Lung protective mechanical ventilation
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Chapter 5

Adoption of Lower Tidal Volume Ventilation Improves with Feedback and Education

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Abstract

Background: To determine whether feedback and education improve adoption of lung-protective mechanical ventilation (ie, with lower tidal volume [VT])

Methods: We conducted a retrospective study of ventilator settings; we used data from 3 consecutive studies of patients with acute lung injury and/or acute respiratory distress syndrome, in the intensive care units of 2 university hospitals in the Netherlands. At site 1 we conducted a time series study of before and after feedback and education about lung-protective mechanical ventilation, and we compared the results from site 1 to the ventilation strategies at site 2, which did not undergo the feedback and education intervention. Feedback and education consisted of presentations of actual ventilator settings, advised ventilator settings, and discussions on potential reasons for not using lower VT.

Results: Two studies were performed at site 1, in 1999–2000 (study 1, n = 22) and in 2002 (study 2, n = 12). In 2003–2004, study 3 was performed simultaneously at site 1 (n = 8) and site 2 (n = 17). At site 1, mean VT was 10.9 ml/kg (95% confidence interval [CI] 10.3 – 11.6) predicted body weight (PBW) in study 1 and 9.9 ml/kg (95% CI 9.0 – 10.8) PBW in study 2 (not significant). After the feedback and education intervention at site 1, VT declined to 7.6 ml/kg (95% CI 6.5 – 8.7) PBW in study 3 (p = 0.003). At site 2, where no feedback and education was given, VT was 10.3 ml/kg (95% CI 9.5 – 11.0) PBW (p < 0.001 vs. site 1).

Conclusions: Adoption of lower VT ventilation strategy in patients with acute lung injury or acute respiratory distress syndrome is far from complete in the Netherlands. Adoption of a lower VT strategy improves after feedback and education.
Introduction
One major advance in the field of mechanical ventilation (MV) has been the clear demonstration that use of lower tidal volumes ($V_t$) (6 ml/kg predicted body weight, PBW) significantly reduces mortality in patients with acute lung injury (ALI) or its more severe form, acute respiratory distress syndrome (ARDS) [1]. Although guidelines support the use of lower $V_t$ in ALI/ARDS–patients [2], physicians have been reluctant to adopt lung–protective ventilation [3-5]. Poor recognition by physician of patients with ALI/ARDS [6], concerns over hypercapnia, acidosis, and hypoxemia [7], as well as fear of increased need for sedation to maintain ventilator synchrony and comfort are several of the barriers to use lower $V_t$ [8,9]. In addition, the importance of using PBW (i.e., weight based on patient’s height, instead of actual body weight) may have been neglected [10].

In the present investigation, we determined ventilator settings in 3 consecutive ALI/ARDS–studies performed in the Netherlands before and after publication of the landmark study by the ARDS Network [1]. We focused on the effect of feedback and education on use of lung–protective MV using lower $V_t$ at one single intensive care unit (ICU) (Academic Medical Center, Amsterdam, site 1). Feedback and education was not given because of one of the abovementioned studies, but because ICU–team members did not follow recommendations in the local MV–guideline, in particular those on use of lower $V_t$, several years after this guideline became effective.

Methods
We collected data on ventilator settings of patients recruited in 3 consecutive randomized controlled ALI/ARDS–studies in the intensive care units (ICUs) of 2 university hospitals. Site 1 was the Academic Medical Center, University of Amsterdam, Amsterdam, the Netherlands. Site 2 was the University Medical Center, University of Utrecht, Utrecht, the Netherlands. We conducted 3 separate studies. Study 1 (performed in 1999–2000) and study 2 (in 2002) were performed at site 1 (figure 1). Study 3 (in 2003-2004) was performed simultaneously at site 1 and site 2. The feedback and education intervention on lung–protective mechanical ventilation occurred at site 1, but not at site 2. Participating subjects met the standard definition of ALI/ARDS [11]. The 3 studies tested the safety and efficacy of instillation of surfactant versus standard therapy (these 3 studies are as yet unpublished).

Study centres
The ICU at site 1 is a 28–bed department; the ICU at site 2 is a 32–bed department. Both ICUs are so–called “closed–format” units (i.e., all patients are under the direct care of the members of the ICU–team). As part of the team ICU–nurses can make ventilator therapy recommendations, but unit policy mandates that all changes in ventilator settings be
ordered by ICU–physicians. However, since in all patients’ pressure controlled MV was used, ICU–nurses were allowed to change applied airway pressures to assure the use of correctly sized VT at all times. The ICU–team at site 1 comprises 5–8 full–time intensivists, 6–8 subspecialty fellows, 12 residents, and occasionally 1 intern. The ICU–team at site 2 comprises 6–8 full and part–time intensivists, 3–4 subspecialty fellows 15 residents and 3 interns.

![Figure 1](image_url) Diagram of studies of which ventilator settings were analyzed. Three consecutive studies were performed during a period of 6 years. Study 1, study 2 and study 3 were all performed at site 1; study 3 was also performed at site 2. The grey boxes illustrate what was compared: ventilator settings of patients recruited in study 1 and study 2 at site 1 were compared with study 3 – in addition, ventilator settings of patients recruited in study 3 at site 1 and site 2 were compared. The black box illustrates the moment at which feedback and education was given at site 1.

### Intervention: feedback and education

At site 1, in between study 2 and study 3, the intervention consisted of: (1) a concise presentation to all ICU–physicians on results from several animal studies [12,13] and clinical studies of lung–protective MV using lower $V_T$ in ALI/ARDS–patients [1,14-19]; (2) a recall on what was stated in the local MV–guideline on size of $V_T$ (“size of $V_T$ should be 6 – 8 ml/kg PBW”) and a recall on that we all agreed on use of lower $V_T$ when this guideline was made effective; (3) presentation on data on actual size of $V_T$ before this intervention (“feedback”, for this, two of us (EKW and MJS) collected all ventilator settings of all patients during a period of 2 weeks); and (4) a discussion on potential reasons for not using lower $V_T$, including the importance of using PBW instead of actual bodyweight to set $V_T$, and potentially existing fear of increased need for sedation to maintain ventilator synchrony and comfort (“education”). The same strategy was practiced in the ICU–nurse team of site 1. This was repeated 3 times. Finally, the patient data management system (PDMS; Metavision, iMDsoft, Sassenheim, the Netherlands) was equipped with a special tool that automatically calculated the ideal $V_T$ from patient’s height, after which the
targets were automatically readable in the “respiratory tab” (i.e., for all patients it was easy to check whether \( V_T \) was between 6 – 8 ml/kg PBW).

**Mechanical ventilation protocols**

During conduct of the first 2 studies no specific recommendations were made on \( V_T \) in the study–protocols. It was advised to follow local MV–guidelines. The protocol of study 3, however, contained a recommendation on \( V_T \)–settings – \( V_T \) was advised to be 6 – 8 ml/kg PBW. At site 1 and site 2, the local MV–guidelines recommended using pressure-controlled (PC) MV or pressure-support (PS) MV. Levels of positive end–expiratory pressure (PEEP) were to be adjusted to PaO\(_2\) levels (at site 1 the algorithm advised higher PEEP levels as compared to site 2). Use of prone positioning was recommended in patients requiring FIO\(_2\) levels > 0.6. Mild hypercapnia was accepted in patients with ALI/ARDS (but no limits for PaCO\(_2\) were given).

**Patients and data–collection**

The following data were extracted from the trial record files at 0, 4, 8, 12, 16, 20, 24, 30, 36, 40, 48, 60 and 72 hours after randomization: \( V_T \), respiratory rate (breaths/min), level of PEEP (cm H\(_2\)O), maximum airway pressure (Paw–max) in cm H\(_2\)O, FiO\(_2\), PaO\(_2\), PaCO\(_2\), and arterial pH. \( V_T \) was expressed in ml/kg PBW.

**Statistical analysis**

All ventilator settings (including \( V_T \)) and blood gas analysis results were similar between patients in the different treatment arms of the studies. Therefore data of each study were pooled and further analysis compared settings between the 3 consecutive studies, and between the 2 sites. To detect differences regarding baseline data in the studies an ANOVA test and post–hoc analysis with Tukey test was performed. These data are all presented as mean ± SD or median [interquartile range (IQR)]. Ventilator data of the studies were all statistically analyzed using a linear mixed model analysis. The fixed effects were study, sample time and study x sample time. The random effect was patient. These data are all presented as mean [95% confidence interval (CI)]. For categorical data the Chi–square test was used. Data in the figures are presented as mean ± standard deviation (SD). A p-value < 0.05 was considered significant. The analysis was performed with SPSS version 12.0 (SPSS Inc., Chicago, IL).

**Results**

**Study subjects**

The present analysis included 22 patients and 12 patients in study 1 and study 2, respectively. Study 3 consisted of 8 patients at site 1 and 17 patients at site 2. Demographics of patients are given in table 1. There were significantly less women in
study 3 at site 1 as compared to the other studies (p < 0.001 versus study 1 and 2 and study 3 at site 2). In accordance, height and PBW values were significantly lower in study 1 and study 2 as compared to study 3. Acute Physiology and Chronic Health Evaluation II scores were lower in study 1 as compared to study 2 and study 3 (p = 0.013 vs. study 2, p = 0.004 vs. study 3 at site 1 and p < 0.001 vs. study 3 at site 2).

**Tidal volume and respiratory rate**

All patients in all 3 studies were initially ventilated with pressure controlled MV. In addition, proning was used in all patients in the first few days after start of MV. During weaning pressure support MV was used. Mean VT in study 1 and study 2 were similar: 10.9 (95% CI 10.3 – 11.6) ml/kg PBW and 9.9 (95% CI 9.0 – 10.8) ml/kg PBW, respectively (not significant). In study 3, at site 2 mean VT was 10.3 (95% CI 9.5 – 11.0) ml/kg PBW as compared to 7.6 (95% CI 6.5 – 8.7) ml/kg in that study at site 1 (p < 0.001 vs. study 3 at site 2, p < 0.001 and p = 0.003 vs. study 1 and study 2, respectively) (figure 2) The number of data points with VT > 10ml/kg PBW declined from 62% and 49% in study 1 and study 2, respectively, to 3% in study 3 at site 1 (p < 0.001). At site 2 the number of data points with VT > 10ml/kg PBW was 48%. The number of observations with VT > 8 ml/kg PBW decreased from 95% and 86% in study 1 and study 2, respectively, to 28% in study 3 at site 1 (p < 0.001). At site 2 the number of observations with VT > 8 ml/kg PBW was 81%.

With the use of lower VT, the respiratory rate increased from 15.6 breaths/min (95% CI 16.6 – 20.1) and 18.3 breaths/min (95% CI 16.5 – 20.2) in the first 2 studies (not significant between study 1 and study 2) to 20.4 breaths/min (95% CI 18.1 – 22.7) in study 3 at site 1 (p = 0.001 vs. study 1). At site 2, respiratory rate was significantly lower: 17.1 breaths/min (95% CI 15.5 – 18.6) (p = 0.002 vs. study 3 at site 1).

**Table 1** Baseline characteristics of patients in the studies

<table>
<thead>
<tr>
<th>Study</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study location</td>
<td>Site 1</td>
<td>Site 1</td>
<td>Site 1</td>
<td>Site 2</td>
</tr>
<tr>
<td>Number of patients</td>
<td>n = 22</td>
<td>n = 12</td>
<td>n = 8</td>
<td>n = 17</td>
</tr>
<tr>
<td>Gender; M/F</td>
<td>15/7</td>
<td>9/3</td>
<td>8/0*</td>
<td>13/4</td>
</tr>
<tr>
<td>Age (years); mean ± SD</td>
<td>59 ± 14</td>
<td>59 ± 15</td>
<td>60 ± 11</td>
<td>56 ± 18</td>
</tr>
<tr>
<td>APACHE II; mean ± SD</td>
<td>17.1 ± 5.7</td>
<td>19.2 ± 6.8</td>
<td>19.8 ± 8.6</td>
<td>19.9 ± 6.3</td>
</tr>
<tr>
<td>Mortality n (%) at day 28</td>
<td>4 (18.2)</td>
<td>2 (16.7)</td>
<td>1 (12.5)</td>
<td>2 (11.8)*</td>
</tr>
<tr>
<td>Reason for ALI/ARDS:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sepsis</td>
<td>6</td>
<td>4</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>6</td>
<td>3</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Trauma</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Shock</td>
<td>8</td>
<td>3</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Height, cm; mean ± SD</td>
<td>173 ± 9</td>
<td>171 ± 8.3</td>
<td>178 ± 7.2</td>
<td>177 ± 11.7</td>
</tr>
<tr>
<td>Actual BW (kg); mean ± SD</td>
<td>73.1 ± 12.5</td>
<td>77.6 ± 17.2</td>
<td>80.5 ± 18.7</td>
<td>84.9 ± 13.7</td>
</tr>
<tr>
<td>Predicted BW (kg); mean ± SD</td>
<td>67.2 ± 9.6</td>
<td>65.9 ± 8.0</td>
<td>73.6 ± 6.6</td>
<td>70.5 ± 12.5</td>
</tr>
</tbody>
</table>

Abbreviations: APACHE II, Acute Physiology And Chronic Health Evaluation II; IQR, interquartile range; BW, body weight. Adjusted p-values:* p < 0.001 vs. study 1, 2 and study 3 at site 2; † p < 0.05 vs. study 2 and 3; ‡ p < 0.05 vs. study 1 and study 3 at site 1; § p < 0.001 vs. study 1 and 3; ¶ p < 0.01 vs. study 3; ¶¶ p < 0.05 vs. study 1 and 3. See text for exact p-values.
Adoption of Lower Tidal Volume Ventilation Improves with Feedback and Education

Figure 2 Tidal volumes (ml/kg predicted body weight) in three consecutive trials (●, study 1; ●, study 2; ■, study 3 at site 1; ▲, study 3 at site 2) in the first 72 hours after inclusion. Area between the dotted lines indicate target VT as explicitly mentioned in the mechanical ventilation protocol during conduct of study 3. Data are means and SE.

PEEP and Paw–max

Individual PEEP levels decreased significantly over time in all patients in the 3 studies (p < 0.001). The mean PEEP level in study 3 at site 2 (9.5 cm H\(\text{O}\) [95% CI 8.5 – 10.5]) was lower as compared to the mean PEEP level in study 1, study 2, and study 3 at site 1 (11.2 cm H\(\text{O}\) [95% CI 10.3 – 12.1], 13.7 cm H\(\text{O}\) [95% CI 12.5 – 14.9] and 14.1 cm H\(\text{O}\) [95% CI 12.6 – 15.6], respectively) (p = 0.059 vs. study 1, p < 0.001 vs. study 2 and study 3 at site 1).

Similarly, individual Paw–max levels decreased over time in all patients in the 3 studies (p < 0.001). The mean Paw–max level in study 2 (31.4 cm H\(\text{O}\) [95% CI 28.7 – 34.0]) was higher as compared to study 3 at site 1 (26.8 cm H\(\text{O}\) [95% CI 23.5 – 30.1], p = 0.034). In the other 2 studies the mean Paw–max levels were 28.1 cm H\(\text{O}\) [95% CI 26.1 – 30.0] and 28.3 cm H\(\text{O}\) [95% CI 26.1 – 30.5] in study 1 and study 3 at site 1, respectively.

\(\text{FiO}_2\), \(\text{PaO}_2\), \(\text{PaCO}_2\) and \text{pH}

Data for \(\text{FiO}_2\), \(\text{PaO}_2\), \(\text{PaCO}_2\) and \text{pH} are given in table 2. No differences were found between the studies regarding \(\text{FiO}_2\) and \text{pH}. Levels of \(\text{PaCO}_2\) were statistically significant (but clinically insignificant) lower in study 1 and study 2 as compared to study 3 at site 2 (p
Levels of PaCO₂ were not different between site 1 and site 2 in study 3. Levels of PaO₂ were significantly higher in study 1 and study 2 as compared to study 3 at site 2 (p = 0.013 and p = 0.01, respectively). Levels of PaO₂ were not different between site 1 and site 2 in study 3.

Table 2 Blood gas analysis variables

<table>
<thead>
<tr>
<th>Study Location</th>
<th>Number of Patients</th>
<th>Site 1</th>
<th>Site 1</th>
<th>Site 1</th>
<th>Site 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study location</td>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>Site 2</td>
</tr>
<tr>
<td>FiO₂</td>
<td>0.50</td>
<td>0.52</td>
<td>0.46</td>
<td>0.51</td>
<td></td>
</tr>
<tr>
<td>[0.47 – 0.54]</td>
<td>[0.47 – 0.56]</td>
<td>[0.41 – 0.52]</td>
<td>[0.47 – 0.55]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PaO₂ (torr)</td>
<td>140</td>
<td>140</td>
<td>122</td>
<td>110</td>
<td></td>
</tr>
<tr>
<td>[128 – 151]*</td>
<td>[125 – 155]*</td>
<td>[104 – 140]</td>
<td>[98 – 122]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PaCO₂ (torr)</td>
<td>36.9</td>
<td>37.8</td>
<td>41.1</td>
<td>40.4</td>
<td></td>
</tr>
<tr>
<td>[35.3 – 38.6]*</td>
<td>[35.6 – 40.1]*</td>
<td>[38.3 – 44.0]</td>
<td>[38.6 – 42.3]</td>
<td></td>
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<tr>
<td>pH</td>
<td>7.40</td>
<td>7.40</td>
<td>7.38</td>
<td>7.41</td>
<td></td>
</tr>
<tr>
<td>[7.38 – 7.42]</td>
<td>[7.37 – 7.43]</td>
<td>[7.35 – 7.42]</td>
<td>[7.39 – 7.44]</td>
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</tbody>
</table>

Data are mean [95% Confidence Interval]. * p < 0.05 vs. study 3 at site 2 (adjusted p-value). See text for exact p-values.

Discussion

Use of lung–protective mechanical ventilation with lower V₁ is recommended for patients suffering from ALI/ARDS [2]. We demonstrate, similar to a growing number of other published manuscripts [3-5], the poor penetration of the use of 6 ml/kg PBW V₁ for ALI/ARDS–patients. Indeed, no adoption of use of lower V₁ was found in the first years after publication of the ARDS Network trial [1]. Although adoption of lower V₁ ventilation improved after feedback and education on lung–protective mechanical ventilation, in most patients V₁ were still larger than 6 ml/kg PBW.

Our analysis has several drawbacks. First, we analyzed different treatment groups within each study together, because neither the study protocols prescribed different ventilator settings for the 2 arms of those studies nor differences regarding respiratory variables were found between the 2 arms. We are uncertain, however, whether changes in the pulmonary condition as a result of the differences in treatment may have resulted in a change in ventilator settings. Groups may be too small to recognize this. Second, as with any secondary subset analysis from a large trial, this report may have significant inherent flaws due to its retrospective design, small sample size, and focus on a single site where the ventilation practices may not be representative of the norm. Finally, a study makes clinicians aware that patients meet criteria for ALI/ARDS, which may change clinical behavior (like use of lung–protective ventilation); in other words VT–practice may not at all have changed in patients not recruited in studies.

An alternative explanation for the change in ventilator settings is secular trends over time. Indeed, one could argue that this decline was (also) an effect of time (i.e., be the result of less lack of awareness about the benefit of lower V₁, less disagreement about the evidence and more motivation to apply lower V₁). For several reasons we consider this less likely, however. First, although a trend towards lower V₁ was noticed between study 1 and
Adoption of Lower Tidal Volume Ventilation Improves with Feedback and Education

study 2, differences were indeed small and not statistically significant. Second, ventilator settings in study 3 did not show a secular trend over time, neither at site 1 nor at site 2. Third, when secular changes over time explain the change in ventilator settings at site 1, why did ventilator settings in the other site remain unchanged? Providing feedback on previous practice has been shown to be more effective than simple education [20]. Recently, Cook and co–workers emphasized the importance of an environmental scan and understanding of current behavior to improve daily practice [21]. In a previous report we demonstrated the effect of a feedback and educational program, targeting a lower VT strategy in all mechanically ventilated ICU-patients [22]. We found that VT declined significantly within 6 months in our ICU and more importantly, after 12 months lower VT were still used. Here we show that in the center in which feedback and education on use of lower VT was given, the use of lower VT–MV improved, while in a neighboring university hospital, where neither feedback nor education had taken place, VT were larger than presently recommended for ALI/ARDS–patients.

Of course, other, yet unrecognized differences between the 2 sites may account for this difference. However, the 2 ICUs are very similar, both being so–called closed format units, with no changes in staffing over time. The only difference that existed between these centers was PEEP levels: lower PEEP levels were used at site 2 in study 3, as compared to site 1 in all studies. The MV–guideline contained different recommendations on the use of PEEP, which completely explains this difference.

It has been shown that clinicians in teaching hospitals only slowly adopted the lower VT–strategy, several years after publication of the ARDS Network study [3]. Although significant reductions in VT in ALI/ARDS–patients were described in another study, wide variation in ventilator practice persisted and the proportion of patients receiving VT within recommended limits (≤ 8 ml/kg PBW) remained modest [4]. In contrast, physicians at ARDS Network centers prescribed significant lower VT after completion of their study (1999 – 2002) as compared to VT during conduct of the study (1996 – 1999) [23]. In an international observational study on 198 European ICU’s, including over 393 ALI/ARDS–patients, in more than half of cases ventilator settings were other than the ARDS Network lung–protective MV strategy [5]. Our data are in line with these reports. Indeed, several years after publication of the ARDS Network trial VT were still large and in fact not different with those set before the benefits of lower VT in ALI/ARDS became clear.

Various reasons for the slow adoption of low VT were recently summarized [24]. Physicians may choose to control plateau pressures (or Paw–max in PC MV) instead of VT, despite the clear benefit of using lower VT at every plateau pressure (i.e., also at lower levels). Physicians may have concerns about the initial worsening of PaO2 and PaCO2 levels when VT are lowered, despite the demonstration that the initial deterioration in PaO2/FiO2–ratio is short–lived [1]. The ARDS Network study demonstrated that low VT–patients had a lower
FiO₂ by the 3rd day as compared to conventional Vₜ—patients. Similarly, although low Vₜ—ventilation causes an increase in PaCO₂ initially, there is no difference in pH by day 7. And finally, many physicians may worry that a low Vₜ—strategy causes increased ventilator dyssynchrony. Two retrospective analysis, however, found no difference either in the number of patients receiving benzodiazepine sedatives or opioid analgesics or in the dosages of these medications [25,26].

From the present analysis we conclude that adoption of lower Vₜ as standard of care in patients with ALI/ARDS is still poor, but may improve with feedback and education.
References


