**The Role Of Ultrasound In Assessment of Positive End-Expiratory Pressure–induced Lung**

**Recruitment In ARDS Patients**

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**ABSTRACT**

In the case of critically sick patients, acute respiratory distress syndrome (ARDS) may be life-threatening and necessitate the need for intensive care unit (ICU) admission. Continuous monitoring is required for mechanical ventilation and recruitment movements as necessary. In this research, the goal is to investigate the use of ultrasonography in the evaluation of positive end exhalatory pressure–induced Lung Recruitment in ARDS patients. Methods and Subjects: A total of 25 ARDS patients were included in this research, which was done in the hospital's respiratory care unit. All of the patients were seen by a doctor, had a chest X-ray, and had laboratory tests. Mechanical ventilation was used in the care of all patients. Using PEEP values of 5 and 15, we measured PV and LUS tracings. The PV curve approach was used to assess PEEP-induced lung recruitment. Between PEEP 5 and PEEP 15, there was an extremely strong positive connection between reaeration score and the change in lung volume (r = 0.737, P 0.001). Results: Between PEEP 5 and PEEP 15, there was a substantial (r=0.577, P=0.003) positive association between the reaeration score and the decrease in PaO2. There was a substantial negative association between reaeration score and mortality (rpb = - 0.842, P 0.001), in which mortality reduces as the score increases. Conclusion: For quantitative evaluation of PEEP-induced lung recruitment, bedside LUS is equal to the PV curve approach. In patients with ARDS, positive end-expiratory pressure (PEEP)-induced Lung Recruitment may be assessed using ultrasonography.

**Keywords:** lung ultrasound; acute respiratory distress syndrome; positive end-expiratory pressure; lung recruitment.

**Introduction**

 Patients in severe condition are more likely to develop acute respiratory distress syndrome (ARDS), a clinical illness (1). A chest X-ray or computed tomography is required to detect bilateral pulmonary infiltrates, which is the current diagnostic standard for ARDS according to the Berlin definition of 2012. (2). The Kigali Modification of the Berlin criteria, among other revisions, allows for either chest radiography or lung ultrasonography to be utilised to determine bilateral pulmonary infiltrates (3). Chest radiography is less sensitive than other imaging modalities, such as computed tomography, in detecting pulmonary infiltrates, and it also uses radiation (4). For up to 30 percent of patients, lung CT has led to changes in clinical care, but since it entails transporting the patient to a radiological department and exposing them to high radiation doses, CT cannot be administered frequently and repeated conveniently (5). Intensive care units are increasingly using ultrasound treatments (ICUs). They are noninvasive and may be done at the bedside (6). An alternative to chest radiography in the detection of ARDS may be lung ultrasonography. In the diagnosis of particular clinical characteristics such as interstitial edoema, consolidation, and pleural effusion it has been shown effective (7). When a patient has ARDS, mechanical ventilation is almost always needed to help them breathe easier and provide more oxygen to their tissues. An increase in positive end-expiratory pressure may help oxygenation in a large number of individuals (PEEP). PEEP is used in ARDS patients to prevent lung derecruitment at the end of expiration and to promote oxygenation via increased lung aeration (8). Positive end-expiratory pressure (PEEP) and other treatment methods in critically sick patients benefit greatly from bedside visualization of lung shape and aeration loss (9). Medical ultrasound (US) may be regarded a reliable tool for detecting nonaerated lung areas and optimizing positive end-expiratory pressure (PEEP) in patients undergoing mechanical ventilation (8). Static pressure–volume (PV) curve analysis has been suggested and recently confirmed against CT and ultrasonography in order to improve PEEP in the bedside technique. Deep sedation and muscular relaxation are required, and this procedure cannot be conducted on individuals who are still able to breathe on their own (10).

Patients and methods

In all, 25 patients with ARDS were included in this trial, which took place from December 2020 to April 2022 at Benha University Hospital's respiratory care unit.

**Inclusion criteria:**

ARDS patients were identified according to Berlin criteria 2012 that have declared new classification of ARDS; PaO2 / FiO2 ratio ≤300 and >200 is mild ARDS; PaO2 /FiO2 ratio 100- 200 is moderate ARDS; PaO2 /FiO2 ratio <100 is severe ARDS. In this new criteria, the minimum level of PEEP required for diagnosing ARDS is 5cmH2O. This value excludes hypoxemia caused by atelectasis. Imaging criterion of ARDS is bilateral infiltrate on chest X-ray that can't be explained by effusion, collapsed lung, or lung **(11)**.Additionally, imaging can be derived from CT chest that reveals a heterogeneous bilateral pulmonary infiltrate mainly in gravity dependent lung regions **(12)**.The new Berlin definition stated that the maximum period between risk factor exposure and ARDS development is 7 days. The choice of 7 days was made because nearly all patients developed it within 7 days after exposure to risk factor **(13)**.

**Exclusion criteria (8)**

The presence of subcutaneous emphysema was an exclusion criterion

Pneumothorax, severe obesity, pregnancy, and patients who couldn't keep their arterial oxygen saturation over 85% while PEEP was being decreased are all reasons for concern.

**Methods:**

Following are the procedures for all patients in this study:

Informed written consent was obtained from patient's relatives.

• Complete history taking.

This includes a full physical exam (General& Local).

• X-ray of the chest.

• Chest CT (when needed).

• Echocardiography

• Experiments in the laboratory (e.g. kidney function tests "KFTs", liver function tests "LFTs", complete blood count "CBC" and erythrocyte sedimentation rate "ESR").

A steady 8 litres per minute flow rate and an inspiratory pressure of 40 centimeters of water are used in mechanical ventilation in the pressure assist-control mode using CARESCAPE R860 software Revision 10, Madison WI53707-7550, Made in USA.

• Pressure–Volume Programmable Ventilator (PV) software was used to assess PEEP-induced Lung Recruitment (LR) curves. After an expiratory pause at PEEP 5 and PEEP 15 cm H2O in anaesthetized and paralysed patients. The difference in lung volumes between PEEP 5 cm H2O and PEEP 15 cm H2O was used to measure the effect of PEEP.

• Lung Ultrasound "LUS": using Philips Hd5 color Doppler Ultrasound Machine, Tokyo, Japan. A Philips C5-2 Curved Array Probe with frequency 5 MHz was used to conduct LUS. Examined the upper and lower intercostal gaps of anterior, lateral, and posterior regions of left and right chest (12 areas were examined 6 areas on right and 6 areas on left). We spent a lot of time looking at every single one of the potential areas of concern. **(Figure 1)** a) Normal aeration (N): presence of lung sliding with A lines or less than two isolated B lines on ultrasound

As a result, there are many distinct B lines in the lungs (B1 lines)

Severe air loss in the lungs with several B lines coalescing (B2 lines)

Consolidation of the lungs (C): the existence of dynamic air bronchograms in the tissues.

Within 15 minutes after adjusting PEEP to 5 cm H2O, a LUS and ABG were done. An ultrasound reaeration score was then derived from changes in the ultrasound pattern in each location after the procedure was repeated after 15 minutes at PEEP 15 cm H2O. Calculation of the ultrasonography reaeration score was as follows: Before and after 15 cm H2O of positive end-expiratory pressure, ultrasonography lung aeration (N, B1, B2, and C) was measured in each of the 12 lung areas studied. Secondly, the ultrasonography lung reaeration score was generated by summing up the scores for each lung area evaluated as given in the table.

|  |
| --- |
| Quantification of reaeration |
| 1 point | 3 points | 5 points |
| B1 N | B2 N |
|  B2 B1 | C B1 | C N |
| C B2 |

The PEEP-induced lung recruitment PV curves were compared to the ultrasound lung reaeration score.

The statistical analysis was conducted using the Software, Statistical Package for Social Science, (SPSS Inc. Released 2009- PASW Statistics for Windows Version 21.0. Chicago: SPSS Inc.). Data were presented and suitable analysis was done according to the type of data obtained for each parameter. Shapiro-Wilk test was done to test the normality of data distribution. Significant data was considered to be nonparametric. The collected data were summarized in terms of Mean ± Standard deviation (± SD) and range (minimum - maximum) for parametric numerical data, while Median (Q2), lower quartile (Q1), upper quartile (Q3) and IQR (IQR = Q3 − Q1) for non-parametric numerical data. Qualitative data presented as number (No.) and percentage (%). Paired sample t test (for parametric) or Wilcoxon signed rank sum test (for non-parametric) was used to assess changes in parameters over 2 occasions. Marginal Homogeneity test used for categorical data to analyze the significance difference between different stages, it’s an extension of the McNemar test for dependent samples. Pearson’s correlation (r) used to measure the strength and direction of association between two numerical variables. Point-biserial correlation (point-biserial correlation coefficient (rpb) used to measure the strength and direction of association between continuous and dichotomous variables. Linear regression analysis was used for detection of predictors of change in lung volume, using generalized linear models. Receiver Operating Curve (ROC) analysis was carried out to evaluate the diagnostic performance of aeration score for change in lung volume. The cutoff point and the corresponding sensitivity and specificity, and Area Under the Curve (AUC) were estimated. After the calculation of each of the test statistics, the corresponding distribution tables were consulted to get the “P” (probability value). Statistical significance was accepted at P value <0.05 (SS). A P value <0.001 was considered highly significant (HS) while a P value > 0.05 was considered non-significant (NS).

**RESULTS**

Twenty-five patients were assessed in this study. The mean age of the studied group was 57.72 ± 17.4 and the age ranged between 10 and 85 years. Median age for studied group was 60 years, ranged from 42 to 69 years. Sixty percent of them were males and 40 % were females. Thirty six percent of the patients had diabetes mellitus, 20% had stroke and 20% had past history of trauma. About 12% of patients had hypertension. Ischemic heart disease, systemic lupus eryromatosis"SLE", chronic kidney disease"CKD", acute kidney disease"AKI", Guillain Barre Syndrome, postoperative history, DVT and intracranial hemorrhage were detected in 4% of patients. Community acquired pneumonia"CAP" was the cause of ARDS among 60%, ventilator associated pneumonia"VAP" among 24%, and Aspiration pneumonia among 16%. The primary weaning success had been reported among 5 patients (20%), and weaning success in the second trial had been registered among one patient [5%]; tracheostomy had been indicated for 12%, and the mortality rate was 76%. Increased PEEP was associated with significant progressive increase of lung volume among studied populations (P<0.001). Also, there was a high significant progressive increase of partial oxygen tension with increased PEEP values from PEEP 5 to PEEP 15 (P<0.001). Furthermore, PaO2/FiO2 significantly increased with the progressive increase of PEEP (P <0.001). However, the paired comparison of PaCO2 and PH did not provide any significant differences at PEEP 5 and PEEP 15 (**table 1).** The mean reareation score was 6.36±3.72 and ranged between 3 and 118 and the mean lung volume difference 96.2±62.64 and ranged between 30 – 250 cm H2o (**table 2).** Increased PEEP was associated with significantchangesinaeration patterns(P<0.001) (**table 3).** Increasing PEEP from 5 cm H2O to 15 cm H2O had highly significant effect on chest ultrasound on right lower anterior, right upper axillary, left lower anterior, left upper axillary and left lower axillary areas and has significant effect on right upper anterior, right lower axillary, right upper posterior, right lower posterior and left upper posterior while has no effect on left upper anterior and left lower posterior. There was highly significant negative strong correlation between reaeration score and mortality (*r*pb = - 0.842, P<0.001). Also, there was highly significant positive strong correlation between reaeration score and change of lung volume between PEEP 5 and PEEP 15 (*r*= 0.737, P <0.001).Furthermore, there was significant positive moderate correlation between reaeration score and change in PaO2 between PEEP 5 and PEEP 15 (*r*= 0.577, P=0.003) (**table 4**). The reareation score was significant predictor for change in lung volume (P<0.001). The lung volume was more among patients with higher aeration score. Regression equation (Y= a + b X) was as follow Y=17.42 + 12.39 X indicating that the coefficient for reareation score is 12.39 cmH2o. The coefficient indicates that for every additional unit change in reareation score, we can expect change in lung volume to increase by an average of 12.39 cmH2o. So, the predicted value for lung volume change at reareation score 6 equals 91.76 cmH2o (**table 5).** The cut off value for reareation score that indicates changes in lung volume more than 90 cmH2o is 6.5 with sensitivity 86% and specificity 94%. The area under the curve (AUC) equals 0.952 with statistically significant difference (p = 0.001) (**table 6).**

**DISCUSSION**

When a patient has ARDS, mechanical ventilation is almost always needed to help them breathe easier and provide more oxygen to their tissues. When ARDS was first identified, raising positive end expiratory pressure (PEEP) was suggested as a way to increase oxygenation (14).

Acute respiratory distress syndrome (ARDS) severity assessment, planning recruitment techniques, and establishing appropriate PEEP levels during mechanical ventilation may all depend on the capacity to recruit (15).

Clinical trials have yet to demonstrate any advantage in terms of patient-centered outcomes—and even imply harm—from recruiting methods without the use of any monitoring (16).

Intensivists are increasingly turning to ultrasonography to learn more about the lung in a noninvasive manner at the patient's bedside. If the standard techniques (bedside radiography and CT) did not have limitations (irradiation, limited information content for radiography, and transportation...), then lung ultrasonography would be of little interest. In many circumstances, ultrasonography may be utilized in place of CT scans, according to our research. Using one universal probe and simple machinery, critical ultrasonography, which includes pulmonary ultrasound, is characterized as using a whole-body approach with a single universal probe and developing novel applications (17).

ARDS patients with positive end-expiratory pressure–induced lung recruitment were studied to see whether ultrasonography may help with that evaluation.

In order to better understand the study's goals, a 2- to 4-MHz convex probe was used to conduct LUS on 25 ARDS patients (15 men and 10 women) hospitalized to the respiratory care unit at Benha University Hospital between December 2020 and April 2022.

PV curves were used to determine PEEP-induced lung recruitment and to compare that data with the ultrasonography reaeration score.

Mean PaO2 was found to be 74.4821.64 at PEEP 5 and 87.7233.51 at PEEP 15, with a strong significant rise in partial oxygen tension with increasing PEEP levels (P0.001). When PEEP was raised from 5 to 15, the mean PaO2/FiO2 rose from 94.92 to 114.63 mmHg, a significant increase (P 0.001). But the matched analysis of PaCO2 and PH at PEEP 5 and PEEP 15 showed no significant changes **(table 1)**. Because the solubility of a gas in a liquid is exactly proportional to the pressure above the solution's surface, raising PEEP will raise pressure in the system. This may be explained by Henry's law. Solubility of oxygen and capacity to pass alveolocapillary membrane is increased as a result, resulting in an increase in blood's oxygen concentration. In addition, Extrinsic PEEP may be utilised to correct ventilation-perfusion (VQ) mismatches, as well. Extrinsic PEEP has a direct effect on oxygenation and an indirect effect on ventilation because it may open or "splint" airways that would otherwise be collapsed, reducing atelectasis and enhancing alveolar ventilation, which in turn reduces VQ mismatch. The alveolar surface expands as a result of increased airflow, allowing for greater gas exchange and improved ventilation. The main aim of using extrinsic PEEP is to increase ventilation, however this should never be done (21). To back up this finding, Bouhemad et al. (18) conducted research showing that in patients with focal loss of aeration, the mean PaO2/FiO2 was 205±105 at PEEP 0 and 282±106 at PEEP 15, and that this significantly increased with the progressive increase in PEEP (P 0.001). In patients with diffuse loss of aeration, the mean PaO2/FiO2 was 146±60 at PEEP 0 and 241±92 at PEEP In contrast, the mean PaCO2 was 39± 67 at PEEP 0, and it was 38 ±67 at PEEP 15, indicating no statistically significant changes when PEEP was gradually increased. As PEEP levels increased from 5 to 15 cm H2O in Stefanidis et al. (1), all patients showed a significant increase in PaO2 and PaO2/FiO2 ratios and corresponding decreases in the nonaerated lung area.

Increased PEEP was linked with a substantial progressive increase in lung volume across the examined groups (P0.001), as did mean lung volume at 5 cm H2O (325.4±72.7 ml at PEEP 5 and 421.6±113.125 ml at PEEP 15). **(table 1)**. Alveoli that have previously been vented may be recruited or dilated further to explain this (22). Patients with focal loss of aeration experienced lung recruitment measured with the PV curve at 347 ml, while patients with diffuse loss of aeration experienced recruitment measured at 834ml, according to the findings of a study by Bouhemad et al. (18). The researchers found that increased PEEP was linked to a significant progressive increase in lung volume in all of the populations studied (P0.001).

Mean reareation score: 6.36±3.72; varied from 3 to 118; ranged from 30 to 250 cm H2o; and mean lung volume difference: 96.2±62.64 cm H2o **(table 2)**. According to Mohamed et al. (19), the LUS score dropped from 25.3±6.3 prior to recruitment to 17.4±6.5 following recruitment with a p value of (0.001), which is significant, and after 12 hours it dropped significantly to (15.38±8.62) with a p value of (0.001)... This was in agreement with their findings.

Aeration patterns changed significantly when PEEP was raised (P0.001) (**table 3).** A study by Bouhemad et al. (18) observed an increase in the number of B lines in the anterior and lateral chest walls following the administration of PEEP, as well as an absence of B lines and the transformation of ultrasonic consolidation into B lines. In the back of the chest, PEEP had only a small effect on existing consolidations.

The current study found that increasing PEEP from 5 cm H2O to 15 cm H2O had a highly significant effect (P 0.001) on chest ultrasound on the right lower anterior, right upper axillary, left lower anterior, left upper axillary, and left lower axillary areas, while having no effect on the left upper posterior. These findings are in keeping with the findings of Tang et al. (23) who found that during lung recruitment, ultrasonography demonstrated a reduction in the B line and a shift in consolidation to an air bronchogram under various PEEP levels. The anterior and lateral chest walls were the areas where most of these modifications took place. Few alterations were made to the back of the chest. PEEP reduced ultrasonography B-lines in various locations of the right and left lungs with time, according to Abdelhameed et al. (20). A2 on the right side, where the impact is most pronounced, was shown to be substantial at PEEP 9, but only after PEEP 6. There were 48 consolidations, 19 in the dependent and 29 in the non-dependent intercostal areas, which were studied by Rode et al (24) Two non-dependent and two dependent consolidations were unable to be recruited.

Reaeration score was shown to have a substantial negative connection (rpb = -0.842, P0.001) with mortality in the present research (**table 4).**  For example, as reported by Salem et al. (25), there was a statistically significant difference in survival rates between the LUS (27) and the FiO2 (25.33) groups, who received PEEP levels based on LUS scores. According to Radwan et al. (26), the death rate was 36% in group A, 18 patients, whereas the mortality rate was 40% in group B, six patients, and there was no statistically significant difference in the mortality rate between the two groups.

Between PEEP 5 and PEEP 15, there was a significantly significant (r = 0.737, P 0.001) positive connection between the reaeration score and the change in lung volume (**table 4).** PEEP-induced lung recruitment was assessed by the PV curve technique, and ultrasonography reaeration score (P 0.0001) was shown to be highly statistically significant (Bouhemad and colleagues, 18).

Reaeration score and decrease in PaO2 (r=0.577, P=0.003) showed a strong positive connection between PEEP 5 and PEEP 15 (r = 0.577). (**table 4).** Statistically significant connection was discovered between the LUS reaeration score and a rise in PaO2 generated by PEEP in Bouhemad et al. (18) investigation. Mohamed et al. (19) discovered a significant negative connection between LUS score and PaO2/Fi O2 following recruitment maneuver (p value 0.001r=-0.8) the same after 12 hours with (p value 0.001,r=-0.8). In other words, the higher the PaO2/FiO2the lower the LUS score becomes. There was no significant correlation between the rise in PaO2 and decrease in non-aerated lung area (r = -0.2, P = 0.9) by Stefanidis and colleagues (1).

Reareation score was shown to be a significant predictor of lung volume change (P 0.001). Reareation score is 12.39 cmH2o, which means that for every unit rise in reareation score, we may anticipate a change in lung volume to increase by an average of 12.39 cmH2o (**table 5).** As a result, the cut-off value for the reareation score that shows increases in lung capacity of more than 90 cmH2o is 6.9 (86%) and 94% (94%) specificity. There is a statistically significant change (p = 0.001) in the AUC (area under the curve) (**table 6).**Ultrasound lung reaeration scores of 18 or above were used by Bouhemad et al. (18) to identify PEEP-induced lung recruitment more than 600 ml. PEEP-induced lung recruitment ranging from 75 to 450 ml was linked with an ultrasonography lung reaeration score of 14 or more.

**CONCLUSION**

PEEP-induced lung recruitment may be quantified using bedside LUS, which is identical to the PV curve approach. In patients with ARDS, positive end-expiratory pressure (PEEP)-induced Lung Recruitment may be assessed using ultrasonography. Monitoring may be done on a daily basis using widely accessible, portable ultrasonography, and this information might be used to guide treatment decisions.

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**Table (1): Effect of PEEP on ABG , PFR and lung volume.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Variable** | **PEEP 5** | **PEEP 15** | **t-Test** | **P value** |
| **Mean ±SD**  | **Mean ±SD** |
| **PH** | 7.27±0.293 | 7.35±0.515 | 0.68 | 0.5 |
| **PaO2** **(mmHg)** | 74.48±21.64 | 87.72±33.51 | 4.39 | <0.001 |
| **PaCO2 (mmHg)** | 48.6±9.89 | 47.8±10.21 | 0.28 | 0.78 |
| **PaO2/FIO2** | 94.92±41.97 | 114.63±67.57 | 4.38 | <0.001 |
| **Lung volume at 15 cm H2O**  | 325.4±72.7 | 421.6±113.125 | 4.38 | <0.001 |

*\** PFR: PaO2/FIO2 ratio

**Table (2):** **Mean reareation score and changes in lung volume between PEEP 5 and PEEP 15.**

|  |  |
| --- | --- |
| **Variable** | **Statistics** |
| **Mean ±SD (range)** | **Median (Q1, Q3) (IQR)** |
| **Reareation score** | 6.36± 3.73 (3-18) | 4 (4,7) |
| **Changes in lung volume between PEEP 5 and PEEP 15** | 96.2±62.64 (30-250) | 70 (57.5-125) |

**Table (3): Ultrasound aeration patterns found at PEEP 5 and PEEP 15:**

|  |  |  |
| --- | --- | --- |
| **Ultrasound finding** | **Frequency****(n = 300)****No. (%)** | P value |
| PEEP 5 | PEEP 15 |
| **N** | 35 (11.7% ) | 82 (27.3% ) | <0.001 |
| **B1** | 79 (26.3% ) | 111 (37% ) |
| **B2** | 137 (45.7% ) | 78 (26% ) |
| **C** | 49 (16.3% ) | 29 (9.7% ) |
| **Total** | 300 (100%) | 300 (100%) |

*N =Normal, B1 =* *multiple well-defined B lines, B2=* *multiple coalescent B lines, C=* *consolidation*

**Table (4):** **Correlation between mortality and aeration score, Changes of lung volume and aeration score, Changes in PaO2 and aeration score among patients (n=25).**

|  |  |  |
| --- | --- | --- |
| **Reareation score****Variable** | **Correlation****coefficient (*r*pb)** | **P** |
| **Mortality** | -0.842 | <0.001 |
| **Changes of lung volume** | 0.737 | <0.001 |
| **Changes in PaO2** | 0.577 | 0.003 |

**Table (5): Regression analysis for prediction of higher changes in lung volume.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Change in lung volume (Y)****Predictors** | **F&P of the model** | **Constant (a)** | **Beta (b)** | **t-Test** | **P value** |
| **Reareation score (X)** | F=27.42P <0.001 | 17.42 | 12.39 | 5.24 | <0.001 |

**Table (6): Receiver operating characteristic (ROC) curve for diagnostic performance reareation score for change in lung volume > 90** **cmH2o.**

|  |
| --- |
| **Changes in lung volume** |
| **Cutoff** | 6.5 |
| **Sensitivity (%)** | 86% |
| **Specificity (%)** | 94% |
| **AUC (95% CI)** | 0.952 (0.86 – 1) |
| **P value** | **0.001** |

**Figure (1): Ultrasound areation pattern.** (A) Normal aeration pattern showing pleural line (red arrow), rib (orange arrow), acoustic shadow (blue arrow). (B) B1 areation pattern showing multiple distinct B lines (red arrow). (C) B2 areation pattern showing multiple confluent B lines (red arrow). (D): C aeration pattern showing consolidation with air bronchogram (red arrow

