

Original Article

Outcome of Targeted Driving Pressure Mechanical Ventilation in ARDS patients

Md Shamimur Rahman¹, Saifullah Al Kafi², Md Mozaffer Hossain³, AKM Ferdous Rahman⁴, Md Motiul Islam⁵, Syed Muhammad Shahin-ur Hayat⁶

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Abstract:

Background: Lung protective strategy in acute respiratory distress syndrome (ARDS) patients is based on low tidal volume (V_T), lower end-inspiratory (plateau) pressure and higher positive end-expiratory pressure (PEEP). But to predict body weight adjusted tidal volume, heterogeneous pathology of the lung in ARDS with different respiratory system compliance (C_{RS}) is not considered. In driving pressure ($\Delta P = V_T / C_{RS}$) tidal volume (V_T) is normalized to functional lung size. It is unclear whether mechanical ventilation targeting driving pressure (ΔP) is more effective than low tidal volume ventilation (LTVV) in patients with ARDS.

Materials and Methods: An open labelled randomized controlled trial was conducted at Intensive Care Unit of Dhaka Medical College Hospital, a tertiary care referral hospital over 12 months from March 2021 to February 2022. Ninety two patients with ARDS, defined by the Berlin criteria, requiring mechanical ventilation were randomized to 1:1 ratio after enrollment in the study using simple random sampling, one group receiving targeted driving pressure (ΔP) that is ≤ 14 cm of H_2O ventilation another group receiving low tidal volume ventilation (LTVV) that is 4-6 ml/kg PBW.

Results: The study found no significant differences between the two groups in terms of clinical variables and laboratory parameters ($p > 0.05$), except for the duration of mechanical ventilation (MV), which was significantly shorter in the Targeted ΔP group ($p < 0.05$). Aspiration pneumonia was the most common cause of ARDS, occurring in 34.8% of the Targeted ΔP group and 39.1% of the LTVV group. The Targeted ΔP group demonstrated a significant increase in mean respiratory system compliance compared to the LTVV group ($p < 0.001$), and a significantly shorter length of ICU stay ($p < 0.001$). Additionally, the PaO_2/FiO_2 ratio was significantly higher in the Targeted ΔP group on Days 3, 5, and 7 ($p < 0.05$). Mean exhaled tidal volume was also significantly higher in the Targeted ΔP group on these days ($p < 0.05$). In the Targeted ΔP group, mean driving pressure significantly decreased on Days 3, 5, and 7 ($p < 0.001$), along with a significant reduction in mean plateau pressure (P_{pl}) ($p < 0.001$). Mean positive end-expiratory pressure (PEEP) significantly decreased on Days 3, 5, and 7 ($p < 0.001$). Respiratory rate significantly decreased on Day 7 ($p < 0.05$). Mean set tidal volume (V_T) significantly increased on Days 3, 5, and 7 ($p < 0.001$). Moreover, the 28-day mortality incidence was significantly lower in the Targeted ΔP group compared to the LTVV group (8.7% vs. 26.1%, $p < 0.05$).

Conclusion: Targeted Driving pressure (ΔP) guided ventilation offers significant clinical benefits over LTVV in managing ARDS patients in terms of increased respiratory system compliance (C_{RS}), shorter lengths of hospital and ICU stays, and lower in-hospital mortality.

Key Points: Acute Respiratory Distress Syndrome, Driving Pressure, Low Tidal Volume Ventilation, Targeted Driving Pressure.

Introduction:

Lung protective strategy using tidal volume 4–6 ml/kg of predicted body weight (PBW), FiO_2 guided positive end-expiratory pressure (PEEP), and plateau pressure ≤ 30 cm H_2O in patients with acute respiratory distress syndrome (ARDS) improves survival.¹ The use of conventional protective lung ventilation (PLV) is associated with improved oxygenation and survival in ARDS patients.^{2,3} But mortality is still high despite the use of PLV strategy, which may reflect the imbalance between tidal volume, manipulation of PEEP, lung recruitment, and hyperinflation, as shown in clinical trials. Also, there are conflicting responses for manipulating PEEP and tidal volume during PLV strategy.⁴ While calculating tidal volume according to PBW the heterogeneous pathology of the lung in ARDS with different respiratory system compliance is not considered.⁵ It has been extensively demonstrated that in patients with acute respiratory distress

syndrome (ARDS), the ratio of ventilated to non-ventilated lung is reduced, a phenomenon known as baby lung.⁶ The aerated ARDS lung has near-normal intrinsic compliance.⁷

The respiratory system compliance in patients with ARDS reflects the residual baby lung size (expressed as a percentage of the expected healthy lung volume). Driving pressure (ΔP) is the ratio of tidal volume to respiratory system static compliance.⁸ It can be calculated simply at the bedside as plateau pressure minus PEEP. Amato et al. have shown in their secondary analyses that ΔP was the primary variable that should be optimized during mechanical ventilation (MV) in ARDS patients and associated improved survival.⁹ Another meta-analysis which included nine studies showing that driving pressure was the only independent ventilator variable that was directly associated with mortality in ARDS patients and they also showed that lower driving pressure was with associated better outcome.¹⁰ Targeting driving pressure

improved the outcome of mechanically ventilated ARDS patients.

The Rationale of the study

To determine the best balance between the benefit of providing mechanical ventilation and the risks of mechanical ventilation, Over the past decades, a protective ventilation strategy with a tidal volume (V_T) of 6ml/kg of PBW has shown improved survival compared to a traditional V_T of 12ml/kg PBW.¹¹ However, patients with small aerated compartments can still experience ventilator induced lung injury (VILI) with low V_T ventilation. In some cases, increased V_T has reduced driving pressure and pulmonary complications.¹² Calculating V_T based on PBW does not account for the heterogeneous pathology of ARDS lungs with varying respiratory compliance.

Driving pressure (ΔP), the ratio of tidal volume (V_T) to static respiratory system compliance; i.e. $\Delta P = V_T/C_{RS}$, can be calculated at the bedside as plateau pressure minus PEEP. ΔP is strongly associated with pulmonary injury and mortality, irrespective of PEEP levels, V_T , or plateau pressure. Therefore, targeting ΔP improves ventilation safety and outcomes in ARDS patients. Amato et al found that optimizing ΔP is crucial for improving survival in these patients. This study aims to compare the outcomes of targeted ΔP mechanical ventilation with those of targeted low V_T ventilation in ARDS patients.⁹ Our hypothesis was that targeted ΔP mechanical ventilation resulted in better outcomes than conventional low V_T ventilation based on PBW. Our findings demonstrated that targeted ΔP ventilation provides superior outcomes compared to conventional low V_T ventilation in ARDS patients.

Methodology:

Study Design: This study was designed as a prospective randomized controlled trial conducted in the Non-COVID ICU at the Department of Anesthesia, Pain, Palliative & Intensive Care, Dhaka Medical College Hospital, Dhaka,

1. Register (Critical Care Medicine), Department of Anesthesia, Pain, Palliative & Intensive Care, Dhaka Medical College Hospital, Dhaka.
2. Phase B Resident, Critical Care Medicine, Department of Anesthesia, Pain, Palliative & Intensive Care, Dhaka Medical College Hospital
3. Professor & Head, Department of Anesthesia, Pain, Palliative & Intensive Care, Dhaka Medical College Hospital, Dhaka.
4. Associate Professor, Critical Care Medicine, Dhaka Medical college
5. Consultant and Head, Dept. Of Critical Care Medicine, Asgar Ali Hospital, Dhaka.
6. Junior Consultant, In-charge of ICU & HDU, BRB Hospital Ltd,

Corresponding Author:

Dr. Md. Shamimur Rahman
Register (Intensive Care Unit)
Department of Anesthesia, Pain, Palliative & Intensive Care
Dhaka Medical College Hospital, Dhaka
Email: dr.shamim022@gmail.com

from March 2021 to February 2022. Using simple random sampling, 92 patients with ARDS, defined by the Berlin criteria, requiring mechanical ventilation were included after thorough history taking, examination, and appropriate investigations based on inclusion and exclusion criteria. The main outcome variable studied was the effectiveness of targeted driving pressure mechanical ventilation in ARDS patients. Approval from ethical review committee (ERC) was taken from the ERC of Dhaka Medical College after finalizing the study protocol.

Participant Selection: The study included patients aged 18 years and older, of both sexes, who were intubated and receiving mechanical ventilation for at least 3 days. All participants were diagnosed with ARDS based on the Berlin definition. The study did not incorporate lung recruitment or adjustment therapies, focusing solely on the targeted driving pressure mechanical ventilation strategy.

Patients meeting any of the following criteria were excluded from the study: those who were immunocompromised due to chemotherapy or radiation therapy, experiencing fluid overload or cardiac failure without a definite ARDS cause, or had a positive pregnancy test. Additionally, patients with hemodynamic instability (mean arterial pressure less than 65 mmHg or requiring vasopressor or inotrope support), intubation due to COPD, pneumothorax, or organ dysfunctions other than lung dysfunction as assessed by the sequential organ failure assessment (SOFA) score were not included.

Data Collection & Evaluation Parameters: Demographic information, symptoms at the time of admission, physical examination results, laboratory findings, were thoroughly assessed. Data was collected immediately before randomization (baseline data) and then Day 1 (that was count as non-interventional day data), Day 3, Day 5, Day 7, Day 14 and on Day 28 after randomization. When patients were discharged from the hospital before the 28th day after randomization patients or their relatives were contacted by telephone to obtain follow-up data.

For each patient, the following data was collected: 28th day mortality (the primary outcome), P/F ratio, organ(s) dysfunction by SOFA score, hemodynamics (mean arterial pressure and heart rate), duration of MV, weaning categories (simple, difficult or prolonged weaning), MV free days (without assisted breathing after successful extubation) at 28th day and length of ICU stay. Patients were followed up for 28 days.

Variable Assessment: The analysis focused on comparing targeted driving pressure (ΔP) mechanical ventilation with low tidal volume ventilation (LTVV) in terms of respiratory system compliance (CRS), hospital and ICU stay durations, and in-hospital mortality. Additionally, we compared PaO_2/FiO_2 ratio, mean exhaled tidal volume, mean driving pressure, mean plateau pressure (P_{Plr}), mean positive end-expiratory pressure (PEEP), mean respiratory rate, and mean set tidal volume (V_T) between the ΔP -guided and LTVV groups

Statistical analysis: Following collection of the data, all data were edited and encoded into a statistical software named statistical program Statistical Package for Social Science (SPSS) version 25.0. Data was inputted into the software (termed as variable) according to the prior analysis plan. In this study, continuous data was displayed as mean ± standard deviation if normally distributed and were compared by unpaired t-test. But when data was abnormally distributed it was expressed as median, interquartile ranges (IQR) and was compared using the Mann-Whitney test between both groups. Qualitative data were expressed as frequency, percentage (%) and compared using Kaplan-Meier curve with log-rank test. Diagnostic accuracy measures of sensitivity and specificity was calculated with 95% exact binomial confidence intervals (CIs). Nonparametric receiver operating curve (ROC) analysis was used to determine area under the curve (AUC). Each assessment was treated as independent in primary analysis based on frequent changes in individual patients' clinical status over 1-day intervals, but sensitivity analysis was restricted to initial assessments. In the whole study, significance level was set $p < 0.05$ in all cases.

Results:

This was a open labelled randomized control trial conducted in Non-COVID ICU, Department of Anesthesia, Pain, Palliative & Intensive Care DMCH. Patients allocated to the targeted driving pressure–strategy group was ventilated using volume-controlled or pressure control modes and patients allocated to low tidal volume (control) group was ventilated using the volume-controlled mode according to the ARDS Net strategy, or pressure-support mode. The main objective of the study was to evaluate the outcome of targeted Driving pressure mechanical ventilation in ARDS patients.

Table-I: Age and gender distribution of the study subjects between two groups (N=92)

| Variables | Targeted ΔP group (n=46) | LTVV group (n=46) | p-value |
|------------------|-----------------------------|----------------------|---------|
| Age group | | | |
| 20-40 | 12(26.1%) | 4(8.7%) | |
| 41-60 | 21(45.7%) | 24(52.2%) | |
| >60 | 13(28.3%) | 18(39.1%) | |
| Mean±SD | 51.41±14.77 | 57.00±13.75 | 0.064 |
| Gender | | | |
| Male | 27(58.7%) | 28(60.9%) | 0.832 |
| Female | 19(41.3%) | 18(39.1%) | |

Table-II: Comparison of clinical and laboratory parameters between two group (N=92)

| Variables | Targeted ΔP group (n=46) Mean±SD | LTVV group (n=46) Mean±SD | p-value |
|----------------------------|--|---------------------------------|---------|
| Temp (°F) | 99.57±1.22 | 99.9±1.43 | 0.180 |
| SBP (mmHg) | 109.00±20.41 | 106.30±11.37 | 0.436 |
| DBP (mmHg) | 77.39±93.97 | 61.52±6.57 | 0.256 |
| Respiratory rate (/min) | 24.63±3.64 | 26.67±3.80 | 0.089 |
| FiO ₂ (mmHg) | 0.81±0.23 | 0.92±0.14 | 0.086 |
| PaO ₂ (mmHg) | 65.22±9.68 | 63.13±8.96 | 0.285 |
| pH | 7.17±0.91 | 7.30±0.04 | 0.333 |
| S creatinine (mg/dl) | 1.22±1.03 | 1.05±0.09 | 0.272 |
| Hematocrit | 33.57±4.45 | 32.30±3.91 | 0.107 |
| WBC (/mm ³) | 12160.43±2692.54 | 12798.07±1695.70 | 0.178 |
| Height (cm) | 158.93±5.82 | 158.76±5.59 | 0.884 |
| Weight (kg) | 63.52±7.57 | 63.87±7.24 | 0.822 |
| APACHE II score | 15.65±1.22 | 17.02±1.95 | 0.081 |

Regarding age and gender distribution, no significant difference was found between two groups ($p > 0.05$) (table I). Table-II showed that there was no significant difference regarding clinical variables and laboratory parameters between Targeted ΔP and LTVV group ($p > 0.05$) except duration of MV which was statistically significant difference between groups ($p < 0.05$).

Table-III: Distribution of the study patients by causes of ARDS in two group (N=92)

| Causes of ARDS | Targeted ΔP group (n=46) No. (%) | LTVV group (n=46) No. (%) | p-value |
|---------------------------|--|---------------------------------|---------|
| Community-acquired | | | |
| Pneumonia | 7(15.2%) | 4(8.7%) | 0.537 |
| Aspiration Pneumonia | 16(34.8%) | 18(39.1%) | 0.665 |
| Sepsis | 8(17.4%) | 10(21.7%) | 0.778 |
| Trauma | 6(13.0%) | 7(15.2%) | 0.765 |
| Near drowning | 2(4.3%) | 1(2.2%) | 1.000 |
| TRALI | 2(4.3%) | 1(2.2%) | 1.000 |
| Acute | | | |
| Pancreatitis | 5(10.9%) | 5(10.9%) | 1.000 |
| Total | 46(100.0%) | 46(100.0%) | |

Table-III showed the cause of ARDS. No significant difference of cause of ARDS was found between two groups ($p > 0.05$). Mean respiratory system compliance significantly was increased in Targeted ΔP group compare to LTVV group ($p < 0.001$), and length of ICU stay significantly decreased in

Targeted ΔP group compare to LTVV group (p<0.001) (table IV). PaO₂/FiO₂ ratio was significantly increased in ΔP-guided ventilation group compared to control group at Day 3, Day 5 and Day 7 (p<0.05).

Table-IV: Comparison of respiratory system compliance, ICU stay, PaO₂/FiO₂ ratio between Targeted ΔP group and LTVV group (N=92)

| Variables | Targeted ΔP group (n=46) Mean±SD | LTVV group (n=46) Mean±SD | p-value |
|--|--|---------------------------------|---------|
| Respiratory System Compliance | 27.74±1.51 | 24.02±1.13 | <0.001* |
| ICU stay | 10.02±1.31 | 12.43±2.47 | <0.001* |
| PaO ₂ /FiO ₂ ratio | | | |
| Day 3 | 79.30±12.07 | 74.52±7.33 | 0.024* |
| Day 5 | 140.51±29.91 | 119.15±16.67 | 0.001* |
| Day 7 | 235.02±57.4 | 204.10±60.1 | 0.013* |

Table-V: Comparison of mean exhaled tidal volume (V_T) between Targeted ΔP group and LTVV group (N=92)

| Exhaled Tidal volume (V _T) (ml/k) | Targeted ΔP group (n=46) Mean±SD | LTVV group (n=46) Mean±SD | p-value |
|---|--|---------------------------------|---------|
| Day 3 | 347.74±29.56 | 336.54±16.32 | 0.027* |
| Day 5 | 387.93±31.06 | 369.09±20.19 | 0.001* |
| Day 7 | 420.39±35.20 | 406.6±21.19 | 0.029* |

Mean exhaled tidal volume was significantly increased at Day 3, Day 5 and Day 7 in Targeted ΔP group compare to LTVV group (p<0.05) (table V). In the Targeted ΔP group mean driving pressure significantly reduced at Day 3, Day 5 and Day 7 (p<0.001) (table VI).

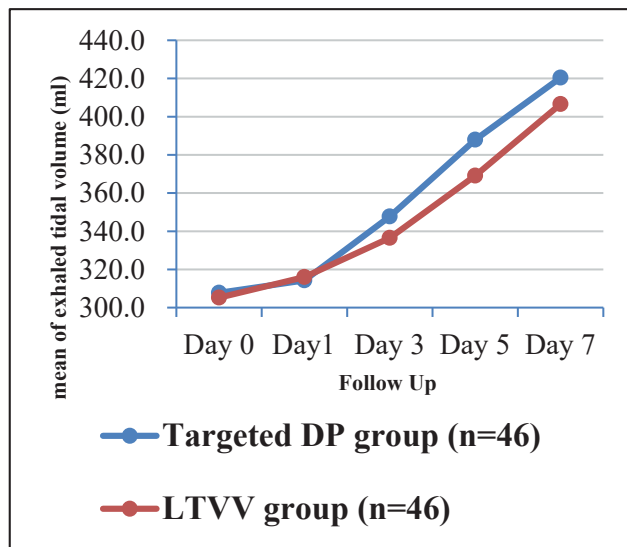


Figure-1: Line diagram showing the mean of exhaled tidal volume (ml/k) in two groups

Table-VI: Comparison of mean driving pressure between Targeted ΔP group and LTVV group (N=92)

| Driving Pressure (cm of H ₂ O) | Targeted ΔP group (n=46) Mean±SD | LTVV group (n=46) Mean±SD | p-value |
|---|--|---------------------------------|---------|
| Day 3 | 13.33±1.50 | 16.21±1.47 | <0.001* |
| Day 5 | 11.69±1.55 | 14.20±1.51 | <0.001* |
| Day 7 | 11.39±1.44 | 13.24±1.20 | <0.001* |

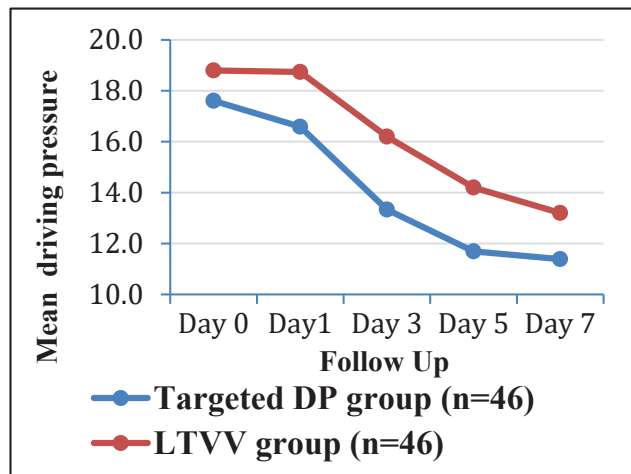


Figure-2: Line diagram showing the mean of driving pressure in two groups

Table-VII: Comparison of mean P_{Pit} between Targeted ΔP group and LTVV group (n=92)

| P _{Pit} (cm of H ₂ O) | Targeted ΔP group (n=46) Mean±SD | LTVV group (n=46) Mean±SD | p-value |
|---|--|---------------------------------|---------|
| Day 3 | 25.48±1.17 | 30.46±1.17 | <0.001* |
| Day 5 | 19.02±1.32 | 26.11±1.39 | <0.001* |
| Day 7 | 16.46±1.66 | 22.22±1.62 | <0.001* |

In the Targeted ΔP group mean P_{Pit} significantly reduced at Day 3, Day 5 and Day 7 (p<0.001) (table VII).

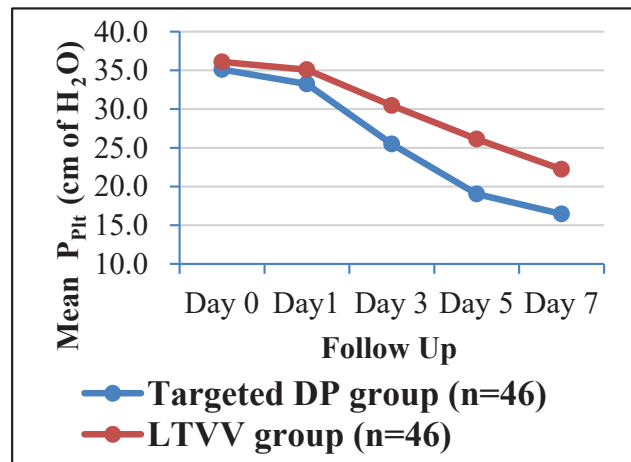


Figure-3: Line diagram showing the mean of P_{Pit} (cm of H₂O) in two groups

Table-VIII: Comparison of mean PEEP between Targeted ΔP group and LTVV group (N=92)

| PEEP (cm of H ₂ O) | Targeted ΔP group (n=46) Mean±SD | LTVV group (n=46) Mean±SD | p-value |
|-------------------------------|-------------------------------------|------------------------------|---------|
| Day 3 | 12.96±1.38 | 14.63±1.51 | <0.001* |
| Day 5 | 7.98±1.39 | 10.96±1.35 | <0.001* |
| Day 7 | 6.09±1.07 | 7.98±1.00 | <0.001* |

In the Targeted ΔP group mean PEEP was significantly reduced at Day 3, Day 5 and Day 7 (p<0.001) (table VIII). In the same group, respiratory rate was also significantly reduced at Day 7 (p<0.05) (table IX). Mean set V_T was significantly increased at Day 3, Day 5 and Day 7 (p<0.001) in the Targeted ΔP group (table X). Incidence of mortality at 28th day was significantly reduced in Targeted ΔP-guided ventilation group compared to LTVV group (8.7% vs. 26.1%) (p<0.05) (table XI).

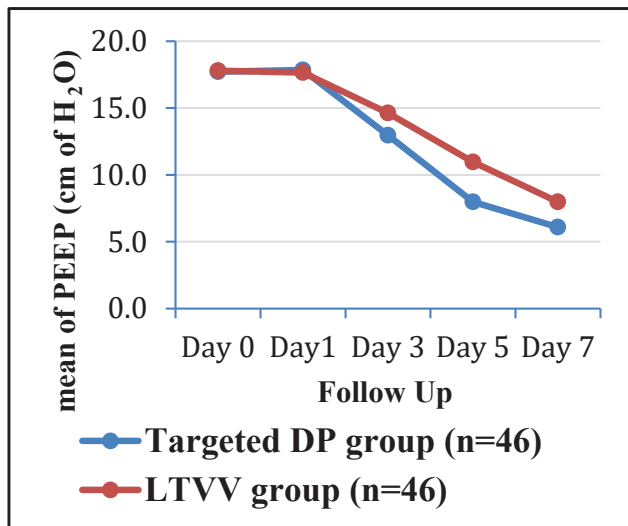


Figure-4: Line diagram showing the mean of PEEP (cm of H₂O) in two groups

Table-IX: Comparison of mean Respiratory rate between Targeted ΔP group and LTVV group (N=92)

| Respiratory rate (/min) | Targeted ΔP group (n=46) Mean±SD | LTVV group (n=46) Mean±SD | p-value |
|-------------------------|-------------------------------------|------------------------------|---------|
| Day 3 | 19.26±1.71 | 19.65±1.77 | 0.283 |
| Day 5 | 15.54±1.22 | 15.17±1.02 | 0.119 |
| Day 7 | 14.96±1.26 | 15.85±1.33 | 0.001* |

Table-X: Comparison of mean set V_T between Targeted ΔP group and LTVV group (N=92)

| Set V _T (ml/kg) | Targeted ΔP group (n=46) Mean±SD | LTVV group (n=46) Mean±SD | p-value |
|----------------------------|-------------------------------------|------------------------------|---------|
| Day 3 | 385.85±19.35 | 365.65±9.23 | <0.001* |
| Day 5 | 416.96±20.26 | 389.35±11.09 | <0.001* |
| Day 7 | 450.61±20.45 | 425.22±14.37 | <0.001* |

Table-XI: Distribution of the study patients by 28 days mortality of ARDS patients in two group (N=92)

| Mortality | Targeted ΔP group (n=46) No. (%) | LTVV group (n=46) No. (%) | p-value |
|--------------|-------------------------------------|------------------------------|---------|
| Survived | 42 (91.3%) | 34 (73.9%) | 0.028 |
| Not survived | 4 (8.7%) | 12 (26.1%) | |
| Total | 46 (100.0%) | 46 (100.0%) | |

Data were expressed as frequency and percentage Chi-square test was performed to see the association between two groups p<0.05 considered as a level of significance

Discussion:

This open labelled randomized controlled trial was conducted in the non-COVID ICU at the Department of Anesthesia, Pain, Palliative & Intensive Care, Dhaka Medical College, from March 2021 to February 2022. The study aimed to evaluate the outcomes of targeted driving pressure (ΔP) mechanical ventilation in ARDS patients. A total of 92 ARDS patients, as defined by the Berlin criteria, requiring mechanical ventilation were included. Patients in the targeted ΔP group were ventilated using volume-controlled or pressure control modes, while those in the low tidal volume (LTVV) group were ventilated using volume-controlled mode per ARDSNet strategy or pressure-support mode. Most patients were aged 41-60 years, with 21 (45.7%) in the ΔP group and 24 (52.2%) in the LTVV group. Male patients comprised 58.7% of the ΔP group and 60.9% of the LTVV group. Baseline characteristics, clinical, and laboratory findings showed no significant differences between the ΔP and LTVV groups (p>0.05). This finding aligns with Hamama et al, who also reported no significant baseline differences between groups (p>0.05).¹³

The common cause of ARDS was aspiration pneumonia 34.8% and 39.1% in Targeted ΔP group and LTVV group respectively. Next common causes of ARDS were sepsis 17.4% and 21.7%. No significant difference of cause of ARDS was found between two groups (p>0.05). Similar findings reported by Hamama et al.¹³

In Targeted ΔP group mean driving pressure observed in Day 0, Day 1 (non-interventional day data), Day 3, Day 5 and Day 7 were 17.61±1.73, 16.59±1.09, 13.33±1.55, 11.69±1.55 and 11.39±1.44 respectively. In LTVV group it was 18.80±0.91, 18.74±0.85, 16.20±1.51, 14.20±1.51 and 13.24±1.20 respectively. In the Targeted ΔP group mean driving pressure significantly reduced at Day 3, Day 5 and Day 7 (p<0.001). In patients with ARDS, a driving pressure-limited mechanical ventilation strategy was feasible in comparison with the conventional strategy, resulting in reductions of driving pressure from the 3rd day up to the 7th day, without an increased risk of severe adverse events such as severe acidosis. There were no differences regarding clinical endPoints, but our trial was not powered to detect effect on those endPoints. In agreement this study Romano et al

reported primary endPoint in the driving pressure–limited strategy group, right after the first hour, a reduction in driving pressure was observed after adjustment of the target tidal volume for that day, dropping from 15.3 cmH₂O to 10.6 cmH₂O ($p < 0.001$).¹⁴ The main analysis showed that the mean driving pressure on the first 3 days was 4.6 cmH₂O (95% CI, 6.5–2.8; $p < 0.001$) smaller in the driving pressure–limited group than in the low tidal volume ventilation group.

A safety concern regarding the use of very low tidal volumes to decrease driving pressure is the emergence of severe respiratory acidosis. To achieve target driving pressure tidal volume was compromised some times. In fact, previous studies evaluated the use of very low tidal volumes (3 or 4 ml/kg PBW) added extracorporeal carbonic dioxide removal to the treatment regimen for all of the study patients.^{15,16}

Present study showed mean respiratory system compliance significantly increased in Targeted ΔP group compare to LTVV group ($p < 0.001$), Length of ICU stay significantly decreased in Targeted ΔP group compare to LTVV group ($p < 0.001$). PaO₂/FiO₂ ratio was significantly increased in ΔP -guided ventilation group compared to control group at Day 3, Day 5 and Day 7 ($p < 0.05$).

Romano et al reported in their feasibility trial, PaCO₂ difference was 10 mm Hg in the first hour to first day, with smaller differences afterward in ΔP vs LTVV ventilation group.¹⁴ Mean PaCO₂ and pH in the driving pressure–limited group were 60 mmHg and 7.27, values that are reasonable in patients with ARDS provided that severe acidosis is avoided. In this regard, there were only three cases of severe acidosis (pH 7.10) in the driving pressure–limited group and one case in the control group (absolute difference 12.1; 95% CI, 241.5 to 17.3). These results suggest that the driving pressure–limited strategy does not frequently cause severe acidosis in patients with ARDS. However, a more precise estimation of the risk of severe acidosis caused by the driving pressure–limited strategy can only be obtained in larger trials.

This study showed mean exhaled tidal volume was significantly increased at Day 3, Day 5 and Day 7 in Targeted ΔP group compared to LTVV group ($p < 0.05$). Similarly Targeted ΔP group mean P_{pit} significantly reduced at Day 3, Day 5 and Day 7 ($p < 0.001$). Romano et al reported the first hour up to the third day, tidal volume was kept lower in the driving pressure–limited strategy group than in the control group (mean difference [ml/kg of PBW], 1.3; 95% CI 1.7–0.9; $p < 0.001$).¹⁴ The mean plateau pressure was significantly lower in the driving pressure–limited group than in the control group in 3rd day to 7th days, and in both cases was below 30 cm H₂O). The respiratory rate was higher in the driving pressure–limited group on Days 2 and 3 ($p < 0.05$). According to this study the Targeted ΔP group mean PEEP significantly reduced at Day 3, Day 5 and Day 7 ($p < 0.001$). Inconsistently Romano et al reported that no statistically significant difference between groups with regard to respiratory system static compliance PEEP in any of the first 7 days.

Incidence of mortality at 28th day was significantly reduced in Targeted ΔP -guided ventilation group compared to LTVV

group (8.7% vs. 26.1%) ($p < 0.05$). Also, ΔP -guided ventilation improved oxygenation, lung compliance, and weaning outcomes. Furthermore, it reduced the length of ICU stay and MV duration. ΔP 14 cm H₂O was the variable associated with improved hospital survival in ARDS patients, as reported by Amato et al and Laffey et al.^{9,17} Amato et al, in a retrospective analysis of data from several RCTs, concluded that ΔP was a better mortality predictor than C_{RS} or tidal volume.⁹ They explained the benefit of ΔP ventilator variable to the optimization of MV in ARDS patients by adopting ventilation to the aerated lung units only. Laffey and his colleagues, in the Lung Safe study, found that $\Delta P \leq 14$ cmH₂O was associated with better survival outcomes in patients with moderate to severe ARDS.¹⁷

Moreover, the results of this study came in agreement with those of Grieco et al and Borges et al.^{18,19} Kassis et al reported improved 28th day mortality, improved oxygenation, and respiratory system compliance with ventilator strategy leading to decreased ΔP .²⁰ Guerin et al noted that ΔP was a risk parameter of mortality, along with P_{plat} and C_{RS}. They noticed that patients with lower ΔP values have better survival outcomes with a significant decreased in SOFA score among survivors compared to those with higher values of ΔP .²¹

In disagreement with this study, Villar et al stated that P_{plat} was better than ΔP in predicting hospital mortality.²² They found that in a secondary analysis of observational studies, including patients with moderate to severe ARDS managed with PLV strategy, comparing the effect of P_{plat} versus ΔP on the prediction of mortality. They found that there were insignificant differences between both groups regarding oxygenation, C_{RS}, and organ dysfunction.²² This disagreement can be explained by the higher cut-off value of ΔP (19 cmH₂O) in Villar et al. study. Cavalcanti et al compared the effects of a PLV method vs titrated PEEP lung recruitment.²² Despite the low value of ΔP at the 7th day in the lung recruitment group, they found that utilizing PLV with a tidal volume of 4–6 ml/kg increased survival and reduced the duration of MV and ICU stay when compared to lung recruitment using titrated PEEP. Potential alveolar distention in the lung recruitment group might explain this discrepancy. Evidence from this study driving pressure is strongly associated with pulmonary injury and mortality, regardless of PEEP levels, tidal volume, or plateau pressure. Therefore, it is possible that targeting driving pressure may improve the safety of ventilation strategies for patients with acute respiratory distress syndrome (ARDS).

Limitations of the study:

This study has several limitations. The small sample size reduced the power to assess patient-centered clinical end points, and the trial was unblind, as blinding clinicians was unfeasible. Most participants had mild ARDS, limiting data applicability to severe cases without extracorporeal membrane oxygenation.^{24,25} Driving pressure measurements were intermittent, requiring an absence of respiratory effort, and assumed minimal variability in respiratory system static compliance over 24 hours, despite potential rapid changes in critically ill patients. The study also lacked esophageal

pressure measurements to evaluate transpulmonary pressure effects²⁶ and did not assess any biomarkers due to resource constraints.

Conclusion:

In patients with ARDS, a mechanical ventilation strategy that limits driving pressure by using very low tidal volumes is feasible in comparison with the conventional strategy. The results presented here will be useful for planning a larger randomized controlled clinical trial to evaluate the effect of a driving pressure-limited strategy on clinical end points. Due to heterogenous pathology mechanical ventilation in ARDS, patient should be based on low driving pressure that is below or equal to 14 cm of H₂O and, not depending only low tidal volume which was set according to the predicted body weight.

Ethical Measures:

After finalizing the study protocol approval from ethical review committee (ERC) was taken from the ERC of Dhaka Medical College. Informed written consent was taken from the patient or legal guardian of the patient who was unable to communicate properly. For safeguarding confidentiality and protecting anonymity, each of the patients was given a special ID no. which was followed in each step of data collection, editing, storage and analysis.

Conflict of Interest

The authors have no conflict of interest to declare.

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