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Clinical paper

Lung ultrasound during newborn resuscitation predicts the need for surfactant therapy in very- and extremely preterm infants

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Abstract

Introduction: Early identification of infants requiring surfactant therapy improves outcomes. We evaluated the accuracy of delivery room lung ultrasound (LUS) to predict surfactant therapy in very- and extremely preterm infants.

Methods: Infants born at $<32^{0/7}$ weeks were prospectively enrolled at 2 centres. LUS videos of both sides of the chest were obtained 5–10 min, 11–20 min, and 1–3 h after birth. Clinicians were masked to the results of the LUS assessment and surfactant therapy was provided according to local guidelines. LUS videos were graded blinded to clinical data. Presence of unilateral type 1 ('whiteout') LUS or worse was considered test positive. Receiver Operating Characteristic (ROC) analysis compared the accuracy of LUS and an FiO_2 threshold of 0.3 to predict subsequent surfactant therapy.

Results: Fifty-two infants with a median age of $27^{6/7}$ weeks (IQR $26^{0/7}$–$28^{6/7}$) were studied. Thirty infants (58%) received surfactant. Area under the ROC curve (AUC) for LUS at 5–10 min, 11–20 min and 1–3 h was 0.78 (95% CI, 0.66–0.90), 0.76 (95% CI, 0.65–0.88) and 0.86 (95% CI, 0.75–0.97) respectively, outperforming FiO_2 at the 5–10 min timepoint (AUC 0.45, 95% CI 0.29–0.62, p = 0.001). At 11–20 min, LUS had a specificity of 95% (95% CI 77–100%) and sensitivity of 59% (95% CI, 39–77%) to predict surfactant therapy. All infants born at 23–$27^{6/7}$ weeks with LUS test positive received surfactant. Twenty-six infants (50%) had worsening of LUS grades on serial assessment.

Conclusions: LUS in the delivery room and accurately predicts surfactant therapy in infants $<32^{0/7}$ weeks.

Keywords: Lung ultrasound, Preterm, Neonate, Surfactant, Oxygen, Delivery room, Diagnostic accuracy

Introduction

Non-invasive respiratory support has replaced routine mechanical ventilation and surfactant therapy as the initial respiratory strategy for premature infants with respiratory distress syndrome (RDS).[1] However, approximately 50% of infants born at $<32^{0/7}$ weeks eventually require surfactant.[2] Early surfactant decreases the risk of death and significant pulmonary injury in infants with RDS compared to delayed treatment.[1,3–5] Infants with RDS often have oxygen requirements that increase gradually until a predetermined threshold is reached for surfactant.[6] Thus, identifying infants in the

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delivery room who will eventually require exogenous surfactant may be beneficial.

Animal studies have shown that surfactant therapy increases both the uniformity and degree of lung aeration.[7,8] At birth, the surface area for gas exchange is initially low but increases exponentially as the lung aerates.[9] Increasing the fraction of inspired oxygen (FiO_2) increases the partial pressure gradient for oxygen diffusion and counteracts the effect of a low surface area on oxygen exchange of the partially liquid-filled lung. Thus, a higher FiO_2 in the delivery room likely indicates poor lung aeration, whereas surfactant therapy can increase the degree of lung aeration and thereby reduce the oxygen requirement.

In preterm infants, observational studies have shown that LUS reliably predicts the need for surfactant therapy after admission to the neonatal unit, typically 1–2 h after birth.[10–15] The characteristic LUS signs may however be identifiable immediately after birth. This would widen the diagnostic capability to include infants who may require surfactant therapy, including minimally invasive surfactant therapy (MIST), prior to admission to neonatal intensive care.[16] In healthy term infants, serial LUS showed the quick transition from a liquid-filled lung to an aerated lung capable of adequate gas exchange.[17,18] LUS can be performed at the bedside in real time, may be easily repeated in response to clinical changes, and avoids exposure to ionizing radiation.[19]

We aimed to characterise changes in LUS images immediately after birth for infants born at $<32^{0/7}$ weeks gestation and evaluate the diagnostic accuracy of LUS in predicting the need for surfactant therapy.

Methods

We performed a prospective, observational study of infants born at $<32^{0/7}$ weeks gestational age between January 2018 and December 2019. Study sites were two perinatal hospitals, Monash Medical Centre (MMC) and the Royal Women's Hospital (RWH), in Melbourne, Australia, together averaging more than 300 very and extremely preterm births per year. The study was approved by the ethics committees at both institutions (RWH reference number 16/35, MMC reference number RES-18-0000-693A) and registered with the Australian New Zealand Clinical Trials Registry (ACTRN12617001256369). This study is reported in accordance with the Standards for Reporting of Diagnostic Accuracy (STARD) guidelines.[20,21]

Study design

Infants born at $<32^{0/7}$ weeks without an antenatal diagnosis of congenital cardiopulmonary pathology were eligible for participation if a researcher was available to perform LUS scans. Antenatal parental consent was sought if time permitted at both hospitals. At MMC, infants were eligible for written, retrospective parental consent if there was insufficient time to discuss the study prior to birth.

At both institutions, most infants were initially managed with facemask CPAP using un-heated, un-humidified gases, pressures of 5–8 cmH_2O, and FiO_2 0.3, titrated to maintain SpO_2 of 80% by 5 min

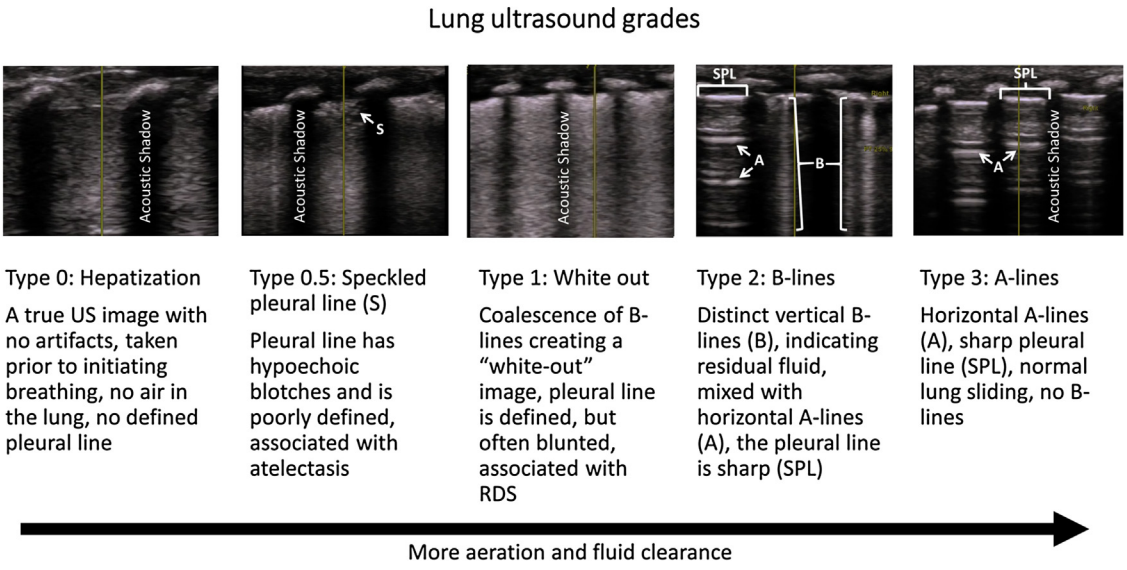


Fig. 1 – Grading system for lung ultrasound video recordings. Type 3 is seen in healthy lungs with a sharp pleural line, full aeration and liquid clearance, characterised by a lack of B-lines and the presence of horizontal, hyperechoic, repetitive A-lines. Normal lung motion with respirations, called lung sliding of the pleural line, should be present to distinguish type 3 lungs from an air leak syndrome. Type 2 is characterised by the discrete vertical B-lines, arising from a clearly defined pleural line, that cover A-lines. A-lines can be seen between the discrete B-lines. Type 1 images are created by the coalescence of vertical B-lines that produce a uniform, hyperechoic image called the "white-out" lung. A-lines are not visible in type 1 images. Type 1 is associated with respiratory distress syndrome. Type 0.5 and type 0 are associated with partially aerated lungs and liquid filled lungs, respectively. These images have been seen transiently as infants initiate breathing after birth, prior to establishment of the pleural line. Type 0.5 depicts the pleural line with a patchy appearance with poor definition, consisting of speckled hyperechoic areas mixed with hypoechoic lung tissue. Type 0 has been seen prior to the initiation of breathing and establishment of the pleural line. This is a true US image (no air artifacts) as the US beam passes exclusively through liquid and is described as lung hepatisation.

and 91–95% after 10 min. At MMC, at the discretion of the clinical team, bubble CPAP via a nasal mask with heated, humidified air was available for initial respiratory support. Infants requiring more support to maintain SpO_2 in this range were considered for intubation and surfactant therapy or minimally invasive surfactant therapy (MIST).[16,22] Indications for intubation while on CPAP included frequent apneas requiring stimulation, regardless of FiO_2 requirement. Intubation-surfactant-extubation (INSURE) and nasal intermittent positive pressure ventilation for primary respiratory support were not practiced at either institution.[23,24] At the RWH, high flow nasal cannula could be used for primary respiratory support following admission in infants ≥30 weeks with an FiO_2 requirement ≤0.3.[25]

Data collection

We obtained serial LUS video recordings using a GE Venue 50 ultrasound machine (GE Healthcare, USA) and an L8-18i transducer with a depth of 2 cm and a gain of 60. LUS was performed at 5–10 min, 11–20 min, 1–3 h, 12–24 h, and 24–72 h after birth.

The infant was placed in a plastic bag after birth to retain warmth and moisture. The LUS transducer was maneuvered into the bag and placed directly on the infant's skin on each side of the chest, in the axillary region, with the notch pointed towards the infant's head. The ultrasound gel was placed under the radiant warmer for a few minutes prior to the scan. The transducer was 3.5 cm long, typically capturing images from 2 to 3 intercostal spaces. During the first three timepoints, the infants were assessed in a supine position. At subsequent timepoints, the infants could be assessed in either prone or supine positions, thereby minimising handling. The transducer was adjusted until a "bat sign" was achieved and the image was optimised for the sharpest pleural line, most aeration, and least fluid retention.[26] Interpretation of LUS findings were not provided to the clinical team unless the researcher detected additional pulmonary pathology (e.g. pneumothorax, effusion). Lung ultrasound to determine RDS is not used in clinical practice in our institutions and most clinicians were not familiar with the interpretation of lung ultrasound images. When the attending clinician had ultrasound expertise, the investigators kept the images out of view of the clinical team. Mode of respiratory support, CPAP level or mean airway pressure, and FiO_2 were collected by the researcher at the time of each LUS. We also collected clinical and demographic information until discharge from hospital.

Lung ultrasound grading

LUS videos were scored at the end of study recruitment by 2 assessors blinded to all clinical data (SB and DB) using a previously validated system that grades each side of the chest on a scale of type 0–3 (Fig. 1).[17,18,27] For instance, Type 1/2 represents Type 1 lung on one side of the chest, and Type 2 lung on the other. Along this scale, type 1 (whiteout) is characterised by coalescence of "B-lines" representing retention of lung liquid/atelectasis, and type 3 is characterised by a lack of B-lines and the presence of "A-lines", representing full lung aeration. In instances of score disagreement, a third blinded assessor acted as an arbiter (OK).

Analysis

In the absence of data allowing formal sample size calculation, we prespecified a convenience sample of 50 participants for this observational study. Means and standard deviations with Student's t-test for comparisons are reported for normally distributed continuous variables. Medians with interquartile ranges with Mann Whitney U test for continuous variables or Wilcoxon signed rank test for ordinal variables, are reported when the distribution was skewed. The scores of the right and left side of the chest of each infant at each timepoint were summed and analyzed using a Friedman's test to determine changes in LUS over time. Three investigators, blinded to the infant's clinical condition, independently assigned LUS scores for 100 images. Interobserver agreement was tested using Kendall's W coefficient of concordance. We used Receiver Operating Characteristic (ROC) analysis to determine and compare the accuracy of LUS performed on infants receiving non-invasive ventilation at 5–10 min, 11–20 min,

Table 1 – Demographic and clinical information based on gestational age at birth.

N	Total 52	23–27 weeks 28	28–31 weeks 24
Gestational age, weeks ^{days}	$27^{6/7}$ ($26–28^{6/7}$)	26 ($25^{6/7}–27^{2/7}$)	29 ($28^{3/7}–30^{3/7}$)
Weight (g)	922 (744–1166)	775 (653–925)	1161 (926–1480)
Sex, male (%)	28 (54%)	17 (61%)	11 (46%)
Fetal growth restriction	14 (27%)	6 (21%)	8 (33%)
Two or more doses of antenatal steroids	32 (62%)	21 (75%)	11 (46%)
Antenatal magnesium sulfate	47 (90%)	25 (89%)	22 (92%)
Vaginal birth	16 (31%)	11 (39%)	5 (21%)
Rupture of membranes (hours)	0 (0–6)	0 (0–1)	0 (0–7)
Apgar 1 min	6 (5–8)	6 (4–7)	8 (6–8)
Apgar 5 min	8 (7–9)	8 (6–8)	9 (8–9)
Intubation in the delivery room	8 (15%)	7 (25%)	1 (4%)
Surfactant therapy	30 (58%)	22 (79%)	8 (33%)
Intubation (<72 h)	20 (38%)	18 (63%)	2 (8%)
Days invasive ventilation	0 (0–8)	8 (0–24)	0 (0–0)
Days invasive and non-invasive ventilation	57 (20–82)	79 (59–95)	19 (5–47)
Chronic lung disease	23 (44%)	17 (61%)	6 (25%)
Death	1 (2%)	1 (4%)	0 (0%)

and 1–3 h, and of FiO_2 at the time of each LUS, to predict ST using the DeLong method.[28] We used Youden's method to determine the optimum cut-off score for LUS and threshold for FiO_2.[29] For the selected cut-off values, we report test characteristics in terms of sensitivity, specificity, positive predictive and negative predictive values with corresponding 95% confidence intervals (CIs).

We used the pROC package in *R* version 3.6.2 (R Foundation, Vienna, Austria) and MedCalc for Windows, version 15.0 (MedCalc Software, Ostend, Belgium) for analysis.[30] Other statistical analyses were performed using IBM SPSS Statistics 21.0 (SPSS, Inc., Chicago, USA). Statistical significance was defined as $p < 0.05$.

Results

Fifty-two infants $<32^{0/7}$ weeks postmenstrual age were enrolled. Demographic and clinical details are shown in Table 1. We included 463 video recordings for analysis with no exclusions due to image quality. There were no pneumothoraces, pleural effusions, or congenital lung malformations. Infants remained stable during all LUS assessments. Kendall's W coefficient of concordance confirmed excellent inter-rater reliability between three assessors ($W = 0.96$, $p < 0.001$), which was consistent with previous studies.[17,18]

No LUS images were obtained for 2 infants at the 5–10 min timepoint due to the absence of an investigator (Fig. 2). Twenty-two infants were managed with non-invasive respiratory support and did not receive surfactant therapy. Ten additional infants did not require intubation but received surfactant therapy via MIST. Twenty infants were intubated by 72 h after birth, all received surfactant.

Lung ultrasound versus fraction of inspired oxygen to predict surfactant

Diagnostic accuracy evaluation was performed independently for each study timepoint for all infants until they were intubated, upon which subsequent assessments did not contribute to the diagnostic evaluation (Fig. 2). The optimal thresholds for predicting ST across timepoints were type 1 on at least one side of the chest for LUS, and FiO_2 of 0.3. While managed on CPAP, we observed the following test positive LUS grades: 1/2, 1/1, 0.5/1, and 0.5/0.5. We did not see LUS type 0 or the combinations of 1/3, 0.5/2, or 0.5/3. Using ROC analysis of diagnostic ability (Fig. 3), we found that LUS had an area under the curve (AUC) at 5–10 min, 11–20 min, and 1–3 h of 0.78 (95% CI 0.66–0.90), 0.76 (95% CI 0.65–0.88) and 0.86 (95% CI 0.75–0.97) respectively. FiO_2 produced lower AUCs of 0.45 (95% CI 0.29–0.62), 0.60 (95% CI 0.44–0.76) and 0.81 (95% CI 0.68–0.95) at the same three points after birth respectively. There was a statistically significant difference in AUC for LUS compared to FiO_2 at the first (5–10 min) timepoint ($p = 0.001$), but not at the 11–20 min ($p = 0.088$) or 1–3 h timepoints ($p = 0.473$).

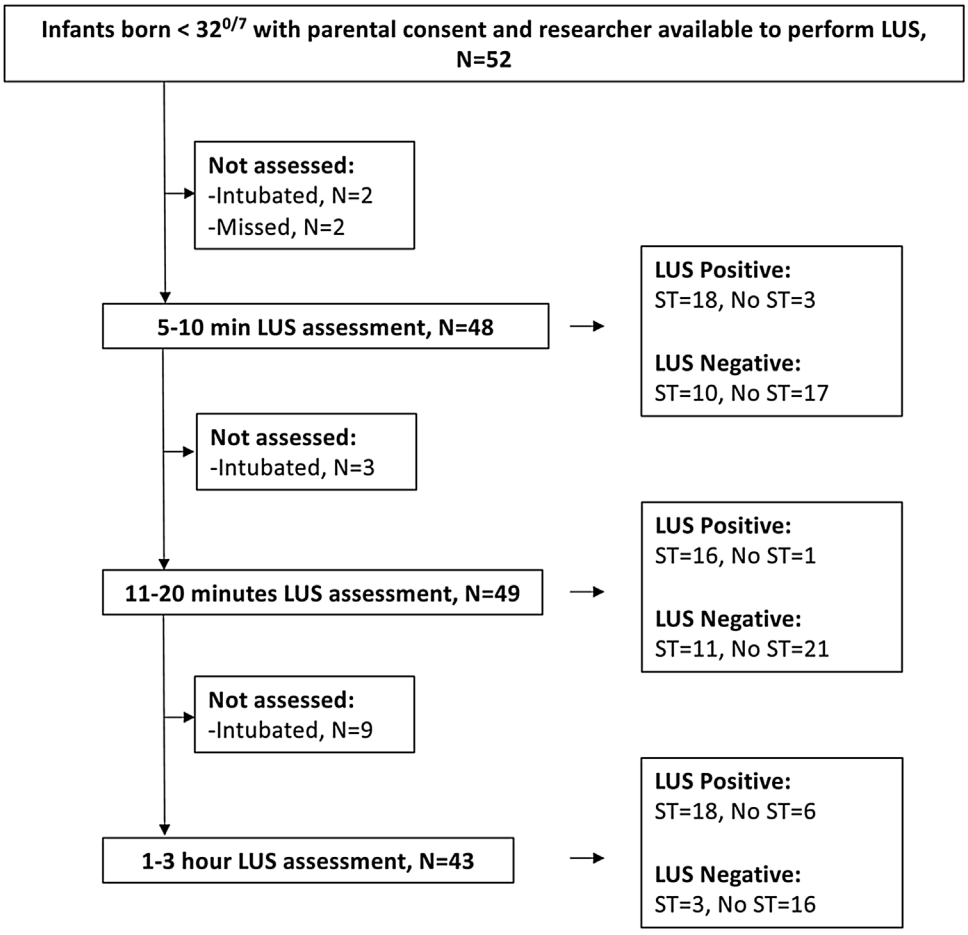


Fig. 2 – Participant flow diagram. Min = minutes, LUS = lung ultrasound, ST = surfactant therapy. Test positive for lung ultrasound is any type 1 grade or worse, on either side of the chest (i.e. grade 1/2, 1/1 or 1/0.5). Test negative is type 2 grade or better on both sides of the chest (i.e. grade 2/2, 2/3 or 3/3).

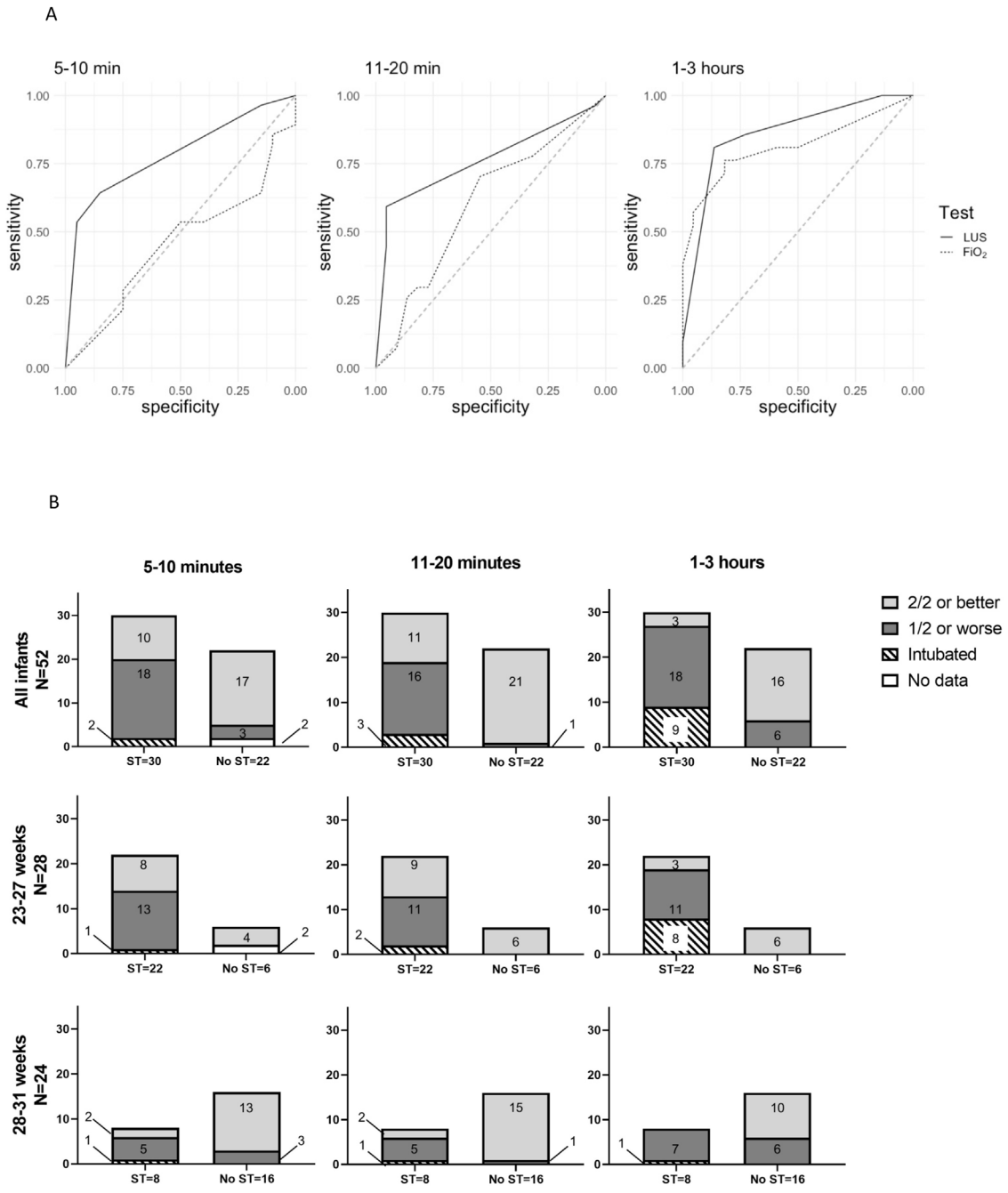


Fig. 3 – (A) Receiver Operating Characteristics curves for prediction of surfactant replacement therapy by lung ultrasound score (LUS, solid line) and fraction of inspired oxygen (FiO_2, interrupted line) at the 3 study timepoints (a, b and c, min = minutes). The diagonal interrupted line shows prediction by chance (Area Under the Curve = 0.5). (B) Distribution of lung ultrasound grades at each study timepoint for infants who did and did not subsequently receive surfactant. Top panel shows all infants, middle and lower panels show data within gestational age subgroups. In two infants, the researcher was unable to acquire LUS images at 5-10 min after birth. ST: surfactant replacement therapy, 1/2: type 1 or worse on at least one side of the chest, 2/2: type 2 or better on both sides of the chest.

Table 2 shows the test characteristics to predict surfactant therapy for type 1/2, type 1/1, and FiO_2 >0.3. Type 1/2 LUS had a specificity of 95% (95% CI 77−100%) and sensitivity of 59% (95% CI 39−77%) at 11−20 min to predict surfactant therapy. Type 1/1 LUS had 95% specificity (95% CI 77−100%) at both 5−10 min and at 11−20 min after birth for predicting surfactant therapy. Type 1/1 LUS reflects more severe lung atelectasis and impaired liquid clearance, thus improving specificity at the cost of sensitivity, which may be desirable in clinical practice. Further test characteristics by gestational age subgroup are given in the supplemental file [Supplemental Tables 1 and 2].

Table 2 – Test characteristics at each study timepoint to independently predict surfactant therapy. Test positive for lung ultrasound (LUS) 1/2 is type 1 grade or worse (i.e. grade 0 or 0.5) on either side of the chest. Test positive for LUS 1/1 is type 1 or worse on both sides of the chest. Results are presented as test characteristics with 95% confidence intervals. Min = minutes, hr = hours, FiO_2 = fraction of inspired oxygen.

Surfactant therapy

Time from birth	Sensitivity			Specificity		
	LUS 1/2	LUS 1/1	FiO_2 >0.3	LUS 1/2	LUS 1/1	FiO_2 >0.3
5–10 min, N = 48	64% (44–81%)	54% (34–72%)	46% (28–66%)	85% (62–97%)	95% (75–100%)	50% (27–73%)
11–20 min, N = 49	59% (39–78%)	44% (25–65%)	30% (14–50%)	95% (77–100%)	95% (77–100%)	77% (55–92%)
1–3 hr, N = 43	86% (64–97%)	81% (58–95%)	57% (34–78%)	73% (50–89%)	86% (65–97%)	95% (77–100%)
Time from birth	Negative predictive value			Positive predictive value		
	LUS 1/2	LUS 1/1	FiO_2 >0.3	LUS 1/2	LUS 1/1	FiO_2 >0.3
5–10 min, N = 48	63% (50–74%)	59% (49–69%)	40% (28–54%)	86% (67–95%)	94% (68–99%)	57% (42–70%)
11–20 min, N = 49	66% (55–75%)	58% (50–67%)	47% (39–56%)	94% (70–99%)	92% (63–99%)	62% (38–81%)
1–3 hr, N = 43	84% (64–94%)	83% (66–92%)	70% (59–79%)	75% (60–86%)	85% (66–94%)	92% (63–99%)

False positives and false negatives to predict surfactant: LUS and FiO_2

Eleven infants with an FiO_2 requirement >0.3 in the delivery room did not receive surfactant therapy and were considered false positives for FiO_2 requirement. Ten of the 11 (91%) infants had LUS type 2/2 or better and were correctly identified by LUS as not needing surfactant therapy. There were 20 infants with an FiO_2 requirement <0.3 in the delivery room who eventually received surfactant therapy and were considered false negatives for FiO_2 requirement. Fourteen of the 20 (70%) infants had LUS type 1/2 or worse and were correctly identified by LUS as needing surfactant therapy.

Eighty-five and 95% of infants who did not receive ST had LUS 2/2 or better at 5–10 and 11–20 min respectively. Three infants with type 2/2 at the 1–3 h assessment who received ST were 23–27 weeks (Fig. 4). Two were intubated for apneas with a low FiO_2 requirement and received surfactant after intubation. The third received ST via MIST. No infant ≥28 weeks with type 2/2 or better after neonatal intensive care unit (NICU) admission received ST. All infants born at $23–27^{6/7}$ weeks with type 1/2 LUS or worse received ST. There were 3 infants with type 1/2 or worse in the delivery room who did not receive ST and were considered false positives. All three infants were ≥30 weeks and ≥1400 g at birth.

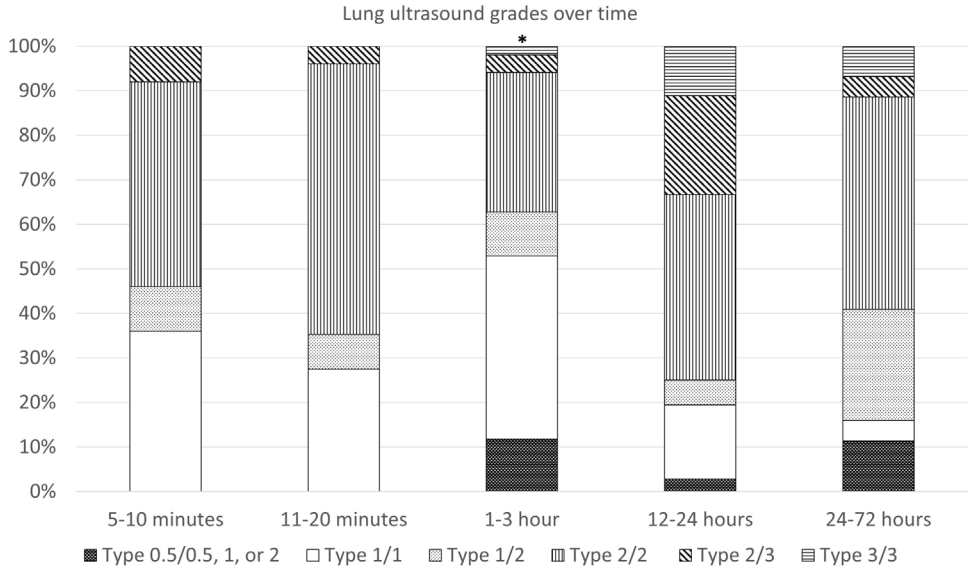


Fig. 4 – Changes in lung ultrasound over time. At each timepoint, the percentage of infants with each grade of lung ultrasound score is shown. For instance, Type 1/2 represents Type 1 lung on one side of the chest, and Type 2 lung on the other. For comparison between timepoints, the scores of the right and left sides of the chest for each infant at each timepoint were summed. Lung ultrasound grades at 1-3 h after birth were significantly lower than the other timepoints, shown by * ($p < 0.001$). There were no differences between the any other timepoints. All infants were included for this analysis (N = 52) regardless of level of respiratory support.

Lung ultrasound over time and "backsliding"

The median LUS grade assessed across all study participants (N = 52) changed over time, with the lowest median score measured at 1 −3 h after birth ($p < 0.001$), which was significantly different from all other timepoints (5−10 min, $p = 0.009$; 11−20 min, $p = 0.005$; 12−24 h, $p = 0.001$, 24−72 h $p = 0.001$, Fig. 4). No differences were seen between the other timepoints.

Twenty-six infants (50%) had lower LUS grades on subsequent assessments compared to their previous LUS score, either in the delivery room (11−20 min, 6 infants) or on admission to the NICU (1 −3 h, 20 infants). We have termed this "backsliding."[18] Infants with backsliding while on CPAP had a longer duration between rupture of membranes and birth ($p = 0.046$), otherwise, there were no significant predictive patient characteristics (Supplemental Table 3). Infants with backsliding while on CPAP were more likely to require intubation than infants on CPAP who did not have backsliding ($p = 0.01$).

Seven of the eight (88%) infants intubated in the delivery room had backsliding following intubation, prior to the administration of surfactant in the NICU. Two of these infants had backsliding twice, seen at 11−20 min while on CPAP and, again, after intubation, at the 1 −3 h timepoint.

There were 10 infants that had a grade of 0.5 on at least one side of the chest, at a minimum of one timepoint. All 10 infants received surfactant therapy and 9/10 were intubated. No grades of 0.5 were seen at 5−10 min. In 4 infants, type 0.5 was observed only after intubation including the only infant with type 0.5 at 11−20 min.

Response to surfactant therapy and lung ultrasound

Thirty infants received surfactant. Two infants were intubated prior to the first LUS assessment. The first dose was given at a median time of 2.5 h (IQR 2−3.4) with median FiO_2 of 36.5% (IQR 28−49%). Adding the LUS score of both sides of the chest together, the median LUS score prior to receiving surfactant while on CPAP was 2 (IQR 2−2), which improved to 3 (IQR 2−4, $p = 0.001$) at a median of 2.5 h (IQR 0.5 −21) after surfactant was given. Supplemental oxygen decreased to 25% (IQR 21−28, $p = 0.001$) after surfactant therapy. Five out of thirty infants had backsliding after surfactant therapy was given. Two of these infants had received MIST and showed backsliding while on CPAP, backsliding was seen in the other 3 after intubation.

Discussion

This is the first delivery room study to assess the utility of LUS and report on the evolution of LUS score after birth in very- and extremely preterm infants. We found that LUS is feasible to perform, has good diagnostic accuracy for surfactant therapy using the axillary view, and can track the progress of lung aeration over the first few hours after birth.

Studies have shown that LUS performed upon admission to neonatal intensive care can predict the need for surfactant therapy.[10,12] A recently published trial suggests that using LUS after NICU admission to guide surfactant therapy decreased the time to receive surfactant and increased the clinical response to surfactant versus using an FiO_2 threshold in infants <32 weeks.[14] Our study suggests that delivery room LUS may identify infants requiring surfactant therapy even sooner after birth, while also widening the diagnostic capability to include the significant proportion of infants who are intubated and/or receive surfactant therapy prior to NICU admission. Although we did not measure the time taken to obtain LUS images, they were typically acquired with less than 30 s of direct patient contact on each side of the chest. Images were captured at ≥5 min after birth, when the infant was typically breathing regularly while being supported on facemask CPAP. We targeted periods of relative physiologic stability for the LUS assessments to minimise interference with the clinical care and to capture images during the time that the clinical team would be considering transfer to the NICU on CPAP versus intubation prior to transport.

Early surfactant administration in premature infants with RDS have improved outcomes.[5] LUS changes consistent with RDS may precede clinical signs which may not appear until several hours after birth. In the delivery room, an FiO_2 threshold of 0.3 produced more false positives (11 infants) and false negatives (20 infants) than LUS. LUS correctly identified that 10/11 of the FiO_2 false positives would not need surfactant and that 14/20 of the FiO_2 false negatives would need surfactant, including 100% of the extremely preterm infants.

Furthermore, we found that surfactant therapy significantly improved the LUS grading indicating better lung aeration. This is consistent with the observation that surfactant therapy greatly increases the uniformity of lung aeration and the distribution of ventilation in preterm rabbits.[7] Rapid identification of poor lung aeration using LUS may facilitate targeted surfactant in the delivery room for infants likely to benefit most from the treatment.

LUS may be able to provide critical feedback in real time to optimise respiratory management in neonates. A high proportion (88%) of infants displayed backsliding following intubation in the delivery room, suggesting that an increase in positive end-expiratory pressure may have reversed backsliding in infants being managed with invasive ventilation.[31] Further studies are warranted to determine whether LUS has utility for determining optimal PEEP levels in intubated and ventilated infants. Similarly, 21 of the 26 infants demonstrating backsliding were initially managed on CPAP, which raises the question as to whether the introduction of CPAP or higher CPAP levels may have reversed the backsliding.

The time related changes in LUS grading and the relatively high incidence of backsliding is particularly interesting and provides further evidence that lung aeration is not a unidirectional process. It has been well documented in animal studies that airways can refill with liquid, particularly in the immature lung in the absence of an end-expiratory pressure.[9] The finding that overall LUS grading was lowest at 1−3 h after birth, even compared with 5−10 min after birth, raises several important questions. As spontaneous breathing is primarily responsible for lung aeration after birth and the clearance of liquid that re-enters the airways between breaths, backsliding may indicate breathing fatigue leading to airway reflooding and/or atelectasis. As infants with backsliding while on CPAP were more likely to be intubated, backsliding may provide an early signal that an infant's respiratory drive is unable to maintain lung aeration or that distending pressure from the CPAP was insufficient. However, we did not observe a consistent pattern in FiO_2 changes in infants with backsliding, albeit, our numbers are small. Specifically, looking at the 21 infants with backsliding while on CPAP: 9 had an increase in FiO_2, 6 had no changes in FiO_2, and 6 had a decrease in FiO_2. We feel backsliding warrants consideration in future studies and validation by other investigators.

Like backsliding, LUS type 0.5 was seen most in intubated infants. Type 0.5 was previously observed in term infants as they initiated breathing after birth and is theorised to represent atelectasis.[17]

Atelectasis may be caused by more severe RDS, a poorly positioned endotracheal tube, or loss of functional residual capacity in infants who receive muscle relaxants prior to intubation.[32,33]

Our study has several limitations, including the observational design, a small cohort, and a clinically important variation in gestational age. Nevertheless, the fact that over 50% of infants were <28 weeks gestation allows generalization of our findings to extremely preterm infants. A further strength was that LUS score was graded blind to the clinical course. It will be important to validate the accuracy and reliability of our findings when LUS is performed in real-time at the bedside, alongside clinical information by a wider range of clinicians.

Future studies are needed to investigate whether adjustments in respiratory support change the appearance of LUS in preterm infants with poor lung aeration. LUS may be able to optimise individual patient care by enabling clinicians to improve the timeliness and appropriate targeting of interventions. Such work would establish the basis for larger trials investigating clinically important outcomes for preterm infants managed using LUS as an auxiliary tool in the delivery room.

Conclusions

Lung ultrasound in the delivery room is a specific predictor of failure of non-invasive respiratory support, especially in extremely preterm infants. Earlier detection of infants needing an increase in CPAP pressure or surfactant may improve clinical outcomes, but larger studies are needed.

Authors' contributions

I can confirm that all authors have made substantial contributions to all of the following: (1) the conception and design of the study, or acquisition of data, or analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, (3) final approval of the version to be submitted. We received no writing assistance for the preparation of this manuscript.

Conflicts of interest

None.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.resuscitation.2021.01.025.

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