ORIGINAL ARTICLE

Lung Ultrasound Score as a Predictor of Clinical Severity and Prognosis in Patients of Ventilator-associated Pneumonia

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Abstract

Background*:* To estimate a correlation between change in lung ultrasound aeration score (LUSS) and mortality in patients with ventilator-associated pneumonia.

Materials and methods*:* We conducted a prospective observational study in which lung ultrasound, the partial pressure of arterial oxygen to fraction of inspired oxygen ratio (PaO_2/FiO_2 ratio), and static lung compliance were performed for five consecutive days since the diagnosis of ventilator-associated pneumonia (day 1–5) in a 20-bed multidisciplinary intensive care unit in at a tertiary care academic institute in Northern India. A hundred and seventeen ventilated patients were studied for the first 5 days after ventilator-associated pneumonia (VAP) development. Lung ultrasounds were performed with an ultrasonography machine using a round-tipped probe of 2–5 MHz at six different areas of each hemithorax, which includes superior and inferior in anterior, lateral, and posterior lung fields. Patients with a decreased LUSS of 2 were labeled as responders. A decrease of LUSS of less than 2 or an increase of LUSS were leveled as nonresponders.

Results: The correlation between the change in LUSS between days 1 and 5 was significant with 28-day mortality (26.3% in responders vs 87.8% nonresponses with $p < 0.001$)

Conclusion: The responders to treatment for VAP described by LUSS had lower mortality than non-responders.

Keywords: Lung compliance, Lung monitoring, Oxygenation, Pneumonia, Ultrasonography, Ventilator-associated.

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Highlights

- The responders to treatment for ventilator-associated pneumonia (VAP) described by the lung ultrasound aeration score (LUSS) had lower mortality than nonresponders.

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Introduction

Ventilator-associated pneumonia is a commonly occurring hospital-acquired infection, affecting up to one-quarter of mechanically ventilated patients.[1] It adversely affects patient care by prolonging intensive care stay, needs for a prolonged duration of mechanical ventilation, and tremendous use of hospital resources.[2–4] Early diagnosis and monitoring of VAP is an essential step in treatment and reducing the cost arising from the infection.

Although a chest radiograph is an essential element in monitoring VAP, due to its inherent shortcomings, it lacks reliability and diagnostic accuracy in mechanically ventilated patients.[5,6] Although computed tomography (CT) thorax is the most appropriate investigation for measuring lung aeration and its variations, it requires the patient to be transported out of the intensive care unit (ICU). It exposes them to high radiation and the risk of transportation.[7,8] Lung ultrasound (LUS) is a simple, non-invasive bedside tool that was considered unsuitable for lung scanning for decades as the ultrasound beam cannot cross the air-filled structures at the interface of visceral pleura, and ordinarily, aerated lung tissue is ultimately reflected.[9] However, in lung consolidations, as the air is replaced by fluid, ultrasound transmission is possible if the lesion and the pleural surface are in direct touch.[10,11] Lung ultrasound has been used to diagnose VAP in the previous study.[12] The LUSS has also been proven reliable for quantifying lung aeration compared to the gold standard CT scan in VAP.[13] Different levels of aeration loss correlate with different ultrasonic imaging patterns. Hence, various treatment options for VAP should change the LUSS. Whether the change in LUSS is correlated to the patient's clinical outcome during VAP is not yet established. So, this prospective observational study was conducted to establish a correlation between change in LUSS and 28-day mortality in VAP.

Materials and Methods

Patients with a diagnosis of VAP as per clinical pulmonary infection score (CPIS) of ages >18 years were included in the study. The diagnosis of VAP was established with CPIS ≥ 6.[14] Patients with morbid obesity, evidence of disseminated malignancy, chronic obstructive pulmonary disease, interstitial lung disease, and subcutaneous emphysema, and the presence of thoracic dressings were excluded from the study.

Ethical approval was granted by the institutional ethics committee, AIIMS, Rishikesh, AIIMS/IEC/19/828 (dated 10/05/19). The trial was prospectively registered with Clinical Trials Registry-India CTRI/2020/10/028480. All procedures followed were by the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Patients meeting the study protocol were enrolled for the trial after receiving informed permission and approval from the institutional ethical committee. An investigator not involved in patient management performed an LUS with an ultrasonography machine using a 2–5 MHz round-tipped probe (LOGIQe, GE Healthcare, USA). Using the parasternal, anterior-axillary, and posterior axillary lines as anatomic landmarks, respectively, it was assessed at six locations of each hemithorax, superior, and inferior area in anterior, lateral, and posterior fields. Outcome data were recorded. A lung ultrasound was performed for five consecutive days since the diagnosis of ventilator-associated pneumonia (Day 1 to Day 5). The change in LUSS between the first and the fifth day was calculated by subtracting the Day 5 LUSS from Day 1 LUSS. We assumed a delta change of 2 in LUSS would favor an improvement in the clinical outcome because the change of 2 in LUSS is required for the diagnosis of VAP.[15] Patients with a decreased LUSS of 2 were leveled as responders. Those patients without a decrease of LUSS of 2 or an increase of LUSS were levelled as nonresponders. The change in LUSS between the first and the third day was also calculated by subtracting the Day 3 LUSS from Day 1 LUSS. Patients with a decrease of LUSS of 2 were levelled as responders on day 3. The partial pressure of arterial oxygen to fraction of inspired oxygen ratio (PaO_2/FiO_2 ratio) was also calculated within 15 minutes of LUS on those five days by obtaining PaO_2 from arterial blood gas analysis (ABG) (Phox ultra ABG machine; Nova Biomedical, US). Plateau pressure was also measured at the same time by using an inspiratory pause on the ventilator (Nellcor Puritan Bennett, Medtronic, US), and static lung compliance (Cstat) was calculated by using the formula (Cstat = Tidal volume/Plateau PEEP). An independent investigator blinded to other outcome parameters recorded the ABG variables and lung compliance. A physician blinded to the study protocols was involved in patient care and management. Following their ICU hospitalization, all study participants received conventional medical management and care in accordance with evidence-based guidelines, which were monitored for a period of 28 days, if discharged it was followed up with a telephone conversation.

Primary Outcome

The primary outcome of this study was to estimate a correlation between the change in LUSS between the first day to the fifth day of development of VAP with 28-day mortality.

Secondary Outcome

The secondary outcomes were (i) to compare the difference between baseline characteristics between responders and non-responders, (ii) to estimate a correlation between responders and nonresponders on day 3, and (iii) to estimate a correlation between LUSS with oxygenation and (iv) to estimate a correlation between LUSS with lung compliance and plateau pressure in patients with VAP.

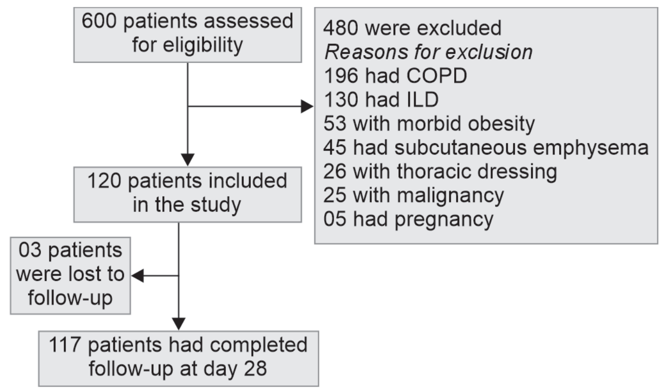

Fig. 1: STROBE diagram of patients recruited for the study

Lung Ultrasound Score Measurement

Ultrasound parameters are characterized into four patterns and defined as follows:

- Normal aeration: The presence of lung sliding with A lines (N).
- Moderate loss of aeration: Three or more well-spaced B-lines. (B1).
- More severe loss of aeration: Coalescent B-lines or subpleural consolidation (B2).
- Complete loss of aeration: The presence of dynamic bronchograms (C).

The lung ultrasonography aeration score was computed as follows: points were assigned based on the least favorable ultrasonography pattern detected for every location of interest., and the total score is 0–36:

- $N \rightarrow 0$
- $B1 \rightarrow 1$
- $B2 \rightarrow 2$
- $C \rightarrow 3$

Statistical Analysis

The statistical program for social science, version 23 (SPSS-23, IBM, USA), was used to conduct the statistical analysis. The median interquartile range (IQR) or number (percentage), whichever is appropriate is used to summarize the findings, which are displayed as descriptive statistics. The primary outcome was analyzed using the Chi-square test, and the secondary outcome analysis was done using Pearson Correlation.

Results

A total of 600 patients were assessed for eligibility during this study period from June 2019 to November 2021, of which 480 patients were excluded due to various reasons as mentioned above. A total of 120 patients were enrolled in the study; of these, 3 patients were lost to follow-up, and finally, 117 patients had complete follow-up at day 28 (Fig. 1). The two groups' baseline patient characteristics were comparable (Table 1).

Of the 117 patients, 76 were responders and 41 were non-responders. Mortality among responders was 26.3% (20 out of 76)

Table 1: Baseline characteristics of participants

Characteristic	*All*	*Responder*	*Non-responder*	*p-value*
Age	45 (40–58)	48 (40–60)	45 (40–58)	0.61
Sex-no. (%) Male	81 (69.2)	50 (65.7)	31 (75.6)	
BMI	25.4 (23.2–27.8)	25.5 (24.5–27.3)	24.7 (22.8–28.8)	0.56
APACHE II	14 (10–20)	12 (10–18)	16 (14–23)	<0.001
SOFA	8 (5–12)	8 (5–12)	9 (5–12)	0.224
HR	118 (103–133)	109 (100–132)	120 (118–141)	<0.001
SBP	107 (96–137)	107 (96–136)	110 (100–140)	0.397

All data are shown in median (Interquartile Range). APACHE, acute physiology and chronic health evaluation II; BMI, body mass index; HR, heart rate; SBP, systolic blood pressure; SOFA, sequential organ failure assessment

Table 2: Clinical outcomes of responder vs non-responders

Characteristic	*Responder*	*Non-responder*	*p-value*
Days of hospitalization	33 (31–52)	24 (13–30)	<0.001
Days of mechanical ventilation	20 (10–26)	14 (11–25)	0.235
28-day mortality	26.31% (20/76)	87.8% (36/41)	<0.001

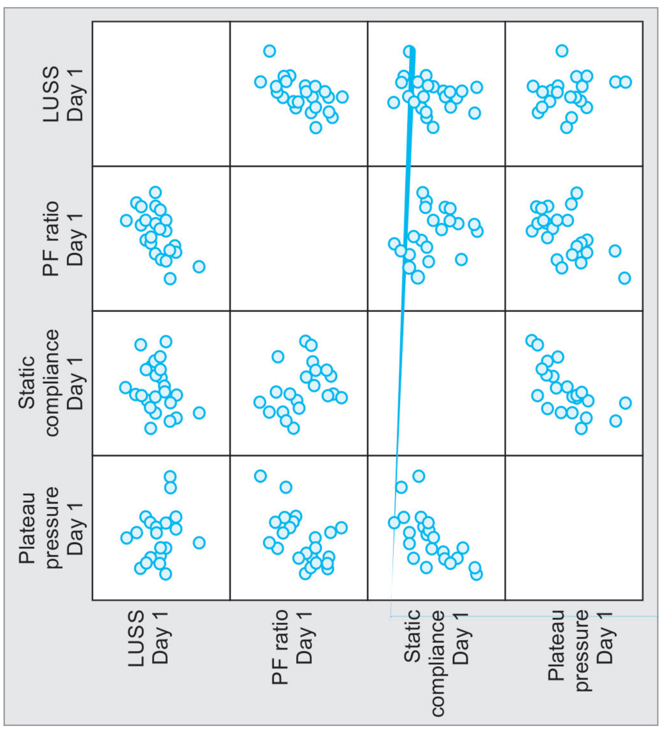

Fig. 2: Scatter plot depicts the correlation between LUSS and PaO_2/FiO_2 ratio, static compliance, and plateau pressure on day 1

and 87.8% (36 out of 41) among nonresponders. This difference was found to be statistically significant ($p < 0.001$) (Table 2).

The correlation was calculated for all five days (Day 1–5) between

- LUSS with PaO_2/FiO_2, static compliance and plateau pressure.

A Pearson correlation analysis was performed to explore these relationships, which has been shown using scatter plots. (Figs 2 to 6). Significant correlations were found between LUSS and with PaO_2/FiO_2 ratio on all 5 days.

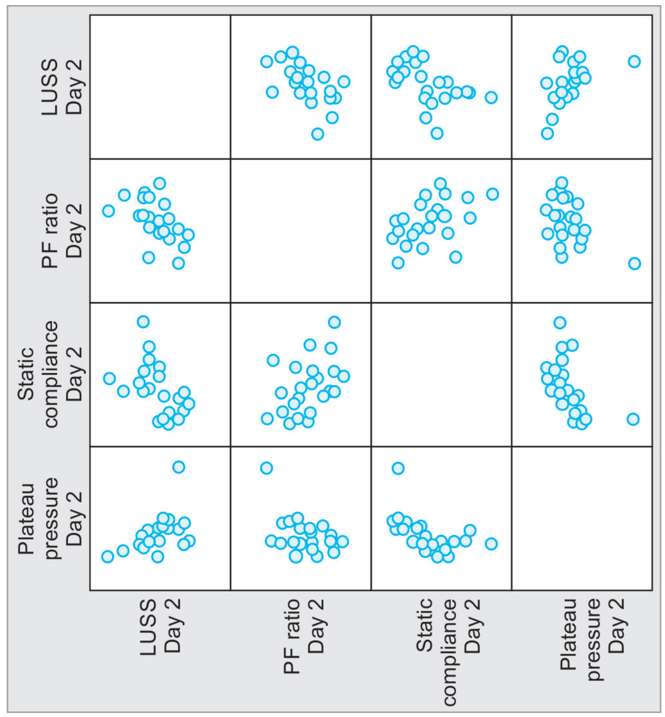

Fig. 3: Scatter plot depicts the correlation between LUSS and PaO_2/FiO_2 ratio, static compliance, and plateau pressure on day 2

The first-day results revealed several significant correlations. First, a strong negative correlation ($r = -0.601$, $p < 0.01$) was found between LUSS and PaO_2/FiO_2, indicating that as LUSS increased, PaO_2/FiO_2 tended to decrease. Second, a moderate negative correlation ($r = -0.229$, $p < 0.05$) was observed between LUSS and static compliance. Third, a significant positive correlation ($r = 0.277$, $p < 0.01$) emerged between LUSS and plateau pressure. Furthermore, our analysis revealed a moderate positive correlation ($r = 0.347$, $p < 0.01$) between PaO_2/FiO_2 and static compliance, a strong negative correlation ($r = -0.543$, $p < 0.01$) between PaO_2/FiO_2 and plateau pressure, and an even stronger negative correlation ($r = -0.668$, $p < 0.01$) between static compliance and plateau pressure. These findings provide valuable insights into the relationships among these variables, which may have important implications for understanding and managing the studied condition.

Utilizing Pearson's correlation analysis, we also observed a moderate positive correlation ($r = 0.577$) between the responder and responder on day 3 with a p-value of less than 0.001.

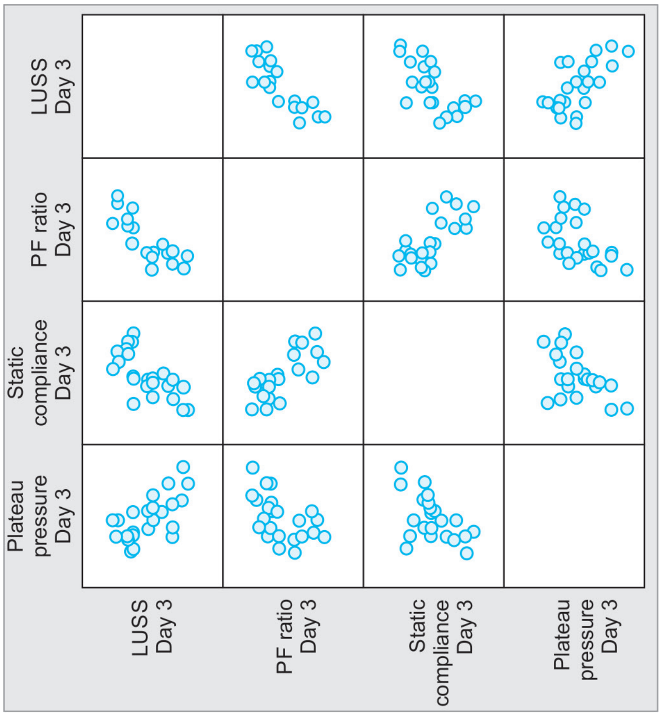

Fig. 4: Scatter plot depicts the correlation between LUSS and PaO_2/FiO_2 ratio, static compliance and plateau pressure on day 3

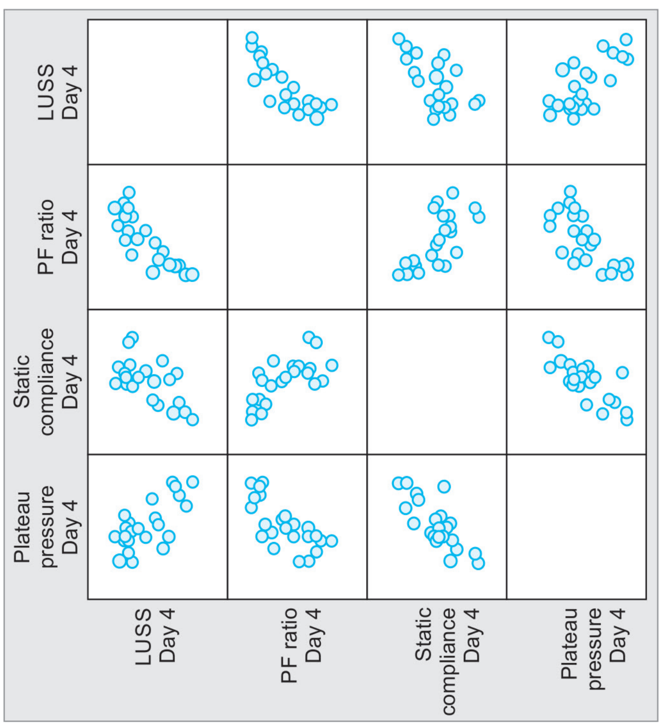

Fig. 5: Scatter plot depicts the correlation between LUSS and PaO_2/FiO_2 ratio, static compliance and plateau pressure on day 4

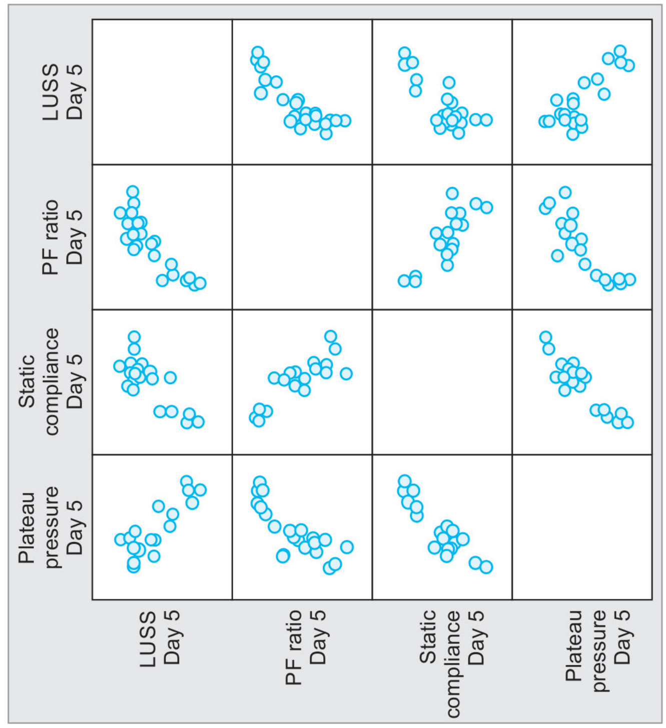

Fig. 6: Scatter plot depicts the correlation between LUSS and PaO_2/FiO_2 ratio, static compliance and plateau pressure on day 5

Discussion

The preliminary work in this prospective observational study provides validation for the use of change in LUSS in patients with VAP. We found that the decrease of LUSS of 2 on the fifth day of development of VAP in comparison to the first day is associated with reduced 28-day mortality. We also found significant negative correlations between LUSS with oxygenation (PaO_2/FiO_2 ratio) on all 5 days. The correlation of LUSS with static compliance and plateau pressure was also statistically significant in all 5 days.

Chest radiographs, although an essential element in monitoring VAP, lack diagnostic accuracy in mechanically ventilated patients.[5,6] They are limited by the posture of the patient, the presence of several indwellings and monitoring lines, its anteroposterior nature, and the presence of common pathologies like pleural effusion and atelectasis in a critically ill patient.[16] CT, though considered the gold standard for measuring lung aeration and its variations,[7,8] is limited by the risk of high radiation exposure and transportation out of the ICU.[9,10] However, LUS is a simple, nonradiating, noninvasive bedside technique that has been successfully applied to diagnose VAP.[17–19] Bouhemad et al. established a significant correlation between CT thorax and ultrasonography lung reaeration following antibacterial therapy in ventilator-associated pneumonia.[13] Tsubo et al. also found a significant correlation of consolidated areas in the left lung evaluated using transesophageal echocardiography with those estimated with CT.[19]

In this study, we did LUS, ABG, static compliance, and plateau pressure measurements simultaneously to reflect the effect of the particular ventilator settings on each of these parameters. In a prospective study, Luna et al. evaluated the performance of the CPIS and its components to identify the initial course of VAP. They demonstrated that patients who received appropriate therapy saw a significant improvement in their PaO_2/FiO_2 ratio, whereas those who received insufficient therapy saw a deterioration. Only the PaO_2/FiO_2 ratio among the CPIS's constituent components was able to distinguish survivors from non-survivors.[20] We found significant negative correlations between LUSS with oxygenation (PaO_2/FiO_2 ratio) in all 5 days. Our findings are in line with those of Li L et al., who found that LUSS and the PaO_2/FiO_2 ratio in ARDS patients had a comparable negative connection ($r = -0.755$, $p < 0.001$).[21] In line with the earlier research, there was a statistically significant link between LUSS and static compliance throughout each of the 5 days.[22] Our study revealed that a decrease of LUSS of 2 on the fifth day of development of VAP in comparison to the first day is associated with reduced 28-day mortality. The association of mortality with lack of improvement in LUSS may be used clinically for escalation of therapy or prolonging the course of antibiotics therapy in VAP. We also found a good correlation between the responder and the non-responder at day 3. Hence, by day 3, there is a good chance to review antibiotics based on LUS findings. After therapeutic interventions such as optimizing positive end expiratory pressure (PEEP) and antibiotics, LUSS significantly decreases as aeration of the lung increases and static lung compliance increases. It might be a useful, non-invasive bedside tool for clinical weaning decision-making. As the calculation of static compliance requires an absence of any spontaneous effort, the use of LUSS can be used for patients with spontaneous respiratory effort. Ntoumenopoulos G et al. in their prospective cohort study involving ten patients on VV ECMO established a robust negative correlation between LUSS and dynamic compliance (r_s (33) = −0.66, $p < 0.001$).[23] This study provides some insight into the use of LUSS as a surrogate measure of lung aeration and lung mechanics for weaning during VV-ECMO. Tsubo et al. also observed a significant correlation between PaO_2/FiO_2 ratio and consolidated area in ARDS, and during the application of PEEP, as the area of consolidation decreased, oxygenation also improved.[19]

Our study has a few limitations; first, LUS detects the infection extending to the visceral pleura so that it can underestimate the severity, and with therapy as pneumonia resolved from visceral sites, it may underestimate LUSS on follow-up. However, a strong correlation between LUSS and PaO_2/FiO_2 ratio suggests that the change at the periphery represents the change in the whole lung. Second, monitoring static compliance in sedated patients who were not on neuromuscular blockade may have a minor influence on the results. Third, LUS is unsuitable for certain conditions like subcutaneous emphysema, morbidly obese patients, and thoracic dressing, which may interfere with optimal ultrasonography image acquisition.

Conclusion

The responders to treatment for VAP described by lung ultrasound score had lower mortality than non-responders.

Ethics Approval and Consent to Participate

Ethical approval was granted by the institutional ethics committee, AIIMS, Rishikesh AIIMS/IEC/19/828 (dated 10/05/19). The trial was prospectively registered with Clinical Trials Registry-India CTRI/2020/10/028480.

Quick Look

The LUSS has also been proven reliable for quantifying lung aeration compared to the gold standard CT scan in VAP. Different ultrasound patterns correspond to different degrees of aeration loss. Hence, therapeutic interventions for VAP should change the LUSS. Whether the change in LUSS is correlated to the patient's clinical outcome during VAP is not yet established.

This prospective observational study showed a strong correlation between LUSS and oxygenation. We also observed that those who were responders to treatment as described by LUSS had lower mortality than the non-responders.

Clinical Trials Registry India (CTRI) Registration

The trial was prospectively registered with Clinical Trials Registry India CTRI/2020/10/028480.

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