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Use of Neonatal Lung Ultrasound for the Early Detection of Pneumothorax

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Abstract

Objective Pneumothorax (PTX) can be diagnosed using lung ultrasonography (LUS) in adult patients, but there are only a few reports of LUS in PTX diagnosis in neonates. The aim of the study was to assess the diagnostic accuracy for PTX.

Study Design This was a retrospective review study performed in our neonatal intensive care unit (level III) between June 2015 and June 2018. All eligible patients underwent an LUS scan before undergoing a chest X-ray (CXR), which was considered the reference standard. When a diagnosis of PTX was inconsistent between LUS and CXR, a chest computed tomography (CT) scan or chest drain was considered the gold standard.

Results Among 86 infants included in the study, 30 (34.9%) were diagnosed with PTX. In these 30 infants, 35 PTXs were detected by bedside LUS (five bilateral PTXs). Moreover, 11 infants with 14 PTXs were diagnosed only by LUS and were missed by CXR. Out of these 11 infants, 7 underwent a CT scan, whereas the remaining 4 underwent thoracentesis that confirmed PTX diagnosis.

Conclusion In neonates with PTX, LUS was more sensitive and specific for the early detection of PTX compared with CXR.

Keywords
- pneumothorax
- lung ultrasonography
- neonate
- diagnosis

Pneumothorax (PTX) is not an uncommon disease among neonates with respiratory difficulty, but it can be life-threatening. Even for a small or medium PTX, delayed diagnosis and treatment may result in the progression of respiratory and circulatory compromise. The incidence of PTX is even higher in infants with meconium aspiration syndrome (MAS), respiratory distress syndrome (RDS), or transient tachypnea of neonate (TTN), especially those who receive assisted ventilation.[1,2] Thus, early detection of PTX in those infants is critically important.

Traditionally, diagnosis of PTX can be achieved by chest X-ray (CXR) or computed tomography (CT). Despite CT being considered the gold standard for the diagnosis of PTX in adults, neonatologists always try to avoid CT because it requires infant transportation and exposure to excessive radiation. On the other hand, it has been shown that supine CXR fails to identify a significant number of PTXs, especially small and medium PTXs.[3] Over the past decade, lung ultrasonography (LUS), as a radiation-free, inexpensive, point-of-care tool that the clinician can use at the bedside, has been successfully used in the diagnosis of PTX and proved to be more accurate than conventional radiology in adults, especially in unstable patients with trauma in the emergency

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room.[4–6] LUS has great value in the diagnosis and differential diagnosis of lung disease in neonates, such as MAS, RDS, TTN, and pneumonia.[7] However, there are only a few reports on the use of LUS to diagnose PTX in infants in the neonatal intensive care unit (NICU).[8–13]

The aim of this study was to assess the accuracy of LUS in the diagnosis of PTX in infants with respiratory distress and suspected PTX in the NICU compared with conventional CXR.

Materials and Methods

Study Protocol

This was a retrospective review study performed in the NICU (level III) of the Guangdong Medical University affiliated Dongguan Children's Hospital, China, between June 2015 and June 2018. The inclusion criteria were as follows: (1) infants who had sudden deterioration of respiratory symptoms and required higher oxygen demand and (2) infants who were assessed with LUS first and then CXR within 1 hour after the initial examination and essential resuscitation. The following exclusion criteria were used: (1) infants who had suspected PTX but did not undergo an LUS and/or CXR within 1 hour after initial resuscitation and (2) infants who underwent a CXR before undergoing LUS. Approval from the Ethics Committee of Dongguan Children's Hospital was obtained prior to the commencement of this study.

According to the routine procedure in our NICU (►Fig. 1), when infants present with sudden respiratory difficulty and PTX is suspected, bedside LUS and CTX are performed within 1 hour after an initial rapid assessment by physical examination and essential resuscitation. Both LUS and CXR are usually performed with the patient in the supine position. In a stable infant, if the diagnosis of PTX was inconsistent between LUS and CXR, a chest CT scan was performed within 1 hour as the gold standard protocol. The volume of the PTX as evaluated by LUS was compared with that evaluated by a CXR or CT scan. In an unstable infant whose clinical situation precluded performing a CT scan and/or in an infant with a clinical suspicion of a large or tension PTX requiring

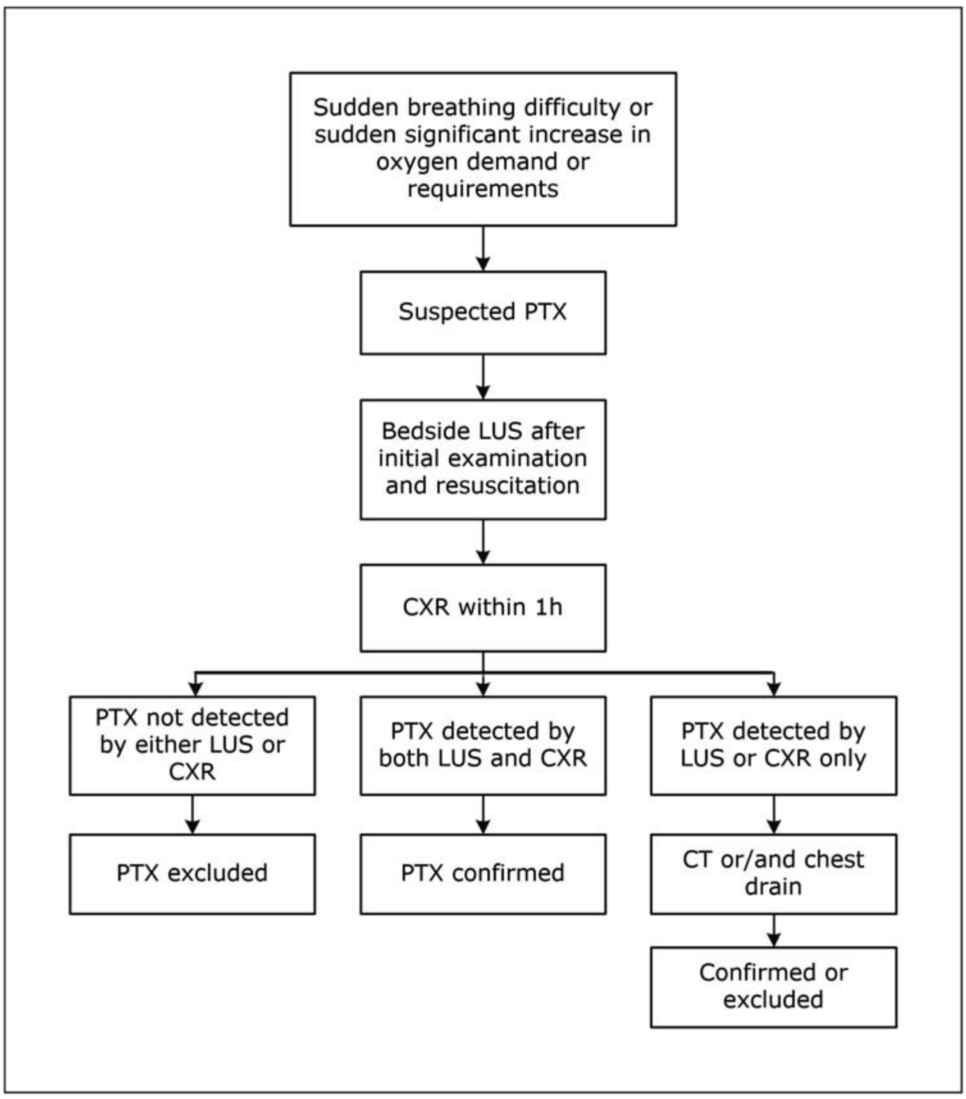

Fig. 1 Routine diagnostic procedure for pneumothorax at our neonatal intensive care unit. CT, computed tomography; CXR, chest X-ray; LUS, lung ultrasonography; PTX, pneumothorax.

immediate chest tube placement, the chest tube was placed after LUS and/or CXR. PTX was then confirmed by the air bubbles released from the chest tube, and the chest drain was considered the gold standard. The criteria for chest drain placement in our NICU include the following: (1) tension PTX, (2) medium- or large-size PTX, and (3) PTX with severe respiratory and/or circulatory embarrassment. All LUS scans were performed by three NICU clinicians who received formal training of point-of-care LUS. All images were reviewed by two senior neonatologists.

Equipment

A portable CXR (MUX-10J) was used in this study. Chest CT was acquired with a 16-slice spiral CT scanning unit (Brilliance, Philips Co.). A portable ultrasound machine (CX50, Philips Co.) was used regularly in our department, and a linear array probe with a frequency of 9 to 12 MHz was used in all LUS scans.

Lung Ultrasonography Examination Methods

LUS scans were performed while infants were in the supine position. Each lung was divided into three regions—anterior, lateral, and posterior regions—based on the anterior and posterior axillary lines. The probe was positioned perpendicular to the ribs. The anterior and lateral regions of both lungs were carefully scanned in either real-time or time-movement mode. Bilateral ultrasonic images were compared.

The observation indices during the LUS examination included (1) pleural line and lung sliding, (2) A-lines, (3) B-lines, and (4) lung point. The pleural line is visible as a hyperechoic horizontal line. During real-time ultrasound, the motion of the visceral pleura relative to the parietal pleura is known as lung sliding. A-lines are a series of echogenic parallel lines equidistant from one another and below the pleural line. B-lines are linearly hyperechoic reflections caused by an ultrasound wave encountering the alveolar gas–liquid interface. B-lines arise from the visceral pleura, are roughly vertical, and spread to the edge of the screen without fading (►Fig. 2). A lung point is the interface between the lung sliding and the lack of lung sliding and represents the physical boundary of the PTX.[14]

Ultrasound signs used to diagnose PTX in this study were (1) absence of lung sliding sign, (2) absence of B-lines in the affected area, and (3) presence of lung point. The diagnostic algorithm used to define a sonographic diagnosis of PTX was described by Volpicelli et al.[15]

The volume of the PTX was determined by LUS as follows. The probe was placed parallel to the ribs on the anterior and lateral chest depending on the extension of the PTX. The lung point, where the normal lung sliding and PTX coexisted in a single view, indicates a boundary between air and the edge of the lung and is accurately detected and located on the body surface. The size of the PTX was estimated by identifying or localizing the lung point at the different intercostal spaces. When these points line up, the contour of the PTX is also outlined. Even if there is no strict correlation between the extension on the chest wall and the volume of intrapleural air, the extension of the PTX allows for a semiquantitative assessment of the volume and, thus, accurately discriminates between large and mild forms. Zhang et al classified the size of the PTX as small (<30%), medium (30–70%), and large (>70%).[16]

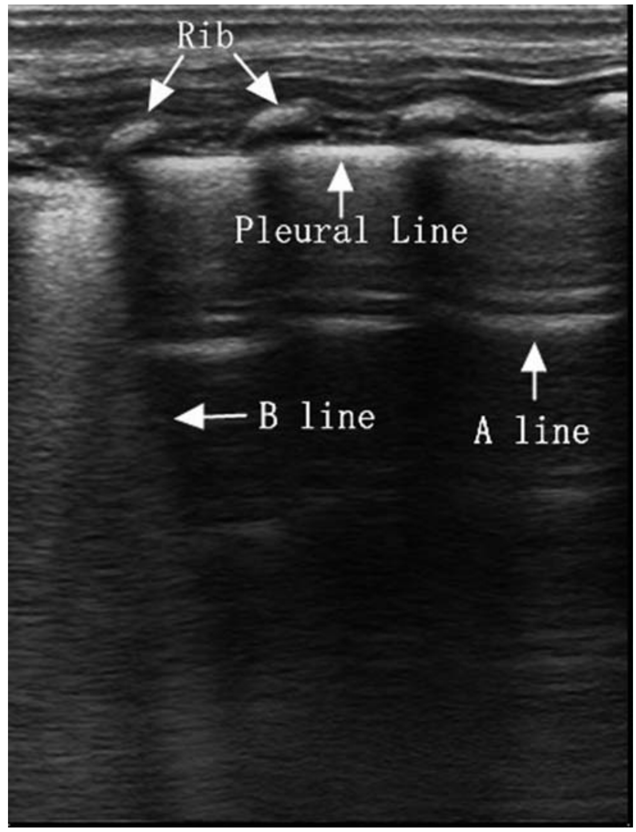

Fig. 2 Conventional ultrasonic signs in the lung. A-lines are a series of echogenic parallel lines that are equidistant from one another and below the pleural line. The B-lines are linearly hyperechoic reflections caused by an ultrasound wave encountering the alveolar gas–liquid interface.

Outcomes Measurement

The diagnostic sensitivity, specificity, positive predictive value, and negative predictive value of PTX were measured to assess the accuracy of LUS.

Statistical Analysis

The Statistical Package for the Social Sciences 17.0 software (SPSS Inc., Chicago, IL) was used to statistically analyze all the data. The overall diagnostic accuracy of LUS signs in the diagnosis of PTX was assessed using receiver operator characteristics (ROC) curves and calculating the area under the curve. The diagnostic sensitivity, specificity, positive predictive value, and negative predictive value of the LUS were calculated as follows. Sensitivity = true positive/(true positive+ false negative); specificity = true negative/(true negative + false positive); positive, positive predictive value = true positive/(true positive + false positive); and negative predictive value = true negative/(true negative + false negative). The agreements between CT and LUS for PTX diagnostic criterion were calculated using the kappa coefficient (κ). A value of $p < 0.05$ indicated a statistically

Table 1 General characteristics of patients

Characteristic	PTX ($n = 30$)
Birth weight, grams	3,076.7 ± 585.9
< 1,500, *n* (%)	1/30 (3.3)
1,500–2500, *n* (%)	3/30 (10.0)
> 2,500, *n* (%)	26/30 (86.7)
Sex, *n* (%)	
Male	24/30 (80.0)
Female	6/30 (20.0)
Gestational age, weeks	38.3 ± 2.2
< 37	3/30 (10.0)
≥37	27/30 (90.0)
Mode of delivery, *n* (%)	
Vaginal, *n* (%)	11/30 (36.7)
Cesarean section, *n* (%)	19/30 (63.3)
Primary disease	
MAS, *n* (%)	11/30 (36.7)
Pneumonia, *n* (%)	8/30 (26.7)
RDS, *n* (%)	3/30 (10.0)
Neonatal asphyxia, *n* (%)	2/30 (6.7)
Pulmonary hemorrhage, *n* (%)	1/30 (3.3)
Spontaneous PTX, *n* (%)	1/30 (3.3)
Others, *n* (%)	4/30 (13.3)
Respiratory support, *n* (%)	
None, *n* (%)	7/30 (23.3)
NCPAP/HFNC, *n* (%)	8/30 (26.7)
Mechanical ventilation, *n* (%)	15/30 (50.0)
Chest drain	
Yes, *n* (%)	25/30 (83.3)
No, *n* (%)	5/30 (16.7)
Outcomes	
Died, *n* (%)	2/30 (6.7)
Survived, *n* (%)	28/30 (93.3)

Abbreviations: HFNC, high-flow nasal cannula; MAS, meconium aspiration syndrome; NCPAP, nasal continuous positive airway pressure; PTX, pneumothorax; RDS, respiratory distress syndrome.

significant difference. The information reported was evaluated by an expert.

Results

Patients

Among the 86 infants, 30 (34.9%) were diagnosed with PTX. ►Table 1 describes the general characteristics of the 30 infants, of whom 15 were mechanically ventilated prior to PTX assessment and 20 had a chest tube placement after PTX was diagnosed. Twenty-eight infants recovered and two infants died of severe MAS and severe persistent pulmonary hypertension.

Performance of LUS and CXR Compared with the Gold Standard

In all the 30 infants, 35 diagnoses of PTX were made using bedside LUS, of which 5 were determined to be bilateral PTX. A total of 21 PTXs in 19 infants were diagnosed by both LUS and CXR (2 were bilateral PTX). In 11 infants diagnosed by LUS, 14 PTXs were missed by CXR (3 were bilateral PTX). Of the 11 infants, 7 underwent a chest CT scan and were observed to have 10 PTXs (3 were bilateral PTX), consistent with LUS findings ($\kappa = 1.000$; $p < 0.001$) (►Fig. 3). Five of the seven infants required chest tube placement soon after CT scan. The remaining four infants were too unstable to undergo a chest CT scan; therefore, we performed thoracentesis to confirm the diagnosis of PTX.

Regarding the volume of the PTXs, 13 PTXs diagnosed by LUS but missed by CXR were small (less than 30%), except one that was medium. Among the 21 PTXs confirmed by both LUS and CXR, the volume of the bilateral PTXs in one infant was graded as medium by LUS and small by CXR. A chest CT scan for that infant was consistent with the LUS finding of a medium PTX. This infant required a chest tube placement afterward (►Table 2).

In the 35 PTXs diagnosed by LUS, all had presented with an absence of B-lines and an absence of lung sliding, whereas 33 had lung points in the LUS images. The sensitivities of these three signs were 100, 100, and 94%, respectively, and the specificities were 100, 100, and 100%, respectively, compared with the results of the CXR, CT scan, and chest drain. ►Table 3 and ►Fig. 4 show the diagnostic accuracy and ROC curves of the individual PTX signs on the LUS. There was the appearance of fixed A-lines without lung points in two lung fields diagnosed as large PTXs (►Fig. 5).

Discussion and Conclusion

In 2012, the international evidence-based recommendations for point-of-care lung ultrasound were established under the auspices of the International Liaison Committee on Lung Ultrasound.[15] LUS has proven to be a fast and reliable diagnostic tool, with the additional benefit of being radiation-free, and is gradually being accepted by clinicians for patient examination, monitoring, and disease management. In addition, LUS has great value in the diagnosis and differential diagnosis of lung disease in neonates, such as TTN, pneumonia, MAS, RDS, and bronchopulmonary dysplasia.[17–22] Recently, Raimondi et al described the main ultrasound features of neonatal respiratory disorders and functional applications of LUS aiming to help a clinical decision and proposed SAFE (Sonographic Algorithm for liFe-threatening Emergencies) as a standardized protocol for emergency functional LUS in critical neonates.[7]

LUS has been applied more extensively in PTX in the emergency setting for adults more than for neonates. Several studies on multiple trauma adult patients demonstrated that bedside LUS as performed by emergency department clinicians enabled for rapid and reliable detection of PTX compared with CXR, using CT and chest drain as the gold standard, especially in cases involving small and medium PTXs.[6,7] Also, LUS was proved to be more accurate than

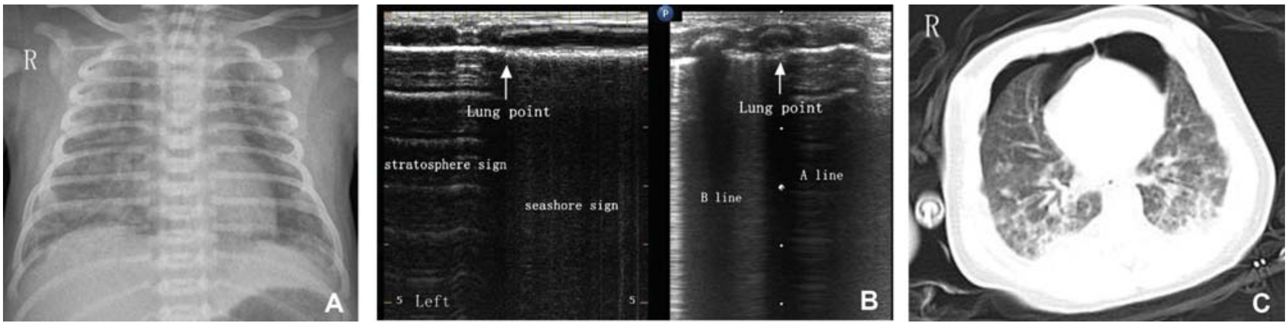

Fig. 3 A typical patient with pneumothorax (PTX) correctly diagnosed by lung ultrasonography (LUS) and missed by chest X-ray (CXR). The gestational age of the infant was $41^{5/7}$ weeks, and the birth weight was 3,210 g. The amniotic fluid was meconium-stained and the infant was admitted to our neonatal intensive care unit due to breathing difficulties and hypoxemia requiring mechanical ventilation after birth. (**A**) Supine CXR showed meconium aspiration syndrome in both lungs and did not enable a diagnosis of PTX. (**B**) Bedside LUS indicated bilateral small PTXs (the absence of B-lines, the existence of lung points, and a stratosphere sign in M mode). (**C**) Diagnosis was confirmed afterward by a chest computed tomography (CT). Arterial oxygenation improved after chest drain.

Table 2 Size of the PTX on LUS, CXR, CT scan, and chest tube placement to highlight the results

	LUS	CXR	LUS plus CT[a]	LUS plus chest tube placement[b]
Small PTX (*n*)	19	8	10	3
Medium PTX (*n*)	7	4	2	1
Large PTX (*n*)	9	9	0	0
Total (*n*)	35	21	12	4

Abbreviations: CT, computed tomography; CXR, chest X-ray; LUS, lung ultrasonography; PTX, pneumothorax.
[a]PTXs were diagnosed inconsistently by LUS and CXR and were confirmed by CT later.
[b]PTXs were diagnosed by LUS but missed by CXR and were later confirmed by chest tube placement.

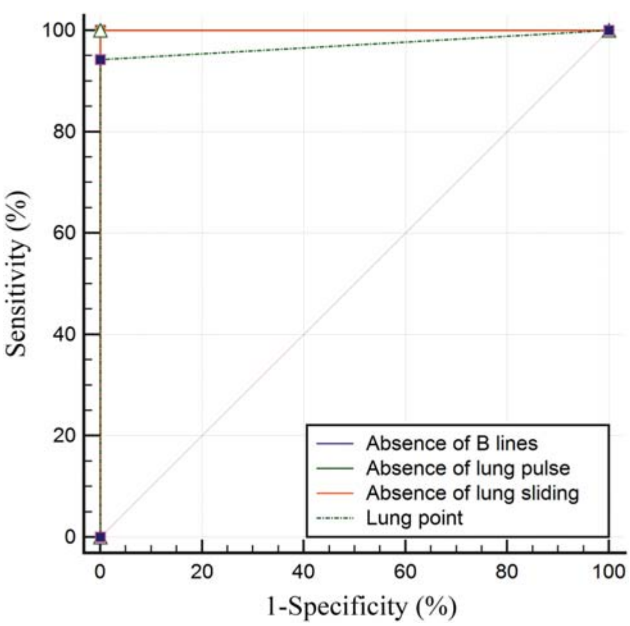

Fig. 4 Receiver operator characteristic curves for the lung ultrasonography signs when used to diagnose pneumothorax.

Table 3 Diagnostic accuracy of PTX signs on LUS in individual lung fields

	Absence of B-lines	Absence of lung sliding	Absence of lung pulse	Lung point
True positives (n^*)	35	35	35	33
False positives (*n*)	0	0	0	0
True negatives (*n*)	137	137	137	137
False negatives (*n*)	0	0	0	2
Sensitivity	100%	100%	100%	94.28%
Specificity	100%	100%	100%	100%
Positive predictive value	100%	100%	100%	100%
Negative predictive value	100%	100%	100%	98.56%

Abbreviations: PTX, pneumothorax; LUS, lung ultrasonography.
Note: The numbers indicate the total counts of individual lung fields from 86 patients including 172 lung fields.

conventional radiology for PTX detection in adults. In a study with 135 trauma patients, the diagnostic sensitivity for LUS versus radiography was 86.2 versus 27.6% and specificity was 97.2 versus 100%, respectively.[16] A meta-analysis including 25 original research articles showed that LUS had a pooled sensitivity of 78.6% and a specificity of 98.4% in the detection of PTX in adults, whereas chest radiography had a pooled sensitivity of 39.8% and a specificity of 99.3%.[4]

The incidence of PTX is increased in neonates with lung disease especially after mechanical ventilation and can be life-threatening. However, to our knowledge, there are few reports on PTX diagnosed by LUS in neonates. A two-phase study of 90 neonates by Liu et al demonstrated that LUS was accurate and reliable in diagnosing and ruling out neonatal

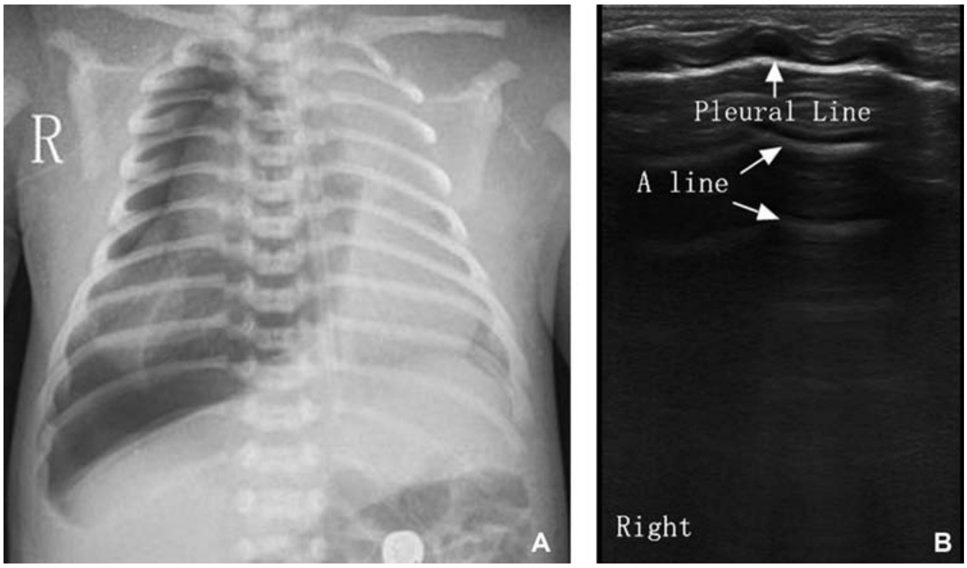

Fig. 5 Ultrasonic manifestation of a large pneumothorax (PTX) in an infant. The gestational age of the infant was 39 weeks, and the birth weight was 3,240 g. The infant was delivered by Cesarean section because of fetal distress in the uterus and admitted to our neonatal intensive care unit due to breathing difficulty for 20 minutes. The amniotic fluid was meconium-stained. (A) The chest X-ray showed a severe PTX in the right lung. (B) The lung ultrasonography showed a pleural line as well as A-lines in the right lung and (alveolar–interstitial syndrome in the left lung, whereas no lung point was found in the right lung. In real-time ultrasound, the lung sliding disappeared in the whole right lung field and appeared in the left lung field.

PTX and was as accurate as CXR.[9] Raimondi et al evaluated the accuracy of LUS in the diagnosis of PTX in the sudden decompensating patient in an international, prospective study, concluding that LUS showed high accuracy in detecting PTX in the critically ill infants, outperforming the clinical evaluation and reducing the time to imaging diagnosis and drainage.[8] However, in both of the studies, ultrasound results were not compared with CT but rather with CXR findings as a reference standard to evaluate the accuracy and reliability of ultrasound in the diagnosis of PTX; thus, the sensitivities of CXR and LUS in PTX diagnosis in neonates were not compared.

Ultrasound signs used to diagnose PTX are the absence of B-lines, the absence of lung sliding, and the appearance of a lung point.[8,11,23] Notably, a lung point sometimes will not be present in patients with a large PTX because the area below the probe is entirely air.[9] In this condition, the appearance of extremely clear and fixed A-lines and the absence of B-lines are important indicators of PTX. Inflammatory exudation and alveolar collapse, which are the main pathological characteristics of the common lung diseases in neonates with respiratory distress, such as MAS, RDS, and pneumonia, are shown as dense B-lines and/or alveolar interstitial syndrome with alveolar consolidation by LUS. The A-lines, which normally present in normal lung fields, should be unclear or disappear in these conditions. If the image of dense B-lines suddenly changes to fixed A-lines in parallel arrays, gas in the pleural cavity must be considered, and the junction where the B-lines change to A-lines is likely the landmark of lung point. In our study, the sensitivity of the absence of B-lines, the absence of lung sliding, and the existence of lung point were 100, 100, and 94.28%, respectively; the specificities were all 100%. The appearance of fixed A-lines without lung points in two lung fields was diagnosed as large PTX (more than 80%), similar to the 10 severe neonatal PTXs presenting without the presence of lung point in LUS images in Liu's study.[9]

Although small PTXs are important to be diagnosed early, especially in patients receiving positive pressure ventilation, and those with unstable hemodynamics, they are sometimes missed by CXR. In our study, a chest CT scan was performed as the gold diagnostic standard when the diagnosis of PTX was inconsistent between LUS and CXR. Eight infants underwent CT scan, including seven infants who were diagnosed PTX by LUS while missed by CXR and one infant who was graded medium bilateral PTX by LUS while small bilateral PTX by CXR. Chest CT scans for all the eight infants proved to be consistent with LUS diagnosis. Most of the PTXs were small and required chest tube placement soon after the CT scan. As far as we know, our study might be the only one in which a CT scan was performed to compare the sensitivity and specificity between LUS and CXR in the diagnosis of neonatal PTX.

In conclusion, our study confirms that the diagnosis of neonatal PTX by LUS is as reliable as conventional CXR and is even more sensitive, especially for small PTXs. The application of LUS in infants with suspected PTX can help with rapid and timely diagnosis, and thus in bedside treatment, and avoid unnecessary exposure to radiation. The limitation of our study is the retrospective nature of the study, and not all infants with PTX detected by LUS underwent a chest CT, which remains the gold standard for the diagnosis of PTX.

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Conflict of Interest

None declared.

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