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Original Research

The importance of lung recruitability: A novel ultrasound pattern to guide lung recruitment in neonates

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Abstract.

BACKGROUND: Lung Ultrasound (LUS)-guided Lung Recruitment Maneuver (LRM) has been shown to possibly reduce ventilator-induced lung injury in preterm infants. However, to avoid potential hemodynamic and pulmonary side effects, the indication to perform the maneuver needs to be supported by early signs of lung recruitability. Recently, a new LUS pattern (S-pattern), obtained during the reopening of collapsed parenchyma, has been described. This study aims to evaluate if this novel LUS pattern is associated with a higher clinical impact of the LUS-guided LRMs.

METHODS: All the LUS-guided rescue LRMs performed on infants with oxygen saturation/fraction of inspired oxygen (S/F) ratio below 200, were included in this cohort study. The primary outcome was to determine if the presence of the S-pattern is associated with the success of LUS-guided recruitment, in terms of the difference between the final and initial S/F ratio (Delta S/F).

RESULTS: We reported twenty-two LUS-guided recruitments, performed in nine patients with a median gestational age of 34 weeks, interquartile range (IQR) 28–35 weeks. The S-pattern could be obtained in 14 recruitments (64%) and appeared early during the procedure, after a median of 2 cmH2O (IQR 1–3) pressure increase. The presence of the S-pattern was significantly associated with the effectiveness of the maneuver as opposed to the cases in which the S-pattern could not be obtained (Delta S/F 110 +/- 47 vs 44 +/- 39, $p = 0.01$).

CONCLUSIONS: Our results suggest that the presence of the S-pattern may be an early sign of lung recruitability, predicting LUS-guided recruitment appropriateness and efficacy.

Keywords: Intensive care, mechanical ventilation, neonatal, respiratory distress syndrome, point-of-care diagnostics, respiratory insufficiency, ventilator-induced lung injury

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List of Abbreviations

CDP Continuous Distending Pressure
D-Pattern Dead space-Pattern
HFOV High-frequency oscillatory ventilation
IQR Interquartile range
LUS Lung Ultrasound
LUSTR Lung Ultrasound Targeted Recruitment
LRM Lung Recruitment Maneuver
NICU Neonatal Intensive Care Unit
OSI Oxygen Saturation Index
S/F Oxygen Saturation/ Fraction of Inspired Oxygen ratio
S-group Sunray-Pattern group
nS group group not showing the Sunray Pattern
S-Pattern Sunray-Pattern
VILI Ventilator Induced Lung Injury

1. Introduction

Ventilator-induced lung injury (VILI) is a major determinant of mortality and morbidity in the Neonatal Intensive Care Units (NICUs) [1]. The lung recruitment maneuver (LRM) is often performed in ventilated patients to optimize mechanical ventilation and decrease the risk of VILI, by reducing atelectotrauma and regional overdistension [2, 3]. LRMs provide a transient increase in transpulmonary pressure, "recruiting" collapsed respiratory units [4], to evenly distribute the tidal volumes in the lungs and improve gas exchange. Since no reliable measure of lung volumes and/or direct evidence of lung derecruitment and recruitability are currently available in neonates, LRMs are routinely guided by oxygen saturation as a surrogate of lung aeration [5, 6]. Recently, LUS has been proposed as a tool to increase the effectiveness of LRMs performed in the first hours of life, improving the overall outcome of preterm infants suffering from respiratory distress syndrome before surfactant administration [7]. The impact of LUS in rescue LRMs in ventilated critically ill infants has not been investigated yet. Particularly in this critical setting, the indication to perform the maneuver needs to be supported by early signs of lung recruitability in order to avoid detrimental hemodynamic and pulmonary side effects. We recently described a novel LUS pattern, named Sunray(S)-pattern [8], developing in the reopening parenchyma during LRM as a sign of lung recruitability. This retrospective study aimed to evaluate if the presence of the S-pattern was associated with a higher rate of success of the LUS-guided LRM in terms of oxygen saturation/fraction of inspired oxygen (S/F) improvement after the procedure. We also provided a detailed description of the LUS pattern evolution in the patients undergoing rescue LUS-guided LRM.

2. Material and methods

2.1. Patients and equipment

All the infants undergoing LUS-guided recruitments between January 2019 and August 2021 were included in this retrospective cohort study. The maneuver was performed in the case of severe respiratory conditions, expressed as an S/F ratio below 200 [9].

LUS examination was executed by an expert neonatologist, trained and experienced in LUS, using a high-frequency linear probe (9–16 MHz) with General Electric Medical System LOGIQ S8 or with Mindray DC8-EXP ultrasound machines. Lung recruitment procedures were performed in mechanically ventilated patients either with VN500 (Draeger, Lubecca, Germany) or with Sensor medics 3100A (Carefusion, San Diego, USA).

This retrospective study was approved by the local ethics committee (Board name: Comitato Etico della Romagna, C.E.ROM.; approval number: 4510; protocol number 8317/2021; study ID number 2484), and conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki.

All the infants were well sedated during the maneuver. No muscle relaxant was used.

2.2. LUS-guided Lung Recruitment Maneuver

The procedure was designed according to a standardized protocol [10]. Before the LRM, LUS was systematically performed on all lung fields: anterior superior, lateral superior, posterior superior, anterior inferior, lateral inferior, and posterior inferior for the right and left sides [11].

Four sonographic aeration patterns could be obtained before starting an LRM (Fig. 1):

- A-pattern – normal aeration represented by pleural sliding and A-lines with no more than 2 well-defined B-lines per lung field;
- B1-pattern – presence of A-lines and at least 3 B-lines per lung field;
- B2-pattern – complete disappearance of A-lines due to coalescent B lines;

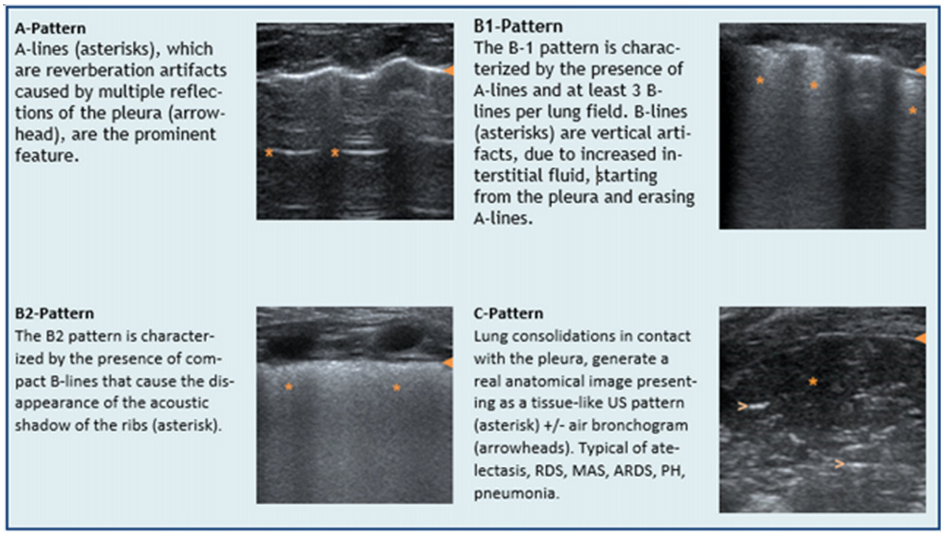

Fig. 1. Main Lung Ultrasound (LUS) patterns before Lung recruitment (LR).

– C-pattern – lung consolidation in contact with the pleura, presenting as a tissue-like ultrasound pattern.

If a B2- or C-pattern was detected on LUS before LRM (Fig. 2), after the exclusion of any corrigible causes of lung collapse (e.g., endotracheal tube misplacement), a LUS guided recruitment was started.

In the case of uneven distribution of the sonographic aeration, the neonate was positioned to maintain the most severely affected lung fields on the upper side, with a constant ultrasound monitoring during the maneuver to visualize the progressive parenchymal re-aeration. Lung recruitment was performed through a stepwise increase of airway pressure, either positive end-expiratory pressure (PEEP) during conventional mechanical ventilation (CMV) or continuous distending pressure (CDP) during high-frequency oscillatory ventilation (HFOV).

Airway pressure was augmented by 1 cmH2O every 1-2 minutes until the lung consolidation completely disappeared (C-pattern converted into a B2 or B1 pattern) or the aeration loss significantly improved (B2 pattern converted in B1 or A): the corresponding level of airway pressure was defined as opening PEEP/CDP. In cases where no improvement of the initial LUS pattern could be obtained during the LUS guided recruitment, the opening pressure was set at the pressure where oxygen saturation did not improve for 2 steps of pressure or began to fall, as a sign of lung over-distension.

After finding the opening pressure, PEEP/CDP was reduced stepwise until LUS began to show signs of lung consolidation or aeration loss in the lung field previously monitored. The corresponding airway pressure was defined as closing PEEP/CDP

Then, the optimal PEEP/CDP was set right above the closing pressure. In the case of atelectasis development/persistence in other lung fields, the infant was positioned again to maintain the atelectatic lung field on the upper side and another LRM was performed.

A thorough LUS follow-up was performed 1 hour, 6 hours, and 12 hours after the end of the maneuver.

2.3. Study groups

After retrospectively revising all the LUS material, the study group was divided into two cohorts of lung recruitments based on the development or the absence of the S-pattern during the procedure, constituting the S-group and the nS-group, respectively.

The S-pattern is characterized by the presence of vertical hyperechoic lines starting from the reopening bronchi and therefore represents the sonographic sign of lung re-aeration. These vertical artifacts were named Sunray(S)-lines, as they resemble the sun rays crossing the clouds. The S-pattern was defined by the appearance of at least one S-line per field (13).

2.4. Data collection

Clinical data were retrospectively retrieved from medical records. The following clinical characteristics were collected: gestational age (GA); birth weight (BW); underlying lung disease, defined as (i) respiratory distress syndrome (RDS) [12], (ii) neonatal acute respiratory distress syndrome (NARDS), following neonatal sepsis [13], (iii) lung derecruitment during MV detected at chest X-ray or LUS, (iv) meconium aspiration syndrome (MAS); days of life at recruitment; incidence of bronchopulmonary dysplasia (BPD), defined as oxygen dependency at 36 weeks post-menstrual age in infants with less than 32 week's GA [14]; duration of MV; length of stay; survival. In regards to the LRM, the following data were retrieved: mode of ventilation (HFOV or CMV); type of ventilator (VN500, Draeger, Lubecca, Germany or Sensormedics 3100A, Carefusion, San Diego, USA); Continuous Distending Pressure (CPD) or Positive End Expiratory Pressure (PEEP), FiO2, pre-ductal SpO2, blood pressure, and heart rate at each time point (start, opening, and optimal pressure); duration of clinical/sonographic benefit, defined as hours without respiratory deterioration and/or LUS evidence of atelectasis after LRM; air leaks within 12 hours from the LRM. To assess the severity of the lung disease we used the following parameters: the S/F ratio [9] and oxygen saturation index (OSI = CDP × FiO2/pre-ductal SpO2) [15].

Sonographic data included: the type of lung pattern before LRM; the development or the absence of the S-pattern; the steps of pressure needed to obtain the S-pattern (when applicable) and the lung pattern at the end of the procedure.

Ultrasound images and videos for the LRMs were retrospectively analyzed by two independent operators to assess the presence of the S-pattern and the type of lung patterns throughout the procedure. No disagreements were reported in this phase.

2.5. Study bias

Selection bias was avoided by including all the infants undergoing the rescue procedure (S/F) ratio below 200 during the period of time taken into consideration. Bias due to loss to follow-up, was not relevant to this study, as there is no follow-up. The misclassification bias was avoided by applying the same protocol for measuring or evaluating the health outcomes in exposed patients. Confusion bias and interaction bias were addressed through multiple linear regressions including the most important confounding variables.

2.6. Primary and secondary outcomes

The primary outcome was the efficacy of the LRM, defined as the difference between the final and the initial S/F ratio (delta S/F ratio). A secondary efficacy outcome in patients undergoing HFOV ventilation was the difference between the final and the initial oxygen saturation index (delta OSI). A secondary safety outcome was the development of pneumothorax with and without the need for chest drain within 12 hours from the LRM.

2.7. Statistical analysis

In order to determine the sample size, we performed an internal analysis of the LRMs performed with the standard method and found a mean delta S/F ratio of 70 + /-25 during the procedure. Assuming an improvement of 50% with LUS guidance developing S-pattern, the minimal sample size to detect significance was 8 recruitments per group considering an alfa error of 0.05 and a beta error of 0.2. However, in order to further avoid selection bias, all the recruitments meeting the inclusion criteria during the study period were included.

To compare the characteristics across the S-group and nS-, the Chi-square test of independence and an F-test were performed for categorical and continuous variables, respectively. A one-way nested ANOVA (ANalysis Of VAriance) was conducted for each comparison group to determine whether the differences between the group means were statistically significant and to take into account the nested structure of the data as multiple observations are associated with the same patient. To this end, the response variable was log-transformed to normalize its distribution when needed.

Finally, a multiple linear regression model was used to estimate the association between the S/F ratio and relevant explanatory variables based on the theory. The same multiple linear regression model was used with OSI as the response variable. The mean was reported with the SD (standard deviation), and the IQR (interquartile range) with the median for the characteristics related to the observations and the patients, respectively. All model assumptions were checked for each model, furthermore, the models were evaluated for multicollinearity, without detecting any relevant effect.

No missing data regarding the variables of interest (delta S/F and delta OSI) were reported. Variables with a significant number of missing data were excluded from the analysis.

As a result of the multiple linear regression, we reported the unstandardized regression coefficient (B) which describes how much the dependent variable is expected to increase when an independent variable increases by one, holding all the other independent variables constant. We then reported the standard error for the unstandardized beta (SE B), to describe the variation around the estimates of the regression coefficient; the *t*-test statistic (t), and the *p*-value.

All statistical analyses were performed by a statistician (LA), using the statistical software R (Version 4.1.2, R Development Core Team, Austria).

Table 1
Clinical characteristics of the patients included in the LUSTR group

Characteristics	LUSTR group $n = 9$
Weeks of gestation, median (IQR)	34 (28 – 35)
BW in grams, median (IQR)	2015 (750 – 2320)
Days of invasive ventilation, median (IQR)	18 (10 – 22)
Days of non-invasive ventilation, median (IQR)	40 (30 – 53)
BPD incidence, n (%)*	2 (100)
Survival, n (%)	5 (55.5)
Days of hospital stay, median (IQR)	114 (80 – 126)

Abbreviations: IQR, interquartile range; GA, gestational age; BW, birth weight; BPD, bronchopulmonary dysplasia. *BPD refers to patients with GA below 32 weeks only ($n = 2$).

3. Results

3.1. LUS pattern evolution during LUS-guided recruitment

Twenty-two LUS-guided recruitments, performed on nine infants, were included in the study. The main characteristics of the patients enrolled are reported in Table 1. The LUS pattern before recruitment was B2 (Fig. 2) in four cases (18.1%), while the remaining eighteen recruitments (81.9%) started from C-pattern (Fig. 2). No correlation was found between the starting LUS pattern and underlying pulmonary condition. Moreover, the underlying pulmonary condition was neither correlated with the initial respiratory picture (starting S/F, starting OSI) nor with the efficacy of the LRM (delta S/F, delta OSI) (data not shown).

The initial LUS findings were correlated with the severity of the pulmonary disease, expressed as the initial S/F ratio. In particular, an initial C-pattern reflected a more severe pulmonary condition as opposed to the B2 pattern (83.2 +/- 12.9 vs 112.8 +/- 36.4, p 0.014). However, the success of the maneuver, in terms of delta S/F was not significantly associated with the initial LUS pattern (45.5 +/- 58.9 vs 95.1 +/- 50.6, p 0.19, for B2 and C-pattern, respectively).

During the procedure, the C-pattern evolved into the S-pattern in 77.8% of the cases ($n = 14$), within a median of 2 steps of pressure increase (IQR 1–3, range 1–4). Subsequently, the S-patten evolved into a homogeneous B2-pattern in all the cases, within a median of 9 pressure steps (IQR 6–11, range 3–18) (Fig. 2). No clinical deterioration or oxygen desaturation was detected in any of the patients that developed the S-Pattern during the maneuver. In the remaining four cases starting from the C-pattern and not developing the S-pattern (22.2%), LUS showed only an increased air bronchogram during the stepwise augmentation of airway pressure, without signs of parenchymal re-aeration, suggesting that only dead space was being recruited. For this reason, we named this pattern dead space (D)-pattern (Fig. 2). In these cases, the opening pressure was set at a median of 4.5 steps of pressure (IQR 3–5.5, range 2–6), when oxygenation started to drop as a sign of pulmonary over-distention, although LUS opening pressure could not be obtained. None of the 4 LRMs starting from the B2-pattern developed the S-pattern. In one case (25%) the B2 evolved into the B1-pattern, while the other 3 LUS findings remained unchanged throughout the recruitment procedure (Fig. 2). In these cases, the opening pressure was set at a median of 9 steps of pressure (IQR 7.5–10, range 4–11), after the drop in oxygenation. The lung recruitment evolving from B2 to B1-pattern did not show any improvement in the S/F ratio, while the other 3, had modest improvement in S/F ratio with very high variability (60.7 +/- 61.9).

3.2. Comparison between S-group and nS-group

To verify if the evolving LUS pattern could early predict the success of the maneuver, and therefore constitute a sign of lung recruitability, the group of LRMs that developed the S-pattern, S-group ($n = 14$), was compared to the nS-group ($n = 8$), constituted by the LRMs in which the S-pattern could not be obtained. The main clinical and procedural charac-

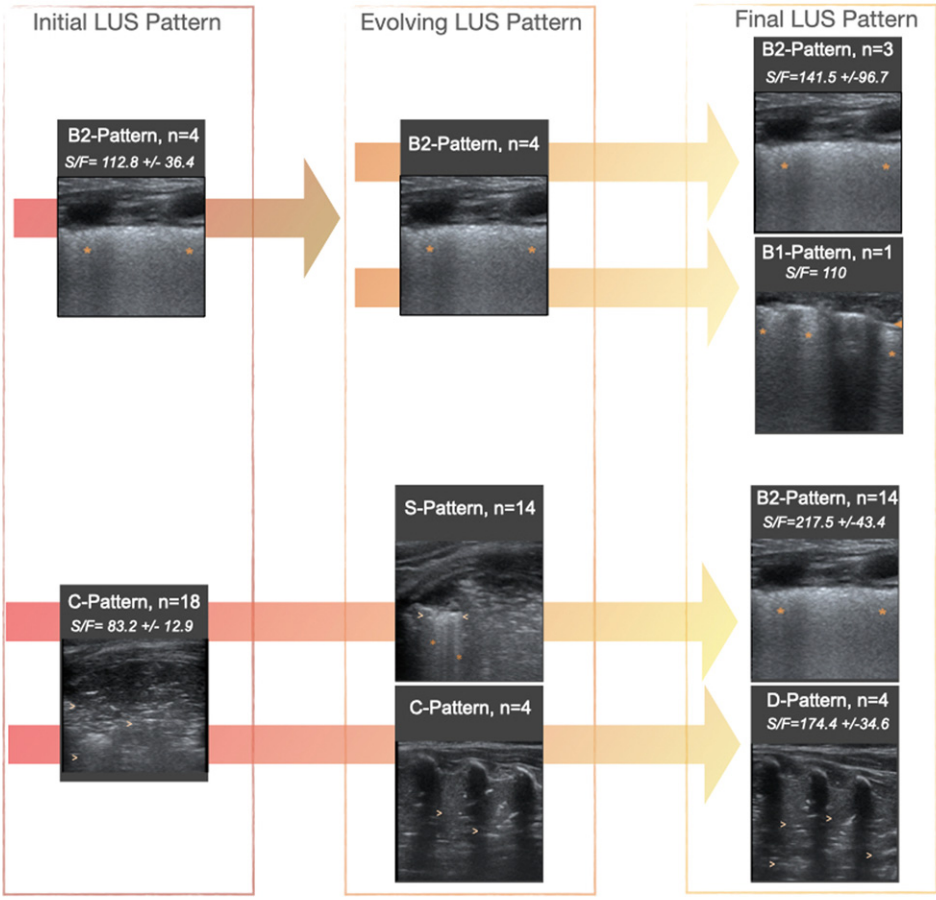

Fig. 2. Possible sonographic trajectories during Lung recruitment. The initial B2-pattern evolved into a final B1 pattern in 3 out of 4 cases and remained unchanged throughout LR in the remaining 3 cases. The C-pattern evolved in the Sunray (S) Pattern and finally into a B2-pattern in 14 out of 18 LRs. In the remaining 4 cases, the C-pattern ultimately converted into a Deadspace (D)-pattern. *D-lines. The different LUS patterns are correlated with the saturation/fraction of inspired oxygen (S/F) ratio reported as means +/- standard deviation.

teristics of the maneuvers are summarized in Table 2. There were no significant differences in the clinical conditions before LRM between the two groups.

In the S-group, the improvement in the S/F ratio (Delta S/F) was significantly more pronounced than in the nS-group (110 +/- 47.3 vs 44.2 +/- 39.2, p 0.003) (Fig. 3). This difference remained significant (p 0.007) after adjusting for initial S/F ratio, underlying lung disease, gestational age, ventilation mode, type of ventilator, and days of life (Table 3). The delta OSI showed a trend towards an improved value in the S-group as compared to the nS-group, without reaching statistical significance (8.2 +/- 6.8 vs 4.6 +/- 6.9, p 0.31). The opening CDP was higher in the S-group as opposed to the nS-group (27.1 +/- 2.7 vs 22.6 +/- 3.1, p 0.008). No air leaks were detected in either group.

4. Discussion

Our study shows the association between the recently described S-pattern and the success of the LUS-guided pulmonary recruitment in critically ill neonates suffering from severe respiratory insufficiency. The S-pattern represents the sonographic counterpart of the anatomical distal lung unit aeration during LRMs. Therefore, it can only be visualized in the recruitable lung, potentially identifying the neonates that can benefit from the recruitment maneuvers. In the last years, LUS has increasingly been used by neonatologists as it is a non-invasive, low-cost, fast, repeatable tool, which does not require patient transportation outside the NICU [20]. Moreover, the point-of-care LUS learning curve is relatively “shallow”[16], with very good reliability on lung aeration

Table 2
Characteristics of the S-group and nS-group

Characteristics	nS-group ($n = 8$)	S-group ($n = 14$)	*p*
Day of life, mean (SD)	19.4 (20.7)	14.8 (7.9)	0.46
Lung condition, n (%)			0.42
Derecruitment during MV	4 (50)	5 (35.7)	
NARDS	2 (25)	7 (50)	
RDS	1 (12.5)	2 (14.3)	
MAS	1 (12.5)	0	
LUS starting pattern, n (%)			**0.019**
b2	4 (50)	0	
c	4 (50)	14 (100)	
LUS final pattern, n (%)			**0.003**
b1	1 (12.5)	0	
b2	3 (37.5)	14 (100)	
D	4 (50)	0	
SpO2, mean (SD)			
Starting	86 (9)	82 (12.5)	0.41
Final	92 (3)	95 (3)	**0.01**
FiO2, mean (SD)			
Starting	0.85 (0.18)	0.82 (0.19)	0.75
Final	0.66 (0.22)	0.45 (0.08)	0.005
S/F ratio, mean (SD)			
Starting	107.3 (31.8)	107.5 (38.1)	1
Final	151.6 (45)	217.5 (43.4)	**0.003**
Delta	44.2 (39.4)	110 (47.3)	**0.003**
OSI, mean (SD)			
Starting	16.6 (5.4)	16.9 (8.1)	0.93
Final	12 (5.9)	8.8 (6.8)	0.11
Delta	4.6 (6.9)	8.2 (6.8)	0.31
HFOV, n (%)	6 (75)	13 (92.9)	0.59
CDP(cmH2O), mean (SD)			
Starting	14.7 (2.1)	15.9 (4.5)	0.53
Opening	22.6 (3.1)	27.1 (2.7)	**0.008**
Optimal	14.7 (2.1)	18.4 (4.2)	0.062
CMV, n (%)	2 (25)	1 (7.1)	
PEEP (cmH2O), mean (range)			
Starting	5.5 (5 – 6)	5	0.67
Opening	8	10	NA
Optimal	6.5 (6 – 7)	7	0.88
Ventilator type, n (%)			0.36
VN500	4 (50)	11 (78.6)	
Sensormedics 3100A	4 (50)	3 (21.4)	
Duration of benefit (hours), median (IQR)	2 (1.5 – 8)	7 (5 – 27)	0.29

Abbreviations: SD, Standard deviation; MV, mechanical ventilation; NARDS, Neonatal Acute Respiratory Distress Syndrome; RDS Respiratory distress syndrome; MAS, meconium aspiration syndrome; LUS, lung ultrasound; LR, Lung recruitment; SPO2, Oxygen Saturation; FiO2, Fraction of Inspired Oxygen; S/F, SpO2/FiO2; OSI, Oxygen saturation index; HFOV, High-frequency oscillatory ventilation; CDP, Continuous distending pressure; CMV, Conventional mechanical ventilation; PEEP, Positive end-expiratory pressure.; IQR, interquartile range.

[17]. LUS-guided recruitment is a promising strategy to optimize invasive ventilation, as it is based on the direct visualization of the reopening pulmonary parenchyma. LUS-guided recruitment, performed in premature infants suffering from RDS, was shown to mitigate lung inflammation, shorten the duration of invasive ventilation and reduce the length of stay as opposed to the standard oxygenation-guided procedure [7]. In this study, Shady and colleagues found no failure of the LRM with a constant improvement in the LUS pattern after the LRM (mostly starting from a B2 pattern). Only B1 or A patterns were detected at the end of the procedure. On the contrary, we did find LRM not showing any sonographic improvement and not leading to a significant increase in terms of the S/F ratio. In particular, LRMs with an initial B2-pattern did not benefit from a LRM. The recruitments starting from a B2 pattern remained unchanged, except for one case that evolved into a B1 pattern and showed the worst absolute outcome in terms of delta S/F ratio.

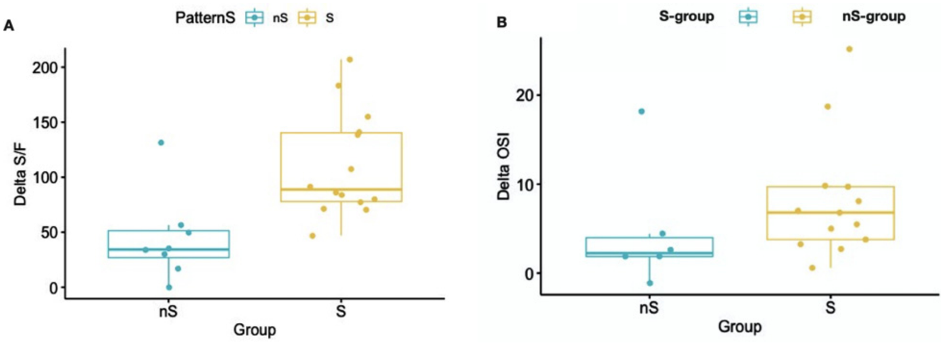

Fig. 3. A: Difference between initial and final Oxygen saturation/Fraction of inspired oxygen ratio (Delta S/F) in the S group and nS group. B: Difference between initial and final Oxygen saturation Index (Delta OSI) in the S-group and nS-Group.

Table 3
Multiple linear regression for the difference (delta) between the final and the initial Oxygen Saturation/Fraction of Inspired Oxygen (S/F) ratio

Variables	B	SE B	*t*	*p*
S pattern, present	70.57	22.32	3.16	**0.007**
Ventilator type, Sensormedics 3100A	7.69	32.03	0.24	0.81
Days of life	0.71	1.08	0.66	0.52
GA	–3.72	3.19	–1.17	0.26
Starting S/F	–0.45	0.35	–1.28	0.22
Underlying lung disease,				
NARDS	–16.91	23.82	–0.71	0.50
RDS	45.03	34.97	1.29	0.33
MAS	40.57	55.57	0.73	NA

Abbreviations: B, unstandardized beta; SEB, standard error for the unstandardized beta; t, *t* test statistic; p, probability value; GA, Gestational age, NARDS, Neonatal Acute Respiratory Distress Syndrome; RDS Respiratory distress syndrome; MAS, meconium aspiration syndrome.

On the other hand, when the LUS guided recruitment started from a C-pattern we found 2 possible scenarios. In the case of early S-pattern development, the maneuver was associated with a significantly better clinical outcome. The presence of the S-pattern allowed to considerably increase the airway pressure until the consolidation was no longer visible on LUS (disappearance of the S-pattern and appearance of the B-pattern), without clinical deterioration or risk of air leaks. However, although the S-pattern could only develop from the C-pattern, the presence of the initial C-pattern itself was not predictive of the success of the maneuver. In fact, if no S-pattern was visualized within 4 pressure steps, the retrospective revision of the LUS material showed increased air bronchogram without any evidence of respiratory unit reopening. We named this pattern D-pattern, being a sign of dead-space recruitment. This scenario was associated with a poor response to the LRM.

Infants enrolled by Shady et al. were all suffering from RDS (yet untreated with surfactant), which may account for differences in clinical and sonographic outcomes between our two studies. Infants with RDS are known to benefit from recruitment maneuvers before surfactant administration [18]. Indeed, both groups (the LUS-guided recruitment and the oxygen guided recruitment group) showed a striking improvement in the oxygen saturation and oxygen need [7]. On the contrary, in our population, LUS-guided LRM was performed as a rescue approach in severe cases of respiratory failure, demonstrated by the dramatically low starting S/F ratio as compared to the previous study [7]. Moreover, we did not perform LUS guided recruitment as elective procedures (i.e. before the first surfactant administration in preterm infants suffering from RDS). Patients with more heterogeneous underlying respiratory diseases in terms of physiopathology and spatial distribution, such as neonatal acute respiratory distress syndrome [13], may show in some cases a poor response to the procedure [19]. However the factors associated with response the LRM have not been identified yet [19]. Consistently, in our analysis, neither the initial LUS pattern nor the initial conditions were associated with the success of the LRM, leaving no reliable indications to choose the good candidates for the LRM. Patients with poor response to surfactant or severe neonatal acute respiratory distress syndrome are known to be difficult to ventilate, often failing standard approaches [13]. In this population, that constituted our study group, we found that the development of the S-pattern was the only variable independently associated with the success of the LRM, as demonstrated by the multivariate analysis including gestational age, days of life, severity of lung disease (expressed as initial S/F ratio), underlying lung disease and type of ventilator. The recruitments displaying the S-pattern obtained delta S/F ratios with an average of 70-point higher than the LRM in which the S-pattern could not be detected (Table 3). None of the infants displaying the S-pattern suffered from clinical deterioration during the maneuver despite the need of a much higher increase in airway pressure to obtain lung derecruitment resolution. On the contrary, the LRM that did not obtain an S-patter had to be interrupted because of oxygen desaturation during the maneuver. When present, the S-pattern appeared during the early phase of the procedure, making it a promising sonographic sign to guide the LRM. Moreover, the evaluation of the S-pattern revealed a very good level of inter-operator agreement, since no conflicts emerged from the retrospective evaluation of the LUS material. LUS offers the possibility to early detect the responder to lung recruitment through the presence of the S-pattern. The absence of the S-pattern may allow to early interrupt the LRM in patients that are going to show a poor response possibly avoiding further cardiorespiratory instability, that may be detrimental. In support of these observations, our group recently compared in a case-control study the fourteen LUS guided recruitment maneuvers described in this paper that displayed the S-pattern, to fourteen lung recruitment maneuvers guided by the standard oxygenation method. The LRMs were matched by severity of lung disease and type of lung disease [20]. As compared to the standard approach, the sonographic guidance of lung recruitability based on the S-pattern development, was associated with a higher success of the procedure in terms of Delta S/F and a trend towards a lower incidence of pneumothorax, suggesting that a Lung Ultra Sound Targeted Recruitment (LUSTR) protocol, based on early detection of lung recruitability and LUS-guided postural recruitment, may improve the efficacy and safety of LRMs in critically ill neonates [20].

Our work has limitations, including the retrospective nature of the study and the technical impossibility in neonates to compare the LUS results with other pulmonary measurements (such as pressure-volume curves and static compliance values). To avoid volutrauma, pressure step-up was interrupted as soon as the LUS signs of consolidation disappeared, and the B-pattern was obtained. However, higher airway pressure may be necessary to achieve full recruitment of the most peripheral lung units. No X-ray was systematically performed before and after the recruitment, and overdistension could not be excluded in any of the groups.

The primary outcome is focused on the respiratory improvement given by the specific LRM. Other clinically relevant outcomes could not be compared as four patients had both LRM with and without S-pattern development during their ventilation.

Lastly, despite no conflicts emerging in the retrospective evaluation of LUS material, it must be mentioned that LUS is an operator-dependent technique.

5. Conclusions

The development of a rescue LUS guided recruitment protocol including the S-pattern as an early sign of lung recruitability and appropriateness of the procedure may improve the success rate of the LUS guided recruitment in infants failing standard approaches. The absence of the S-pattern after a maximum of 4 pressure steps and the development of the D-pattern suggests that the LRM should be interrupted, to avoid clinical deterioration and potential side effects. Further large prospective trials are needed to confirm our results.

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Conflict of interest

The authors have no conflict of interest to disclose. Preliminary results of this study were presented as a poster presentation at the jENS congress 2021. The data of this article are available upon request.

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Reprints

No reprints will be ordered.

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