THE ULTRASOUND JOURNAL 2026; VOL. 18: 18843 DOI: 10.5826/TUJ.2026.18843 MATTIOLI 1885

ORIGINAL RESEARCH PAPERS

The predictive value of different lung ultrasound protocols for extravascular lung water in septic shock patients

YUAN DING[1,2], FENG QIAN[3], YANG FENG[3], BIN ZHU[2] AND YIBO MA[3]

[1]Department of Critical Care Medicine, Jiangsu Province Hospital of Chinese Medicine, Nanjing, China; [2]Department of Critical Care Medicine, The Third Affiliated Hospital of Soochow University, Changzhou, China; [3]Department of Ultrasound, The Third Affiliated Hospital of Soochow University, Changzhou, China

ABSTRACT

Background: Currently, the role of lung ultrasound (LUS) in the diagnosis and treatment of patients with septic shock is widely recognized. Various LUS protocols and scoring criteria have been proposed, yet a unified LUS protocol for assessing lung water in these patients remains lacking.

Methods: Forty-six septic shock patients underwent LUS with three scanning schemes (4-region, 8-region, BLUE) alongside pulse indicated continuous cardiac output (PiCCO) monitoring. Spearman correlation analysis was used to compare the correlation between the three ultrasound scoring schemes, PiCCO and other clinical laboratory indicators. At the same time, the value of three LUS protocols for assessing pulmonary water in septic shock patients was evaluated using receiver operating characteristic (ROC) analysis.

Results: Spearman's correlation analysis showed a significant correlation between extravascular lung water index (EVLWI) and 4-region, 8-region, or the Bedside Lung Ultrasound Examination (BLUE) protocol. More importantly, the BLUE protocol showed a stronger correlation with EVLWI than the 4-region protocol and the 8-region protocol (r=0.634, 0.458, 0.546, $p<0.001$). The ROC curve analysis showed that ultrasound protocols could predict the early occurrence of pulmonary edema in septic shock patients (EVLWI>7 mL/kg), diagnosis of pulmonary edema (EVLWI>10 mL/kg), and evaluation of pulmonary fluid severity (EVLWI≥15 mL/kg).

Conclusions: Our study found that septic shock patients were prone to pulmonary edema during fluid resuscitation, and ultrasound scoring could help us quantify pulmonary edema. Among the 4-region, 8-region and BLUE protocols, the BLUE protocol shows relatively better overall performance in predicting lung water elevation and evaluating edema severity.

Key words: Septic shock, Extravascular pulmonary water index, Pulmonary edema, Lung ultrasound

Received: 13 March 2026 | Accepted: 14 April 2026

Correspondence: Yibo Ma / Department of Ultrasound, The Third Affiliated Hospital of Soochow University, Changzhou, China / E-mail: mayibo@czfph.com;
Bin Zhu / Department of Critical Care Medicine, The Third Affiliated Hospital of Soochow University, Changzhou, China / E-mail: drzhubin@126.com

Introduction

Septic shock is a dysregulated immune response caused by infection, which leads to microcirculation changes and organ dysfunction (1). According to a study published in The Lancet, there are more than 10 million new cases of septic shock worldwide every year, with a mortality rate of 50% (2). Fluid resuscitation is considered the primary measure for the treatment of patients with septic shock. It can rapidly supplement circulating blood volume, restore preload, improve peripheral tissue perfusion, and ultimately reduce the mortality of patients with septic shock (3).

Without proper evaluation and close monitoring, once the fluid volume exceeds a certain limit, it can lead to fluid overload and serious effects (4). Especially for the lung, the inflammation itself leads to the destruction of the pulmonary capillary barrier. At the same time, a large amount of fluid input will increase hydrostatic pressure and further aggravate edema (5). At present, there are many fluid responsiveness assessment methods to guide fluid resuscitation, such as the passive leg raising test (6), the inferior vena cava diameter (7), and so on. However, these methods are not only limited by many conditions, but also cannot monitor the volume status of patients in real time (8). Chest computed tomography and bedside chest radiography are commonly used in the diagnosis of pulmonary edema (9,10), but they are time-consuming and expose patients to ionizing radiation, making repeated examinations difficult. At the same time, these tests can only diagnose pulmonary edema, but lack a quantitative assessment of lung water content.

Pulse-indicated continuous cardiac output (PiCCO) can be used to monitor extravascular lung water index (EVLWI) (11), cardiac output (CO), polyvinylpyrrolidone iodine (PVPI), and other indicators, which can effectively reflect the dynamic changes of body fluid. However, PiCCO monitoring also has limitations: (1) PiCCO requires specific instruments, which are expensive and difficult to carry out in primary hospitals (12). (2) PiCCO is invasive hemodynamic monitoring, which can not be carried out for patients with local skin infection at the puncture site or abnormal coagulation function. At the same time, partial lung resection, pneumothorax, and serious arrhythmia can lead to invalid or large error measurement results (13). (3) EVLWI represent global lung water content rather than regional lung water content. Therefore, there is an urgent need to find a simple, less contraindicated, and repeatable method for monitoring extravascular lung water.

In recent years, the role of lung ultrasonography in diagnosing and treating patients with septic shock has been widely recognized, especially since the COVID-19 pandemic (14). Lung ultrasound (LUS) has been widely used in atelectasis, pneumothorax, pneumonia, pulmonary edema, and other diseases (15,16). Compared with PiCCO, LUS presents intuitive images, and can be performed multiple times for different patients at any time to observe the dynamic changes of the disease.

B-line is a valuable sonographic indication of pulmonary edema. Some studies have quantified lung water according to the distribution and morphology of B-line (17). However, on the one hand, it has been proposed that LUS score may lead to overestimation of local pathological status. Such quantitative or semi-quantitative assessment schemes are controversial (18). On the other hand, the areas of LUS examination are diverse, including 28-region, 12-region, 8-region, and 4-region (19,20,21). At the same time, some experts have proposed the bedside lung ultrasound examination (BLUE) for critically ill patients (22). In addition, there are many scoring standards corresponding to the examination protocols. There is a lack of a unified ultrasound protocol to guide the assessment of lung water in patients with septic shock because of the large number of ultrasound protocols and their corresponding scores.

Therefore, we designed this experiment and selected patients with septic shock as the research subjects. Patients underwent simultaneous PiCCO monitoring and LUS examination. The ultrasound scoring scheme recognized by the current authoritative journals and their corresponding scoring standards included 8-region and 4-region. In addition, we also innovatively combined the BLUE scheme with the widely used semi-quantitative scoring method. On the one hand, the correlation between these three LUS protocols and other variables was compared. On the other hand, we also compared the value of different ultrasound schemes for assessing the severity of pulmonary edema based on specific EVLWI levels, to identify a suitable and convenient zoning scheme and scoring standard for monitoring extravascular lung water in patients with septic shock. Although lung ultrasound has been validated for semi-quantitative evaluation of extravascular lung water in critically ill patients, there remains a lack of unified consensus on the optimal bedside scanning protocol. The novelty of this study is that we, for the first time, applied a standardized semi-quantitative scoring system to the BLUE protocol and directly compared it with the classic 4-region and 8-region lung ultrasound protocols. This head-to-head comparison provides simple, clinically applicable evidence for selecting the optimal lung ultrasound scheme in bedside hemodynamic management of patients with septic shock.

Patients and methods

Patient selection

Patients with septic shock admitted to the ICU of the Third Affiliated Hospital of Soochow University from February 2021 to February 2023 were enrolled. This study was approved by the Ethics Committee of the Third Affiliated Hospital of Soochow University and registered in the Chinese Clinical Trial Register (clinical trial number: ChiCTR2100041999).

The inclusion criteria were (1) Diagnosis of septic shock (refer to diagnostic criteria of Sepsis-3.0) (1); (2) PiCCO monitoring was performed; (3) Age ≥ 18 years old. The exclusion criteria were (1) Trauma, wound dressing, prone position, and other reasons affecting ultrasound examination; (2) Circulatory instability.

Clinical and laboratory data

Fluid resuscitation was performed as soon as septic shock was diagnosed. Fluid resuscitation was performed according to the patient's condition and the criteria recommended by the Survival Sepsis Campaign. PiCCO parameters were collected within 24 hours after enrollment. Ultrasound scans with different protocols were performed immediately after PiCCO. Clinical and laboratory data were recorded on the day of ultrasound examination.

General demographic data: gender, age, source of infection, acute physiology and chronic health evaluation score in ICU, sequential organ failure score, 28-day mortality, and hospital mortality.

Laboratory data: white blood cell (WBC), neutrophil (NEU), hemoglobin (Hb), C-reactive protein (CRP), procalcitonin (PCT), B-type natriuretic peptide (BNP), albumin (Alb), lactic acid (Lac), and creatinine (Cr). Blood gas analysis was performed during PiCCO measurement, and the oxygenation index (arterial oxygen pressure/fraction of inspired oxygen) was calculated according to the blood gas results.

PiCCO monitoring

PiCCO data were collected using a system designed by PULSION, Germany. The subclavian or internal jugular vein catheter was selected as the central vein for connection to the pressure transducer and monitor. The patient was placed in the supine position, and the nurse measured the central venous pressure (CVP). PiCCO measurement was performed by the attending physician: after a rapid injection of 20 mL of 0°C 0.9% saline into the central vein, the arterial temperature was monitored with a temperature sensor in the femoral artery catheter to obtain a thermodilution curve. After three consecutive injections, EVLWI, pulmonary vascular permeability index (PVPI), cardiac output index (CI) and global end diastolic volume index (GEDVI) were calculated.

According to the literature, increased lung water was defined as EVLWI>7 mL/kg (23), lung edema was defined as EVLWI>10 mL/kg (24). A cut-off of EVLWI≥15 was chosen for severe edema (25).

Ultrasound examination and scoring

Lung ultrasound images were acquired using a Konica Minolta ultrasound machine by physicians who were specially trained in lung ultrasound and were not involved in the diagnosis and treatment of patients. The 2-5 MHz curved array probe was used for examination.

We selected lung ultrasound score of 4-region (LUS_4), 8-region (LUS_8) and BLUE (LUS_b), which were convenient for the operation of critically ill patients. The scanning methods and scoring criteria were referred to authoritative magazines. The three protocols and their scoring methods are as follows: (1) LUS_4: The 3rd and 6th intercostal Spaces of the bilateral anterior chest were scanned. The number of B-lines in each partition was counted. Finally summed to calculate the total score of the 4-region(19). (2) LUS_8: The lungs were divided into eight regions based on the parasternal line, anterior axillary line, posterior axillary line and bilateral nipple line (Table 1) (21, 22). (3) LUS_b: Based on the size of the patient's hand as the standard, the two index fingers are placed on the chest wall, the left hand is on the top, and the right hand is on the bottom. Superior blue point: between the third and fourth palm fingers above. Lower blue point: the palm of the right hand. Diaphragm point: the intersection of the little finger of the lower hand and the midaxillary line. The posterolateral alveolar and/or pleural syndrome (PLAPS) point: the intersection of the posterior axillary line and the lower blue dot (26).

Statistical analysis

IBM Corp SPSS 25.0 (Armonk, NY, USA) was used for statistical analysis of the data. GraphPad Prism 8 and ChiPlot tools were used to plot. Data with normal distribution were shown as mean ± standard deviation. Skewed distribution data were shown as median (25%–75% interquartile ranges). We used the Student's t-test, Fisher's exact test, and the Mann-Whitney U-test according to the variables evaluated. Count data were expressed as rate (%) and compared by chi-squared test.

Spearman correlation analysis was performed between different ultrasound scores and laboratory indicators. Finally, we performed ROC curves to analyze the diagnostic value of different ultrasound scores in evaluating the severity of pulmonary edema. A post-hoc power analysis was performed for the primary endpoint (correlation between BLUE protocol score and EVLWI). With an effect size of r=0.634, two-tailed α=0.05, and sample size n=46, the statistical power was calculated to be 76.9%, confirming that the current sample size was sufficient for the core statistical analysis.

Results

Clinical characteristics of 46 patients with septic shock

A total of 50 patients were identified, 4 were excluded from this study: 2 patients with pneumothorax and severe subcutaneous emphysema, 1 patient with severe circulatory instability, and 1 patient with chest dressing coverage affecting the examination. Table 2 shows the clinical characteristics of 46 patients with septic shock who were ultimately included. There were 32 males (69.6%). The age of patients ranged from 40 to 94 years, with an average age of 65.80±15.78 years. The average BMI of the patients was 22.49±2.52 kg/m^2. Pulmonary infection was the main primary infection, accounting for 43.5% of the total. Regarding ventilatory status, 44 patients (95.7%) received mechanical ventilation, and 2 patients (4.3%) breathed spontaneously without ventilatory support.

Extravascular lung water increased in 70% of patients (EVLWI>7 mL/kg). 37% of patients had pulmonary edema (EVLWI>10 mL/kg). The PiCCO parameters and the total scores of the three ultrasound protocols are shown in Table 3. EVLWI was 9.50(7.00-12.25) within 24 hours of fluid resuscitation. At the same time, the total score of 4-sector protocol was 2.50(0.75-7.00), while the total score of 8-sector and BLUE protocol was 8.30±5.18 and 7.72±4.44, respectively. The EVLWI and corresponding ultrasound

Table 1. LUS_8 and LUS_b scoring system.

	Normal aeration	**Moderate loss of lung aeration**	**Severe loss of lung aeration**	**Pulmonary consolidation**
score	0	1	2	3
ultrasound patterns	A line/one or two B-lines	three or more B-lines	multiple coalescent B-lines	the presence of a tissue pattern

Table 2. Patients Clinical Characteristics.

Variable	
Age (years)	65.80±15.78
Male (n, %)	32(69.6)
BMI (kg/m^2)	22.49±2.52
APACHE II	26.83±6.91
SOFA	10.17±3.37
Infection sites (n, %)	
pulmonary infections	20(43.5)
abdominal infection	19(41.3)
urinary tract infection	4(8.7)
Other	3(6.5)
WBC (10^9/L)	10.59(7.17-16.28)
NEU (%)	89.50(86.00-94.13)
PCT (ng/mL)	6.40(1.31-38.16)
BNP (pg/mL)	864.85(333.50-2298.65)
CRP (mg/L)	126.55(37.95-207.58)
Hb (g/L)	104.41±21.99
Alb (g/L)	33.05±7.46
Lac (mmol/L)	2.70(1.88-4.58)
PaO_2/FiO_2 (mmHg)	305.83±105.39
28-day mortality (n, %)	20(43.5)
hospital mortality (n, %)	25(54.3)

Abbreviations: APACHE II: acute physiology and chronic health evaluation; Alb: albumin; BMI: body mass index; BNP: B-type natriuretic peptide; CRP: C-reactive protein; Hb, hemoglobin; Lac, lactic acid; NEU: neutrophil; PaO_2/FiO_2, arterial oxygen pressure/fraction of inspired oxygen; PCT: procalcitonin; WBC: white blood cell.

Table 3. PiCCO parameters and the total scores of the three ultrasound protocols.

Variable	
CVP (mmHg)	14.07±5.22
CI[L/(min·m^2)]	2.98±1.03
GEDVI (mL/m^2)	855.20±181.68
EVLWI (mL/kg)	9.50(7.00-12.25)
PVPI	1.60(1.30-2.00)
LUS_4	2.50(0.75-7.00)
LUS_8	8.30±5.18
LUS_b	7.72±4.44

Abbreviations: CVP: central venous pressure; CI: cardiac output index; GEDVI, global end diastolic volume index; EVLWI: extravascular lung water index; PVPI: pulmonary vascular permeability index.

scores of 46 patients with septic shock are shown in Figure 1.

Correlation between different variables

Spearman correlation coefficient was used to analyze the correlation of 18 variables including PiCCO monitoring indicators, ultrasound score and clinical data. The correlation heatmap (Figure 2) was used to show the correlations between them. Spearman rank correlation coefficient r values are presented in different colors in the heat map.

The results showed a significant positive correlation between EVLWI and the scores of the three protocols ($p < 0.05$), with the BLUE scoring scheme showing the strongest correlation with EVLWI (r=0.634). To formally compare the strength of correlations, Fisher's z-transformation was performed. The BLUE protocol showed a significantly stronger correlation with EVLWI than the 4-region protocol (z=2.01, p=0.044). The correlation of the BLUE protocol was also numerically higher than that of the 8-region protocol, although the difference did not reach statistical significance (z=1.25, p=0.211). The linear correlations between the three scoring schemes and EVLWI are described in Figure 3.

In addition, the BLUE and 8-region protocols were found to be significantly negatively correlated with the oxygenation index, with the highest correlation observed for the BLUE protocol (r=0.417). However, there was no significant correlation between the 4-region protocol and PaO_2/FiO_2 ($p>0.05$), probably because it only collected the number of B-lines of the anterior chest wall. The correlation between ultrasound score and PaO_2/FiO_2 is depicted in Figure 4.

Predictive value of three ultrasound protocols for the severity of lung water

The ROC curve was drawn to analyze the predictive value of 4-region, 8-region, and BLUE protocol for the severity of pulmonary edema in patients with septic shock. Fortunately, we found that all three protocols show excellent predictive performance for assessing the severity of pulmonary edema in septic shock, as shown in Table 4. First of all, compared

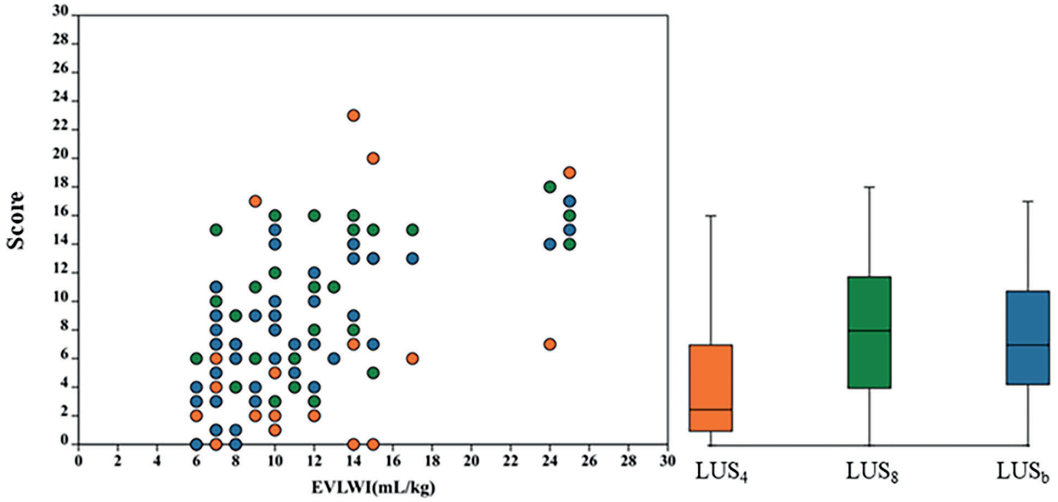

Figure 1. Results of lung ultrasound scores for the three protocols.

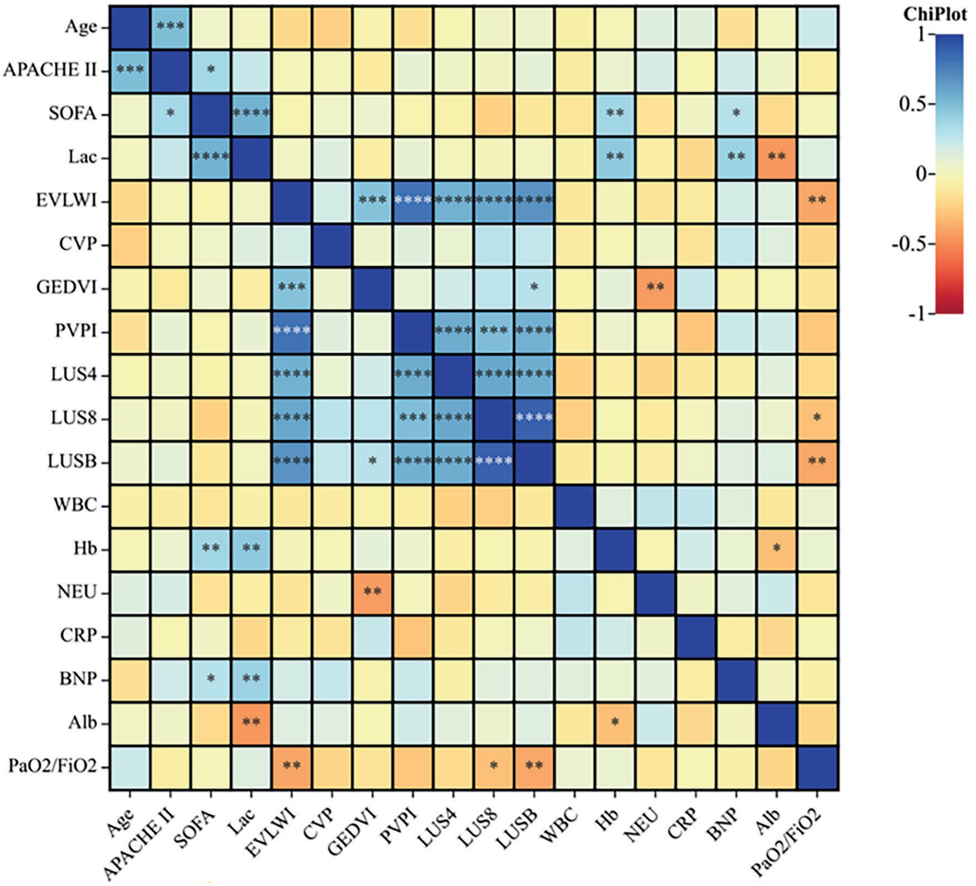

Figure 2. Correlation between different variables.

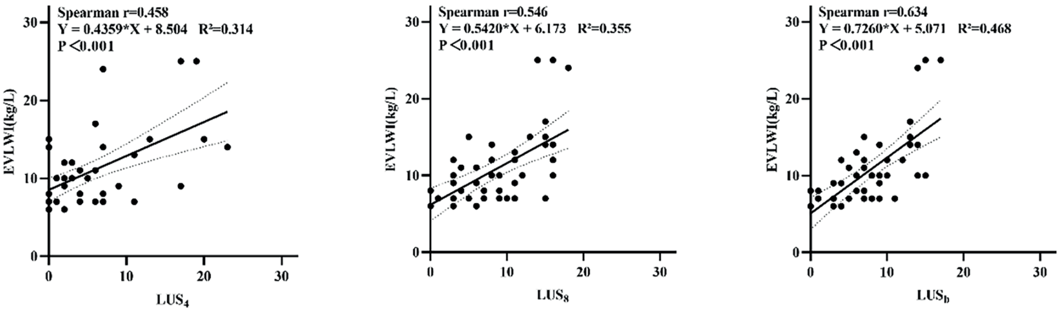

Figure 3. Correlation between the score of three lung ultrasound protocols and EVLWI.

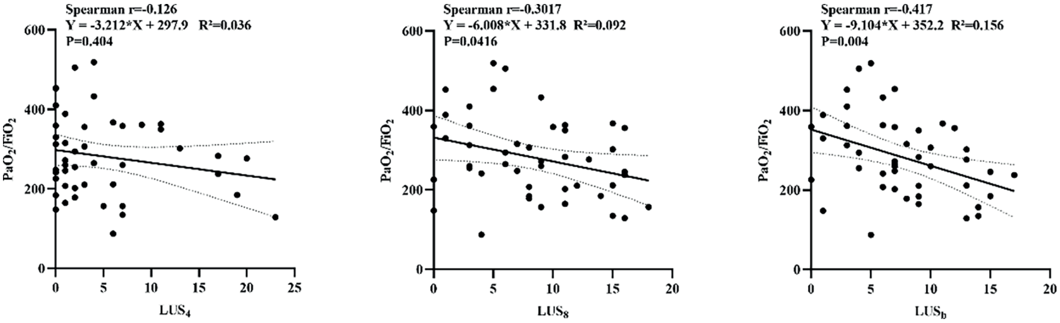

Figure 4. Correlation between the score of three lung ultrasound protocols and PaO_2/FiO_2.

Table 4. PiCCO parameters and the total scores of the three ultrasound protocols.

EVLWI level (mL/kg)	Protocol	AUC	95%CI	*P* value	Youden index	cut-off point	Sensitivity (%)	Specificity (%)
EVLWI>7	LUS_4	0.685	0.522-0.848	0.048	0.362	1.50	71.9	64.3
	LUS_8	0.688	0.524-0.851	0.045	0.299	7.50	65.6	64.3
	BLUE	0.739	0.589-0.889	0.011	0.384	5.50	81.3	57.1
EVLWI>10	LUS_4	0.755	0.605-0.904	0.004	0.434	1.50	88.2	55.2
	LUS_8	0.765	0.620-0.910	0.003	0.460	12.5	52.9	93.1
	BLUE	0.775	0.637-0.913	0.002	0.460	11.5	52.9	93.1
EVLWI≥15	LUS_4	0.799	0.578-1	0.013	0.601	5.50	85.7	74.4
	LUS_8	0.835	0.667-1	0.005	0.729	12.5	85.7	87.2
	BLUE	0.886	0.760-1	0.001	0.755	12.5	85.7	89.7

Abbreviations: AUC: area under the curve; EVLWI: extravascular lung water index.

with the 4-region and 8-region protocols, the BLUE protocol had a higher diagnostic value for pulmonary edema, with an area under the ROC curve (AUC) of 0.775, and high specificity and sensitivity (specificity 93.1%, sensitivity 52.9%), while the AUC of the BLUE protocol for the diagnosis of pulmonary edema was 0.755(sensitivity 88.2%, specificity 55.2%). The AUC of 4-region was 0.765(sensitivity 52.9%, specificity 93.1%). We compared the potential of three protocols to identify whether increased lung fluid had occurred (EVLWI>7 mL/kg). The AUC of the 4-region, 8-region and BLUE were 0.685, 0.688 and

0.739, respectively. Furthermore, the ROC analyses were performed to identify severe lung edema with EVLWI>15 mL/kg. The AUC of 4-region, 8-region, and BLUE were 0.799, 0.835, and 0.886, respectively. Pairwise comparisons of AUCs were performed using the DeLong test. The BLUE protocol had a significantly higher AUC for severe pulmonary edema (EVLWI ≥15 mL/kg) than the 4-region protocol (p=0.032). Although the difference between BLUE and 8-region protocols was not statistically significant (p=0.187), the BLUE protocol achieved consistently higher AUC values across all EVLWI thresholds. The ROC curve for the scores of three protocols was plotted (Figure 5).

Discussion

First of all, this study found that 37% of the patients had increased lung water, even though all the enrolled patients had taken PiCCO monitoring. A study of 372 patients with septic shock who underwent fluid

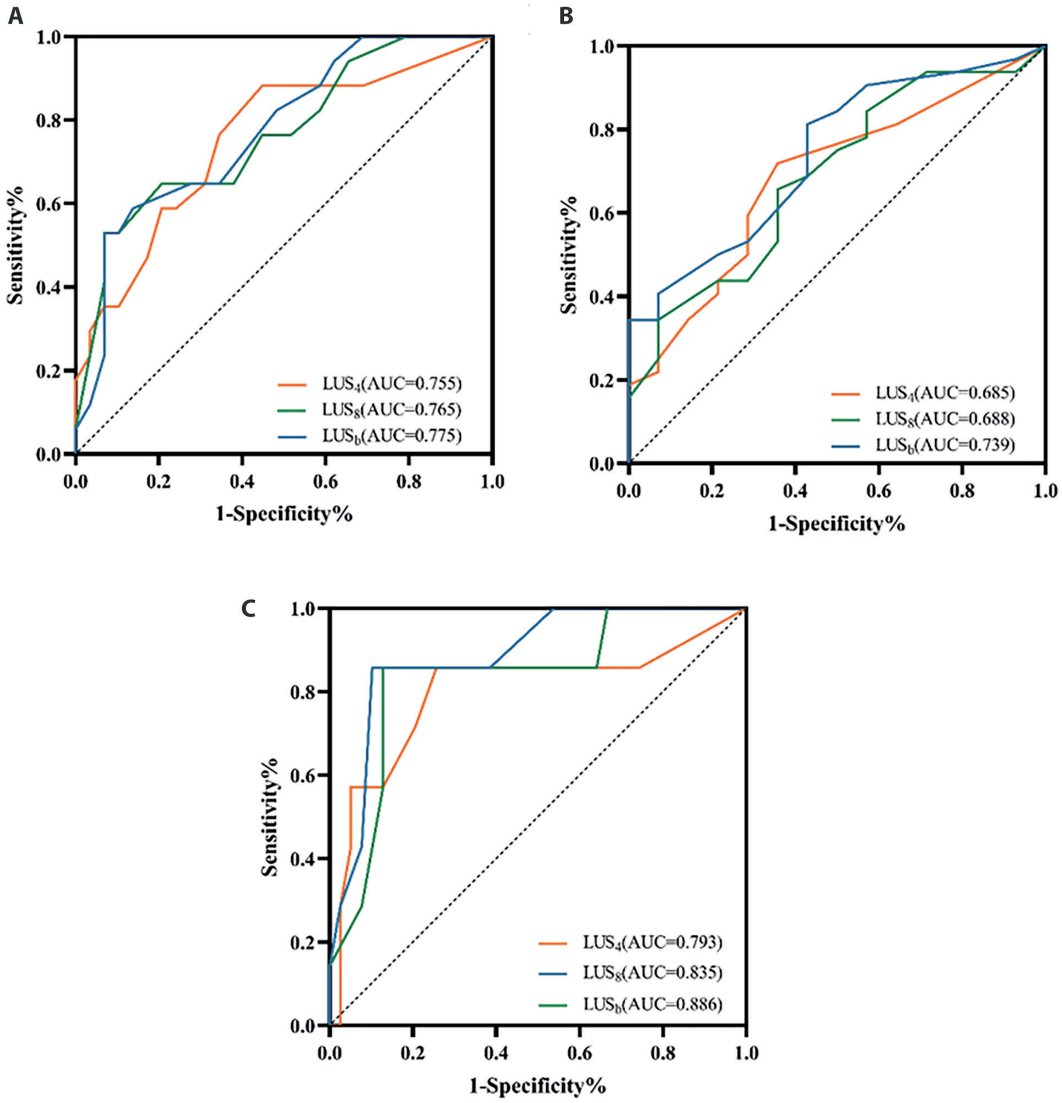

Figure 5. Receiver operating characteristic curves of lung ultrasound score. A) EVLWI>7 mL/kg; B) EVLWI>10 mL/kg; C) EVLWI≥15 mL/kg severe pulmonary edema).

resuscitation according to the early goal-directed therapy showed that 67% of the patients had fluid overload on the first day of resuscitation, and nearly 48% of the patients had fluid overload for more than three days (26). In recent years, more and more studies have found the harm caused by excessive fluid resuscitation to patients. Aggressive fluid can cause pulmonary edema, gas exchange disorder, decreased lung compliance, increased work of breathing, resulting in respiratory failure, and ultimately affecting the prognosis of patients with septic shock (27, 28, 29). Therefore, the fluid resuscitation strategies are constantly changing. From supplementation of about 5 L of fluid within 6 hours to advocating fluid infusion at a speed of 30 mL/h within a limited time (30, 31), some studies also put forward the liquid management strategy of "Less is more" (29).

In addition, it has been emphasized that the resuscitation process should be guided by dynamic monitoring rather than by physical examination or static parameters alone (3,32). By comparing the PiCCO parameters with the collected ultrasound scores, we concluded that LUS was a non-invasive and effective method for predicting lung water status in patients with septic shock. More importantly, our innovative BLUE protocol is a time-saving method with good correlation with transpulmonary thermodilution for pulmonary scanning in patients with septic shock.

In our study, we found that the ultrasound score has potential in the early prediction of pulmonary edema (EVLWI>7 mL/kg), the diagnosis of pulmonary edema (EVLWI>10 mL/kg), and the evaluation of severe pulmonary edema (EVLWI≥15 mL/kg). The final B-line score showed a good correlation with EVLWI, whether it was the measurement of the anterior chest B-line or the semi-quantitative measurement of different regions or points. In conclusion, ultrasound images of the comet tail provide an indirect method to measure EVLWI and provide a sensitive and accurate way to assess the severity of pulmonary edema.

After further analysis of the three ultrasound protocols, we found that although the 8-region and BLUE protocols adopted the same semi-quantitative scoring method, the final scoring results of the two protocols were not consistent because they scored the worst signs of the points and regions respectively. Notably, the BLUE protocol showed an advantage over the more comprehensive octant scan in diagnosing pulmonary edema and in its correlation with EVLWI. We speculate that, on the one hand, the semi-quantitative scoring of 8-region selects the serious parts of each region as the scoring objects, and the incidence of lower atelectasis is relatively high in severe patients due to long-term bed rest (33), so the position from the anterior axillary line to the posterior axillary line is easily scored 3 points. However, atelectasis can not represent increased lung water to some extent, and including atelectasis in the total score may lead to serious bias. On the other hand, pulmonary infection was the main source of infection in the study subjects, which resulted in the signs of the local most severe region being largely affected by pulmonary infection, resulting in higher scores. Positive pressure ventilation markedly altered pulmonary aeration status and lung tissue density, which directly modulated B-line ultrasound presentations and further weakened the correlation between ultrasound scores and real EVLWI. In our cohort, most patients received mechanical ventilation support, which was an inherent confounding factor in this analysis. This ventilatory interference effect should be fully considered in clinical protocol application and result interpretation.

Regarding the diagnostic performance of BLUE protocol, we observed an unbalanced profile with relatively low sensitivity and high specificity. From a clinical perspective, this performance characteristic indicated that this ultrasound protocol was more suitable for ruling-out pulmonary edema and identifying contraindications for excessive fluid resuscitation in septic shock patients, rather than as a standalone definitive diagnostic tool. The limited sensitivity may be attributed to concomitant pulmonary comorbidities, focal pulmonary lesions, and limited anterior chest scanning range in this study. We have to admit that the LUS scoring schemes has limitations: different signs including pulmonary edema, atelectasis, pneumonia, etc. all show comet tail sign, and the B-line morphology is similar, which is difficult to distinguish, resulting in large scoring errors (34). The 4-region protocol scanned fewer locations and mainly represented the anterior wall, which may also explain why its correlation with EVLWI was weak. However, the 4-region has its unique advantages, fewer examination positions, the signs of the anterior chest wall are easy to identify, significantly shortening the examination time. It is of great significance to quickly assess the condition, especially the occurrence of severe pulmonary edema, and is suitable for beginners to scan quickly. Rapid scanning for beginners is of great significance for rapid judgment of the condition. In conclusion, different regions have their own advantages and limitations.

In addition to the advantages and disadvantages of ultrasound scoring across different areas, there is also a lack of standards for scoring different signs. We summarized several quantitative methods mentioned in recent years as follows:

1. Count the number of B-lines directly (19). When the confluent B-lines could not be counted, the percentage of B-lines in intercostal space could be scored.
2. According to the score of the number of positive quadrants, positive quadrants were defined as ≥3 B-lines (35).
3. Define the score of each ultrasound sign.

At present, the scoring regulations that are commonly used are shown in Table 1 (21). We must admit that, no matter which scheme is used, it can only predict extravascular lung water and there are "visual differences" in the quantitative or qualitative B-line among different doctors, so the scoring results also differ (36). Thus, although an ultrasound scoring system is a good measure for quantifying lung disease, precision has been elusive. The choice of scoring standard should be based on the patient's condition and the purpose of the examination, and the quantitative and qualitative criteria should be combined.

In the present study, the correlation between ultrasound semi-quantitative scores and reference EVLWI was moderate at maximum, which is consistent with previous reports (37). Multiple factors contributed to this correlation limitation. Concomitant pulmonary lesions, positive pressure ventilation-induced lung aeration changes, subjective bias in visual semi-quantitative scoring, and ultrasound partial volume effect all attenuated the direct correlation between ultrasound manifestations and pulmonary water volume. Therefore, lung ultrasound should be regarded as a rapid bedside screening tool for pulmonary edema, rather than an alternative quantitative monitoring modality to replace invasive EVLWI detection.

Nevertheless, conventional B-line semi-quantitative scoring has inherent limitations, including high operator dependence and subjective scoring variability. Emerging quantitative ultrasound techniques, such as computer-aided diagnosis and ultrasonic scattering signal analysis, can help overcome these drawbacks through objective, signal-based quantification (38). These innovative methods offer promising strategies to improve the accuracy and reliability of lung ultrasound evaluation in clinical practice.

Simplified lower-lung ultrasound protocols are advantageous for rapid bedside evaluation of diffuse pulmonary diseases including ARDS. Nonetheless, these simplified strategies cannot fully reflect the morphological heterogeneity of ARDS, including variable focal and diffuse lesion distributions (39, 40). Full multi-region scanning provides more comprehensive pulmonary information but requires longer examination time. Thus, clinical ultrasound protocols should be selected to balance diagnostic comprehensiveness and efficiency according to lesion patterns.

Furthermore, the scoring system in this study was based on the 2012 international consensus and cannot fully conform to modern updated concepts of critical care ultrasound (40). Corradi et al. pointed out that remarkable quantification inaccuracy existed in conventional manual counting and scoring of ultrasound B-lines, and such systematic biases were commonly underappreciated in clinical practice. Accordingly, objective quantitative ultrasonographic techniques are required to achieve precise evaluation of pulmonary edema (41).

Brusasco et al. demonstrated that second-order grey-scale texture analysis based on pleural ultrasound images could effectively distinguish acute respiratory distress syndrome from cardiogenic pulmonary edema (42). Such quantitative ultrasonographic features beyond visual B-line assessment provide objective evidence for etiological diagnosis of pulmonary edema. Advanced imaging modalities and multi-parametric ultrasound integration are promising solutions, which will be the major future research focus.

Limitations

Our study has several limitations. First, we collected only PiCCO data and ultrasound scores at a single time point and lacked an overall assessment of the patient's course. Second, this was a single-center study with a relatively small sample size. However, post-hoc power analysis confirmed that the current sample size achieved acceptable statistical power to support the primary correlation analysis. Multi-center and large-sample studies are still needed to further verify our findings in the future. On the one hand, data acquisition is highly dependent on the experience of operators and raters. On the other hand, the scanning method selected in the study mainly focused on the anterior chest wall and did not include the back scan in the scoring part. Therefore, we hope that future studies can continue to expand the sample size and increase the scanning of the posterior chest wall. At the same time, PiCCO parameters and LUS data were collected at multiple periods during the treatment to further verify the clinical value of different ultrasound schemes. We explicitly acknowledged that the optimal ultrasound score cut-off values derived in this study lacked external independent validation, and multivariate regression analysis as well as inter-protocol diagnostic agreement analysis were not conducted. We also stated that future multi-center studies are required to verify these cut-off thresholds and further explore independent predictive value of ultrasound scores.

Conclusion

In conclusion, ultrasound scores can help quantify extravascular lung water, but the scoring scheme and criteria should be selected based on the specific condition. The BLUE protocol presents a relatively favorable correlation with EVLWI and acceptable diagnostic performance for pulmonary edema. It can be used as a simple and effective tool to guide fluid resuscitation and is worthy of further clinical application and research.

Abbreviations

LUS: Lung Ultrasound
PiCCO: Pulse indicated Continuous Cardiac Output
ROC: Receiver Operating Characteristic
EVLWI: Extravascular Lung Water Index
BLUE: Bedside Lung Ultrasound Examination
CO: Cardiac Output
CI: Cardiac Output Index
GEDVI: Global End Diastolic Volume Index
ICU: Intensive Care Unit
APACHE II: Acute Physiology and Chronic Health Evaluation II
SOFA: Sequential Organ Failure Assessment
WBC: White Blood Cell
NEU: Neutrophil
Hb: Hemoglobin
CRP: C-reactive Protein
PCT: Procalcitonin
BNP: B-type Natriuretic Peptide
Alb: Albumin
Lac: Lactic Acid
Cr: Creatinine
CVP: Central Venous Pressure
BMI: Body Mass Index
AUC: Area Under the Curve
PLAPS: Posterolateral Alveolar and/or Pleural Syndrome

Acknowledgements: Not applicable.

Author’s Contributions: Yuan Ding designed and conducted the study, performed data analysis and drafted the manuscript. Bin Zhu contributed to the design of the study and reviewed the manuscript. Yibo Ma, Feng Qian, Yang Feng assisted in the collection of ultrasound data. All the authors critically revised the manuscript and approved the submission.

Funding: This study was supported by the Programs of Major Science and Technology Project of Changzhou Health Commission (No: ZD202501), Program of Major Science and Technology Project of Changzhou Health Commission (No: ZD202101), Top Talent of Changzhou medical innovation talent training (NO:201627), and Medical young talent of Jiangsu (NO: QNRC2016276).

Ethics Approval and Consent to Participate: Written consent was obtained for all patients and the protocol was registered at www.chictr.org.cn (ChiCTR2100041999).

Consent for Publication: Not applicable.

Competing Interests: The authors declare no competing interests.

Declaration on the Use of AI: None

References

1. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA 2016;315:801-10. doi: 10.1001/jama.2016.0287.
2. Fleischmann-Struzek C, Mellhammar L, Rose N, Cassini A, Rudd KE, Schlattmann P, et al. Incidence and mortality of hospital- and ICU-treated sepsis: results from an updated and expanded systematic review and meta-analysis. Intensive Care Med 2020;46:1552-62. doi: 10.1007/s00134-020-06151-x.
3. Evans L, Rhodes A, Alhazzani W, Antonelli M, Coopersmith CM, French C, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Intensive Care Med 2021;47:1181-247. doi: 10.1007/s00134-021-06506-y.
4. Adamantos S. Fluid therapy in pulmonary disease: how careful do we need to be? Front Vet Sci 2021;8:624833. doi: 10.3389/fvets.2021.624833.
5. Jaffee W, Hodgins S, McGee WT. Tissue edema, fluid balance, and patient outcomes in severe sepsis: an organ systems review. J Intensive Care Med 2018;33:502-9. doi: 10.1177/0885066617742832.
6. Su CH, Liu SH, Tan TH, Lo CH. Using the pulse contour method to measure the changes in stroke volume during a passive leg raising test. Sensors (Basel) 2018;18:3420. doi: 10.3390/s18103420.
7. Khajehpour H, Behzadnia MJ. The role of internal jugular vein Doppler ultrasonography in predicting hypovolemic shock in polytrauma patients. Ultrasonography 2022;41:317-24. doi: 10.14366/usg.21144.
8. Hu X, Li L, Hao X, Niu N, Tang Y. Passive leg raising combined with echocardiography could evaluate volume responsiveness in patients with septic shock. Zhonghua Wei Zhong Bing Ji Jiu Yi Xue 2019;31:619-22. doi: 10.3760/cma.j.issn.2095-4352.2019.05.019.
9. Assaad S, Kratzert WB, Shelley B, Friedman MB, Perrino A. Assessment of pulmonary edema: principles and practice. J Cardiothorac Vasc Anesth 2018;32:901-14. doi: 10.1053/j.jvca.2017.08.028.
10. Wang Y, Shen Z, Lu X, Zhen Y, Li H. Sensitivity and specificity of ultrasound for the diagnosis of acute pulmonary edema: a systematic review and meta-analysis. Med Ultrason 2018;20:32-6. doi: 10.11152/mu-1223.
11. Zhang F, Li C, Zhang JN, Guo HP, Wu DW. Comparison of quantitative computed tomography analysis and single-indicator thermodilution to measure pulmonary edema in patients with acute respiratory distress syndrome. Biomed Eng Online 2014;13:30. doi: 10.1186/1475-925X-13-30.
12. Siegenthaler N, Giraud R, Saxer T, Courvoisier DS, Romand JA, Bendjelid K. Haemodynamic monitoring in the intensive care unit: results from a web-based Swiss survey. Biomed Res Int 2014;2014:129593. doi: 10.1155/2014/129593.
13. Gassanov N, Caglayan E, Nia A, Erdmann E, Er F. Hämodynamisches monitoring auf der Intensivstation: Pulmonalarterienkatheter versus PiCCO. Dtsch Med Wochenschr 2011;136:376-80. doi: 10.1055/s-0031-1272539.
14. Allinovi M, Parise A, Giacalone M, Amerio A, Delsante M, Odone A, et al. Lung ultrasound may support diagnosis and monitoring of COVID-19 pneumonia. Ultrasound Med Biol 2020;46:2908-17. doi:10.1016/j.ultrasmedbio.2020.07.018.
15. Peng QY, Wang XT, Zhang LN. Findings of lung ultrasonography of novel corona virus pneumonia during the 2019-2020 epidemic. Intensive Care Med 2020;46:849-50. doi: 10.1007/s00134-020-05996-6.
16. Koenig S, Mayo P, Volpicelli G, Millington SJ. Lung ultrasound scanning for respiratory failure in acutely ill patients: a review. Chest 2020;158:2511-6. doi: 10.1016/j.chest.2020.08.2052.
17. Lajili F, Toumia M, Sekma A, Bel Haj Ali K, Sassi S, Zorgati A, et al. Value of lung ultrasound sonography B-lines quantification as a marker of heart failure in COPD exacerbation. Int J Chron Obstruct Pulmon Dis 2024;19:1767-74. doi: 10.2147/COPD.S447819.
18. Enghard P, Rademacher S, Nee J, Hasper D, Engert U, Jörres A, et al. Simplified lung ultrasound protocol shows excellent prediction of extravascular lung water in ventilated intensive care patients. Crit Care 2015;19:36. doi: 10.1186/s13054-015-0756-5.
19. Zhao Z, Jiang L, Xi X, Jiang Q, Zhu B, Wang M, et al. Prognostic value of extravascular lung water assessed with lung ultrasound score by chest sonography in patients with acute respiratory distress syndrome. BMC Pulm Med 2015;15:98. doi: 0.1186/s12890-015-0091-2.
20. Mayr U, Lukas M, Habenicht L, Wiessner J, Heilmaier M, Ulrich J, et al. B-lines scores derived from lung ultrasound provide accurate prediction of extravascular lung water index: an observational study in critically ill patients. J Intensive Care Med 2022;37:21-31. doi: 10.1177/0885066620967655.
21. Liteplo AS, Marill KA, Villen T, Miller RM, Murray AF, Croft PE, et al. Emergency thoracic ultrasound in the differentiation of the etiology of shortness of breath (ETUDES): sonographic B-lines and N-terminal pro-brain-type natriuretic peptide in diagnosing congestive heart failure. Acad Emerg Med 2009;16:201-10. doi: 10.1111/j.1553-2712.2009.00347.x.

22. Eichhorn V, Goepfert MS, Eulenburg C, Malbrain ML, Reuter DA. Comparison of values in critically ill patients for global end-diastolic volume and extravascular lung water measured by transcardiopulmonary thermodilution: a meta-analysis of the literature. Med Intensiva 2012;36:467-74. doi: 10.1016/j.medin.2011.11.014.
23. Kushimoto S, Taira Y, Kitazawa Y, Okuchi K, Sakamoto T, Ishikura H, et al. The clinical usefulness of extravascular lung water and pulmonary vascular permeability index to diagnose and characterize pulmonary edema: a prospective multicenter study on the quantitative differential diagnostic definition for acute lung injury/acute respiratory distress syndrome. Crit Care 2012;16:R232. doi: 10.1186/cc11898.
24. Tagami T, Kushimoto S, Yamamoto Y, Atsumi T, Tosa R, Matsuda K, et al. Validation of extravascular lung water measurement by single transpulmonary thermodilution: human autopsy study. Crit Care 2010;14:R162. doi: 10.1186/cc9250.
25. Lichtenstein DA, Mezière GA. Relevance of lung ultrasound in the diagnosis of acute respiratory failure: the BLUE protocol. Chest 2008;134:117-25. doi: 10.1378/chest.07-2800.
26. Kelm DJ, Perrin JT, Cartin-Ceba R, Gajic O, Schenck L, Kennedy CC. Fluid overload in patients with severe sepsis and septic shock treated with early goal-directed therapy is associated with increased acute need for fluid-related medical interventions and hospital death. Shock 2015;43:68-73. doi: 10.1097/SHK.0000000000000268.
27. Malbrain ML, Marik PE, Witters I, Cordemans C, Kirkpatrick AW, Roberts DJ, et al. Fluid overload, de-resuscitation, and outcomes in critically ill or injured patients: a systematic review with suggestions for clinical practice. Anaesthesiol Intensive Ther 2014;46:361-80. doi: 10.5603/AIT.2014.0060.
28. Loflin R, Winters ME. Fluid resuscitation in severe sepsis. Emerg Med Clin North Am 2017;35:59-74. doi: 10.1016/j.emc.2016.08.001.
29. Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med 2001;345:1368-77. doi: 10.1056/NEJMoa010307.
30. Levy MM, Evans LE, Rhodes A. The surviving sepsis campaign bundle: 2018 update. Intensive Care Med 2018;44:925-8. doi: 10.1007/s00134-018-5085-0.
31. Pinsky MR, Cecconi M, Chew MS, De Backer D, Douglas I, Edwards M, et al. Effective hemodynamic monitoring. Crit Care 2022;26:294. doi: 10.1186/s13054-022-04173-z.
32. Mingoia A, Wittebole X, Gérard L. Diagnosis of middle lobe atelectasis with lung ultrasonography. Intensive Care Med 2021;47:906-7. doi: 10.1007/s00134-021-06421-2.
33. Heldeweg MLA, Haaksma ME, Smit JM, Smit MR, Tuinman PR. Lung ultrasound to discriminate noncardiogenic interstitial syndrome from cardiogenic pulmonary edema: is "gestalt" as good as it gets? J Crit Care 2023;73:154180. doi: 10.1016/j.jcrc.2022.154180.
34. Anile A, Russo J, Castiglione G, Volpicelli G. A simplified lung ultrasound approach to detect increased extravascular lung water in critically ill patients. Crit Ultrasound J 2017;9:13. doi: 10.1186/s13089-017-0068-x.
35. Haaksma ME, Smit JM, Heldeweg MLA, Pisani L, Elbers P, Tuinman PR. Lung ultrasound and B-lines: B careful! Intensive Care Med 2020;46:544-5. doi: 10.1007/s00134-019-05911-8.
36. Corradi F, Ball L, Brusasco C, Riccio AM, Baroffio M, Bovio G, et al. Assessment of extravascular lung water by quantitative ultrasound and CT in isolated bovine lung. Respir Physiol Neurobiol 2013;187:244-9. doi: 10.1016/j.resp.2013.04.002.
37. Corradi F, Brusasco C, Vezzani A, Santori G, Manca T, Ball L, et al. Computer-aided quantitative ultrasonography for detection of pulmonary edema in mechanically ventilated cardiac surgery patients. Chest 2016;150:640-51. doi: 10.1016/j.chest.2016.04.013.
38. Corradi F, Brusasco C, Pelosi P. Chest ultrasound in acute respiratory distress syndrome. Curr Opin Crit Care 2014;20:98-103. doi: 10.1097/MCC.0000000000000042.
39. Luecke T, Corradi F, Pelosi P. Lung imaging for titration of mechanical ventilation. Curr Opin Anaesthesiol 2012;25:131-40. doi: 10.1097/ACO.0b013e32835003fb.

---

40. Corradi F, Via G, Forfori F, Brusasco C, Tavazzi G. Lung ultrasound and B-lines quantification inaccuracy: B sure to have the right solution. Intensive Care Med 2020;46:1081-3. doi: 10.1007/s00134-020-06005-6.
41. Brusasco C, Santori G, Tavazzi G, Via G, Robba C, Gargani L, et al. Second-order grey-scale texture analysis of pleural ultrasound images to differentiate acute respiratory distress syndrome and cardiogenic pulmonary edema. J Clin Monit Comput 2022;36:131-40. doi: 10.1007/s10877-020-00629-1.