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Physiology-Based Individualized PEEP Titration and Its Effect on Respiratory Mechanics and Oxygenation in ARDS: A Prospective Observational Study

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ABSTRACT

Acute Respiratory Distress Syndrome (ARDS) has high morbidity and mortality and often requires mechanical ventilation. Bedside, physiology-guided titration of positive end-expiratory pressure (PEEP) may improve lung mechanics, oxygenation, and reduce ventilator-induced lung injury. **Objectives:** To determine the impact of physiology-based PEEP titration individualized on respiratory mechanics, oxygenation, hemodynamics, and clinical outcome in patients with ventilated ARDS. **Methods:** This is a pre and post-quasi-experimental study (Jan-Dec 2025) at the Medical and Surgical ICUs of Bahria International Hospital, Lahore. Adult patients with ARDS in need of invasive ventilation were enrolled. PEEP was progressively regulated at the bedside depending on compliance, driving pressure, oxygenation, and imaging. The main outcome measurements consisted of compliance, driving pressure, and PaO2/FiO2 changes, whereas secondary measures were the length of ventilation, ICU hospitalization, barotrauma, and death in the ICU. **Results:** Among 120 patients (mean age 54.2 ± 14.6 years; 60% male), individualized PEEP titration improved compliance (32.5 ± 6.8 → 38.7 ± 7.2 mL/cmH_2O, p<0.01), reduced driving pressure (15.6 ± 3.4 → 12.8 ± 3.0 cmH_2O, p<0.01), and increased PaO_2/FiO_2 (140 ± 35 → 195 ± 42 mmHg, p<0.01). There were minimal hemodynamic effects. Median ventilation period was 9 days, ICU stay 12 days; barotrauma 5%, ICU mortality 28%. **Conclusions:** PEEP titration based on physiology and monitored at the bedside is safe, feasible, and effective in enhancing lung mechanics and oxygenation in patients with ARDS, and it should be included in lung-protective ventilation.

INTRODUCTION

Acute Respiratory Distress Syndrome (ARDS) is a respiratory failure of a serious type, which is associated with diffuse destruction of alveoli, elevation of pulmonary capillary permeability, and dysfunction of the gas exchange [1]. Nevertheless, regardless of the improvements in critical care, ARDS is linked to high morbidity and mortality rates, especially in resource-limited environments [2]. Supportive therapy relies on mechanical ventilation, which, however, in the wrong environment, can cause further lung damage resulting in ventilator-induced lung injury (VILI) [3]. Out of the ventilatory parameters, the central role is played by positive end-expiratory pressure (PEEP) in the process of balancing alveolar recruitment and the risks of overdistension and hemodynamic compromise [4]. PEEP

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helps to avoid end-expiratory alveolar collapse, increases functional residual capacity, enhances oxygenation, and decreases cyclic atelectrauma [5]. The ARDS lungs are also heterogeneous, with such dependent areas that they can be collapsed and such non-dependent areas that they can be overinflated (the so-called baby lung concept), which means that they require an individual PEEP adjustment [6]. Excessive PEEP may cause excessive transpulmonary pressure, venous congestion, high pulmonary vascular resistance, and right ventricular dysfunction, which are crucial factors in the individual modification approach as opposed to a generalized one [7]. Conventional PEEP-FiO_2 tables, which are mainly grounded on oxygenation, do not deliver reliable clinical results [8]. The modern interventions focus on the adjustment of PEEP according to the lung mechanics, recruitability, and cardiopulmonary interactions [9]. To close the gap between physiological concepts and clinical practice, bedside assessment tools, including respiratory compliance, driving pressure, pressure-volume curves, esophageal manometry, lung ultrasound, and electrical impedance tomography, are useful [10]. PEEP titration art must be coupled with the lung-protective interventions that include the low tidal volume ventilation, plateau and driving pressure limits, permissible hypercapnia, and prone positioning [11]. ARDS is also a disease that is still associated with high morbidity and mortality rates despite the enhancement in the management of critical care. The optimal titration of positive end-expiratory pressure (PEEP) is a controversial topic, even though positive end-expiratory pressure (PEEP) is one of the foundations of lung-protective ventilation. Conventional techniques, such as standardized PEEP-FiO_2, do not take into account inter-patient differences in the recruitability and mechanics of alveoli, and may lead to suboptimal outcomes due to either overdistension or collapse of alveoli. The latest advances are dedicated to physiology-related, individualized PEEP-setting based on bedside measurements, such as compliance of the respiratory system, driving pressure, and oxygenation indices.

However, in patients on mechanical ventilation in ARDS, there is a paucity of clinical data on such resource-constrained conditions to determine clinical usefulness, safety, and physiological effects of individualized strategies in such patients. Therefore, the study was conducted with an aim to identify whether the physiology-based bedside PEEP titration can improve respiratory mechanics and oxygenation without causing significant hemodynamic impairment, which will help close a critical gap between hypothetical recommendations and practical application. This study aimed to evaluate the effect of physiology-based individualized PEEP titration on respiratory mechanics (respiratory system compliance and driving pressure) and oxygenation (PaO_2/FiO_2 ratio) in mechanically ventilated patients with ARDS.

METHODS

This pre and post-quasi-experimental study was conducted in the Medical and Surgical Intensive Care Units of Bahria International Hospital, Lahore, for 12 months (January–December 2025), following ethical approval (IRB No. IRBEC/BIH/73-2025, dated 1st January 2025). Sample size was calculated using the single population proportion formula (95% confidence level, p=50%, margin of error=9%), yielding 119 patients. Written informed consent was taken. Given the feasibility considerations, it was decided to include 120 patients, which was found to be satisfactory to show clinically meaningful differences in respiratory mechanics and oxygenation. The attrition-adjusted sample size was 131, but the recruited sample size was 120, given the feasibility considerations. This was still greater than the minimum unadjusted required sample size of 119 and was thus considered adequate to analyze the primary physiological outcomes. The sampling method involved the use of a non-probability continuous sampling technique, which involved enrolling patients consecutively over the study period, provided the patients were eligible and met the inclusion criteria. Consecutive enrolment of adult patients (18 years or older) with ARDS as defined by the Berlin criteria, including invasive mechanical ventilation. The severity of ARDS was determined according to the proportion of PO_2/FiO_2 at the minimum PEEP of 5 cmH_2O. Patients who are pregnant, have advanced chronic lung disease, intracranial hypertension, or are severely hemodynamically unstable were excluded. Demographic and clinical data were taken at baseline. All patients received lung-protective ventilation with a target tidal volume of 6 mL/kg predicted body weight and plateau pressure < 30 cmH_2O. The baseline mean tidal volume was 6.1 ± 0.3 mL/kg PBW, mean PEEP was 8.5 ± 2.1 cmH_2O, mean plateau pressure was 26.4 ± 3.2 cmH_2O, mean driving pressure was 15.6 ± 3.4 cmH_2O, mean PaO_2/FiO_2 was 140 ± 35 mmHg, and mean respiratory system compliance was 32.5 ± 6.8 mL/cmH_2O. PEEP was titrated by a stepwise incremental–decremental method using 2–3 cmH_2O increments up to 18–20 cmH_2O. At each step, compliance, driving pressure, oxygenation, and hemodynamics were monitored. The optimal PEEP was defined as the pressure that achieved optimal compliance and minimum driving pressure without causing hemodynamic instability. The mean optimal PEEP after titration was 12.3 ± 2.7 cmH_2O. ARDS severity was determined by PaO_2/FiO_2 measured at a minimum PEEP of 5 cmH_2O, according to the Berlin criteria. At enrollment, 38 patients (32%) had mild ARDS, 54 (45%) had moderate ARDS, and 28 (23%) had severe ARDS.

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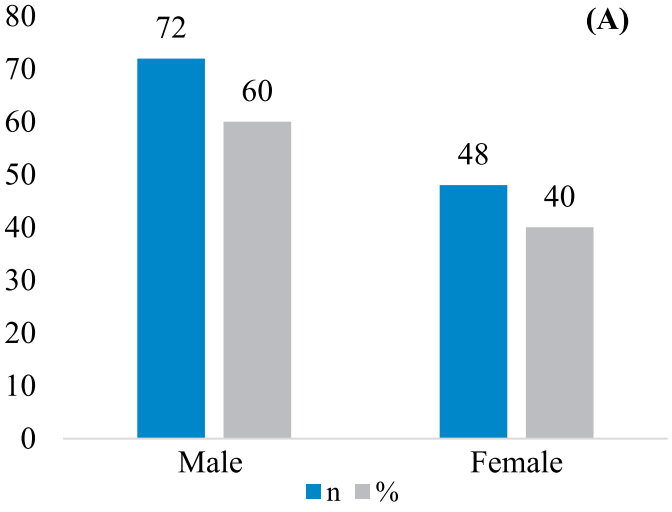
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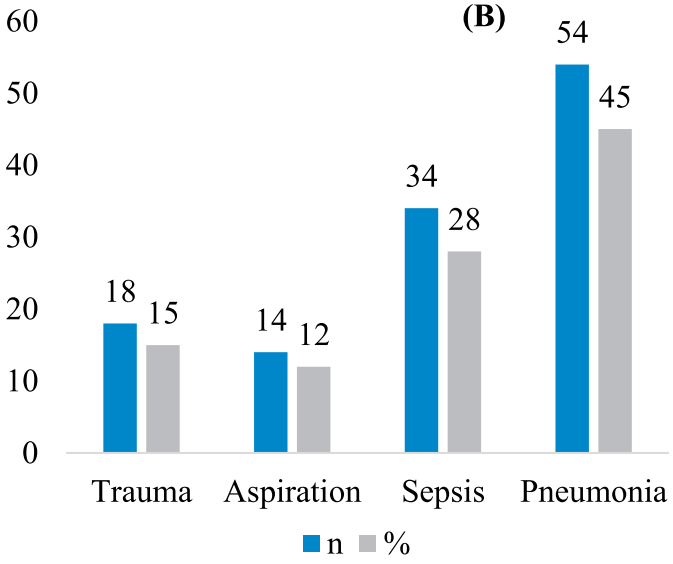
Respiratory system compliance was reported as 32.5 ± 6.8 mL/cmH_2O before PEEP titration and 38.7 ± 7.2 mL/cmH_2O after titration. Driving pressure was reported as 15.6 ± 3.4 cmH_2O before titration and 12.8 ± 3.0 cmH_2O after titration. PaO_2/FiO_2 was reported as 140 ± 35 mmHg before titration and 195 ± 42 mmHg after titration. The key outcomes were the change of respiratory compliance, driving pressure, and the ratio of PaO2/FiO2. The secondary outcomes included length of mechanical ventilation, length of stay in the ICU, barotrauma, and ICU mortality.

Data were analyzed using SPSS version 26.0. Continuous variables were expressed as mean ± SD, and categorical variables as frequencies and percentages. The pre-post changes in respiratory compliance, driving pressure, and oxygenation demonstrated moderate-to-large effect sizes, supporting adequate statistical validity of the paired comparisons. Before applying one-way ANOVA, assumptions of normality and homogeneity of variance were assessed using the Shapiro–Wilk test and Levene's test, respectively. Data met these assumptions, and parametric tests were applied accordingly. A p-value <0.05 was considered statistically significant. The association between optimized PEEP levels (and changes in driving pressure and compliance) and clinical outcomes (ICU mortality and barotrauma) was assessed using the chi-square test and logistic regression analysis to adjust for potential confounders.

RESULTS

It summarizes the baseline characteristics of the 120 ARDS patients. Panel A shows a male predominance (72/120, 60%). Panel B indicates pneumonia was the most common etiology (45%), followed by non-pulmonary sepsis (28%), trauma (15%), and aspiration (12%). Panel C shows most patients had moderate ARDS (45%), with mild (32%) and severe (23%) disease being less common, and severity groups did not differ significantly ($p > 0.05$) figure 1.





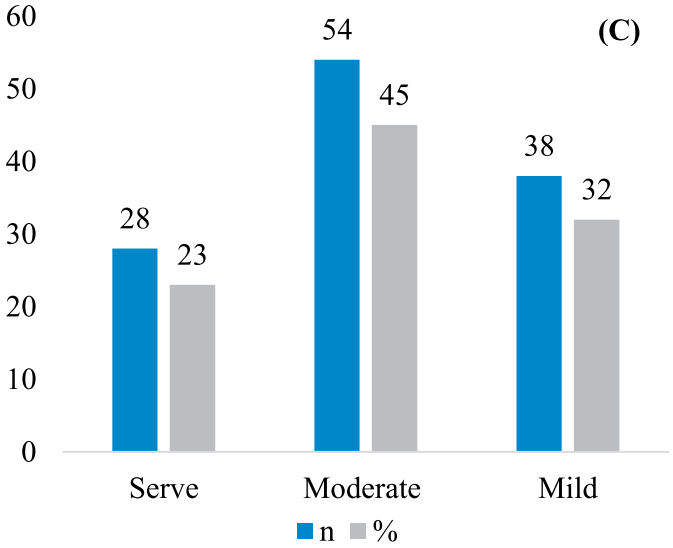


Figure 1: Distribution of Gender (A), ARDS Etiology (B), and ARDS Severity (C) among the Study Population

At the initiation of mechanical ventilation, ARDS patients had a mean tidal volume of 6.1 ± 0.3 mL/kg predicted body weight, a mean PEEP of 8.5 ± 2.1 cmH_2O, a plateau pressure of 26.4 ± 3.2 cmH_2O, a driving pressure of 15.6 ± 3.4 cmH_2O, PaO_2/FiO_2 ratio of 140 ± 35 mmHg, and a respiratory system compliance of 32.5 ± 6.8 mL/cmH_2O. One-way ANOVA for continuous variables was used to compare baseline ventilatory and respiratory parameters among ARDS severity groups (Table 1).

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Table 1: Baseline Ventilatory and Respiratory Parameters

Parameters	Mild ARDS (n=38), Mean ± SD	Moderate ARDS (n=54), Mean ± SD	Severe ARDS (n=28), Mean ± SD	F-value	p-value
Tidal Volume (mL/kg PBW)	6.1 ± 0.3	6.0 ± 0.4	6.2 ± 0.3	0.89	0.41
PEEP (cmH_2O)	8.3 ± 2.0	8.6 ± 2.2	8.7 ± 2.1	0.97	0.38
Plateau Pressure (cmH_2O)	26.1 ± 3.0	26.6 ± 3.3	26.8 ± 3.2	1.25	0.29
Driving Pressure (cmH_2O)	15.2 ± 3.1	15.8 ± 3.5	15.9 ± 3.4	1.12	0.33
PaO_2/FiO_2 (mmHg)	155 ± 30	138 ± 32	120 ± 28	1.34	0.27
Respiratory Compliance (mL/cmH_2O)	33.8 ± 6.5	32.1 ± 6.9	31.4 ± 7.2	1.05	0.35

Legend: Baseline Ventilatory and Respiratory Parameters of ARDS Patients (n=120). Data are presented as mean ± SD. Statistical comparisons across ARDS severity groups were performed using one-way ANOVA; all comparisons were not statistically significant ($p>0.05$)

Following bedside-guided individualized PEEP titration, the mean optimal PEEP increased from 8.5 ± 2.1 to 12.3 ± 2.7 cmH_2O. As shown in table 2, respiratory system compliance improved significantly from 32.5 ± 6.8 to 38.7 ± 7.2 mL/cmH_2O (paired t-test: $t = 11.6$, $p<0.01$), driving pressure decreased from 15.6 ± 3.4 to 12.8 ± 3.0 cmH_2O ($t = 9.42$, $p<0.01$), and PaO_2/FiO_2 ratio increased from 140 ± 35 to 195 ± 42 mmHg ($t = 14.1$, $p<0.01$), indicating improved lung mechanics and oxygenation after PEEP optimization (Table 2).

Table 2: Effect of Individualized PEEP Titration on Respiratory Mechanics and Oxygenation

Parameters	Before PEEP, Mean ± SD	After PEEP, Mean ± SD	Mean Difference (95% CI)	Cohen's d	Test Used	t-value	p-value
Respiratory Compliance (mL/cmH_2O)	32.5 ± 6.8	38.7 ± 7.2	+6.2 (4.8 to 7.6)	0.89	Paired t-test	11.6	<0.01
Driving Pressure (cmH_2O)	15.6 ± 3.4	12.8 ± 3.0	−2.8 (−3.6 to −2.0)	0.82	Paired t-test	9.42	<0.01
PaO_2/FiO_2 (mmHg)	140 ± 35	195 ± 42	+55 (44 to 66)	1.10	Paired t-test	14.1	<0.01
Optimal PEEP (cmH_2O)	8.5 ± 2.1	12.3 ± 2.7	—	—	Descriptive	—	—

Legend: Effect of individualized PEEP titration on respiratory mechanics and oxygenation (n=120). Values are mean ± SD. Paired t-tests showed significant improvements in compliance ($t = 11.6$, $p<0.01$), driving pressure ($t = 9.42$, $p<0.01$), and PaO_2/FiO_2 ($t = 14.1$, $p<0.01$). Optimal PEEP is descriptive

Bedside PEEP titration caused a modest but statistically significant decrease in mean arterial pressure from 82.3 ± 9.5 to 79.8 ± 10.1 mmHg (paired t-test: $t = 2.36$, $p=0.02$), while heart rate remained stable (92.1 ± 14.2 → 90.8 ± 13.6 bpm, $t = 1.56$, $p=0.12$). No patient required escalation of vasopressor therapy, indicating that individualized PEEP titration was hemodynamically well tolerated (Table 3).

Table 3: Hemodynamic Parameters Before and After PEEP Titration

Parameters	Before PEEP Titration, Mean ± SD	After PEEP Titration, Mean ± SD	Test Used	Test Statistic	p-value
Mean Arterial Pressure (mmHg)	82.3 ± 9.5	79.8 ± 10.1	Paired t-test	t = 2.36	0.02
Heart Rate (beats/min)	92.1 ± 14.2	90.8 ± 13.6	Paired t-test	t = 1.56	0.12

Legend: Hemodynamic parameters before and after PEEP titration (n=120). Values are mean ± SD. Paired t-tests showed a significant decrease in mean arterial pressure ($t = 2.36$, $p=0.02$); heart rate change was not significant ($t = 1.56$, $p=0.12$)

The median duration of mechanical ventilation was 9 days (IQR 6–14), and the median ICU length of stay was 12 days (IQR 8–18). Barotrauma occurred in 6 patients (5%), and ICU mortality was 28% (n=34). No significant association was observed between optimized PEEP levels and ICU mortality ($p=0.25$) or barotrauma ($p=0.50$) (Table 4).

Table 4: Clinical Outcomes of the Study Population

Outcome	Value
Duration of Mechanical Ventilation, median (IQR)	9 (6–14) Days
ICU Length of Stay, median (IQR)	12 (8–18) Days
Barotrauma, n (%)	6 (5%)
ICU Mortality, n (%)	34 (28%)

DISCUSSION

The paper compared the outcomes of physiology-based individualized PEEP titration with respiratory mechanics, oxygenation, hemodynamics, and clinical outcomes in patients receiving mechanical ventilation in ARDS. These findings indicate that bedside-guided PEEP adjustment led to better respiratory system compliance and oxygenation and lesser driving pressure; however, there were slight alterations in hemodynamics. Mechanical ventilation and ICU length of stay were not very low, and barotrauma was not very high. Overall, individualized PEEP titration was safe and effective in optimizing lung mechanics and gas exchange in ARDS patients. The observed improvements in respiratory compliance and oxygenation following individualized PEEP titration reflect the principle that alveolar recruitment and stabilization reduce cyclical

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atelectasis and improve ventilation-perfusion matching [14]. Previous studies have reported that physiology-based PEEP, based on lung mechanics and recruitment capabilities, improves oxygenation relative to fixed-PEEP strategies [15]. Equally, this decrease in driving pressure is consistent with evidence that optimal PEEP, based on compliance minimization, reduces lung stress and strain, which may decrease the risk of ventilator-induced lung injury [16]. The slight reduction in the mean arterial pressure that we observed is also in agreement with the existing literature, which suggests that a moderate amount of PEEP increase can have a slight impact on preload and cardiac output, but close monitoring usually can prevent clinically significant hypotension [17]. The observed low incidence of barotrauma supports the safety of the individualized PEEP titration in combination with low tidal volume ventilation and monitoring plateau pressure [18]. The result of clinical outcomes in ICU mortality rate and duration of mechanical ventilation are similar outcomes in cohorts with the intervention of lung protective ventilatory strategies at individual personalized PEEP [19]. It is also worth noting that patients with moderate to severe ARDS showed the greatest improvements in oxygenation and compliance, which supports the notion that recruitable lung domains are more vulnerable to changes in adjusted PEEP [20]. The findings underscore the importance of bedside assessment using lung mechanics, imaging, and, where applicable, esophageal manometry or electrical impedance tomography to inform PEEP decisions.

This research has several limitations. First, the results are likely to have limited external validity and cannot prove causation, as it is a single-centre prospective observational study. Second, the lack of a control group with the standardized PEEP titration strategy limits the ability to compare and determine the superiority of the individualized PEEP titration strategy. Third, despite attempts to standardize ventilatory settings and control confounding factors, residual confounding from variations in disease severity, comorbidity, and sedation level cannot be fully eliminated.

CONCLUSIONS

The conclusion is that a physiology-based individualized PEEP titration in mechanically ventilated patients with ARDS significantly improves respiratory system compliance, reduces driving pressure, and improves oxygenation without causing clinically significant hemodynamic compromise. Nonetheless, ICU mortality or barotrauma were not significantly associated with it. These results support the ability and safety of bedside, physiology-informed optimization of PEEP as a component of lung-protective ventilation, but additional randomized controlled trials are required to determine its impact on clinical outcomes.

Authors' Contribution

Conceptualization: AM
Methodology: AM, EY
Formal analysis: AM
Writing and Drafting: AM, MAR, EY, RP, RK, YAZ
Review and Editing: AM, MAR, EY, RP, RK, YAZ, FS

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflict of Interest

All the authors declare no conflict of interest.

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