What is Lung Protective Ventilation?

NBART 2016
Disclosure

- Full time employee of Draeger
Outline

• 1. Why talk about Lung Protective Ventilation?
• 2. What is Lung Protective Ventilation?
• 3. How to apply Lung Protective Ventilation?
Outline

1. Why talk about Lung Protective Ventilation?
2. What is Lung Protective Ventilation?
3. How to apply Lung Protective Ventilation?
Is the Ventilator Contributing to the Pathogenesis of ARDS?

Is acute respiratory distress syndrome an iatrogenic disease?

Jesús Villar qualities and Arthur S Slutsky qualities Critical Care 2010, 14:120

• “..injurious ventilation strategies have been shown to cause all of the pathology associated with ALI/ARDS.”

• “..should we begin to consider that ALI/ARDS is a consequence of our efforts rather than progression of the underlying disease?”

• “..ALI/ARDS is largely a ‘man-made’ syndrome.”

• “..ALI/ARDS is no longer a syndrome that must be treated, but is a syndrome that should be prevented.”
No Reduction in ARDS Mortality since 1998

**FIGURE 1.** Schematic representation of average reported mortality in observational and randomized controlled trials in adult patients with acute respiratory distress syndrome since 1967. Data have been compiled from [6,11,12,26,27].

Villar et al. Curr Opin Crit Care 2014;20:3-9
How Does the Ventilator Cause Injury?
Ventilator Induced Lung Injury (VILI)

Mechanisms:

- **Volutrauma & Barotrauma (Stress/Strain)**
  - **Stress** = High ΔTranspulmonary Pressure, not necessarily high PIP!
  - **Strain** = High tidal volume (Volume above the FRC) & may occur even with low VT of 4-6 ml/kg IBW in heterogenous lung disease (ARDS Baby Lung)

- **Atelectrauma**
  - Repetitive opening and closing of Alveoli (recruitment/derecruitment injury)
  - Disruption of surfactant monolayer → Shear stress injury
  - Altered A/C membrane → permeability to proteins and other solutes → pulmonary edema and intrapulmonary floating

- **Biotrauma (Systemic Organ Failure)**
  - Resultant effect of initial insult and above injuries
Outline

• 1. Why talk about Lung Protective Ventilation?
• 2. What is Lung Protective Ventilation?
• 3. How to apply Lung Protective Ventilation?
What is lung protective ventilation?

- Any ventilation strategy that aims to minimize or prevent VILI
- ARDSnet Low VT, Pplateau < 30 & PEEP/FiO2 table
- Open Lung Ventilation (Recruitment, HFO, APRV, Optimal PEEP)
- Prone Ventilation
- Adjunctive Therapies: Pulmonary vasodilators, ECLS, gene therapy, pharmacological, etc.....

- Mechanical ventilation strategies that minimizes Lung Strain and Stress, as well as prevention of recruitment-derecruitment injury
What is LPV?
What is LPV?

Can be done in every ICU!!!
How Does the Ventilator Cause Injury?
Ventilator Induced Lung Injury (VILI)

Mechanisms:
• **Volutrauma & Barotrauma (Stress/Strain)**
• **Atelectrauma (shear injury)**
• **Biotrauma (Systemic Organ Failure)**
What is LPV?
Low Tidal Volume (LTV)

Presumed to prevent or minimize Volutrauma by limiting overdistension and therefore limits Dynamic Strain and the resulting lower Pplateau may decrease ΔTranspulmonary pressure and therefore Stress injury ??????
### Table 1. Summary of Ventilator Procedures.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group Receiving Traditional Tidal Volumes</th>
<th>Group Receiving Lower Tidal Volumes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventilator mode</td>
<td>Volume assist--control</td>
<td>Volume assist--control</td>
</tr>
<tr>
<td>Initial tidal volume (mL/kg of predicted body weight)</td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td>Petco2 pressure (cm of water)</td>
<td>&lt;50</td>
<td>&lt;30</td>
</tr>
<tr>
<td>Ventilator rate setting needed to achieve a pH goal of 7.3 to 7.45 (breaths/min)</td>
<td>6–55</td>
<td>6–55</td>
</tr>
<tr>
<td>Ratio of the duration of inspiration to the duration of expiration</td>
<td>1:1–1:3</td>
<td>1:1–1:3</td>
</tr>
<tr>
<td>Oxygenation goal</td>
<td>$\text{PaO}_2$, 55–80 mm Hg, or $\text{SpO}_2$, 88–95%</td>
<td>$\text{PaO}_2$, 55–80 mm Hg, or $\text{SpO}_2$, 88–95%</td>
</tr>
<tr>
<td>Allowable combinations of $\text{FiO}_2$ and PEEP (cm of water)‡</td>
<td>0.3 and 5</td>
<td>0.3 and 5</td>
</tr>
<tr>
<td></td>
<td>0.4 and 5</td>
<td>0.4 and 5</td>
</tr>
<tr>
<td></td>
<td>0.5 and 5</td>
<td>0.4 and 8</td>
</tr>
<tr>
<td></td>
<td>0.5 and 8</td>
<td>0.5 and 8</td>
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<tr>
<td></td>
<td>0.5 and 10</td>
<td>0.5 and 10</td>
</tr>
<tr>
<td></td>
<td>0.7 and 10</td>
<td>0.7 and 10</td>
</tr>
<tr>
<td></td>
<td>0.7 and 12</td>
<td>0.7 and 12</td>
</tr>
<tr>
<td></td>
<td>0.7 and 14</td>
<td>0.7 and 14</td>
</tr>
<tr>
<td></td>
<td>0.8 and 14</td>
<td>0.8 and 14</td>
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<tr>
<td></td>
<td>0.9 and 14</td>
<td>0.9 and 14</td>
</tr>
<tr>
<td></td>
<td>0.9 and 16</td>
<td>0.9 and 16</td>
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<tr>
<td></td>
<td>0.9 and 18</td>
<td>0.9 and 18</td>
</tr>
<tr>
<td></td>
<td>1.0 and 18</td>
<td>1.0 and 18</td>
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<tr>
<td></td>
<td>1.0 and 20</td>
<td>1.0 and 20</td>
</tr>
<tr>
<td></td>
<td>1.0 and 22</td>
<td>1.0 and 22</td>
</tr>
<tr>
<td></td>
<td>1.0 and 24</td>
<td>1.0 and 24</td>
</tr>
</tbody>
</table>

### Table 4. Main Outcome Variables.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group Receiving Lower Tidal Volumes</th>
<th>Group Receiving Traditional Tidal Volumes</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death before discharge home and breathing without assistance (%)</td>
<td>31.0</td>
<td>39.8</td>
<td>0.007</td>
</tr>
<tr>
<td>Breathing without assistance by day 28 (%)</td>
<td>65.7</td>
<td>55.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No. of ventilator-free days, days 1 to 28</td>
<td>12±11</td>
<td>10±11</td>
<td>0.007</td>
</tr>
<tr>
<td>Barotrauma, days 1 to 28 (%)</td>
<td>10</td>
<td>11</td>
<td>0.43</td>
</tr>
<tr>
<td>No. of days without failure of nonpulmonary organs or systems, days 1 to 28</td>
<td>15±11</td>
<td>12±11</td>
<td>0.006</td>
</tr>
</tbody>
</table>
Meta-Analysis of Acute Lung Injury and Acute Respiratory Distress Syndrome Trials Testing Low Tidal Volumes

Peter Q. Eichacker, Eric P. Gerstenberger, Steven M. Banks, Xizhong Cui, and Charles Natanson

TABLE 1. NUMBER OF PATIENTS, TIDAL VOLUMES STUDIED, AND MORTALITY RATES IN FIVE RANDOMIZED CLINICAL TRIALS

<table>
<thead>
<tr>
<th>Author (Ref.)</th>
<th>Number of Patients</th>
<th>Tidal Volume</th>
<th>Mortality Rate</th>
<th>Reported Mortality Difference (p Value)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low Tidal Volume</td>
<td>Low Tidal Volume* (ml/kg)</td>
<td>Control* (ml/kg)</td>
<td>Low Tidal Volume (%)</td>
</tr>
<tr>
<td>Amato and coworkers (3)</td>
<td>29</td>
<td>6.1 ± 0.2*</td>
<td>11.9 ± 0.5*</td>
<td>38</td>
</tr>
<tr>
<td>Stewart and coworkers (5)</td>
<td>60</td>
<td>7.2 ± 0.8*</td>
<td>10.6 ± 0.2*</td>
<td>50</td>
</tr>
<tr>
<td>Brochard and coworkers (6)</td>
<td>58</td>
<td>7.2 ± 0.2*</td>
<td>10.4 ± 0.2*</td>
<td>47</td>
</tr>
<tr>
<td>Brower and coworkers (7)</td>
<td>26</td>
<td>7.3 ± 0.1*</td>
<td>10.2 ± 0.1*</td>
<td>50</td>
</tr>
<tr>
<td>ARDSNet (4)</td>
<td>432</td>
<td>6.3 ± 0.1*</td>
<td>11.7 ± 0.1*</td>
<td>31</td>
</tr>
</tbody>
</table>

## LTV for everyone?

**Ventilation with lower tidal volumes for critically ill patients without the acute respiratory distress syndrome: a systematic translational review and meta-analysis**

Ary Serpa Neto\[^{a,b,c}\], Liselotte Nagtzaam\[^{c}\], and Marcus J. Schultz\[^{c,d}\]

*Curr Opin Crit Care* 2014, 20; 25-32

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Tidal volume (ml/kg)</th>
<th>Low tidal volume</th>
<th>High tidal volume</th>
<th>Duration mechanical ventilation</th>
<th>Mortality</th>
<th>Inflammatory markers</th>
<th>Development of ARDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lee et al. [39]</td>
<td>1990</td>
<td></td>
<td>6.0</td>
<td>12.0</td>
<td>↓</td>
<td></td>
<td>NR</td>
<td>↓</td>
</tr>
<tr>
<td>Gajic et al. [40]</td>
<td>2004</td>
<td></td>
<td>9.0</td>
<td>12.0</td>
<td>NR</td>
<td></td>
<td>NR</td>
<td>↓</td>
</tr>
<tr>
<td>Wolthuis et al. [41]</td>
<td>2007</td>
<td></td>
<td>8.0</td>
<td>10.0</td>
<td>↔</td>
<td>↔</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Yilmaz et al. [42]</td>
<td>2007</td>
<td></td>
<td>8.0</td>
<td>11.0</td>
<td>↓</td>
<td>↓</td>
<td>NR</td>
<td>↓</td>
</tr>
<tr>
<td>Determann et al. [8]</td>
<td>2010</td>
<td></td>
<td>6.0</td>
<td>10.0</td>
<td>↔</td>
<td>↔</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Pinheiro de Oliveira et al. [43]</td>
<td>2010</td>
<td></td>
<td>5.0</td>
<td>12.0</td>
<td>↔</td>
<td>↔</td>
<td>↓</td>
<td>NR</td>
</tr>
</tbody>
</table>
LTV for everyone?

Ventilation with lower tidal volumes for critically ill patients without the acute respiratory distress syndrome: a systematic translational review and meta-analysis

Ary Serpa Neto\textsuperscript{a,b,c}, Liselotte Nagtzaam\textsuperscript{c}, and Marcus J. Schultz\textsuperscript{c,d}

Curr Opin Crit Care 2014, 20; 25-32
Improper Ventilation Settings in Healthy Can Propagate ARDS

● = 10ml/kg
○ = 6ml/kg

Critical Care 2010, 14:R1

Critical Care 2004, 32(9):1817-1824
LTV for everyone?

Association Between Use of Lung-Protective Ventilation With Lower Tidal Volumes and Clinical Outcomes Among Patients Without Acute Respiratory Distress Syndrome
A Meta-analysis

Neto et al. JAMA 2012, 308, No. 16, p.1651-1659

- 20 Articles Included

Table 2. Demographic, Ventilation, and Laboratory Characteristics of the Patients at the Final Follow-up Visit

<table>
<thead>
<tr>
<th></th>
<th>Protective Ventilation (n = 1416)</th>
<th>Conventional Ventilation (n = 1406)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>59.97 (7.92)</td>
<td>60.22 (7.36)</td>
<td>.93</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>72.71 (12.34)</td>
<td>72.13 (12.16)</td>
<td>.93</td>
</tr>
<tr>
<td>Tidal volume, mL/kg IBW⁠¹</td>
<td>6.45 (1.09)</td>
<td>10.60 (1.14)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>PEEP, cm H₂O⁠²</td>
<td>6.40 (2.39)</td>
<td>3.41 (2.79)</td>
<td>.01</td>
</tr>
<tr>
<td>Plateau pressure, cm H₂O⁠²</td>
<td>16.63 (2.58)</td>
<td>21.35 (3.61)</td>
<td>.006</td>
</tr>
<tr>
<td>Respiratory rate, breaths/min⁠²</td>
<td>18.02 (4.14)</td>
<td>13.20 (4.43)</td>
<td>.01</td>
</tr>
<tr>
<td>Minute-volume, L/min⁠³</td>
<td>8.46 (2.90)</td>
<td>9.13 (2.70)</td>
<td>.72</td>
</tr>
<tr>
<td>PaO₂/Fio₂⁠⁴</td>
<td>304.41 (65.74)</td>
<td>312.97 (68.13)</td>
<td>.51</td>
</tr>
<tr>
<td>Paco₂, mm Hg⁠⁵</td>
<td>41.05 (3.79)</td>
<td>37.90 (4.19)</td>
<td>.003</td>
</tr>
<tr>
<td>pH⁠⁶</td>
<td>7.37 (0.03)</td>
<td>7.40 (0.03)</td>
<td>.11</td>
</tr>
<tr>
<td>Study</td>
<td>RR (95% CI)</td>
<td>Subtotal (95% CI)</td>
<td></td>
</tr>
<tr>
<td>----------------------</td>
<td>-------------</td>
<td>-------------------</td>
<td></td>
</tr>
<tr>
<td>Gajic et al., 2004</td>
<td>0.47 (0.22-1.00)</td>
<td>0.33 (0.23-0.47)</td>
<td></td>
</tr>
<tr>
<td>Michelet et al., 2006</td>
<td>0.43 (0.10-1.97)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yilmaz et al., 2007</td>
<td>0.29 (0.16-0.53)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Licker et al., 2009</td>
<td>0.23 (0.09-0.62)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Determann et al., 2010</td>
<td>0.17 (0.04-0.82)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yang et al., 2011</td>
<td>0.23 (0.03-2.18)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fernandez-Bustamante et al., 2011</td>
<td>0.67 (0.20-2.17)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weingarten et al., 2012</td>
<td>0.32 (0.01-8.26)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Lung injury

Mortality

<table>
<thead>
<tr>
<th>Study</th>
<th>RR (95% CI)</th>
<th>Subtotal (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Michelet et al., 2006</td>
<td>2.08 (0.18-24.51)</td>
<td>0.64 (0.46-0.86)</td>
</tr>
<tr>
<td>Wolthuis et al., 2007</td>
<td>0.82 (0.12-5.71)</td>
<td></td>
</tr>
<tr>
<td>Yilmaz et al., 2007</td>
<td>0.41 (0.25-0.68)</td>
<td></td>
</tr>
<tr>
<td>Licker et al., 2009</td>
<td>0.82 (0.39-1.75)</td>
<td></td>
</tr>
<tr>
<td>Determann et al., 2010</td>
<td>1.02 (0.51-2.04)</td>
<td></td>
</tr>
<tr>
<td>Fernandez-Bustamante et al., 2011</td>
<td>1.47 (0.15-14.38)</td>
<td></td>
</tr>
<tr>
<td>Sundar et al., 2011</td>
<td>0.49 (0.04-5.48)</td>
<td></td>
</tr>
<tr>
<td>Yang et al., 2011</td>
<td>0.33 (0.01-8.21)</td>
<td></td>
</tr>
<tr>
<td>Weingarten et al., 2012</td>
<td>1.00 (0.06-17.18)</td>
<td></td>
</tr>
</tbody>
</table>

Mortality

Heterogeneity: $\chi^2 = 3.74; P = .81, I^2 = 0\%$

Test for overall effect: $z = 6.06; P < .001$

Heterogeneity: $\chi^2 = 6.94; P = .54, I^2 = 0\%$

Test for overall effect: $z = 2.68; P = .007$
Does LTV and Pplateau < 30 Alone Prevent VILI?
What do we actually know?:

1. VT ≤ 8ml/kg decreases development of ALI and ARDS (Maybe 9 - 10ml/kg???)
2. VT ≤ 8ml/kg decreases ARDS mortality.
3. Plateau of ≤ 30cmH2O may still cause VILI, especially in ARDS and with high ΔTranspulmonary pressure.
4. May still see VILI with LTV, especially in ARDS.

• Still disagreement on exactly how low of VT is lung protective?
• Normal Mammal Vt = 6.3ml/kg IBW +/-~30%, so 4 – 8 ml/kg IBW
How Does the Ventilator Cause Injury?
Ventilator Induced Lung Injury (VILI)

Mechanisms:
• Volutrauma & Barotrauma (Stress/Strain)
• Atelectrauma (Shearing injury)
• Biotrauma
Addressing Atelectrauma

• Preventing alveolar collapse and development of heterogeneous lung disease
• Recruit collapse alveoli and prevent derecruitment at end exhalation
• **Open Lung Ventilation?**:
  • PEEP?
  • Recruitment?
  • HFO?
  • APRV?
What is LPV – Preventing Atelectrauma?
Low versus High PEEP

Intensive Care Med. (2012) 38:1573-1582
Preventing Atelectrauma

• Does PEEP prevent atelectrauma?
• How to establish required PEEP level?
Does PEEP really matter?

Higher vs Lower Positive End-Expiratory Pressure in Patients With Acute Lung Injury and Acute Respiratory Distress Syndrome
Systematic Review and Meta-analysis

Briel et al. JAMA 2010, Vol.303; 3:865-873

<table>
<thead>
<tr>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Inclusion criteria</td>
<td>Acute lung injury with PaO₂:FIO₂ ≤300&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Acute lung injury with PaO₂:FIO₂ ≤250&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Acute lung injury with PaO₂:FIO₂ ≤300&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Recruiting hospitals (country)</td>
<td>23 (United States)</td>
<td>30 (Canada, Australia, Saudi Arabia)</td>
<td>37 (France)</td>
</tr>
<tr>
<td>Patients randomized to higher vs lower PEEP</td>
<td>276 vs 273</td>
<td>476 vs 509&lt;sup&gt;b&lt;/sup&gt;</td>
<td>385 vs 383&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Validity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concealed allocation</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Follow-up for primary outcome, %</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Blinded data analysis</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Stopped early</td>
<td>Stopped for perceived futility</td>
<td>No</td>
<td>Stopped for perceived futility</td>
</tr>
<tr>
<td>Experimental intervention</td>
<td>Higher PEEP according to FIO₂ chart, recruitment maneuvers for first 80 patients</td>
<td>Higher PEEP according to FIO₂ chart, required plateau pressures ≤40 cm H₂O, recruitment maneuvers</td>
<td>PEEP as high as possible without increasing the maximum inspiratory plateau pressure &gt;28-30 cm H₂O</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Control intervention</td>
<td>Conventional PEEP according to FIO₂ chart, required plateau pressures ≤30 cm H₂O, no recruitment maneuvers</td>
<td>Conventional PEEP according to FIO₂ chart, required plateau pressures ≤30 cm H₂O, no recruitment maneuvers</td>
<td>Conventional PEEP (5-9 cm H₂O) to meet oxygenation goals</td>
</tr>
</tbody>
</table>
Does PEEP really matter?

<table>
<thead>
<tr>
<th>Variable</th>
<th>Higher PEEP</th>
<th>Lower PEEP</th>
<th>( P ) Value</th>
<th>Higher PEEP</th>
<th>Lower PEEP</th>
<th>( P ) Value</th>
<th>Higher PEEP</th>
<th>Lower PEEP</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tidal volume, mL/kg of predicted body weight</td>
<td>6.3 (1.0)</td>
<td>6.3 (0.8)</td>
<td>.33</td>
<td>6.3 (1.0)</td>
<td>6.3 (1.0)</td>
<td>.47</td>
<td>6.5 (1.4)</td>
<td>6.4 (1.3)</td>
<td>.25</td>
</tr>
<tr>
<td>Plateau pressure, cm H₂O</td>
<td>29 (5.4)</td>
<td>23 (5.6)</td>
<td>&lt;.001</td>
<td>27 (5.6)</td>
<td>23 (5.9)</td>
<td>&lt;.001</td>
<td>27 (6.2)</td>
<td>24 (6.9)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>( F_{\text{IO}_2} )</td>
<td>0.51 (0.18)</td>
<td>0.61 (0.19)</td>
<td>&lt;.001</td>
<td>0.44 (0.15)</td>
<td>0.56 (0.18)</td>
<td>&lt;.001</td>
<td>0.45 (0.15)</td>
<td>0.54 (0.19)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>PEEP, cm H₂O</td>
<td>15.3 (3.4)</td>
<td>9.0 (3.1)</td>
<td>&lt;.001</td>
<td>13.3 (4.3)</td>
<td>8.2 (3.0)</td>
<td>&lt;.001</td>
<td>10.8 (5.0)</td>
<td>7.8 (3.3)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Oxygenation index ( ^a )</td>
<td>13.2 (8.7)</td>
<td>12.7 (7.8)</td>
<td>.16</td>
<td>11.2 (7.0)</td>
<td>11.6 (7.1)</td>
<td>.29</td>
<td>11.2 (7.1)</td>
<td>11.8 (8.4)</td>
<td>.34</td>
</tr>
<tr>
<td>( \text{PaO}_2 ), mm Hg</td>
<td>96 (38)</td>
<td>83 (29)</td>
<td>&lt;.001</td>
<td>87 (31)</td>
<td>82 (28)</td>
<td>&lt;.001</td>
<td>84 (25)</td>
<td>83 (26)</td>
<td>.41</td>
</tr>
<tr>
<td>( \text{PaCO}_2 ), mm Hg</td>
<td>44 (11)</td>
<td>44 (11)</td>
<td>.42</td>
<td>44 (9.9)</td>
<td>44 (11)</td>
<td>.68</td>
<td>45 (12)</td>
<td>46 (12)</td>
<td>.06</td>
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<td>Arterial pH</td>
<td>7.35 (0.09)</td>
<td>7.36 (0.09)</td>
<td>.02</td>
<td>7.38 (0.08)</td>
<td>7.38 (0.08)</td>
<td>.49</td>
<td>7.41 (0.08)</td>
<td>7.40 (0.08)</td>
<td>.08</td>
</tr>
</tbody>
</table>

Briel et al. JAMA 2010, Vol.303; 3:865-873
Does PEEP matter?

Briel et al. JAMA 2010, Vol.303; 3:865-873
So, What Do We Know From This?

- Higher PEEP may confer a mortality benefit in Moderate to Severe ARDS patients with P/F ratio of < 200mmHg.
- In these patients, may actually decrease the need for rescue therapies
- Improves thoracic compliance
- Improves oxygenation
- 
- BUT
- Higher PEEP may actually be detrimental in patients without ARDS or Mild ARDS
What is LPV?
# Study Summary: Prone Positioning

Prone position

---

**Claude Guérin**

*Curr opin crit care. 2014, 20;92-97*

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>No. of patients (SP/PP)</td>
<td>152/152</td>
<td>378/413</td>
<td>60/76</td>
<td>174/168</td>
<td>229/237</td>
</tr>
<tr>
<td>% of ARDS (SP/PP)</td>
<td>93.3/94.7</td>
<td>28/33.9</td>
<td>100/100</td>
<td>100/100</td>
<td>100/100</td>
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<tr>
<td>PaO₂/FIO₂ (mmHg)</td>
<td>127</td>
<td>150</td>
<td>147</td>
<td>113</td>
<td>100</td>
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<td>Tidal volume (ml/kg)</td>
<td>10.3 MBW</td>
<td>8 MBW</td>
<td>8.4 PBW</td>
<td>8 PBW</td>
<td>6.1 PBW</td>
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<tr>
<td>PEEP (cmH₂O)</td>
<td>10</td>
<td>8</td>
<td>12</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>PP session duration (average hours per session)</td>
<td>7</td>
<td>8</td>
<td>17</td>
<td>18</td>
<td>17</td>
</tr>
<tr>
<td>Mortality (SP/PP) (%)</td>
<td>25/21.1</td>
<td>31.5/32.4</td>
<td>58/43</td>
<td>32.8/31</td>
<td>32.8/16</td>
</tr>
</tbody>
</table>
Neuromuscular Blockers in Early Acute Respiratory Distress Syndrome

Laurent Papazian, M.D., Ph.D., Jean-Marie Forel, M.D., Arnaud Gacouin, M.D., Christine Penot-Ragon, Pharm.D., Gilles Perrin, M.D., Anderson Loundou, Ph.D., Samir Jaber, M.D., Ph.D., Jean-Michel Arnal, M.D., Didier Perez, M.D., Jean-Marie Seghboyan, M.D., Jean-Michel Constantin, M.D., Ph.D., Pierre Courant, M.D., Jean-Yves Lefrant, M.D., Ph.D., Claude Guérin, M.D., Ph.D., Gwenaël Prat, M.D., Sophie Morange, M.D., and Antoine Roch, M.D., Ph.D., for the ACURASYS Study Investigators*
Paralysis

- N = 339, Study = 177
- Cisatracurium = 15 mg bolus followed by 37.5 mg/hour infusions X 48 hours

<table>
<thead>
<tr>
<th>Age — yr</th>
<th>58±16</th>
<th>58±15</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tidal volume — ml/kg of predicted body weight</td>
<td>6.55±1.12</td>
<td>6.48±0.92</td>
</tr>
<tr>
<td>PaO₂:FIO₂</td>
<td>106±36</td>
<td>115±41</td>
</tr>
</tbody>
</table>
Outline

• 1. Why talk about Lung Protective Ventilation?
• 2. What is Lung Protective Ventilation?
• 3. How to apply Lung Protective Ventilation?
How to apply Lung Protective Ventilation?

• **Paralysis:**
  • Establish true baseline pulmonary status
  • Optimize mechanical ventilation settings
  • **Need a static state with no patient respiratory efforts!!!**
NIH ARDSnet LPV Protocol At The Bedside: Tidal Volume, RR and Pplateau

8ml/kg
PEEP ≥ 5
RR < 35 bpm

Plateau > 30?

↓ VT to 6ml/kg IBW

Plateau > 30?

↓ VT by 1 ml/kg to low of 4 ml/kg IBW

Plateau < 25?

↑ VT by 1 ml/kg up to 6ml/kg IBW

No Change

Air Hungry or Asynchrony & Plateau < 30?

↑ VT by 1 ml/kg up to 8ml/kg IBW

Maintain at 6ml/kg IBW

↓ VT to 6ml/kg IBW over no more than 2 hours

NO

YES
ARDSnet LPV Protocol At The Bedside: Tidal Volume, RR and Pplateau

YES

pH ≥ 7.30?

No Change

NO

pH 7.15 - 7.30?

↑ RR until pH > 7.30 or PaCO2 < 25, max RR 35bpm

pH < 7.15?

↑ VT by 1 ml/kg up to 8ml/kg IBW, Plateau > 30 allowed, consider NaHCO3
ARDSnet LPV Protocol At The Bedside:

PEEP

P/F ≥ 200 mmHg = Mild ARDS as per Berlin Definition

<table>
<thead>
<tr>
<th>FIO2 (%)</th>
<th>30</th>
<th>40</th>
<th>40</th>
<th>50</th>
<th>50</th>
<th>60</th>
<th>70</th>
<th>70</th>
<th>70</th>
<th>80</th>
<th>90</th>
<th>90</th>
<th>90</th>
<th>90</th>
<th>100</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEEP cmH₂O</td>
<td>5</td>
<td>5</td>
<td>8</td>
<td>8</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>12</td>
<td>14</td>
<td>14</td>
<td>14</td>
<td>16</td>
<td>18</td>
<td>18</td>
<td>20-24</td>
</tr>
</tbody>
</table>

P/F ≤ 200 mmHg = Moderate to severe ARDS as per the Berlin Definition

| Step | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 |
|------|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|----|----|
| FIO₂ | 0.3 | 0.3 | 0.3 | 0.4 | 0.4 | 0.4 | 0.4 | 0.5 | 0.5 | 0.6 | 0.7 | 0.8 | 0.8 | 0.9 | 1.0 | 1.0 |
| PEEP | 5 | 8 | 10 | 10 | 12 | 14 | 16 | 18 | 18 | 20 | 20 | 20 | 22 | 22 | 22 | 24 |
Lung Protective Ventilation: ARDSnet Approach

- Prevent Volumtrauma & Barotrauma
- Prevent Atelectrauma
- Minimize O2 toxicity
- Minimize Biotrauma

- VT 4-6ml/kg with Pplateau of ≤ 30 and permissive hypercapnia, as long as pH is ≥ 7.30
- FiO2/PEEP table (non-physiological).
- Looked at High v. Low PEEP table, concluded no benefit but, subgroup analysis showed benefit for sicker pt. with P/F < 200
- Minimize FiO2 to maintain PaO2 55 to 80mmHg or SpO2 88 to 95%
- 1/3 of pt. still had increase inflammatory markers
LPV at the bedside: ARDSnet approach

- Dx with MRSA Pneumonia
- Intubated for respiratory failure after trial 1 day of Optiflow 50 LPM, FiO2 0.60:
  - Pre-intubation ABG with
    - pH 7.13
    - PaCO2 75
    - HCO3-22
    - PaO2 60
    - SpO2 93%
Initial ventilator settings:

- VC-AC (constant flow)
- VTset 500
- RR 16
- PEEP 8
- FiO2 0.60
- PIP 37
- Pplat 32
- MV 8.3
- SpO2 98%
ARDSnets LPV Protocol At The Bedside

1. Calculate IBW:
   - Males IBW(kg) = 50 + 2.3 (Height(inches) – 60)
   - Females IBW(kg) = 45.5 + 2.3 (Height(inches) – 60)

2. Volume or Pressure Control (Original study was VC, with no plateau time)
   - Pplateau measures minimum Q4h

   - IBW = 54.7 kg
1. What VT to set?
   • 8 ml/kg ~ 438 ml

2. What RR to set?
   • MV for pH > 7.30 ~ MV 10, therefore RR ~ 22

3. What PEEP and FiO2 to set?
   • PaO2 150, therefore decrease FiO2 to 50%
   • P/F > 200, so low PEEP/FiO2 Table

<table>
<thead>
<tr>
<th>FiO2</th>
<th>30</th>
<th>40</th>
<th>40</th>
<th>50</th>
<th>50</th>
<th>60</th>
<th>70</th>
<th>70</th>
<th>70</th>
<th>80</th>
<th>90</th>
<th>90</th>
<th>90</th>
<th>100</th>
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</thead>
<tbody>
<tr>
<td>PEEP</td>
<td>5</td>
<td>5</td>
<td>8</td>
<td>8</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>12</td>
<td>14</td>
<td>14</td>
<td>14</td>
<td>16</td>
<td>18</td>
<td>20–24</td>
</tr>
</tbody>
</table>
ARDSnet LPV Protocol At The Bedside

• What are you going to do over the next 2 hours?
  1. Decrease VT towards 6ml/kg IBW ~ 328 ml
  2. RR is increased to match MV 10 ~ RR – 30bpm
  3. PEEP 8, FiO2 0.50

Pplateau  27
SpO2  97%

• Any changes?
ARDSnet LPV Protocol At The Bedside

- Patient resp. status worsens and now is on the following settings:
  - VT = 4ml/kg
  - RR = 35
  - FiO2 = 0.90
  - PEEP = 22
  - Pplateau = 35

What are you going to do next?????
Is ARDSnet the only way to do LPV? HFO?

- Is it really not beneficial?
- Poor study design?
- Based on old AECC definition of ARDS, so patients had P/F ratios of < 150 and therefore already had moderate ARDS as per the new Berlin Definition of ARDS. Therefore, was it just started too late?
Is ARDSnet the only way to do LPV?

APRV?

A Randomized Prospective Trial of Airway Pressure Release Ventilation and Low Tidal Volume Ventilation in Adult Trauma Patients With Acute Respiratory Failure

• Maxwell R et al. Journal of Trauma Injury, Infection and Critical Care, Sept. 2010
• N = 63 (31 APRV and 32 LOVT)

• Results:
  • No differences in ventilator days, ICU length of stay, mortality and associated complications

• Conclusion:
  • “APRV seems to have a similar safety profile as the LOVT”
Moving Towards Prevention: Evidence from Human Studies

Early application of airway pressure release ventilation may reduce mortality in high-risk trauma patients: A systematic review of observational trauma ARDS literature

Penny L. Andrews, RN, BSN, Joseph R. Shiber, MD, Ewa Jaruga-Killeen, PhD, Shreyas Roy, MD, CM, Benjamin Sadowitz, MD, Robert V. O’Toole, Louis A. Gatto, PhD, Gary F. Nieman, BA, Thomas Scalea, MD, and Nader M. Habashi, MD, Baltimore, Maryland

Andrews et al. J Trauma Acute Care Surg 2013;75:635
Moving Towards Prevention: Evidence from Human Studies

Pre-emptive Use of APRV in Humans

Andrews et al. J Trauma Acute Care Surg 2013;75:635
Moving Towards Prevention: Evidence from Animal Studies


EARLY AIRWAY PRESSURE RELEASE VENTILATION PREVENTS ARDS—A NOVEL PREVENTIVE APPROACH TO LUNG INJURY

Shreyas Roy,* Nader Habashi,† Benjamin Sadowitz,* Penny Andrews,‡ Lin Ge,* Guirong Wang,* Preyas Roy,‡ Auyon Ghosh,* Michael Kuhn,§ Joshua Satalin,* Louis A. Gatto,‖ Xin Lin,‖ David A. Dean,‖ Yoram Vodovoz,∗∗ and Gary Nieman∗
Moving Towards Prevention: Evidence from Animal Studies

Experimental Design:

**APRV** (n=4)
- Phigh = $P_{\text{plat}}$
- Plow = 0
- Tlow PEFR = 75%
- Thigh ≥ 90% CPAP
- Vt = 12 mL/kg

**Sham** (n=5)
- PEEP = 5
- Vt = 10mL/kg
- No Sepsis + I/R

**ARDSnet** (n=3)
- High PEEP table
- Vt = 6mL/kg

Broad Spectrum Antibiotics

Early Goal Directed Therapy Based Fluid Resuscitation and Vasopressors

All Animals Continuously Monitored according to ICU Standards of Care

Roy et al. Shock 2013;39:28-38
Moving Towards Prevention: Evidence from Animal Studies
Moving Towards Prevention: Evidence from Animal Studies

Gross Anatomy

APRV

ARDSnet
Is APRV a viable LPV strategy?

- Animal and small human trials suggest it’s as effective or more effective than ARDSnet, but
- No large randomized trials on mortality benefit
- Still treated by many as a rescue therapy just like HFO
Low VT and Pplateau < 30 the only lung protective strategy?

Driving Pressure and Survival in the Acute Respiratory Distress Syndrome

Marcelo B.P. Amato, M.D., Maureen O. Meade, M.D., Arthur S. Slutsky, M.D., Laurent Brochard, M.D., Eduardo L.V. Costa, M.D., David A. Schoenfeld, Ph.D., Thomas E. Stewart, M.D., Matthias Briel, M.D., Daniel Talmor, M.D., M.P.H., Alain Mercat, M.D., Jean-Christophe M. Richard, M.D., Carlos R.R. Carvalho, M.D., and Roy G. Brower, M.D.

- Multilevel Mediation Analysis
- 3562 patients from 9 published randomized controlled trials
- Increase in ∆P by 7 cmH2O → ↑ Mortality, not VT or Pplateau
Why 7 cmH2O?
Changes in pleural pressures with normal ventilation
Lung Protective Ventilation: Minimizing Dynamic Strain

Is it just low VT and Pplateau < 30 that decreases mortality???????

N = 3652, from 9 previous studies

\[ \Delta P \leq 15 \text{ cmH}_2\text{O} \]

Individualizing Lung Protective Ventilation: Using conventional Ventilation

• Starting a breath from a lower pressure to a higher pressure, with changes in VT > anatomical deadspace

  • Make the lungs as homogenous as possible
  • Recruit collapsed alveoli
  • What’s the best way to do this and how do we know at the bedside?

• Keep the alveoli open at end exhalation (Alveolar Stability)
  • Prevent derecruitment and therefore atelectrauma or shearing injury
  • No agreement on how to do this!!!!!!
  • VT ≤ 8ml/kg is likely a good thing
  • The lower the airway pressure the better??
    • or is it the driving pressure or transpulmonary pressure that’s important?
    • Basically we need to minimize Dynamic Strain and Stress
Individualizing Lung Protective Ventilation: Using conventional Ventilation

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Individualizing Lung Protective Ventilation: Using conventional Ventilation

CT Scan = Gold standard for assessing extend of Collapse and Recruitability

A  Alveolar overdistension
B  Normoventilation
C  Tidal recruitment
D  Alveolar collapse
New and Newer Technological Approach
Dorsal atelectasis – CT and PulmoVista500

Regions subject to overdistension

Regions subject to lung collapse
How to Recruit on a Ventilator
Lung recruitment - patterns

• Sustained inflations / Continuous distending pressure
  – 40 cmH2O for 40 sec

• Incremental PEEP + Pinsp / Pplat increase
  – Keeping same ΔP

• Incremental Pinsp - increase leaving PEEP the same

• Incremental PEEP increase leaving Pinsp the same

• Intermittent sighs / intermittent high level PEEP
Clinical situation
Lung recruitment – incremental PEEP + Pinsp

Conclusions:
Can reverse hypoxemia in majority (95%) of patients with primary or secondary ARDS

Amato et al. 2006 Aug;174(3):268-78
Possible Clinical Application:
Trending Cdyn and ∆P in Volume Control

[Graph showing PaO₂ and Cdyn over time with incremental and decremental PEEP levels]
Conclusions

• Different opinions on what Recruitment Maneuvers should be applied, IF AT ALL:
  • ▪ Variety of Recruitment Maneuvers currently discussed
  • ▪ Available studies show mainly positive outcomes, especially oxygenation
  • ▪ Few adverse effects published

• BUT:
  • ▪ Small numbers of patients/poorly controlled studies
  • ▪ More effective early in disease process
  • ▪ Most publications state that Recruitment Maneuvers are more effective in
    ARDS of extrapulmonary origin(Gattinoni et al., Villagra et al. , Pelosi et al.,Lim et al. , Valente Barbas, Kacmarek et al.)
  ▪ Results short lived if appropriate PEEP is not applied afterwards
Individualizing Lung Protective Ventilation: Using conventional Ventilation

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    - or is it the driving pressure or transpulmonary pressure that’s important?
    - Basically we need to minimize Dynamic Strain and Stress
Characteristical Points on a PV curve and their suggested meaning

Possible Clinical Application:
Trending Cdyn and ΔP
Targeting Dynamic Compliance and driving pressure: Recruitment Trends
Promising technologies

- Transpulmonary Pressure
- Electrical Impedance Tomography
- Volumetric Capnography

- EPVent 2 Trial?
Individualizing Lung Protective Ventilation: Using conventional Ventilation

• Starting a breath from a lower pressure to a higher pressure, with changes in VT > anatomical deadspace

  • Make the lungs as homogenous as possible
    • Recruit collapsed alveoli
    • What’s the best way to do this and how do we know at the bedside?

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    • Basically we need to minimize Dynamic Strain and Stress
Lung Protective Ventilation:

Is it just low VT and Pplateau < 30 that decreases mortality??????

N = 3652, from 9 previous studies

ΔP ≤ 15 cmH2O

# Lung Protective Ventilation Large Trial

<table>
<thead>
<tr>
<th>Trial’s acronym or intervention tested</th>
<th>experimental group</th>
<th></th>
<th>Control group</th>
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<tbody>
<tr>
<td></td>
<td>N patients</td>
<td>Definition</td>
<td>Mortality rate</td>
<td>N patients</td>
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<tr>
<td>ARMA [6]</td>
<td>432</td>
<td>Lower VT</td>
<td>31.0</td>
<td>429</td>
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<tr>
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<td>Restrictive fluid strategy</td>
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<td>Higher PEEP</td>
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<td>EXPRESS [32]</td>
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<td>Recruitment augmented</td>
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<td>LOVS [33]</td>
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<td>475</td>
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<td>178</td>
<td>Neuromuscular blockade</td>
<td>31.6</td>
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<tr>
<td>Aerosolized albuterol [34]</td>
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<td>Inhaled β2 agonist</td>
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<td>BAIT-2 [35]</td>
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<td>I V. β2 agonist</td>
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<td>OSCILLATE [36**]</td>
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<td>HFOV</td>
<td>40.0</td>
<td>273</td>
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<tr>
<td>OSCAR [37**]</td>
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<td>HFOV</td>
<td>41.7</td>
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<td>PROSEVA [19**]</td>
<td>237</td>
<td>Prone position</td>
<td>16.0</td>
<td>229</td>
</tr>
</tbody>
</table>
What is lung protective ventilation?

• General Agreement that lower VT’s are better than higher VT’s
• General Agreement on lower Pplateau safer than higher Pplateau
• Recruit or to not recruit?
• What is the best PEEP and how do you know?
What is Lung Protective Ventilation??????????

• Likely a multi prong approach
• Maintain a fully inflated homogeneously ventilated lung
  • Recruit collapse lungs
• Mitigate or prevent Volutrauma and Barotrauma (Dynamic strain and stress)
• Mitigate or prevent Atelectrauma (Shearing injury)
• Prevent alveolar collapse on exhalation
  • Low/High FiO2/PEEP tables, Individualized PEEP
• Minimize strain at the alveolar level
  • 4 – 8ml/kg with lowest ΔP
Thank you for your attention.