Relationship of End Expiratory Lung Volume, Compliance, and Plateau Pressure in Acute Respiratory Distress Syndrome

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ABSTRACT

COVID-19 ARDS (acute respiratory distress syndrome), caused by *SARS-CoV*-2, involves a decrease in the end expiratory lung volume (EELV), compliance, and hypoxemia. The authors retrospectively analysed the relationship between the EELV, Plateau pressure (Pplat), and compliance of the respiratory system in a group of 21 mechanically ventilated COVID ARDS patients with moderate to severe hypoxia who were subjected to a recruitment manoeuvre. Further, these parameters were studied after dividing them into two groups as Group 1 of clinically non-recruitable and Group 2 of clinically recruitable patients. There was relationship between EELV, compliance, and Pplat among those patients who were clinically recruited *versus* those who were not in a homogeneous group of COVID ARDS patients. In Group 1, the statistical value of EELV and compliance were $r = 0.395$, $p>0.05$, EELV and Pplat were $r = 0.021$, $p>0.05$, and compliance and Pplat were $r = -0.848$, $p<0.001$. In Group 2, the statistical values of EELV and compliance were ($r = 0.605$, $p<0.001$), EELV and Pplat were $r = -0.391$, $p<0.05$, compliance and Pplat were $r = -0.848$, $p<0.001$. The additional information gained after understanding this relationship can help to optimise ventilator settings.

Key Words: *COVID, ARDS, End expiratory lung volume, Plateau pressure, Compliance, Recruitment, Ventilation.*

How to cite this article: Saseedharan S, Patil S, Rambhad S, Kadam V, Yadav A, Bagade R. Relationship of End Expiratory Lung Volume, Compliance, and Plateau Pressure in Acute Respiratory Distress Syndrome. *J Coll Physicians Surg Pak* 2023; **33(10)**:1204-1206.

COVID-19 ARDS (acute respiratory distress syndrome) involves acute hypoxemic respiratory failure (not caused by cardiac failure) presented within one week with worsening respiratory symptoms, along with bilateral shadows on x-ray / CT (computed tomography) scan / ultrasonography, not fully explained by effusion, collapse, or nodules.[1]

ARDS generally leads to a decrease in the end expiratory lung volume (EELV) or functional residual capacity (FRC), heterogeneous affected lung parenchyma (consolidation or fluid-filled alveoli interspersed with normal areas), intrapulmonary shunting, and severe hypoxemia. Only a small proportion of the lung participates in ventilation, termed the baby lung (the functional lung tissue). Recruitment helped to open the lung and PEEP (positive end expiratory pressure) was used to keep it open. Recruitment manoeuvre involving the opening of collapsed alveoli and recruiting more lung units to participate in oxygenation and ventilation had been used as rescue measures for severe hypoxia.[2] The increase in EELV could be due to the addition of lung units participating in gas exchange or overdistension of the alveoli that were already open.

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Received: August 17, 2022; Revised: May 18, 2023;
Accepted: May 19, 2023
DOI: https://doi.org/10.29271/jcpsp.2023.10.1204

The relationship between the EELV, plateau pressure (Pplat), and compliance of the respiratory system in a group of 21 patients was retrospectively analysed. The groups were divided into Group 1: clinically recruitable, and Group 2: clinically non-recruitable, with moderate to severe hypoxia who were subjected to a recruitment manoeuvre.

After Ethics Committee's approval (ECR/70/Inst/MH/2013/R-R-19), data were collected by a retrospective chart review between February and June 2021. The inclusion criteria was PaO_2/FiO_2 ratio less than 150 with PEEP >5 on invasive ventilation, bilateral inhomogeneous opacities on x-ray chest or CT scan, age >16 years, within 5 days of illness onset, and *SARS Cov*-2 RTPCR (Reverse transcription-polymerase chain reaction) or rapid antigen for positive status.

The exclusion criteria was pulmonary oedema from cardiac origin, pneumothorax, chronic obstructive pulmonary disease (COPD), pulmonary embolism, any patient who required vasopressors to maintain hemodynamics, death within 1 day of admission, transfer in from another hospital, prone position for recruitment, and terminally ill patients, lung cancer, emphysema and interstitial lung disease.

Eighty-eight COVID ARDS patients were screened and only 21 met the inclusion criteria. All 21 patients were sedated, paralysed, and ventilated with the Carescape R860, GE Healthcare ventilator equipped with an Escovyx module with the capacity to measure EELV.[3]

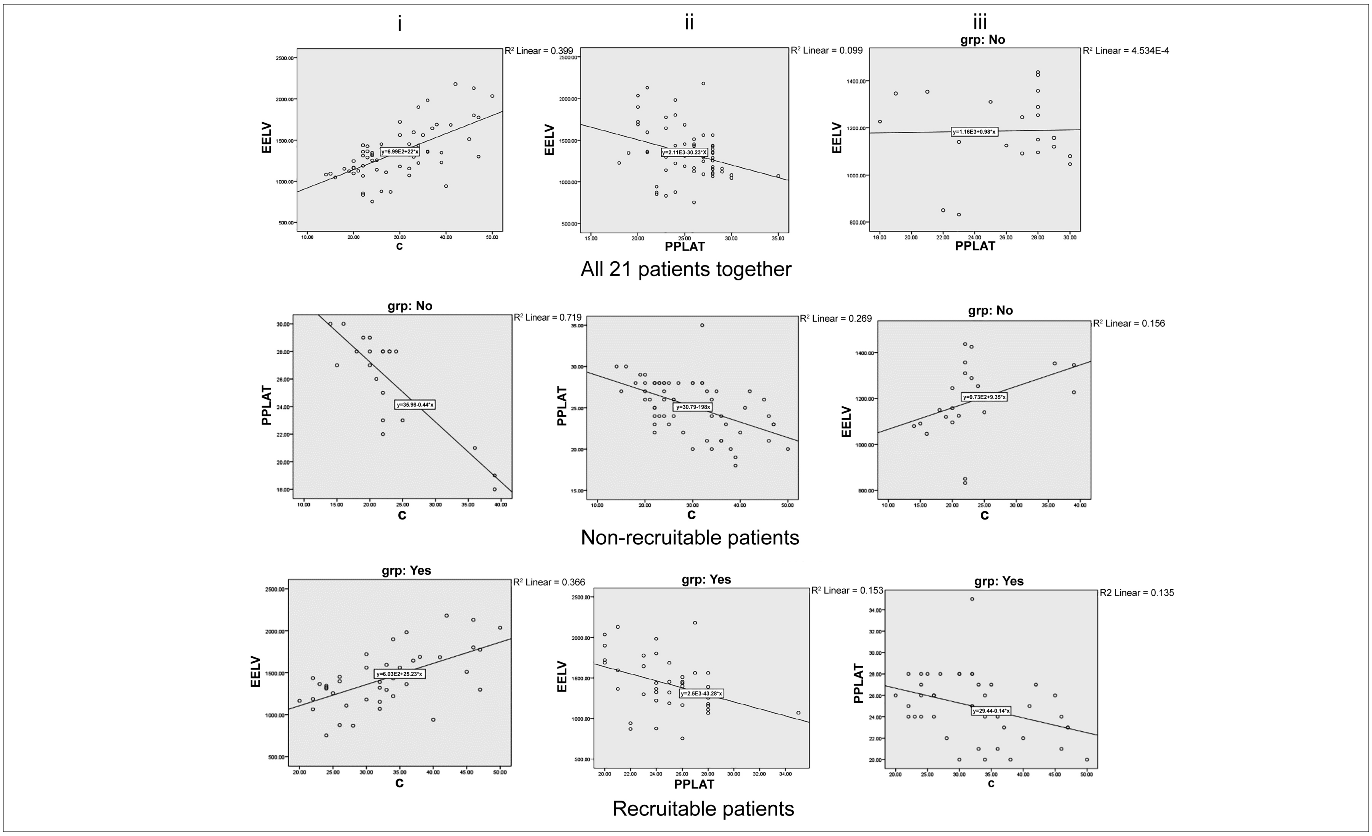

Figure 1: Scatter plots of all 21 patients together; Group 1 of recruitable patients; and Group 2 of non-recruitable patient; (i) Regression lines for end expiratory lung volume (EELV) *versus* compliance; (ii) For functional residual capacity *versus* Plateau pressure (Pplat); (iii) For Compliance *versus* Pplat.

An initial EELV was calculated after the patient was ventilated for 6 hours. A staircase recruitment manoeuvre was performed in indicated patients using pressure control mode with 15 cmH_2O of pressure control above PEEP. While maintaining the driving pressure constant (15 over PEEP) the PEEP was increased from 20 cmH_2O to 30 cmH_2O, followed by 35 cmH_2O every 2 min, reaching a maximum pressure of 50 cmH_2O.[3] The manoeuvre was abandoned immediately at any time that the mean arterial pressure dropped by 10 %. However, none of the study patients developed hypotension during the manoeuvre. The final PEEP was set using the decremental PEEP titration method.

Clinical recruitment was defined as an increase in 3% of the SpO_2 at 2 and 4 hours along with anatomical recruitment seen during the measurement of EELV. The relationship of compliance, plateau pressure, and end EELV was noted at the end of 2 and 4 hours between patient groups that were clinically recruitable (Group 1) and those that were not (Group 2).

Correlations were evaluated by Pearson's linear correlation test. The difference between correlations was evaluated by an equality of dependent correlations test.[4] A p-value <0.05 was considered statistically significant.

The analysis of all the patients together (without dividing into groups) revealed a significant correlation between EELV and compliance (r = 0.632, p<0.00) as well as EELV and plateau pressure (r = -0.315*, p = 0.012).

The scatterplot which explored the correlation of change in EELV with change in compliance suggested a definite positive linear relationship (r = 0.632, p = 0.00), with larger values of EELV tending to be associated with larger values of compliance (Figure 1), a moderate but definite negative correlation (r = -0.315*, p = 0.012) between change in EELV and change in plateau pressure, and a moderate but negative relationship (r = -0.519**, p = 0.00) between compliance and plateau pressure as in Figure 1.

In Group 1, there was no significant correlation between EELV and compliance or EELV and Pplat, with a strong negative relationship between compliance and Pplat as shown in Figure 1.

In Group 2, there was a moderate but positive linear relationship between EELV and compliance in recruitable patients, and a negative linear relationship between change in EELV and change in Pplat as shown in Figure 1.

Similar to Group 1, there was a negative linear relationship between compliance and Pplat in recruitable patients as shown in Figure 1.

The group that recruited showed a larger percentage change in the EELV and compliance as compared to the group that was not recruitable whereas the non-recruitable group also showed a rise in the percentage change in Pplat as compared to the recruitable group as shown in Table I.

Table I: Percentage change of EELV, compliance and Pplat among the recruitable and non-recruitable patients.

		n	Mean percentage change
EELV	Non-recruitable	7	49.6781
	Recruitable	14	82.1232
	Total	21	71.3081
Compliance	Non-recruitable	7	14.1485
	Recruitable	14	31.2364
	Total	21	25.5404
Plateau pressure	Non-recruitable	7	5.2124
	Recruitable	14	-0.1891
	Total	21	1.6114

Conventionally, successful recruitment involves sustained improvement of saturations. However, during recruitment, alveolar recruitment and overdistension can simultaneously occur in various parts (in the heterogenous lung parenchyma in ARDS) of the lung, and oxygenation (on its own) may not be sensitive enough to pick up lung injury.[5]

To calculate EELV, the nitrogen wash-out/wash-in technique is the validated method used by the Carescape R860. Physiologically, an increase in EELV (by recruitment) should ideally cause a decrease in compliance and an improvement in Pplat. The results of this study are as per the experimental study done in which an increase in PEEP caused an increase in the EELV with a corresponding increase in the static compliance of the respiratory system. These experiments demonstrated that beyond a certain level of mean airway pressure, there was a drop in compliance which signified overdistension.[6] There are very few human studies exploring this relationship.

Bikker *et al.* in contrast to other studies showed no correlation between EELV and dynamic compliance during the slow stepwise increase in PEEP. However, in this study, only three levels of PEEP were measured starting at 15, 10, and 5 cm which may not have been an adequate pressure to affect recruitment. Also, dynamic compliance may underestimate the total compliance of the lung and thorax as it is influenced by the resistive part of lung mechanics.[4]

In this study, the scatterplots of the group that was non-recruited showed no relationship between EELV and compliance or Pplat. In the group that was recruited clinically, the scatterplot suggested a linear positive moderate relationship between EELV and compliance, and a negative linear relationship with Pplat. Importantly, the mean percentage change in EELV and compliance in recruited patients were much higher than in the non-recruited patients, respectively (82.1 *vs.* 49.6% and 31.2 *vs.* 14.1%). The mean Pplat in the patients that were recruited showed a very minor reduction as compared to the non-recruited patients where the Pplat showed a percentage rise of 5.2%.

This study had limitations as it did not assess the outcomes of these patients which would have given more information about the benefits or risks of the manoeuvre. The sample size was small, however it is the largest till date (from India) of homogeneous group of ARDS patients.

There was a reasonably clear relationship between EELV, compliance, and Pplat among those patients who were clinically recruited *versus* those who were not in a homogenous group of COVID ARDS patients. The additional information gained after understanding this relationship can help to optimise ventilator settings.

PATIENTS' CONSENT:
Patients' consent was not taken as this study was a retrospective, observational study of routine standard protocols of the ICU.

COMPETING INTEREST:
The authors declared no competing interest.

AUTHORS' CONTRIBUTION:
SS, SP: Contributed to conception of work, acquisition, interpretation of data, drafting and revising of the manuscript.
SP, SR, VK, AY: Contributed to conception of work and drafting.
RB: Contribution to statistics and drafting.
All authors approved the final version of the manuscript to be published.

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