e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2024; 16(10); 358-363

Original Research Article

Assessing the Utility of Extravascular Lung Water Measurement in Managing Lung Injury in the Intensive Care Unit

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Received: 19-07-2024 / Revised: 25-08-2024 / Accepted: 20-10-2024
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Conflict of interest: Nil

Abstract

Background: Extravascular lung water (EVLW) reflects the lung fluid outside the pulmonary vasculature and is critical in conditions such as hydrostatic pulmonary edema and acute respiratory distress syndrome (ARDS). Its quantification using transpulmonary thermodilution (TPTD) has been validated and provides valuable insights into lung injury.

Objective: This study aimed to evaluate the utility of EVLW and PVPI (pulmonary vascular permeability index) in managing lung injury in critically ill patients, exploring their correlation with oxygenation parameters, radiographic assessments, and differentiation between ARDS and other pulmonary conditions.

Methods: In a prospective observational study conducted between Department of Anesthesiology and Critical care, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India for 12 months, 20 patients aged 18–60 years with septic shock requiring mechanical ventilation were included. EVLW and PVPI were measured using the Volume View® and EV1000® Clinical Platform. Oxygenation indices (PaO_2:FiO_2, $AaDO_2$) and chest radiograph scores were correlated with EVLW and PVPI. Statistical analysis included Pearson correlation and subgroup analyses for ARDS and non-ARDS cohorts.

Results: EVLW and PVPI showed strong correlations with chest radiograph scores ($r = 0.75$, $p < 0.0001$; $r = 0.63$, $p < 0.0001$) and significant negative correlations with PaO_2: FiO_2 ($r = -0.28$, $p = 0.0003$; $r = -0.35$, $p = 0.0005$). A positive correlation with $AaDO_2$ was also observed ($r = 0.34$, $p = 0.001$; $r = 0.37$, $p = 0.0011$). These parameters differentiated ARDS from non-ARDS with notable accuracy, aiding targeted fluid management and prognostication.

Conclusion: EVLW and PVPI are valuable tools for characterizing pulmonary edema, assessing oxygenation, and guiding fluid management in critically ill patients. Their integration into ICU protocols may enhance ARDS diagnosis and treatment precision.

Keywords: Acute respiratory distress syndrome (ARDS), Extravascular lung water (EVLW), Transpulmonary thermodilution (TPTD), Oxygenation, Prognostication

Introduction

Extravascular lung water (EVLW) represents the volume of fluid in the lungs outside the pulmonary circulation, encompassing interstitial, intracellular, alveolar, and lymphatic fluids, but excluding pleural effusions [1]. Elevated EVLW is a hallmark of hydrostatic pulmonary edema and acute respiratory distress syndrome (ARDS) [2], reflecting the severity of diffuse alveolar injury in ARDS cases. The measurement of EVLW, primarily achieved through transpulmonary thermodilution (TPTD), has been validated against gravimetry, the gold-standard method, in human autopsy studies [3]. TPTD can detect subtle and rapid increases in EVLW, underscoring its diagnostic precision.

The “pulmonary vascular permeability index (PVPI)”, calculated as the ratio of EVLW to “pulmonary blood volume (PBV)”, provides an indirect assessment of pulmonary capillary integrity [4]. Commercial TPTD devices are available for measuring the extravascular lung water index (EVLWI) and PVPI alongside other “hemodynamic parameters”. While EVLW reflects the total lung water volume, EVLWI normalizes EVLW to the patient’s actual or expected body weight, mitigating variability due to anthropometric differences.

In managing septic shock, maintaining organ perfusion is critical [5]. However, fluid resuscitation aimed at countering systemic vasodilation and capillary leakage can risk pulmonary edema and impaired oxygenation [6]. Traditional resuscitation endpoints often neglect volumetric measures like EVLW, which can guide decisions on fluid administration or removal. Parameters such as EVLW and PVPI help balance adequate fluid resuscitation with the prevention of over-resuscitation.

Recent critical care studies have validated EVLW measurement as a tool to characterize lung edema, predict outcomes in critically ill patients, and refine lung-targeted therapies and fluid management strategies [7]. This study aims to evaluate the role of EVLW measurement in ICU management of lung injury by correlating it with oxygenation metrics, PVPI, and chest radiograph scores while exploring its utility in distinguishing ARDS from other causes of pulmonary edema.

Material and Methods

Study Design

This prospective observational study was conducted over 12 months Department of Anesthesiology and Critical care, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India . all participants or their legally designated representatives were fully told about the study's goals, methods, possible risks, and advantages, and their written informed permission was obtained. This process ensured that participants were fully informed and voluntarily agreed to participate in the research. The study's ethical framework emphasized respect for autonomy, confidentiality, and the well-being of all participants, aligning with the principles of the Declaration of Helsinki.

Sample Size

The study included 20 critically ill patients, ages 18 to 60, who had an APACHE II score of ≥20, needed mechanical ventilation, and were diagnosed with septic shock with or without ARDS

Sample Selection Criteria

The study population consisted of patients diagnosed with septic shock, with or without accompanying ARDS, who required mechanical ventilation for respiratory support. To ensure the safety and relevance of the study, specific exclusion criteria were applied. Pregnant patients were excluded due to potential risks and physiological variations unique to pregnancy. Other exclusion criteria included individuals with coagulopathy, defined by an international normalized ratio (INR) >1.5 or a platelet count <100,000/mm³, to minimize bleeding risks. Patients with a history of pneumonectomy or lobectomy were excluded to avoid confounding factors related to altered lung anatomy.

Additionally, individuals with peripheral arterial disease or contraindications to femoral artery catheterization were excluded, as these conditions could complicate the placement of monitoring devices. Patients with deep vein thrombosis or pulmonary embolism were omitted to prevent complications during study procedures. Finally, those requiring extracorporeal membrane oxygenation (ECMO) support were excluded, as ECMO significantly alters hemodynamic and pulmonary parameters, potentially interfering with study outcomes. These criteria ensured the selection of a homogenous patient group suitable for analyzing the study objectives.

Procedure

EVLWI was measured using the EV1000® Clinical Platform and VolumeView®. To achieve exact placement in the inferior portion of the superior vena cava, the procedure involved inserting a central venous catheter through the right internal jugular vein and using chest radiography to confirm the catheter tip's position. Twenty milliliters of ice-cold saline were administered via the catheter three times, and the mean of the readings was documented. The predicted body weight (PBW) was computed using the patient's height with gender-specific equations: for males, 0.91 × (height in cm – 152.4) + 50; and for females, 0.91 × (height in cm – 152.4) + 45.5.

Anteroposterior chest radiographs were acquired simultaneously with the EVLWI readings for the radiographic evaluation of pulmonary diseases. Each lung was partitioned into six regions: upper, lower, and perihilar. The zones were evaluated on a scale from 0 to 65 according to the severity of pulmonary edema, resulting in a cumulative score ranging from 0 to 390. Two blinded radiologists separately analyzed the radiographs to guarantee an impartial assessment.

Concurrently, oxygenation and hemodynamic metrics were documented, encompassing the PaO2:FiO2 ratio and the alveolar-arterial oxygen gradient (AaDO2). The AaDO2 was computed utilizing the alveolar gas equation:

$$\mathrm{AaDO2} = [\mathrm{FiO2} \times (\mathrm{Patm{-}PH2O})] - \frac{\mathrm{PaCO2}}{0.8} - \mathrm{PaO2},$$

where the constants were set as Patm = 760 mmHg, PH2O = 47 mmHg, and R (respiratory quotient) = 0.8. Arterial blood gases provided the partial pressures of oxygen (PaO2) and carbon dioxide (PaCO2).

Measurements of EVLWI, PaO2:FiO2, and AaDO2 were performed bi-daily, and chest radiographs were acquired as clinically warranted. A total of 117 EVLWI readings were documented and examined for their connection with PaO2:FiO2 and AaDO2. Following the exclusion of three radiographs due to pleural effusion, 64 radiographs were evaluated and linked with the respective EVLWI values. The Pulmonary Vascular Permeability Index (PVPI) was assessed 99 times to determine its correlation with EVLWI, chest radiograph scores, PaO2:FiO2 ratio, and AaDO2. This thorough methodology guaranteed the precise linkage of volumetric and oxygenation metrics, yielding significant insights into the management of lung injury in critically ill patients.

Statistical Analysis

The study examined the correlation between the EVLWI and PVPI with chest radiograph scores and oxygenation metrics to understand their diagnostic and prognostic utility. Patients were categorized into ARDS and non-ARDS groups for subgroup analysis. Normality was assessed using the D'Agostino-Pearson test, and Pearson's correlation coefficient was used to assess the relationships between variables. Cohen's kappa test was used to assess inter-observer agreement, and the student's t-test was used to ascertain statistical significance. For accurate and reliable data interpretation, sophisticated statistical software was used for all statistical analyses.

Results

The baseline characteristics of the study population, consisting of 20 participants, revealed a diverse cohort with a mean age of 42 years (range 30–52), predominantly male (60%). Most patients were medical (80%) rather than post-surgical (20%). Half of the participants had acute respiratory distress syndrome (ARDS), and the cohort showed varying hemodynamic and respiratory parameters, including a baseline cardiac index (CI) of 4.10 ± 1.30 $\mathrm{ml/m^2}$, systemic vascular resistance index (SVRI) of 1600.45 ± 800.50 $\mathrm{dyne{\cdot}s{\cdot}m^2/cm^5}$, and extravascular lung water index (EVLWI) of 14.0 ml/kg (range 8.00–18.50). The pulmonary vascular permeability index (PVPI) was 3.60 (range 2.85–4.50), and the global end-diastolic index (GEDI) was 540.00 ± 160.00 $\mathrm{ml/m^2}$. The severity of illness was significant, with an APACHE II score of 21 (range 19–24), SOFA and MODS scores of 9 (range 7–11), and a $\mathrm{PaO_2{:}FiO_2}$ ratio of 190.0 (range 110–270). The $\mathrm{AaDO_2}$ was 160.0 (range 125.00–370.00), while chest radiograph scores showed variability between observers (Observer 1: 185, range 125–250; Observer 2: 125, range 30–230). The thoracic fluid content was 42 (range 30–50), and all participants required mechanical ventilation. Other parameters included baseline tidal volume (V_t) of 7.5 ml/kg (range 6.5–8.5) and positive end-expiratory pressure (PEEP) of 6 cm H_2O (range 5–8).

Table 1. Baseline characteristics of the study population

Baseline Characteristics	N = 20
Male sex	12 (60%)
Baseline SVRI ($\mathrm{dyne{\cdot}s{\cdot}m^2/cm^5}$)	1600.45 ± 800.50
Age	42 (30–52)
Baseline EVLWI (ml/kg)	14.0 (8.00–18.50)
Chest Radiograph score (Observer 1)	185 (125–250)
Thoracic Fluid Content	42 (30–50)
Baseline PEEP (cm H_2O)	6 (5–8)
$\mathrm{PaO_2{:}FiO_2}$ ratio	190.0 (110–270)
Baseline V_t (ml/kg)	7.5 (6.5–8.5)
Baseline CI ($\mathrm{ml/m^2}$)	4.10 ± 1.30
Baseline GEDI ($\mathrm{ml/m^2}$)	540.00 ± 160.00
Mechanical ventilation requirement	20 (100%)
Medical vs post-surgical patients	16 vs 4
Baseline PVPI	3.60 (2.8500–4.5000)
ARDS	10 (50%)

Chest Radiograph score (Observer 2)	125 (30–230)
MODS score	9 (7–11)
SOFA score	9 (7–11)
$AaDO_2$	160.0 (125.00–370.00)
APACHE II score	21.0 (19–24)

Correlation coefficients and corresponding p-values for several parameters are shown in Table 2. There is a considerable positive association between the EVLWI and the chest radiograph ratings from both observers. A somewhat positive association with $AaDO_2$ ($r = 0.34$, $p = 0.001$) and a moderately negative correlation with the $PaO_2:FiO_2$ ratio was also demonstrated by EVLWI. Furthermore, a high positive correlation exists between EVLWI and PVPI. Additionally, there is a negative moderate association with $PaO_2:FiO_2$ ($r = -0.35$, $p = 0.0005$), a positive moderate correlation with $AaDO_2$, and substantial correlations with chest radiograph scores. All the correlations are statistically significant, suggesting meaningful relationships between these variables.

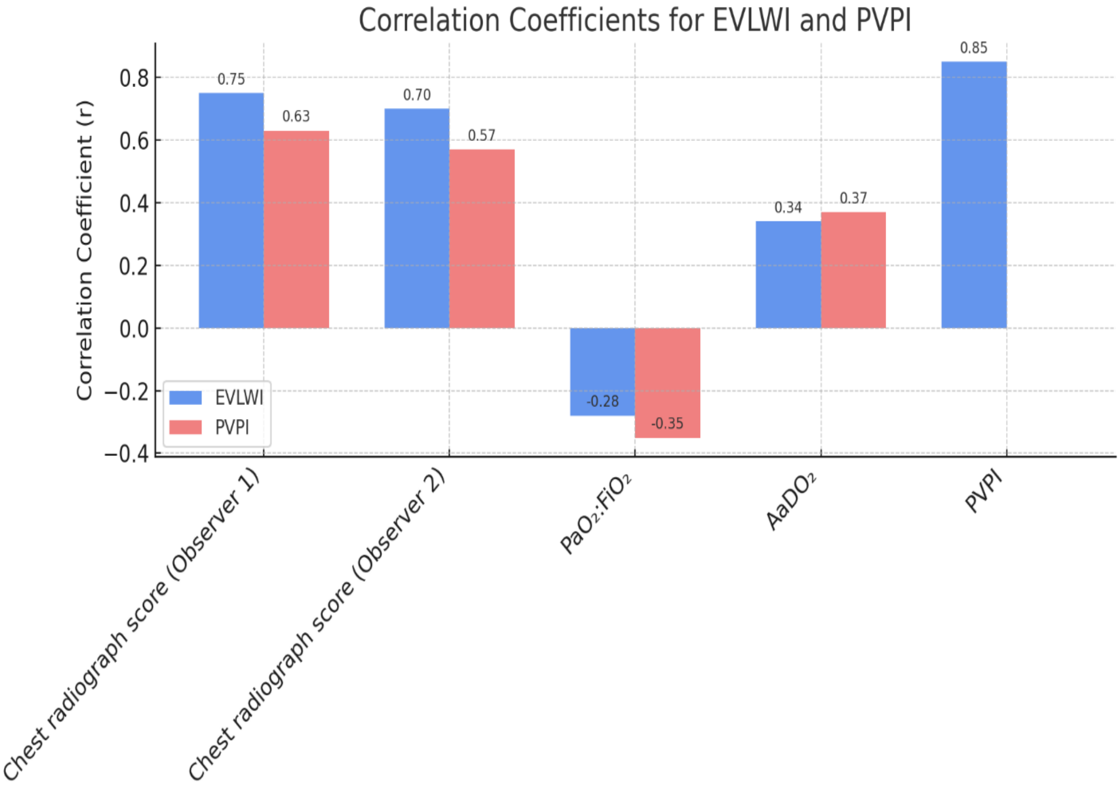

Figure 1. Correlation coefficients and P values of correlation

A subgroup study that compares patients with ARDS and those without non-ARDS on several measures is shown in Table 3. The baseline EVLWI and PVPI did not differ significantly between the two groups (p-values of 0.22 and 0.34, respectively). However, the correlations between EVLWI and other respiratory parameters showed notable differences. In ARDS patients, there was a strong, significant negative correlation between EVLWI and $PaO_2:FiO_2$ ($r = -0.65$, $p < 0.0001$) and a strong, significant positive correlation between EVLWI and $AaDO_2$ ($r = 0.59$, $p < 0.0001$). In contrast, non-ARDS patients showed weaker and non-significant correlations ($PaO_2:FiO_2$: $r = -0.18$, $p = 0.09$; $AaDO_2$: $r = 0.12$, $p = 0.15$). These differences were statistically significant ($p = 0.002$ for $PaO_2:FiO_2$ and $p = 0.004$ for $AaDO_2$). The correlations between PVPI and both $PaO_2:FiO_2$ and $AaDO_2$ were weaker in both groups, with no significant differences between the groups (p-values of 0.057 and 0.112, respectively).

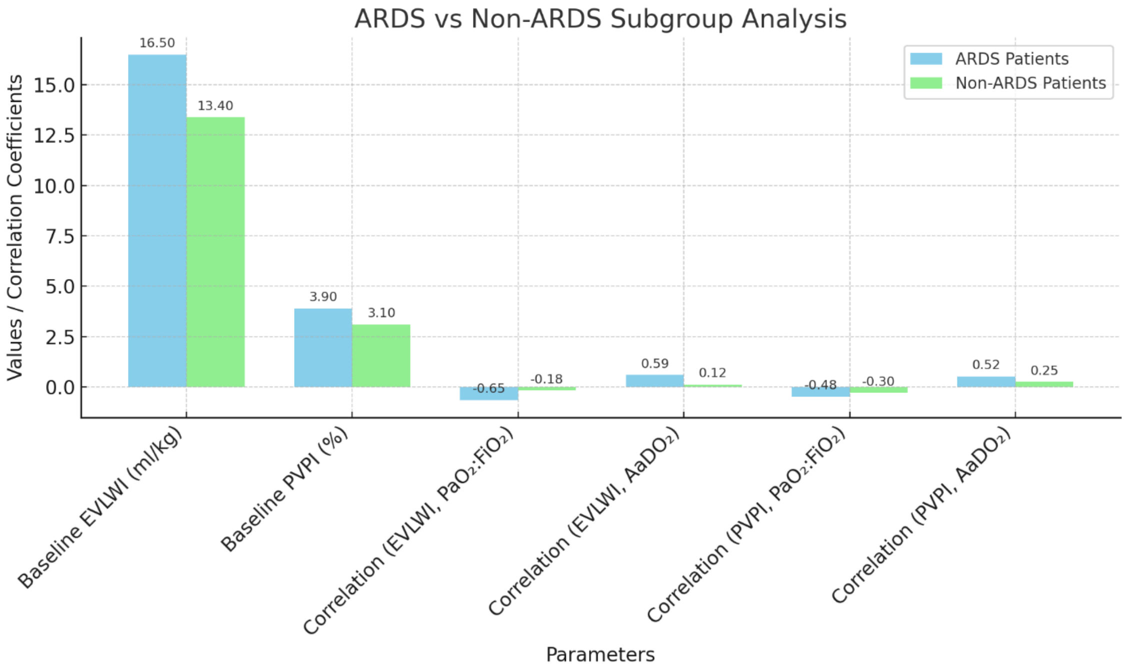

Figure 2. Acute respiratory distress syndrome and nonacute respiratory distress syndrome subgroup analysis

Discussion

This study investigated the relationship between TPTD parameters (EVLWI and PVPI) and the severity of lung injury, as measured by oxygenation metrics, including PaO_2:FiO_2 and $AaDO_2$. We investigated the noninvasive evaluation of pulmonary edema via chest radiograph scoring and its connection with EVLWI and PVPI measurements. EVLW was correlated with anticipated body weight (PBW) rather than actual body weight since it more accurately represents patient prognosis (Jozwiak et al., 2013) [8]. Measuring EVLWI using TPTD is expensive and intricate in critical care unit; yet it offers a consistent, quantitative assessment of pulmonary edema that is responsive to minor variations in lung water (Martin et al., 2012) [9]. Conversely, chest radiographs are more readily available yet susceptible to inter-observer variability and affected by conditions such as pleural effusion, consolidation, and atelectasis, as demonstrated in our study where three radiographs were eliminated due to pleural effusion.

Our findings demonstrated a moderate negative correlation between EVLWI and the PaO_2:FiO_2 ratio, consistent with prior research (Martin et al., 2012) [9], and a moderate positive correlation with $AaDO_2$, which corresponds with earlier studies (Phillips et al., 2009) [10] but contradicts a study employing a double indicator dilution system (Jozwiak et al., 2013) [8]. Elevations in EVLWI and PVPI indicate prevalent physiological disturbances in septic shock and ARDS, attributed to enhanced capillary permeability that permits the effusion of protein-rich fluid across the capillary endothelium (Jozwiak et al., 2013) [8]. The robust connection between EVLWI and PVPI in our study corresponds with the established relationship between these two indices. Clinical investigations indicate elevated PVPI in ARDS relative to hydrostatic pulmonary edema (Martin et al., 2012) [9]. Elevated pulmonary vascular permeability results in augmented extravascular lung water (EVLW) and diminished lung compliance, hence exacerbating hypoxemia by intrapulmonary shunting.

In the subgroup analysis, baseline EVLWI and PVPI were elevated in ARDS patients relative to non-ARDS patients, albeit not significantly, probably due to the confounding influences of sepsis and multiorgan dysfunction. Prior research, including a study by Martin et al. (2012), indicated that certain patients with clinical ARDS did not exhibit increased EVLWI, while individuals with severe sepsis could present elevated EVLWI without fulfilling the Berlin criteria for ARDS. Our results align with existing studies, indicating that sepsis-induced lung damage may lead to elevated EVLWI and PVPI without meeting ARDS criteria. The superior correlation of EVLWI and PVPI with PaO_2: FiO_2 and $AaDO_2$ in ARDS patients illustrates the pathophysiology of ARDS, wherein intrapulmonary shunting significantly contributes to hypoxemia, whereas in non-ARDS patients, sepsis-induced permeability alterations may coexist with additional hypoxemic factors (Phillips et al., 2009) [10].

Our study has multiple limitations, notably a limited sample size, which may have diminished statistical power. Despite numerous measures conducted on each patient to provide sufficient power, an increased sample size could have alleviated some biases. A further concern is the reliability of TPTD in patients exhibiting severe ventilation-perfusion mismatch, which may obstruct access to inadequately perfused regions of the pulmonary vascular bed (Jozwiak et al., 2013). Furthermore, although we omitted chest radiographs exhibiting pleural effusion, we were unable to utilize ultrasonography or CT scans to exclude minor pleural effusion. Ultimately, the limited study population precluded an evaluation of the prognostic significance of EVLWI about mortality outcomes, as well as the effects of a negative fluid balance intended to diminish EVLWI on oxygenation and other physiological parameters. Moreover, fluid balance was not documented consistently, potentially influencing the outcomes due to fluctuations in physician and nurse efforts.

Conclusion

In conclusion, this study underscores the utility of EVLWI and PVPI as robust markers in managing lung injury among critically ill patients in the ICU. EVLWI's diagnostic and prognostic usefulness is highlighted by the substantial connections it has with oxygenation measures (PaO_2:FiO_2 and $AaDO_2$), chest radiograph scores, and PVPI. These indices not only differentiate ARDS from other causes of pulmonary edema but also aid in tailoring fluid management strategies. By integrating EVLWI and PVPI into routine clinical practice, healthcare providers can optimize treatment protocols, improve oxygenation, and potentially enhance outcomes in patients with severe respiratory compromise.

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