Key Pressures in ARDS

PEEP

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Johns Hopkins University
(no disclosures)
no disclosures
ACUTE RESPIRATORY DISTRESS
IN ADULTS

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Lancet 1967; 2:319-323
Setting PEEP

**Traditional Approach**

Adjust PEEP to allow acceptable arterial oxygenation on $\text{FiO}_2 \leq .70$

$\text{PEEP} = 5 - 12 \text{ cm H}_2\text{O}$
Ventilator-Induced Lung Injury

Low Volume
Low Pressure
VILI
## 3 Higher PEEP Trials

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<thead>
<tr>
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ARDSnet NEJM 2004
Meade JAMA 2008
Mercat JAMA 2008
Why Mortality Not Lower with Higher PEEP?

Effects of Higher PEEP in each patient
- Reduce VILI from Low volume/low pressure
- Increase VILI from Overdistention
Effects of PEEP are Variable Among Patients

Diffuse

Recruitment

Overdistention

Lobar

Recruitment

Overdistention
– Who are the PEEP responders?
– How much PEEP in responders?
– When to decrease PEEP in responders?
– How much PEEP in nonresponders?
How to Set PEEP

Table of fixed combinations of PEEP and FiO₂

<table>
<thead>
<tr>
<th>FiO₂</th>
<th>.3</th>
<th>.4</th>
<th>.4</th>
<th>.5</th>
<th>.5</th>
<th>.6</th>
<th>.7</th>
<th>.7</th>
<th>.7</th>
<th>.8</th>
<th>.9</th>
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<tr>
<td>PEEP</td>
<td>5</td>
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<td>8</td>
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<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>18-24</td>
</tr>
</tbody>
</table>
# How to Set PEEP

Table of fixed combinations of PEEP and FiO₂

<table>
<thead>
<tr>
<th>FiO₂</th>
<th>0.3</th>
<th>0.4</th>
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<th>0.5</th>
<th>0.5</th>
<th>0.6</th>
<th>0.7</th>
<th>0.7</th>
<th>0.8</th>
<th>0.9</th>
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<td>16</td>
<td>18</td>
</tr>
</tbody>
</table>

<table>
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<tr>
<th>Higher PEEP/Lower FiO₂</th>
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</thead>
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<td>FiO₂</td>
</tr>
<tr>
<td>PEEP</td>
</tr>
</tbody>
</table>

Note: PEEP values for higher PEEP and lower FiO₂ are generally higher than those for fixed combinations of PEEP and FiO₂.
Lower PEEP → Higher PEEP
Tables

• Easy
• No special equipment
• How to identify PEEP responders?
• Optimal PEEP?
• Some patients may need lower PEEP than they receive on the lower PEEP table
EXPRESS PEEP

• Raise PEEP until inspiratory Pplat approaches 30 cm H₂O
  – Greater Ventilator-free days
  – Mortality NS but favorable trend

Mercat et al
JAMA 2008
Stress Index

\[ \text{Pao} = a \cdot \text{inspiratory time}^b + c \]

Stress IndexPredicts Lung Injury

Stress Index in “Lobar” ARDS
PEEP, Pplat, and Lung Volume

Effects of Lowering PEEP on Gas Exchange in Lobar ARDS

<table>
<thead>
<tr>
<th></th>
<th>ARDSNet Table</th>
<th>Stress Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>PaO₂/FiO₂</td>
<td>122 ± 44</td>
<td>110 ± 32 (NS)</td>
</tr>
<tr>
<td>PaCO₂ (mm Hg)</td>
<td>46 ± 6</td>
<td>42 ± 6 (&lt;0.01)</td>
</tr>
</tbody>
</table>

Effects of Lower-lower PEEP on Inflammatory Mediators

Stress Index

- Special monitoring equipment needed
- Must be relaxed during inspiration
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.
Trials of Lung-protective Mechanical Ventilation

Clinical Trials (3562 Patients)
1. Amato NEJM 1998 – Lower $V_T$ + Higher PEEP
2. Stewart NEJM 1998 – Lower $V_T$
3. Brochard AJRCCM 1998 – Lower $V_T$
4. Brower CCM 1999 – Lower $V_T$
5. ARDS Network NEJM 2000 - Lower $V_T$
6. ARDS Network NEJM 2004 – Higher PEEP
7. Mercat JAMA 2008 – Higher PEEP
8. Meade JAMA 2008 – Higher PEEP
9. Talmor NEJM 2008 – Pes guided higher PEEP
Driving Pressure ($\Delta P$)

- Volume
- Airway Pressure

Determinants of $\Delta P$
- Tidal Volume ($V_T$)
- Compliance $C_{RS}$
## Model Variables

**Patient variables**
- Days on mech vent
- Age
- APACHE III (1.31)
- # Organ failures
- Arterial pH (0.64)
- PaCO\(_2\)
- PaO\(_2\)/FIO\(_2\)
- Tidal-compliance

**Mech Vent Variables**
- Tidal volume
- Plateau pressure
- PEEP
- FiO\(_2\) (1.32)
- Respiratory rate
- Mean airway pressure
- ΔP (Pplat – PEEP) (1.47)
Driving Pressure

Airway Pressure

Pplat

Driving Pressure

Time

PEEP
Combined population of ARDS (N = 3080)

Relative Risk (adjusted mortality rate*)

\[ \Delta P \text{ (Driving-Pressure, cmH}_2\text{O)} \]

*: adjusted for age, APACHE/SAPS risk, arterial-pH, P/F ratio, and study-trial
$\Delta P$-Guided PEEP

$V_T = 6 \text{ ml/kg}$

$\Delta P = 18$
$\Delta P$-Guided PEEP

Volume

Paw

$V_T = 6 \text{ ml/kg}$

$\Delta P = 14$
$\Delta P$-Guided PEEP

Volume

Paw

$V_T = 6 \text{ ml/kg}$

$\Delta P = 18$
Driving Pressure

- Special monitoring equipment not needed
- Inspiratory efforts OK
- Patient must be relaxed during exhalation
Higher PEEP to Patients with More Recruitable Lung and Lower PEEP to Patients with Less Recruitable Lung?

- Table of fixed combinations of PEEP and FiO$_2$  YES
- Raise PEEP until Pplat approaches 30 cm H$_2$O  No
- Raise PEEP until transpulmonary pressure > 0  No
- Adjust PEEP to Stress Index = 1.0  No
- Adjust PEEP to minimize Driving Pressure  ?

Chiumello D
Crit Care Med 2014
Thank You
Thank You

PEEP
Effect of ventilation on surface forces in excised dogs’ lungs$^1,2$

EDMUND E. FARIDY,3 SOLBERT PERMUTT, AND RICHARD L. RILEY
Department of Environmental Medicine, Johns Hopkins University,
Baltimore, Maryland

Sol Permutt
Mechanical Ventilation and ARDS

- Critical for survival
  - ensure gas exchange
  - buy time …
- Can cause lung injury
  - may prevent recovery
Pao = a \cdot \text{inspiratory time}^b + c

Airway Pressure Decrease with PEEP

Air Flow

Decrease PEEP

Stress index > 1

Stress index = 1

ΔP
Air Flow

Airway Pressure

Raise PEEP

# Driving Pressures in Higher PEEP Trials

<table>
<thead>
<tr>
<th></th>
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<td>PaO₂/FIO₂</td>
<td>ΔP (Pplat – PEEP)</td>
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<td>Tidal-compliance</td>
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</table>
Driving Pressure (Pplat – PEEP) = $V_T/C_{RS}$

E.g., $V_T = 600$, $C_{RS} = 25$ ml/cm H$_2$O

Driving Pressure = $600/25 = 24$ cm H$_2$O
Alveolar Type II Epithelial Cells

Tschumperlin et al. Am J Respir Crit Care Med 2000
Figure 1:

- **Resampling A:** matched PEEP
- **Resampling B:** matched ΔP
- **Resampling C:** matched P_{PLAT}

Airway pressures (cmH_2O):

- Higher P_{PLAT}:
  - not always risky
- Higher PEEP:
  - not always protective

*: adjusted for age, APACHE/SAPS risk, arterial-pH, P/F ratio, and study-trial
**Figure 4:** ∆P-changes driven by randomization mediate survival in the higher-PEEP arms

P = 0.002 (survival difference across terciles)

- mean ∆P-change = -3.7 cmH₂O
- mean ∆P-change = +0.4 cmH₂O
- mean ∆P-change = +4.1 cmH₂O

*: Adjusted for: age, APACHE/SAPS risk, arterial-pH, P/F ratio, study-trial, and Disease-∆P

Low-PEEP arm; N = 794 (mean ∆P-change = +1.3)
Figure 2a: Subsample of patients under "protective settings"

( N = 1745 )

All with Plateau-pressure ≤ 30 cmH₂O & \( V_T \leq 7 \text{ mL} / \text{ibw} \)

**stratification:**

\[ \Delta P \leq 14 \text{ cmH}_2\text{O} \quad (989) \]
\[ \Delta P > 14 \text{ cmH}_2\text{O} \quad (756) \]

\[ P_{PLAT} \leq 25 \text{ cmH}_2\text{O} \quad (955) \]
\[ P_{PLAT} > 25 \text{ cmH}_2\text{O} \quad (790) \]

\[ V_T \geq 6 \text{ mL/kg} \quad (867) \]
\[ V_T < 6 \text{ mL/kg} \quad (878) \]

\[ P < 0.001 \]
\[ P = 0.98 \]
\[ P = 0.30 \]

*: adjusted for age, APACHE/SAPS risk, arterial-pH, P/F ratio, and study-trial
Strain

Ratio of total deformation to the initial dimension of the material body in which the forces are being applied.
Strain

Ratio of total deformation to the initial dimension of the material body in which the forces are being applied.

\[ \text{Strain} = \frac{\Delta L}{L} \]
Figure 2b: Combined population of ARDS (N = 3080)

Relative Risk (adjusted mortality rate*)

\[ P < 0.001 \]
\[ P < 0.01 \]

\[ P = 0.92 \]
\[ P_{PLAT} < 30 \]
\[ P_{PLAT} \geq 30 \]
\[ N = 1406 \]
\[ N = 260 \]
\[ N = 529 \]
\[ N = 882 \]

\[ \Delta P \leq 14 \]
\[ \Delta P > 14 \]

*: adjusted for age, APACHE/SAPS risk, arterial-pH, P/F ratio, and study-trial
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Lower $V_T$/Pressure Ventilation

- VILI from Overdistension
- VILI from Opening-Closing
- Lower $V_T$
ARDS Network Tidal Volume Trial
Mortality Before Hospital Discharge

Mortality (Percent)

P = 0.007

ARDSnet. NEJM 2000
ARDS Network Tidal Volume Trial

Tidal Volume goal = 6 ml/kg PBW

Plateau Pressure limit = 30 cm H$_2$O
Mechanical Ventilation
Traditional Approach

PEEP 0-12 cm H$_2$O

Low Volume/Low Pressure at End-expiration
Lower $V_T$/Pressure Ventilation

- VILI from Overdistension
- VILI from Opening-Closing
- Lower $V_T$
Lower $V_T$ and Higher PEEP

Lung Volume

VILI from
Opening-Closing

VILI from
Overdistension

Time
Ventilator-Induced Lung Injury

Webb and Tierney
Am Rev Resp Dis
110:556-565, 1974
# 3 Higher PEEP Trials

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1 ARDSnet NEJM 2004  
2 Meade JAMA 2008  
3 Mercat JAMA 2008
Effects of PEEP are Variable

Diffuse

Recruitment

Overdistention

Lobar

Recruitment

Overdistention
ARDS Network Trial of Lower Tidal Volume Ventilation in ALI/ARDS

Subset analysis

No “safe” level of $P_{plat}$ identified
Mortality by Day 1 Pplat Quartiles (n=822)

- Highest: >29%
- Third: 29%
- Second: 25%
- Lowest: 20%

Mortality (%) by Day 1 Pplat Quartiles:
- Highest: >37%
- Third: 37%
- Second: 31%
- Lowest: 26%

Note: * represents a range of 10-20 cm H2O for 26 patients.
Lower $V_T$/Pressure Ventilation
and Higher PEEP

Lung Volume

Time

VILI from Overdistension

VILI from Opening-Closing

Higher PEEP and Lower $V_T$
Stress Index

Lung-protective Mechanical Ventilation in ALI and ARDS
PEEP Questions

- Who are the responders?
- How much PEEP in responders?
- How much PEEP in nonresponders?
- When to decrease PEEP in responders?
Ventilator-Induced Lung Injury

High Volume
High Pressure
VILI

Low Volume
Low Pressure
VILI
Effects of PEEP on Elastance Recruiters and Nonrecruiters

Lower $V_T$ and Inspiratory Pressure
Reduced Overdistention AND Opening-Closing

Volume

Pressure

Higher $V_T$

Lower $V_T$
Higher $V_T$ and Inspiratory Pressure
Ventilator-induced Lung Injury

Effect of Positive Pressure Ventilation on Surface Tension Properties of Lung Extracts

Lazar J. Greenfield, M.D., Paul A. Ebert, M.D., Donald W. Benson, M.D., Ph.D.

Anesthesiology 1964; 312-316
Effects of PEEP

Responders | Nonresponders
---|---
PEEP | 9 | 16 | 9 | 15

Pressure Volume Curve
Stress Index

Volume

Pao

Stress Index < 1
Pressure Volume Curve
Stress Index

Volume

Pao

Stress Index = 1
Pressure Volume Curve
Stress Index

Volume

Pao

Stress Index >1
### Effects of PEEP

<table>
<thead>
<tr>
<th></th>
<th>Responders</th>
<th>Nonresponders</th>
</tr>
</thead>
<tbody>
<tr>
<td>PaO$_2$/FiO$_2$</td>
<td>150 (36)</td>
<td>149 (38)</td>
</tr>
<tr>
<td>(SD)</td>
<td>396 (138)</td>
<td>142 (36)</td>
</tr>
<tr>
<td>PEEP</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td></td>
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