Mechanical Ventilation in ARDS

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Outline

• 1. Obesity effects on the abdomen
• 2. Obesity effects on the respiratory system
• 3. Implications for mechanical ventilation
Obesity Effects on Intra-abdominal Pressure
Abdominal Compartment Syndrome

- Syndrome well recognized by surgeons
- Increasing evidence in Medical ICU patients
- Transduce Foley catheter or paracentesis needle or measure gastric pressure
50% had IAP > 12 mmHg
8% had ACS
BMI was the only significant independent predictor of IAP in multivariate analysis
Effects of ACS

High IAP can:
1. overcome the closing pressure of intra-abdominal venules which can lead to renal failure or hepatic necrosis
2. raise pleural pressure with associated pulmonary effects
3. Lead to high pleural pressure which can create confusion with CVP and PAOP
ACS – intra-abdominal

• We have observed cases of apparent hepatorenal syndrome which were reversible with paracentesis.
• Compromise of other organs also reported especially when IAP>40mmHg
• Trauma surgeons perform laparotomy for anuria with good success
ACS can elevate Pleural Pressure

- Diaphragm may remodel with chronicity so more IAP is transmitted to thorax i.e. less recoil across the diaphragm
- Obesity or ascites may effect Ppl more than acute processes
- If Ppl is really positive why would the lung not deflate?
How is Positive Pleural Pressure Sustained? Is Negative Transpulmonary Pressure Possible?

• 1) Atelectasis
• 2) Flow limitation
• 3) Airway closure

• Presumably regional variations in pleural pressure allow some lung regions to remain patent throughout the respiratory cycle
• PEEP could help overcome collapse
Measurement Issues

- CVP and wedge are generally referenced to atmosphere.
- Positive pleural pressure could effectively squeeze the RA and LV.
- The transmural pressure (in-out) is the relevant distending pressure.
- Could have very high CVP or wedge with small volumes i.e. resuscitation may be indicated.
Correlation between intra-abdominal and intracranial pressure in nontraumatic brain injury
Summarize ACS

- Elevated IAP is common in obesity
- Important effects on abdominal viscera
- Raised pleural pressure has implications for mechanical ventilation
- Awareness of pleural pressure is critical for interpretation of CVP and Wedge
- Raised ICP may respond to laparotomy
Outline

• 1. Obesity effects on the abdomen
• 2. Obesity effects on the chest wall/lung
• 3. Implications for mechanical ventilation
Obesity Effects on Chest Wall

- Compliance of the lung but not the chest wall is reduced in a number of obesity studies.
- Baseline position is altered i.e. pleural pressure is positive but pressure/volume characteristic is preserved.
Pes in normal and obese subjects at rest, lateral recumbent.

Owens et al. Obesity 2012
Compliance of the respiratory system and its components in health and obesity

Studied modest obesity by today’s standards

Normal lung compliance

Reduced chest wall compliance

Likely confounded by behavioral influences during wakefulness i.e., chest wall muscle activity
Early chest wall studies were likely confounded by behavioral influences, e.g. muscle activity during wakefulness.

Subsequent studies done during relaxed wakefulness or paralysis or sleep.

Chest wall compliance is likely normal in obesity.
Chest Wall Compliance vs. BMI

Body Mass Index (kg/m²)

Chest Wall Compliance (L/cmH₂O)

Series 1

Suratt JAP 1984
Esophageal and transpulmonary pressures in acute respiratory failure*

Daniel Talmor, MD, MPH; Todd Sarge, MD; Carl R. O’Donnell, ScD; Ray Ritz, RRT; Atul Malhotra, MD; Alan Lisbon, MD; Stephen H. Loring, MD
Summarize Obesity and Chest Wall

• Most data indicate that the lung not the chest wall is stiff
• Evidence of alveolar collapse suggests benefits to PEEP
• Airway opening pressures tell us little about distending pressures across the lung.
• 6 cc/kg tidal volume gives variable lung stretch.
Outline

1. Obesity effects on the abdomen
2. Obesity effects on the chest wall/lung
3. Implications for mechanical ventilation
How Many Have a Good Sense How to Ventilate this patient?

- 45 year old with bilateral infiltrates has ABG of pH=7.35, PaCO2=43 mmHg, PaO2=70 mmHg on FIO2=0.6

- Who would give PEEP=8 cmH2O vs. 15 cmH2O?
Conservative views expressed

6 cc/kg volume pre-set is the gold standard

Lower is better

Goal is to do no harm with ventilator i.e. prevent mechanical injury
Stress Concentration

• Estimated concentration of stress could be > 4 times that applied to the airway

• Airway pressure of 30 cmH₂O ≈ 140 cm H₂O in some regions

Mead, JAP 1970, 28(5):596
Very high shear forces can occur at junctions of normal and abnormal lung
No safe pressure (AJRCCM 2007)
Strategies to promote homogeneity may promote lung protection
“get it open, leave it open”
Homogeneity is everything
Cytokine Release Following Recruitment Maneuvers*

Daniel Talmor, MD, MPH, FCCP; Todd Sarge, MD; Anna Legedza, ScD; Carl R. O’Donnell, ScD; Ray Ritz, RRT; Stephen H. Loring, MD; and Atul Malhotra, MD, FCCP

Plow FEEP 30 – 40 cm H\textsubscript{2}O

PEEP = 5 cmH₂O  
collapsed Area = 54.3%  
collapsed Mass = 69.2%

PEEP = 19 cmH₂O  
(OLA)  
collapsed Area = 21.9%  
collapsed Mass = 36.8%

PEEP = 25 cmH₂O  
(after P_{PLAT} = 55)  
collapsed Area = 0.4%  
collapsed Mass = 0.9%

PEEP = 23 cmH₂O  
(30 minutes later)  
collapsed Area = 0.5%  
collapsed Mass = 1.8%
Effects of recruitment maneuvers in patients with acute lung injury and acute respiratory distress syndrome ventilated with high positive end-expiratory pressure*

The ARDS Clinical Trials Network; National Heart, Lung, and Blood Institute; National Institutes of Health

Magnitude and Duration of RM Effects on Arterial Oxygenation. We monitored SpO₂ continuously. To assess immediate effects of RM maneuvers (RMs), we compared greatest increments in SpO₂ during the first 10 mins after initiating RMs or sham RMs. After the first 10 mins, FIO₂ and PEEP were adjusted in discrete steps according to an explicit protocol (FIO₂/PEEP step, Table 1) to maintain SpO₂ of 88–95%. To assess duration of RM effects, we recorded changes in FIO₂/PEEP-step at 30 mins and 1, 2

Transient oxygenation benefits likely not sustained due to inadequate PEEP
• Open Lung Ventilation
• PEEP > Pflex and Plateau < UIP
• Permissive hypercapnia and recruitment maneuvers
• Studied n=53 RCT sick patients
• 28 day survival 71% vs 38%

Amato et al NEJM 1998; Ranieri JAMA 1999
• Some have argued 71% control mortality too high (3.6 organ failures)
• Small sample size???
• Findings confirmed by Ranieri et al who demonstrated lower cytokines using lung protective strategy

Ranieri JAMA 1999
A high positive end-expiratory pressure, low tidal volume ventilatory strategy improves outcome in persistent acute respiratory distress syndrome: A randomized, controlled trial*

Jesús Villar, MD, PhD, FCCM; Robert M. Kacmarek, PhD, FCCM; Lina Pérez-Méndez, MD, PhD; Armando Aguirre-Jaime, PhD; for the ARIES Network

- Set ventilator based on PV curves
- Similar to Amato’s strategy

Table 2. Main outcome variables

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>$P_{rew}$/LTV</th>
<th>$p$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventilator-free days</td>
<td>6.0 ± 7.9</td>
<td>10.9 ± 9.4</td>
<td>.008</td>
</tr>
<tr>
<td>Barotrauma, n (%)</td>
<td>4 (8.4)</td>
<td>2 (4)</td>
<td>.418</td>
</tr>
<tr>
<td>No. of organ failures: post-pre randomization</td>
<td>1.2 (0.7–1.6)</td>
<td>0.3 (0–0.7)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>ICU mortality rate, %</td>
<td>53.3</td>
<td>32.0</td>
<td>.040</td>
</tr>
</tbody>
</table>

$P_{rew}$, lower inflection point of the pressure volume curve of the respiratory system; LTV, low tidal volume; ICU, intensive care unit.

- one protocol violation kept this out of NEJM

CCM May 2006
Mechanical Ventilation Guided by Esophageal Pressure in Acute Lung Injury


Table 4. Clinical Outcomes.*

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Esophageal-Pressure–Guided (N=30)</th>
<th>Conventional Treatment (N=31)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>28-Day mortality — no. (%)</td>
<td>5 (17)</td>
<td>12 (39)</td>
<td>0.055</td>
</tr>
<tr>
<td>180-Day mortality — no. (%)</td>
<td>8 (27)</td>
<td>14 (45)</td>
<td>0.13</td>
</tr>
<tr>
<td>Length of ICU stay — days</td>
<td></td>
<td></td>
<td>0.16</td>
</tr>
<tr>
<td>Median</td>
<td>15.5</td>
<td>13.0</td>
<td></td>
</tr>
<tr>
<td>Interquartile range</td>
<td>10.8–28.5</td>
<td>7.0–22.0</td>
<td></td>
</tr>
</tbody>
</table>

*Data from Table 4 in the article.
Background

• The pressure applied to the lung itself is usually not known, and is often assumed to be similar to the ventilator airway pressures.

• In some patients, the chest wall contributes a large part of the respiratory system elastance, making the above assumption false.
Transpulmonary Pressure

- Transpulmonary pressure \( (P_L) \) is the pressure actually distending the lung.

\[
P_L = P_{ao} - P_{pl}
\]

- Knowing pleural pressure \( (P_{pl}) \) could allow calculation of transpulmonary pressure \( (P_L) \) to individualize pressures appropriate to the lungs.
Plateau pressure minus PEEP predicts mortality in lots of different trials.

The trials were designed for the most part to limit tidal volume.

Still emphasize importance of transpulmonary pressure in determining lung stress.
Hypothesis

• Depending on the chest wall contribution to respiratory mechanics, a given PEEP or Pplat may be adequate for one patient but potentially injurious for another.

• This may explain equivocal results in clinical trials and discrepancies with animal studies.
Did Prior Studies Use the Right Target?

\[ P_L = P_{ao} - P_{Pl} \]

\( P_L \) 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.
Pressure transducing wafers implanted in dog lungs revealed differences in pleural pressure due to the gravitational effect of the dependent vs. non-dependent regions of the lung.

$P_{es}$ Values Reflect High Pleural Pressures

$r = 0.88$
$p < 0.0001$
$slope = 1.2$
$y$-intercept = -2.5
In Humans

Patient Oxygenation - Repeated Measures

PaO2/FiO2 ratio

EP

conventional

P=0.002
6- Month Survival

Cumulative Survival

Esophageal pressure guided protocol

Conventional protocol

Time from enrollment, days
Esophageal pressures in acute lung injury: do they represent artifact or useful information about transpulmonary pressure, chest wall mechanics, and lung stress?

- EPVENT Small pilot study
- Some have questioned accuracy of Pes
- Magnitude of any artifacts appears small compared to measured values.
- Pes well validated in dogs by Pelosi and Amato
- Can predict Pes with Pabd suggesting not just cardiac weight
- Would seem unlikely that outcome would improve by titrating to artifacts
- Larger studies are needed and are planned
Studied high vs. low PEEP and showed no difference

PEEP set based on oxygenation tables which were reasonably arbitrary.
ALVEOLI Caveats

• 1. Imbalances at randomization
• 2. 2 protocol revisions
• 3. failed to promote lung homogeneity
• 4. not very sick patients
• 5. neglected hemodynamic effects of PEEP
• 6. did not measure individual lung and chest wall characteristics or recruitability

Owens, et al. Critical Care 2009
Ventilation Strategy Using Low Tidal Volumes, Recruitment Maneuvers, and High Positive End-Expiratory Pressure for Acute Lung Injury and Acute Respiratory Distress Syndrome
A Randomized Controlled Trial

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for the Lung Open Ventilation Study Investigators

Context  Low-tidal-volume ventilation reduces mortality in critically ill patients with acute lung injury and acute respiratory distress syndrome. Instituting additional strategies to open collapsed lung tissue may further reduce mortality.

Objective  To compare an established low-tidal-volume ventilation strategy with an experimental strategy based on the original “open-lung approach,” combining low tidal volume, lung recruitment maneuvers, and high positive end-expiratory pressure.

Design and Setting  Randomized controlled trial with concealed allocation and blinded data analysis conducted between August 2000 and March 2006 in 30 intensive care units in Canada, Australia, and Saudi Arabia.

Patients  Nine hundred eighty-three consecutive patients with acute lung injury and a ratio of arterial oxygen tension to inspired oxygen fraction not exceeding 250.

Interventions  The control strategy included target tidal volumes of 6 mL/kg of predicted body weight, plateau airway pressures not exceeding 30 cm H₂O, and conventional levels of positive end-expiratory pressure (n=508). The experimental strategy included target tidal volumes of 6 mL/kg of predicted body weight, plateau pressures not exceeding 40 cm H₂O, recruitment maneuvers, and higher positive end-expiratory pressures (n=475).

Main Outcome Measure  All-cause hospital mortality.

Results  Eighty-five percent of the 983 study patients met criteria for acute respiratory distress syndrome at enrollment. Tidal volumes remained similar in the 2 groups, and mean positive end-expiratory pressures were 14.6 (SD, 3.4) cm H₂O in the experimental group vs 9.8 (SD, 2.7) cm H₂O among controls during the first 72 hours (P<.001). All-cause hospital mortality rates were 36.4% and 40.4%, respectively (relative risk [RR], 0.90; 95% confidence interval [CI], 0.77-1.05; P=.19). Barotrauma rates were 11.2% and 9.1% (RR, 1.21; 95% CI, 0.83-1.75; P=.33). The experimental group had lower rates of refractory hypoxemia (4.6% vs 10.2%; RR, 0.54; 95% CI, 0.34-0.86; P=.01), death with refractory hypoxemia (4.2% vs 8.9%; RR, 0.56; 95% CI, 0.34-0.93; P=.03), and previously defined eligible use of rescue therapies (5.1% vs 9.3%; RR, 0.61; 95% CI, 0.38-0.99; P=.045).

Conclusions  For patients with acute lung injury and acute respiratory distress syndrome, a multifaceted protocolized ventilation strategy designed to recruit and open the lung resulted in no significant difference in all-cause hospital mortality or barotrauma compared with an established low-tidal-volume protocolized ventilation strategy. This “open-lung” strategy did appear to improve secondary end points related to hypoxemia and use of rescue therapies.

Trial Registration  clinicaltrials.gov Identifier: NCT00182195
Positive End-Expiratory Pressure Setting in Adults With Acute Lung Injury and Acute Respiratory Distress Syndrome
A Randomized Controlled Trial

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for the Expiratory Pressure (Express) Study Group

Context The need for lung protection is universally accepted, but the optimal level of positive end-expiratory pressure (PEEP) in patients with acute lung injury (ALI) or acute respiratory distress syndrome remains debated.

Objective To compare the effect on outcome of a strategy for setting PEEP aimed at increasing alveolar recruitment while limiting hyperinflation to one aimed at minimizing alveolar distension in patients with ALI.

Design, Setting, and Patients A multicenter randomized controlled trial of 767 adults (mean [SD] age, 59.9 [15.4] years) with ALI conducted in 37 intensive care units in France from September 2002 to December 2005.

Intervention Tidal volume was set at 6 mL/kg of predicted body weight in both strategies. Patients were randomly assigned to a moderate PEEP strategy (5-9 cm H2O) (minimal distension strategy; n=382) or to a level of PEEP set to reach a plateau pressure of 28 to 30 cm H2O (increased recruitment strategy; n=385).

Main Outcome Measures The primary end point was mortality at 28 days. Secondary end points were hospital mortality at 60 days, ventilator-free days, and organ failure–free days at 28 days.

Results The 28-day mortality rate in the minimal distension group was 31.2% (n=119) vs 27.8% (n=107) in the increased recruitment group (relative risk, 1.12 [95% confidence interval, 0.90-1.40]; P=.31). The hospital mortality rate in the minimal distension group was 39.0% (n=149) vs 35.4% (n=136) in the increased recruitment group (relative risk, 1.10 [95% confidence interval, 0.92-1.32]; P=.30). The increased recruitment group compared with the minimal distension group had a higher median number of ventilator-free days (7 [interquartile range [IQR], 0-19] vs 3 [IQR, 0-17]; P=.04) and organ failure–free days (6 [IQR, 0-18] vs 2 [IQR, 0-16]; P=.04). This strategy also was associated with higher compliance values, better oxygenation, less use of adjunctive therapies, and larger fluid requirements.

Conclusions A strategy for setting PEEP aimed at increasing alveolar recruitment while limiting hyperinflation did not significantly reduce mortality. However, it did improve lung function and reduced the duration of mechanical ventilation and the median number of ventilator-free days.
Figure 2. Probabilities of Death and Breathing Without Assistance From the Day of Randomization (Day 0) to Day 28
Clinical Trial Oxygenation vs. Mechanics

**Oxygenation**
ALVEOLI - negative
LOVS - negative

**Mechanics**
Amato - positive
Villar - positive
EpVent - positive

? Express - equivocal
High-Frequency Oscillatory Ventilation on Shaky Ground

Atul Malhotra, M.D., and Jeffrey M. Drazen, M.D.
High-Frequency Oscillation in Early Acute Respiratory Distress Syndrome

High-Frequency Oscillation for Acute Respiratory Distress Syndrome

Prone Positioning in Severe Acute Respiratory Distress Syndrome

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• Large scale multicenter randomized trials
• HFO vs. conventional.
• No benefit if not harmful
• Mechanisms of toxicity include hemodynamic and/or sedation

NEJM 2013
Table 4. Effects of Positive End-Expiratory Pressure in Patients with Congestive Heart Failure.

- Reduced preload due to increased vena caval resistance
- Reduced left ventricular afterload due to reduced wall stress
- Reduced myocardial oxygen consumption due to decreased ventricular size
- Increased lung compliance due to reduced extravascular lung fluid
- Decreased negative pleural pressure with inspiration
- Suppressed catecholamines due to improved cardiac output and oxygenation
- Reduced mitral regurgitation
Summary

• Oxygenation is one of many factors that should influence ventilator settings.
• Mechanics may be more important than oxygenation per se since patients rarely die from hypoxemia and the goal is to do no mechanical harm with ventilator.
• Multiple factors including individual’s hemodynamics and mechanics should influence PEEP decisions as well as response to therapy (recruitability).
• We need more RCTs but small existing studies which have titrated ventilator settings based on lung and chest wall mechanics have succeeded.
Disclosures /Funding

Grants PI: Malhotra
- NIH and AHA

Industry (none since May 2012)