Ventilator-Induced Lung Injury

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Overview

• Regional lung mechanics vary considerably in ARDS patients

• Abnormal shear stress can produce alveolar epithelial and endothelial damage, which can produce a systemic inflammatory response

• Ventilatory strategies that reduce lung heterogeneity and atelectasis as well as limit overdistension may reduce ventilator-associated lung injury and improve outcomes
Chest CT in ARDS
Heterogeneous Lung Mechanics

- Normal
- Decreased Compliance
- Alveolar Flooding/Collapse
- Bronchio-Constriction
Atelectasis during Induction of General Anesthesia in Obese Patients

Coussa M et al., Anesth Analg 2004;98:1491

With 0 cm H2O PEEP

Before induction

After intubation
Atelectasis during Induction of General Anesthesia in Obese Patients

Coussa M et al., *Anesth Analg* 2004;98:1491

With 10 cm H2O PEEP
VALI
Ventilator Associated Lung Injury
Volutrauma
Static Pressure-Volume Curve of the Respiratory System

- In animal studies, high volume mechanical ventilation produces acute lung injury similar to ARDS.
- This injury is associated with local overdistention of lung units.
Static Pressure-Volume Curve of the Respiratory System

- A minimal level of PEEP is necessary to prevent closure of newly-opened alveoli, increase FRC, and improve effective lung compliance.

- This level of PEEP may reduce trauma associated with the repetitive re-opening of collapsed alveoli.
Fu Z et al., J Appl Phys 73:123, 1992
Atelectotrauma
What’s Wrong with a Little Atelectasis?

Radford EP. Handbook of Physiology, Section 3, Volume 1 1964:429-449
Figure 1: Atelectotrauma
The interface between collapsed and consolidated lung (A) and over-distended lung units (B) is heterogeneous and unstable. Depending on ambient conditions this region is prone to cyclic recruitment and derecruitment and localised asymmetrical stretch of lung units (C) immediately apposed to regions of collapsed lung.
Biotrauma
37 patients with ARDS randomized

Controls: TV 11.1 ml/kg, 6.5 cm H₂O PEEP (best PaO₂), normal PaCO₂

Lung protective strategy: TV 7.6 ml/kg, 14.8 cm H₂O PEEP (both based on P-V curve)

Inflammatory mediators and cells in BAL increased in controls and decreased in experimental group after 36 hours
PMNs in BAL Fluid

Ranieri VM, et al., JAMA, 282:54, 1999
**IL-6 Levels in BAL Fluid**

Ranieri VM, et al., *JAMA*, 282:54, 1999
NIH NHLBI ARDS Network

Prospective, Randomized, Multi-Center Trial of 12 ml/kg Vs 6 ml/kg Tidal Volume Positive Pressure Ventilation for Treatment of Acute Lung Injury and Acute Respiratory Distress Syndrome

NEJM, 342:1301-8, 2000
Proportion Alive and Off Ventilator

Proportion

Study Day

NEJM, 342:1301-8, 2000
28 Day Survival

Proportion Surviving

Days after study entry

NEJM, 342:1301-8, 2000
Median Organ Failure Free Days

- **CNS**: 14 days
- **Hepatic**: 22 days
- **Cardiovascular**: 22 days
- **Coagulation**: 22 days
- **Renal**: 28 days

* = statistical significance

- = 6 ml/kg
- = 12 ml/kg

*NEJM, 342:1301-8, 2000*
Lung protective ventilation strategy for ARDS

### Mortality at end of follow-up period

<table>
<thead>
<tr>
<th>Study</th>
<th>Protective n/N</th>
<th>Conventional n/N</th>
<th>Relative Risk (Fixed) 95% CI</th>
<th>Weight (%)</th>
<th>Relative Risk (Fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amato 1998</td>
<td>13/29</td>
<td>17/24</td>
<td></td>
<td>6.7</td>
<td>0.63 [0.39, 1.02]</td>
</tr>
<tr>
<td>ARDS Network 2000</td>
<td>133/432</td>
<td>170/429</td>
<td></td>
<td>61.5</td>
<td>0.78 [0.65, 0.93]</td>
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<tr>
<td>Brochard 1998</td>
<td>27/58</td>
<td>22/58</td>
<td></td>
<td>7.9</td>
<td>1.23 [0.80, 1.89]</td>
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<tr>
<td>Brower 1999</td>
<td>13/26</td>
<td>12/26</td>
<td></td>
<td>4.3</td>
<td>1.08 [0.62, 1.91]</td>
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<tr>
<td>Stewart 1998</td>
<td>30/60</td>
<td>28/60</td>
<td></td>
<td>10.1</td>
<td>1.07 [0.74, 1.55]</td>
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<tr>
<td>Villar 2006</td>
<td>17/50</td>
<td>25/45</td>
<td></td>
<td>9.5</td>
<td>0.61 [0.38, 0.98]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>655</strong></td>
<td><strong>642</strong></td>
<td></td>
<td><strong>100.0</strong></td>
<td><strong>0.83 [0.72, 0.95]</strong></td>
</tr>
</tbody>
</table>

Total events: 233 (Protective), 274 (Conventional)
Test for heterogeneity chi-square=9.24 df=5 p=0.10 I² =45.9%
Test for overall effect z=2.69  p=0.007
Alternative Protective Strategies

- Prone positioning
- PEEP – how much and how
  - PV curve, transpulmonary/esophageal pressure, electrical impedance, optimal lung compliance, open lung, ARDSnet table
- Ventilator modes – HFOV, APRV
- Neuromuscular blockade
- ECMO; ECCO$_2$R
Summary

- Lung mechanics are often heterogeneous, even without injury
- Lung injury can further alter regional lung mechanics
- Mechanical ventilation can cause lung injury
- Certain patterns of ventilation may worsen lung injury
- Encouraging lung recruitment and limiting overdistention may reduce barotrauma and improve outcome