ORIGINAL ARTICLE

Assessment of Extravascular Lung Water Using Lung Ultrasound in Critically Ill Patients Admitted to Intensive Care Unit

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Abstract

Background: Lung ultrasound (LUS) is a simple bedside tool to assess overhydration. Our study aimed to assess extravascular lung water (EVLW) using B-lines and correlate it with weaning, duration of mechanical ventilation, and mortality in critically ill patients admitted to the intensive care unit (ICU).

Patients and methods: 150 mechanically ventilated ICU patients prospectively observed over 18 months, with their demographic and clinical data noted. Extravascular lung water was monitored using LUS in four intercostal spaces (ICS) from day 1 to day 5, day 7, day 10, and weekly thereafter. Pulmonary fluid burden was graded as low (1–10), moderate (11–20), and high (21–32). Weaning outcome, duration of weaning, mechanical ventilation, ICU stay, and mortality were compared in patients with and without EVLW.

Results: Out of 150, 54 patients (36.0%) had EVLW. The mean lung score amongst our patients was 8.57 ± 6.0. The mean time for detection of EVLW was 1.43 ± 2.24 days. Lung score was low in 40 (26.67%) patients, moderate in 9 (6.00%) patients, and high in 5 (3.33%) patients. Incidence of weaning failure (p-value = 0.006), duration of weaning, mechanical ventilation, ICU stay (p-value < 0.0001 each), and overall mortality were significantly higher in patients with EVLW (p-value = 0.006).

Conclusion: We conclude that a good proportion of critically ill patients have EVLW. Extravascular lung water significantly increases the duration of weaning, mechanical ventilation days, ICU stay, and overall mortality in critically ill patients.

Keywords: B-lines, Bedside lung ultrasound, Extravascular lung water, Intensive care unit, Learning ultrasound in critical care, Ultrasound.

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Highlights

Ultrasonography is a simple and efficient tool to assess extravascular lung water (EVLW) in critically ill patients. Extravascular lung water assessed via ultrasound (USG) also correlates with worse outcomes and increased mortality.

Introduction

Extravascular lung water is the fluid in the lung situated outside its vascular compartment which is influenced by hydrostatic pressure and capillary permeability.[1] Intravenous fluid is the mainstay of resuscitation in a critically ill patient and its overuse culminates in fluid overload manifesting in the form of EVLW. This is clinically associated with pulmonary edema.[2] The increase in lung water content further impairs lung function which is essential for oxygenation.[3] Studies have shown that the reduction of EVLW results in a favorable change in outcome.[4,5]

Diagnostic modalities like chest X-ray, nuclear magnetic resonance imaging, positron emission tomography, and computed tomography have been used to detect EVLW. Radiation hazards, low specificity, high interobserver variability, and the requirement of huge infrastructure limit the use of these modalities.[6] Currently thermodilution technique has emerged as a decent choice but the invasiveness of the technique and the need for regular calibrations are common limitations.[1,7,8]

Ultrasound examination of the lung presents a noninvasive, portable, and radiation-free bedside modality with decent sensitivity and specificity that is less time-consuming.[6,9] Increase in water content of the lungs leads to visualization of well-defined, hyperechoic, laser-like, comet-tail artifact emanating from the pleural line which moves synchronously with lung sliding and is known as B-lines as in Figure 1.[9,10]

Thus, we devised a study to assess the role of lung USG in the determination of EVLW. Our primary objective was to use four sectors LUS in critically ill patients to assess EVLW by means of lung score and time taken to diagnose EVLW. Our secondary objective was to correlate the effect of EVLW with weaning, intensive care unit (ICU) length of stay, duration of mechanical ventilation, and mortality.

Patients and Methods

After Institutional Ethical Committee approval (IEC/2020-11/CC-31), we conducted a prospective observational study on critically ill

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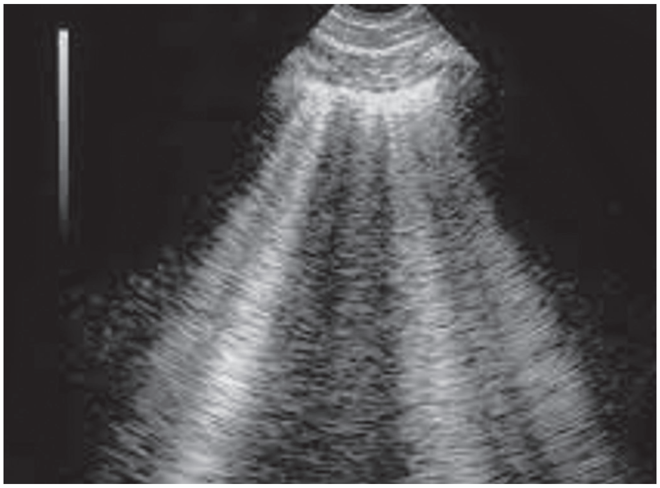

Fig. 1: Ultrasound (USG) with B-lines

patients admitted to the ICU over a period of 18 months. Inclusion criteria were mechanically ventilated patients of either sex aged more than 18 years and expected to stay in ICU for at least 48 hours, after obtaining written informed consent from the patients/relatives. Pregnant females, patients with pulmonary fibrosis, persistent pleural effusion, known lung pathology, and those who would interfere with the interpretation of LUS were excluded from our study. Patients were resuscitated and stabilized as per institutional protocol after ICU admission and a detailed history was taken. On day 1 of admission, blood was sent for routine investigations as per protocol, and a LUS was done to assess EVLW. Acute physiology and chronic health evaluation score II (APACHE II), Glasgow coma scale (GCS), and sequential organ failure assessment (SOFA) scores were also evaluated.

Monitoring of EVLW was done using LUS from day 1 to day 5 (every 24 hours), day 7, day 10, and weekly thereafter by the four-sector method. The point of care ultrasound (POCUS) performer was an anesthesiologist who had performed a minimum of 50 LUSs in ICU.

Biochemical and hematological parameters, SOFA scores, and culture sensitivity were also monitored.

An ultrasound machine with a 2–5 MHz linear/convex probe (Sono Site Micro Maxx Portable Ultrasound machine) was used for the assessment of EVLW in the ICU. In supine or semirecumbent position, we scanned four intercostal spaces (ICS) (bilateral 3rd and 6th inter costal space from sternum till midclavicular line). The number of single and confluent B-lines per ICS was used to grade the field's water content with scores marked as 0–8 (Table 1).[6]

Table 1: Lung ultrasound scoring system

Ultrasound findings	*Score*
No B-line/ICS	0
One B-line/ICS	1
Two B-lines/ICS	2
Three B-lines/ICS	3
Four B-lines/ICS	4
Five B-lines/ICS	5
Confluent B-lines >50% ICS	6
Confluent B-lines >75% ICS	7
Confluent B-lines 100% ICS	8

Thus, the total lung score (0–32) was obtained after adding the four independent values of upper and lower lung fields bilaterally. The pulmonary fluid burden was then graded as

- Low (1–10)
- Moderate (11–20) and
- High (21–32)

Patients with EVLW (EVLW +), defined as lung score >0 in our study population were categorized into low, moderate, or high groups. Extravascular lung water negative (EVLW-) patients were defined as lung score <1. The mean time taken for detection and average lung score were noted. Duration of weaning, weaning outcome, duration of ICU stay, duration of mechanical ventilation, the reason for ICU admission, mortality, demography, head injury, GCS, APACHE II score, SOFA score, serum albumin levels, PaO_2/FiO_2 ratio, serum N-terminal pro-B-type natriuretic peptide (NT Pro-BNP) levels, use of high positive end expiratory pressure (PEEP), need for renal replacement therapy (RRT), use of vasopressor, use of diuretics, sepsis, and fluid balance at 1 week were compared between patients with and without EVLW.

If extubation was successful, and there was an absence of ventilatory support for 48 hours following extubation, it was considered successful weaning. Weaning failure was considered when there was a failure of the spontaneous breathing trial, a need for reintubation and/or resumption of ventilatory support following extubation, or death within 48 hours after extubation.

A study by Bellani G et al. found the incidence of acute respiratory distress syndrome in ICUs in 50 countries (29,144 patients) to be 10.4%.[11] Using this value as a reference value, the minimum required sample size with a 5% level of significance and a 5% margin of error was calculated to be 144 patients. The total sample size taken was 150 to reduce the margin of error.

Categorical variables were represented as percentages (%) and numbers. Chi-square test was used to analyze qualitative data and Fisher's exact test was used if a cell had an expected value of less than 5. Quantitative data was presented as the Mean ± SD (if it had a normal distribution), and as the median with an interquartile range if skewed. Kolmogorov-Smirnov test was used to check data normality. Skewed data was statistically evaluated by the Mann-Whitney test (for two groups) and Kruskal–Wallis test (for more than two groups). Nominal data was statistically evaluated using an unpaired t-test. The p-value of less than 0.05 was considered statistically significant. Statistical analysis was done by using Statistical Package for Social Sciences (SPSS) software, version 25.0, IBM manufacturer, Chicago, USA.

Results

Our cohort had 150 patients with a mean age of 44.7 years 60.7% male predominance and 39.3% females. The mean predicted body weight was 61.9 kilograms. Our patients usually presented to us with a mean GCS of 7. Mean APACHE II at admission was 20.1 which dropped to 15.4 at 48 hours of ICU stay. Our mean SOFA scores on day 1 were 7.4. Most of our patients required admission for medical reasons (49%) followed by surgical reasons (41%). Trauma patients accounted for the remainder 9% of our cohort. The most common comorbidity in our patient cohort was diabetes (21.3%) followed by hypertension (20.7%).

Table 2: Demographic data and overall patient characteristics ($n = 150$)

Mean age (years)	44.68 ± 17.5
Age-group (years)#	
18–30	38 (25.33%)
31–40	31 (20.67%)
41–50	34 (22.67%)
51–60	19 (12.67%)
61–70	14 (9.33%)
>70	14 (9.33%)
Gender (Male:Female)#	91:59 (60.67%:39.33%)
Mean predicted body weight (kilograms)	61.86 ± 10.4
GCS on day 1	7.25 ± 3.26
GCS#	
≤8	85 (56.67%)
9–12	64 (42.67%)
3–15	1 (0.006%)
APACHE II score at the time of admission	20.07 ± 9.18
APACHE II score at 48 hours	15.35 ± 11.94
SOFA score on day 1	7.39 ± 3.89
Reason for admission#	
Medical	74 (49.33%)
Surgical	62 (41.33%)
Trauma	14 (9.33%)
Comorbidities#	
Diabetes	32 (21.33%)
Hypertension	31 (20.67%)
Renal disease	9 (6%)
Neurological	7 (4.67%)
Cardiac disease	5 (3.33%)
Psychiatric	2 (1.33%)
Hepatic disease	1 (0.67%)
Hematological	1 (0.67%)
Gestational hypertension	1 (0.67%)
Head injury#	7 (4.67%)
Extravascular lung water#	54 (36%)
Lung score	8.57 ± 6.01
Mean time taken for detection (days)	1.43 ± 2.24
Pulmonary burden#	
Low (1–10)	40 (26.67%)
Moderate (11–20)	9 (6%)
High (21–32)	5 (3.33%)
Duration of mechanical ventilation (days)	3.34 ± 2.54
Duration of ICU stay (days)	4.76 ± 2.72
Mortality#	34 (22.67%)

Values expressed as Mean ± SD. #Values expressed as number

During the ICU stay, 36% of our patients experienced the development of EVLW with mean lung scores of 8.57. The mean time taken to detect this was 1.4 days. The majority of these patients had low lung scores (26.7%) followed by moderate scores (6%) and the least fell into the high lung scores (3.3%). The average duration of mechanical ventilation in our cohort was 3.34 days with 4.8 days of mean ICU stay. Our cohort had a mortality of 22.7%. This is depicted in Table 2.

Our cohort was divided into those with EVLW (EVLW+) and those without EVLW (EVLW-). 54 (36%) of our patients had EVLW while 96 (54%) did not have EVLW. EVLW+ patients had a significantly higher APACHE II at admission than EVLW-(23 vs 19, $p = 0.044$) (Table 3). APACHE II scores at 48 hours had significantly higher median values in the EVLW+ group (18 vs 10.5, $p < 0.01$) (Table 3). Median day 1 SOFA scores were also significantly higher in patients with EVLW (7 vs 6, $p = 0.045$) (Table 3).

Patients with EVLW+ also required more RRT, had higher NT Pro-BNP, and had poorer PaO_2/FiO_2 ratios (defined as less than 300) on day 1 (20.4 vs 1%, 3636 vs 278 and 74.1 vs 41.7% respectively, $p < 0.01$ for all) (Table 3). The EVLW+ patients had significantly more underlying sepsis (74.1 vs 56.3%, $p = 0.03$) (Table 3) and required higher PEEP (defined as >10 cm water) (11 vs 1%, $p = 0.009$) (Table 3). However, the study failed to detect any significant difference between baseline GCS amongst both the groups. The need for vasopressors also bore no significant difference amongst the groups (Table 3).

The positive fluid balance patients also required more diuretics and had significantly lower cumulative fluid balance after 1 week (83 vs 24% and 119 mL vs 547 mL respectively, $p < 0.001$ for both) (Table 3). The ICU length of stay, duration of mechanical ventilation, and weaning were also significantly more amongst patients with EVLW+ (5 vs 4, 3.5 vs 2, and 2 vs 1 respectively, $p < 0.001$ for all) (Table 3). The failure to wean was also significantly higher amongst EVLW+ patients (19 vs 15%, $p = 0.006$) (Table 3) as was the mortality (19 vs 15%, $p = 0.006$). Mortality was higher in EVLW + than in EVLW – (19 (35.19%) vs 15 (15.63%), $p = 0.006$) (Table 3). High PEEP (≥10) requirement was more EVLW+ than in EVLW – with no statistical significance (11.11 vs 1.04%, $p = 0.009$).

Discussion

We used lung USG on 150 critically ill patients to determine EVLW and found that 36% had evidence of varying amounts of fluid overload. Our findings are corroborated by Papa et al. who found similar results across Italian ICUs with 34.5% of patients out of the 1150 patients on which lung USG was performed.[12] We used the four-sector protocol to determine EVLW in our cohort of patients. Though many approaches to study B-lines such as 28 sectors and 8-sector scans are available, the four-sector protocol is novel, rapid as well as validated for the EVLW index (EVLWI) and correlates well with thermodilution.[13,14] Using this approach, the mean time to detect appreciable fluid on USG in our study was 1.4 days.

The EVLW+ patients in our study had more weaning failure and duration of weaning days. This is probably because of higher plateau pressures and lower static compliance induced by the interstitial lung water.[3,15] This may also have been responsible for the poorer oxygenation as exemplified by poor PaO_2/FiO_2 ratios and the requirement of higher PEEP in EVLW+ patients despite the fact that PEEP can both over-estimate and underestimate EVLW. Thus EVLW+ patients also had significantly higher ventilator days and longer duration of ICU stay. Mitchell et al. had shown earlier that using pulmonary arterial catheters to quantify EVLW and using diuresis to decrease this lung fluid resulted in more ventilator-free days and reduced ICU length of stay.[5,16]

Our results show that EVLW predicted survival is in tune with many studies.[4,17] Using EVLW as a single predictor of mortality though not yet advocated, is probably useful when used in conjunction with other scores like SOFA.[17,18] As EVLW is a reflection of a single organ function, it may not be able to replace scores like SOFA and SAPS II on first day of ICU admission, but continuous monitoring can be beneficial.[19] It was shown that with an increase in EVLW above 9 mL/kg, there was an increase in mortality.[19] Past studies using the well-validated trans pulmonary indication dilution

Table 3: Comparison between those with and without EVLW

	EVLW(+) (n = 54)	*EVLW(–) (n = 96)*	*p-value*
GCS on day 1*	7 (3–10)	8 (4–11)	0.324
APACHE II at admission*	23 (16–26)	19 (12–26)	**0.044**
APACHE II at 48 hours*	18 (9.25–25.75)	10.5 (4.75–19)	**0.0005**
SOFA score on day 1*	7 (5–11)	6 (3–10)	**0.045**
Albumin (gm/dL) on day 1*	2.8 (2.125–3.5)	3.1 (2.275–3.8)	0.29
Need for RRT#	11 (20.37%)	1 (1.04%)	< **0.0001**
Serum NT Pro BNP (ng/mL) levels on day 1*	3636 (1274–11638.5)	278 (50–2825.25)	< **0.0001**
PaO_2/FiO_2 ratio <300 on day 1**	40 (74.07%)	40 (41.67%)	**0.0001**
Sepsis**	40 (74.07%)	54 (56.25%)	**0.03**
Vasopressor**	31 (57.41%)	41 (42.71%)	0.084
High PEEP (≥10)#	6 (11.11%)	1 (1.04%)	**0.009**
Diuretics**	45 (83.33%)	23 (23.96%)	<**0.0001**
Cumulative fluid balance (mL) over 1 week*	–118.96 (–432.396–229.958)	546.67 (320.417–831.125)	<**0.0001**
Weaning failure**	19 (35.19%)	15 (15.63%)	**0.006**
Duration of weaning (days)*	2 (2–3)	1 (1–2)	<**0.0001**
Duration of mechanical ventilation (days)*	3.5 (3–5)	2 (2–3)	<**0.0001**
Duration of ICU stay (days)*	5 (4–7)	4 (3–5)	<**0.0001**
Mortality**	19 (35.19%)	15 (15.63%)	**0.006**

*Mann–Whitney test; Data represented as Median [IQR-Inter quartile range]; #Fisher's exact test; **Chi-square test. *p*-value (< 0.05 is significant)

method have shown that EVLW as a parameter has a good predictive value in further course of disease.[20,21]

In our study, EVLW+ patients had significantly higher SOFA and APACHE II scores on day 1 with higher APACHE II scores even at 48 hours. 74% of our patients in the EVLW+ group had sepsis. During sepsis, inflammatory products such as neutrophil elastase, protease, collagenase, and nitric oxide are released.[22] Similar mediators are also released in trauma and postsurgical patients.[6] These mediators along with alveolar damage result in fluid extravasation in the interstitium, hence adding to the EVLW.[6,22,23] Higher association of sepsis in our cohort of patients is presumably the reason for higher baseline SOFA and APACHE II scores in our cohort.[24,25]

NT Pro-BNP levels of our cohort were significantly higher in the EVLW+ patients than in EVLW-group. The levels of these natriuretic peptides are not only governed by heart function but also by volume status.[26,27] The increased capillary permeability caused by natriuretic peptides also contributes to our study findings.[27] In addition, patients with septic cardiomyopathy also show higher levels of these peptides, and our cohort had a lot of septic patients.[28] Our study showed that day 1 albumin levels amongst EVLW+ patients bore no clinical significance to EVLW-patients despite the fact that median values were lower than the EVLW- group. It is quite possible that albumin losses are multi-factorial. The common ones are fever, malnutrition in sepsis, gut losses, and losses from damage to the glomerular basement membrane and hence it cannot have sole control over the extravasation of fluids in the pulmonary interstitium.[26,29] Also, we obtained albumin values on day 1, and serial monitoring was not analyzed. In our study, we found that the cumulative fluid balance at 1 week was significantly lower amongst the EVLW+ group when compared to the other. This was possibly due to the increased use of diuresis and RRT initiation in this group. Use of diuresis and RRT to remove extra water from the body has been found to be of benefit to patients. Due to the high load of sepsis patients in our cohort, septic AKI would have validated the need for RRT in these patients. Extravascular lung water monitoring in such patients is shown to have a clinical relevance value.[30] The ongoing confidence trial's results will also help analyze the effect of daily LUS examination to guide deresuscitation in critically ill invasively ventilated.[10]

One of the limitations of our study was that it was a single center observational study. Our sample size of 150 was small. Also, the parameters and scores need to be followed up for better generalization and the bedside lung USG was not compared with standard dilution techniques for EVLW. Secondly, scanning of lung fields in the four sectors scan does leave out a few potential areas of fluid distribution in the supine ventilated patients. Hence, further randomized studies are thus required for a better understanding of the goals of monitoring EVLW. The USG images were not stored hence interobserver variability could also have been possible. The doctor performing the POCUS was not blinded. This may add to bias but the doctor had no control over the outcomes as it was an observational study.

We thus conclude that USG is a simple, fast and efficient tool to assess and monitor EVLW in critical patients.

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