Transpulmonary Pressure

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Disclosures

• Research funding
  – NHLBI
  – CMS
  – Gordon and Betty Moore Foundation

• Advisor
  – Intensix
  – Medial

• In debt
  – To many people, but in particular to Dr. Steve Loring
ARDS Patient

- Post traumatic ARDS
- 46 y/o male s/p MVC, fractured pelvis
- Compromise of circulation to the legs
- Anasarca and a tense abdominal wall
- Initial ventilator settings
  - CMV
  - TV= 535 cc
  - FiO2= 1
  - PEEP= 13
ARDS Mortality: What More Can We Do?

Proportion Surviving

Days after study entry

Vt = 6

Vt = 12

Slide courtesy BT Thompson
Animal Experiments Show That Adequate PEEP Can Reduce VILI

- Faridy et al. – Large volume mechanical ventilation increased surface tension. At a given $V_T$, effect attenuated by higher PEEP.

- Wyszogrodski et al. – High volume ventilation inactivated surfactant in cats. At a given $V_T$, effect less with higher PEEP.

- Webb and Tierney – High volume ventilation caused hemorrhagic edema and hyaline membranes in rats. At constant peak pressure, effect less with higher PEEP.

- Muscedere et al. – Even low volume ventilation in lavaged rat lungs caused histological damage. Effects were reduced or eliminated with higher PEEP.

- Chiumello et al. – Ventilation of injured rat lungs released inflammatory cytokines. At a given $V_T$, effects were less with higher PEEP.
Clinical Trials of Higher PEEP

• Amato demonstrated a benefit to a low tidal volume strategy combined with PEEP set by LIP of the PV curve.
• ARIES trial seemed to confirm this
• ALVEOLI trial stopped early for futility
• LOVS trial showed no benefit.
• The EXPRESS trial which set PEEP based on the airway plateau pressure showed mixed results
“The LOV study and the Express study not only should conclude the era of comparing PEEP levels in unselected populations with ALI and ARDS, but also underscore the need for a new definition of ARDS aimed at identifying patients with greater lung edema and larger recruitability ...”

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

### Table 4. Clinical Outcomes in All Patients and Stratified by Presence of ARDS at Baseline

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>All Patients</th>
<th></th>
<th>With ARDS</th>
<th></th>
<th>Without ARDS</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>(n = 1136)</td>
<td>No. (%)</td>
<td>(n = 951)</td>
<td>No. (%)</td>
<td>(n = 220)</td>
</tr>
<tr>
<td>Death in hospital</td>
<td>374 (32.9)</td>
<td>409 (35.2)</td>
<td>0.94 (95% CI: 0.86 to 1.04)</td>
<td>0.25</td>
<td>324 (34.1)</td>
<td>368 (39.1)</td>
</tr>
</tbody>
</table>
Optimal Risk/Benefit of PEEP May Depend on Recruitability

- 6 ml/kg
- Lower PEEP
- Higher PEEP
- Injury > Benefit
- Benefit > Injury

Driving Pressure

PEEP (cm H$_2$O)

$P_{\text{plat}}$
$P_L$ May be more important than $P_{ao}$

$$P_L = P_{ao} - P_{Pl}$$

$P_L$ is the pressure actually distending the lung.
This may be very different from the pressure measured at the airway.
$P_L$ May be Very Different then $P_{ao}$

$P_L = P_{ao} - P_{Pl}$

Titrating ventilation based on ventilator pressures does not allow us to take this variability into account.
Esophageal Pressure to Estimate Pleural Pressure
Mechanical ventilation: Passive

Graph showing Pes (esophageal Pressure) and Volume. The P-V curve of passive Chest Wall is indicated with red arrows.
Pressure transducing wafers implanted in dog lungs revealed differences in pleural pressure due to the gravitational effect of the dependant vs. non-dependant regions of the lung.

**Pes Values Reflect High Pleural Pressures**

\[ r = 0.88 \]
\[ p < 0.0001 \]
\[ \text{slope} = 1.2 \]
\[ y\text{-intercept} = -2.5 \]

Pelosi Am J Respir Crit Care Med 2001; 164:122-130
Relationship Between Transpulmonary and Airway Pressure

Talmor et al. CCM 2006
Sample Data From Anesthetized Obese Subject

- **Paw**
- **Pes**
- **Vol.**
- **Flow**

Graphs showing waveforms for Paw, Pes, Vol, and Flow with various annotations.
Expanded Time Scale

Paw

Pes

Vol.

Flow

Airway Pressure

Gastric or Esophageal Pressure

Volume

Corrected Flow

Threshold Paw

Flow

Vol.
In Humans

PT 1 Initial Ventilator settings on PCV

\[ P_{aw} = 13 \text{ to } 40 \]
\[ P_{es} = 20 \text{ to } 33 \]
\[ P_{tp} = -8 \text{ to } 6 \]
Pt 1 Strategy: Change ventilator pressures to optimize $P_L$

Ventilator pressures:

PEEP 13 → 26

which raised

Pplateau 40 → 46
Pt 1 After Ventilator Changes to Optimize $P_L$
# Mechanical Ventilation Guided by Esophageal Pressure in Acute Lung Injury


## Esophageal-Pressure–Guided Group

<table>
<thead>
<tr>
<th>$F_{iO_2}$</th>
<th>0.4</th>
<th>0.5</th>
<th>0.5</th>
<th>0.6</th>
<th>0.6</th>
<th>0.7</th>
<th>0.7</th>
<th>0.8</th>
<th>0.8</th>
<th>0.9</th>
<th>0.9</th>
<th>1.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>$P_{L_{exp}}$</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>4</td>
<td>6</td>
<td>6</td>
<td>8</td>
<td>8</td>
<td>10</td>
<td>10</td>
</tr>
</tbody>
</table>

## Control Group

<table>
<thead>
<tr>
<th>$F_{iO_2}$</th>
<th>0.3</th>
<th>0.4</th>
<th>0.4</th>
<th>0.5</th>
<th>0.5</th>
<th>0.6</th>
<th>0.7</th>
<th>0.7</th>
<th>0.7</th>
<th>0.8</th>
<th>0.9</th>
<th>0.9</th>
<th>0.9</th>
<th>1.0</th>
</tr>
</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>12</td>
<td>14</td>
<td>14</td>
<td>14</td>
<td>16</td>
<td>18</td>
<td>20–24</td>
<td></td>
</tr>
</tbody>
</table>
6- Month Survival

Cumulative Survival

Time from enrollment, days

Esophageal pressure guided protocol

Conventional protocol
N001 Baseline

Pao
- 17 cmH₂O

Flow
- 0.010 L/s

Pes
- 28 cmH₂O

Ptp
- 11 cmH₂O
N001 Day 1

Pao
- Airway Pressure (Pao) 33 cmH₂O

Flow
- Flow (L/s)

Pes
- Esophageal Pressure (Pes) 34 cmH₂O

Ptp
- Transpulmonary Pressure (Pao-Pes) -0.8 cmH₂O
A. Severe tricuspid regurgitation (TR) is seen in this transthoracic image both by color Doppler (arrow) and spectral display. Maximum peak gradient between right ventricle and atrium is measured at 67 mmHg, indicating severe pulmonary artery systolic hypertension.

B. Twenty four hours after PEEP optimization based on transpulmonary pressure. Almost complete resolution of TR by color Doppler (yellow arrow). Peak gradient between right ventricle and atrium decreased from 67 mmHg (panel A) to 22 mmHg.
Hemodynamics

Proportion of patients on pressors

Length-of-Stay Net Fluid Balance (L)

Baseline
-10 0 10 20 30 40

Day 1
Control
Intervention

Day 2
Control
Intervention

Day 3
Control
Intervention

Proportion of total patients

Baseline Day 1 Day 2 Day 3

Control patients Intervention patients
Mechanical ventilation: Passive
Elastance Derived Measurement of Transpulmonary Pressure

\[ E_{RS} = \frac{\Delta P_{AO}}{VT} \]

\[ \Delta P_{AO} \]

\[ E_{CW} = \frac{\Delta P_{ES}}{VT} \]

\[ P_L = P_{AO} \cdot \frac{E_L}{E_{RS}} \]
**P - based Method**
Assumption: Measured $P_{es}$ is approximately equal to $P_{pl}$

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**$E_{cw}$ - based Method**
Assumption: Measured slope of chest wall $P$-$V$ curve is accurate, but $P_{pl} = 0$ when $P_{ao} = 0$
ECMO criteria for influenza A (H1N1)-associated ARDS: role of transpulmonary pressure
ECMO criteria for influenza A (H1N1)-associated ARDS: role of transpulmonary pressure

PATIENTS TRANSFERRED TO REGIONAL CENTER FOR ECMO
N = 14

partitioning of respiratory mechanics

Oxygenation Index: 34 ± 5
Pplat\(_L\): 27.2 ± 1.2 cmH\(_2\)O
N = 7

ECMO

Oxygenation Index: 37 ± 4
Pplat\(_L\): 16.6 ± 2.9 cmH\(_2\)O
N = 7

INCREASE PEEP UNTIL Pplat\(_L\) ≥ 25 cmH\(_2\)O

Oxygenation Index: 16 ± 1

NO ECMO

RCTs of Higher PEEP

P_{Plat}

Driving Pressure

PEEP (cm H$_2$O)

Amato  Villar  ALVEOLI Express  LOVS  EPVent

+RM  +RM

Vt 6  Vt 7  Vt 6  Vt 7

Slide courtesy BT Thompson
EPVent II- Overall Concept

- A phase II prospective randomized controlled trial of ventilation directed by esophageal pressure measurements.

- Enroll 200 patients with moderate to severe ARDS by the Berlin conference definition in 10 academic medical centers in North America.

- Randomized to EPVent group or empiric high-PEEP control group.
Transpulmonary Pressure

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