accounted for a majority of the hospital admissions to the NICU. In this study, examinations were performed using a high-frequency 10 to 14 MHz linear array probe, which was more effective in visualizing the chest wall and the peripheral lung parenchyma. [13,14]

The signs of normal neonates on LUS included clear pleural lines, A-lines, and/ or B-lines or comet-tail artifacts. The numbers of A-lines were associated with the depth of the probe of the ultrasound machine. When the ultrasonic wave of the probe can penetrate more deeply, more A-lines display on the screen. It has generally been accepted that few B-lines or comet-tail artifacts can be found in normal neonates within 24 to 36 h after birth because the fetal lung is very rich in fluids.[15] This study, however, found that the existing time of B-lines could surpass 36 h and was related to gestational age and mode of delivery. Based on the above results, the B-line on LUS could exist much longer in neonates with smaller gestational ages and cesarean delivery. The longest duration of B-lines was >2 weeks. These neonates were considered normal newborn infants because they had no lung disease with abnormal clinical manifestation, unusual laboratory examination, or signs of CR, whereas congested B-lines and "white lung" could not be observed on LUS in newborn infants without lung disease.

The main signs of lung disease on LUS among the neonates in this study were as follows: the absence of A-lines, pleural line abnormalities, interstitial syndrome, lung consolidation, air bronchograms, pulmonary edema, and lung pulse. Moreover, these abnormal signs were mainly found during examinations of the back, a reason for which could be associated with neonatal position. The priority posture of neonates is the supine position, which can cause pulmonary ventilation/perfusion defect and accumulation of pathogens in the back owing to gravity. This can

Table 4

Lung ultrasonic manifestations in lung diseases.

Lung Diseases	Pleural-line Abnormalities (n) (%)	Absence of A-line (%)	Insterstitial Syndrome (%)	Pulmonary Edema or White Lung (%)	Pleural Effusion (%)	Double Lung Point (%)	Lung Consolidation and Air Bronchograms (%)	Lung Pulse (%)
Pneumonia* (n=725)	659 (90.9%)	725 (100%)	725 (100%)	0 (0%)	63 (8.7%)	0 (0%)	725 (100%)	118 (16.3%)
RDS* (n=492)	492 (100%)	492 (100%)	73 (14.8%)	419 (85.2%)	156 (31.7%)	0 (0%)	492 (100%)	109 (22.2%)
TTN* (n=320)	320 (100%)	320 (100%)	225 (70.3%)	95 (29.7%)	62 (19.4%)	109 (34.1%)	0 (0%)	0 (0%)
MAS* (n=155)	137 (88.4%)	155 (100%)	155 (100%)	0 (0%)	27 (17.4%)	0 (0%)	155 (100%)	37 (23.9%)
Total* (n=1692)	1608 (95.0%)	1692 (100%)	1178 (69.6%)	514 (30.4%)	308 (18.2%)	109 (6.4%)	1372 (81.1%)	264 (15.6%)

MAS=meconium aspiration syndrome, RDS=respiratory distress syndrome, TTN=transient tachypnea of newborn.
*The examination time of cases within 48 hours after admission.

lead to serious pulmonary lesions that often occur in the back and is the reason why these abnormalities are usually found on the back. These findings suggest that the operators of LUS should pay more attention to the examination of backs in neonates.

The specific features of neonatal pulmonary disease on LUS are as follows:

(1) Abnormalities of the pleural line: This includes a thickness of >0.5 mm or an irregular appearance, evidence of small subpleural consolidation, or disappearance.[16] There were 1692 cases with lung disease, which were examined within 48 hours after admission. Of these, 1608 cases (95.0%) were found with pleural line abnormalities classified as pneumonia, RDS, TTN, or MAS. Pleural line abnormalities were easily detected in neonatal lung disease.

(2) A-line disappearance: A total of 1692 cases (100%) with lung diseases were detected with A-line disappearance within 48 hours after admission. Therefore, the disappearance of A-lines is one of the most common abnormal ultrasonic manifestations of lung disease in the NICU, but the absence of A-lines alone failed to distinguish these lung diseases. A-lines arise from the reverberation artifact of the pleural line. The basic reason for A-line formation is the difference in acoustic impedance between the pleural interface and the lung. Therefore, when the pleural line is abnormal, it will certainly be accompanied by A-line abnormalities. However, of all cases with A-line abnormality, there were only 1609 cases (95.0%) with accompanying

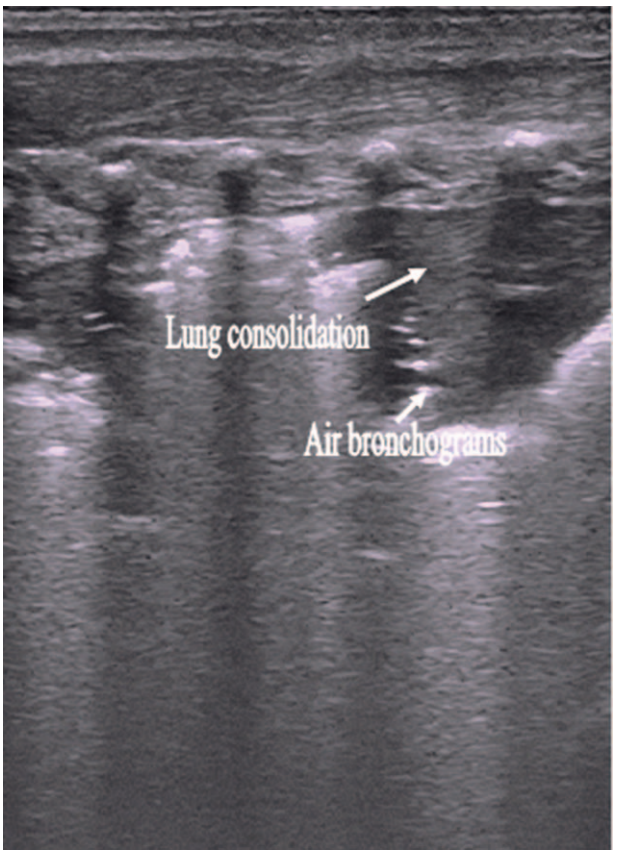

Figure 3. Pneumonia on lung ultrasonography. Lung ultrasound findings of pneumonia in a neonate (gestational age, 36^{+2} weeks; vaginal delivery; birth weight, 3010 g). Lung ultrasound showed pleura lines abnormalities, disappearance of A-line and lung sliding, irregular areas of lung consolidation with air bronchograms.

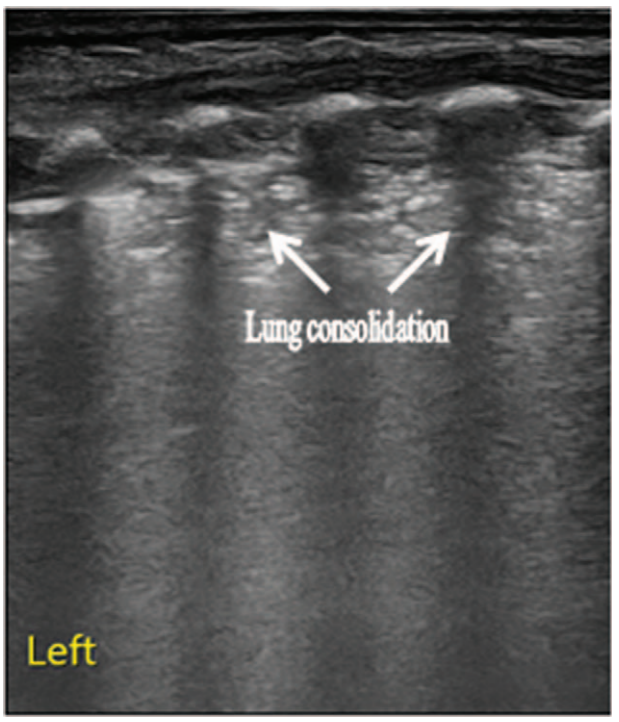

Figure 4. Respiratory distress syndrome (RDS) on lung ultrasonography. Lung ultrasound findings of RDS (grade III RDS on chest radiography) in a neonate (gestational age,33 weeks; cesarean section delivery; birth weight, 1915 g). Lung ultrasound showed pleural line abnormalities, disappearance of A-lines, subpleural lung consolidation with many air bronchograms, and pleural effusion.

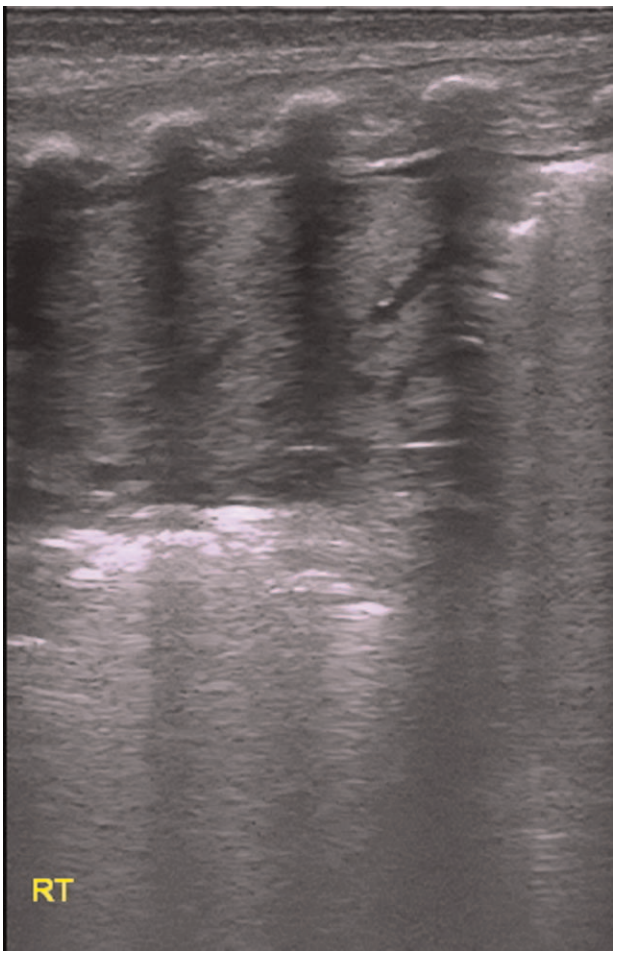

Figure 5. Pulmonary atelectasis on lung ultrasonography. Lung ultrasound showed pleural line abnormalities, disappearance of A-lines, and rules large areas of atelectasis with hyperechogenic air bronchograms and hypoechogenic liquid bronchograms.

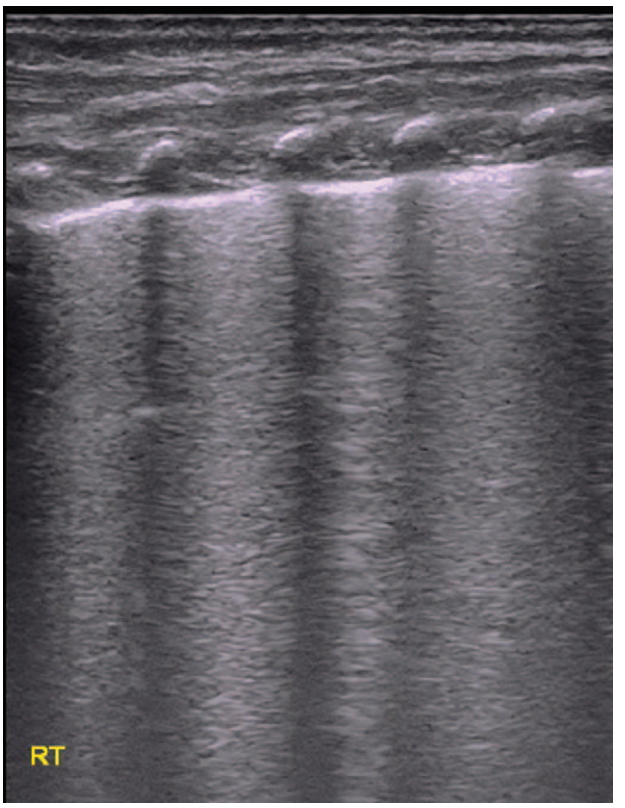

Figure 6. Transient tachypnea of newborn (TTN) on lung ultrasonography. Lung ultrasound findings of TTN in a neonate (gestational age, 36 weeks; virginal delivery; birth weight, 2510 g). Lung ultrasound showed pleural line abnormalities, disappearance of A-lines, and interstitial syndrome.

pleural-line abnormalities. This suggests that although the A-lines of cases were abnormal, the pleural line of the same cases could be normal.

(3) Interstitial syndrome or pulmonary edema: Based on these results, interstitial syndrome is the common sign of lung diseases in the NICU, the possible reasons for which are as follows:
   (a) The percentage of fluid in neonates is relatively higher than that in adults, which will generate relatively more lung liquid.
   (b) The neonates grow and develop quickly; therefore more liquid is needed every day, which also cause the more fluid in lung.
   (c) The glomerular filtration rate is very low in neonates within one week after birth and especially lower in premature infants. Therefore, the excessive water intake can lead to interstitial syndrome or even pulmonary edema.
   (d) When there is lung disease, the inflammation effusion in lung tissue also easily increases the amount of lung fluid present. Along with the increased lung fluid in the neonates, the findings on LUS are range from interstitial syndrome to pulmonary edema and even white lung. From the results above, both interstitial syndrome and pulmonary edema could be found in RDS and TTN, but only interstitial syndrome could be detected in pneumonia and MAS. In general, the lung liquid present in serious cases of TTN or RDS (grade III or IV RDS on CR) was characterized as pulmonary edema or even white lung on LUS; yet, the lung liquid present in less severe cases of TTN and RDS (grade II RDS on CR) was characterized as interstitial syndrome. When assessing lung water content in patients with lung disease, either bilateral lung fields or different lung tissues had different signs on LUS, meaning that the water content in different lung tissues could be different.

(4) Lung consolidation with air bronchograms: Among the 1692 cases with lung disease examined within 48 hours after admission, 1372 cases (81.1%) were detected with lung consolidation and air bronchograms. All cases of pneumonia, RDS, and MAS had been found with lung consolidation and air bronchograms, but cases of TTN had not. The degree and scope of lung consolidation of RDS on LUS usually related to the severity of RDS. A small focal subpleural consolidation with little air bronchograms was detected in RDS (grade II RDS on CR). However, in severe RDS (grade III or IV RDS on CR), the scope of lung consolidation extended deeper, and more air bronchograms were found on LUS. In instances of pneumonia, the character, and size of lung consolidation located in any part of the lung field were different, and air bronchograms appeared dendritic on LUS.

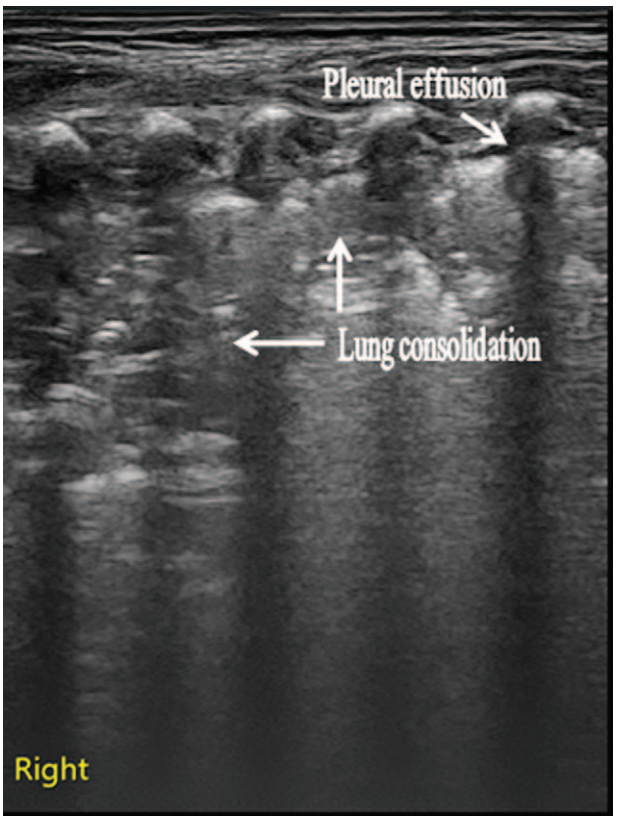

Figure 7. Meconium aspiration syndrome (MAS) on lung ultrasonography. Lung ultrasound findings of MAS in a neonate (gestational age, 41^{+3} weeks; cesarean section delivery; birth weight, 3756 g). Lung ultrasound showed pleural line abnormalities, disappearance of A-lines, lung consolidation with air bronchograms, and pleural effusion.

(5) Lung pulse: Among the 1692 cases with lung disease examined within 48 hours after admission, 264 cases (15.6%) including pneumonia, RDS, and MAS exhibited lung pulse on LUS. Although lung pulse is an important sonographic feature of serious atelectasis, serious lung consolidation is not definitely associated with lung pulse on LUS. For example, in this study,19 cases with outside focal atelectasis of the right lung also exhibited no lung pulse on LUS owing to its farther distance from the heart.

(6) Double-lung point: Previous literature considered a double-lung point to be a specific sign of TTN on LUS.[15] However, this study found that the double-lung point was not a specific sign of TTN and could also appear in other diseases on LUS. In addition to cases of TTN, 33 cases of pneumonia, 9 cases of RDS, and 5 cases of MAS were found with double-lung points during the convalescent phase on LUS. These findings are inconsistent with those from the previous literature.[15] According to the definition of a double-lung point, the reason for its formation is the different degree and nature of pathological changes between the upper and lower lung fields. The pathological changes in the 47 cases referenced above were sufficient so that the double-lung points were detected on LUS. This indicates that the double-lung point was not specific, but rather, a relatively sensitive sign of TTN on LUS. Another study had also shown that the double-lung point had a sensitivity of 33.8% with a specificity of 91.3% in diagnosing TTN.[17]

(7) With regard to the dynamic observation of pneumonia, RDS, and MAS, lung consolidation and pulmonary edema alleviating or disappearing, the gradual appearance of A-lines was representative of patient improvement. In monitoring TTN, the degree of reduction in interstitial syndrome or pulmonary edema and the gradual appearance of A-lines implied better patient conditions.

(8) Among the 212 cases of LTOD diagnosed as bronchopulmonary dysplasia (BPD), 103 cases were detected with atelectasis, lung consolidation, and/or interstitial syndrome, etc. Because these lesions were not easily found on CR and because CT was not utilized, long-term oxygen therapy was used for affected infants, which possibly resulted in iatrogenic BPD. Upon removal of the above-referenced abnormal conditions, the reliance on oxygen among patients with LTOD significantly reduced or disappeared. This suggests that the current diagnosis of BPD was at least partly inaccurate or unreasonable; therefore, increasing the use of LUS in the NICU is necessary.

(9) Children in the "other group" were found with B-lines, and the longest existing B-line duration in this study was 58 days after birth. These patients of the "other group" had been cured over 1 week, and no abnormal clinical manifestations, laboratory examinations, or signs of CR were observed. These observations show that the B-line could still be detected on LUS for a long time even if the cases with lung disease had been cured.

(10) Lung ultrasound compared with traditional CR: LUS is more sensitive than traditional CR in finding lung lesions.[9,12,18,19]From our results above, LUS more easily found the hidden lesions of lung than CR. The possible causes of traditional CR difficulty in finding these lesions were as follows: the scope of lesions was too small; the radiation dose of CR did not meet the requirements; the effect of lesion location and the transillumination angle or direction of CR such as for lesions in the deep lung field were not completely displayed on regular CR. On the contrary, LUS was not only able to easily find the hidden lesions but also had more clinical value in the diagnosis and identification of RDS and TTN and the identification of premature infants with LTOD. Therefore, it is necessary to promote the use of LUS to improve the diagnostic accuracy of lung disease and to reduce misdiagnosis in the NICU.

(11) There are 2 differential signs of lung disease on LUS. First, RDS and TTN: RDS and serious TTN have severe dyspnea, and an oxygen partial pressure drop on blood gas analysis. However, CR failed to distinguish them because their indications on CR are the same as for white lung imaging. But LUS can effectively distinguish between the 2 diseases. Based on this study and previous literature,[7,10,15,16] although both RDS and TTN showed pulmonary edema on LUS, TTN had no lung consolidation, whereas RDS did show lung consolidation on LUS. Second, RDS, pneumonia, and MAS:RDS pneumonia and MAS were common newborn infant diseases. All of them could have the same of clinical manifestations and laboratory examination, and CR failed to distinguish them alone. Whether LUS could differentiate these diseases alone and contribute to the treatment. Based on this study and previous research,[3,11,12,16,20] the main differences between them on LUS are as follows: ① In general, assessing the lung liquid on LUS, severe RDS (grade III or IV RDS on CR) is

characterized as pulmonary edema or even as white lung, whereas less severe RDS (grade II RDS on CR) appears as interstitial syndrome. Pneumonia and MAS primarily show interstitial syndrome, rarely indicating pulmonary edema or white lung. ② Lung consolidation of RDS on LUS showed no clear boundaries from lung tissue but was easy to distinguish. Air bronchograms of RDS were more exquisite and dense than for pneumonia and MAS. In pneumonia, lung consolidation had irregular shape, and air bronchograms appeared dendritic. ③ MAS could be regarded as a special type of pneumonia, with its main signs on LUS being very pneumonia-like. Therefore, there is no apparent difference among RDS, pneumonia, and MAS on LUS, and figures should be combined with clinical data when etiologies are being considered. In short, it is important that the same type of disease can look different on LUS. For example, the signs of RDS (grade II RDS on CR versus grade III or IV RDS on CR) were not the same on LUS. Furthermore, different lung diseases could also show the same type of ultrasonic signs on LUS (as TTN, RDS, pneumonia, and MAS all showed signs of interstitial syndrome). Thus, LUS cannot be completely separated from clinical data when attempting to distinguish among lung diseases, and the results of LUS would have important value for clinical diagnosis and treatment when it can be closely combined with clinical information.

In addition, LUS has the advantages of no radiation, noninvasiveness, and simplicity aside from dynamic observation. Compared with CR, LUS appears more effective in the diagnosis of neonatal lung diseases, especially for the diagnosis and identification of RDS and TTN. Furthermore, LUS has the additional practical value of being able to discriminate the cause of premature infants with LTOD. Routine examination with LUS is an important necessity in the management of pulmonary disease in the NICU.

The limitations of this research include the fact that one single operator performed all LUS examinations; consequently, the results may not generalize to a less-experienced examiner. Any doctors who would like to perform LUS should be properly trained. Furthermore, there were few cases of MAS, and pneumothorax was not included at all. The extent of the dynamic observation of neonatal pulmonary disease was also insufficient. These factors require further attention in future research.

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