Atul Malhotra, MD, is a board-certified pulmonologist, intensivist and chief of Pulmonary, Critical Care and Sleep Medicine. He is active clinically in pulmonary, critical care and sleep medicine. In the sleep clinic, he provides a full spectrum of diagnostic and therapeutic services to patients with sleep-related disorders, including sleep apnea, insomnia, restless leg syndrome, narcolepsy and sleep disorders associated with medical or psychiatric conditions. He has a special interest in the treatment of sleep apnea.

Dr. Malhotra is the president of the American Thoracic Society. He has taught and presented his research on sleep-related disorders locally, regionally, nationally and internationally. He has published more than 200 original manuscripts in leading journals. He is a principal- and co-investigator on numerous projects relating to sleep apnea and serves as an ad hoc reviewer for many leading journals including the New England Journal of Medicine, Mayo Clinic Proceedings, Sleep and the Journal of American Medical Association. To view a full list of his publications, visit PubMed.

As a professor in the Department of Medicine, Dr. Malhotra is involved in training medical students, residents and fellows at UC San Diego School of Medicine.

Before joining UC San Diego Health, Dr. Malhotra practiced pulmonary, critical care and sleep medicine at Massachusetts General Hospital, Beth Israel Deaconess Medical Center and Brigham and Women’s Hospital. He also served as attending physician in intensive care at King Faisal Hospital in Rwanda. He was associate professor at Harvard Medical School and medical director of the Brigham and Women’s Hospital Sleep Disorders Research Program.

Dr. Malhotra completed his fellowship training in pulmonary and critical care medicine at Harvard Medical School and a residency in internal medicine at the Mayo Clinic. He completed an internship at St. Thomas Medical Center in Akron, OH and received his medical degree from the University of Alberta in Canada. Dr. Malhotra is triple board-certified in pulmonary disease, sleep medicine and critical care medicine.
Acute Respiratory Distress Syndrome
Lung Mechanics and Driving Pressure

Atul Malhotra, MD
Pulmonary, Critical Care and Sleep Medicine
UC San Diego

Outline

• 1. Obesity effects on the abdomen
• 2. Obesity effects on the respiratory system
• 3. Implications for mechanical ventilation

Thorax 2008
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
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.

NORMAL

OBESE

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

A. NAIMARK* AND R. M. CHERNIACK*
Faculty of Medicine, University of Manitoba; and Clinical Investigation Unit, Department of Medicine, Winnipeg General Hospital, Winnipeg, Canada

• 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

JAP 1960 Cherniack

Compliance of chest wall in obese subjects

PAUL M. SURATT, STEPHEN C. WILHOIT, HENRY S. HSIAO, RICHARD L. ATKINSON, AND DUDLEY F. ROCHESTER
Department of Internal Medicine, University of Virginia School of Medicine and Pulmonary Function Laboratory, University of Virginia Hospital, Charlottesville, Virginia 22908 and Department of Surgery, University of North Carolina, Chapel Hill, North Carolina 27514

• 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

JAP 1984
Chest Wall Compliance vs. BMI

Body Mass Index (kg/m²)

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

CCM 2006
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?
Malhotra et al, NEJM CPC 2003

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

High-Frequency Oscillatory Ventilation on Shaky Ground
Atul Malhotra, M.D., and Jeffrey M. Drezner, M.D.

NEJM 2013
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
Stress distribution in lungs: a model of pulmonary elasticity

JERE MEAD, TAMOTSU TAKISHIMA, AND DAVID LEITH
Department of Physiology, Harvard University School of Public Health, Boston, Massachusetts 02115

- 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

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
Amato – caveats?

- 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:

Jesus 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>
<thead>
<tr>
<th>Table 2. Main outcome variables</th>
<th>Control</th>
<th>P_{PEEP}/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_{PEEP} 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
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.
Critique of Amato et al.

• Driving pressure independent of tidal volume predictive value is surprising if not implausible
• Statistics were robust but complex
• Primary studies had relatively fixed tidal volume diminishing its predictive value
Driving Pressure and Respiratory Mechanics in ARDS

Stephen H. Loring, M.D., and Atul Malhotra, M.D.

- Plateau pressure minus PEEP predicts mortality in lots of different trials
- Incorporates scaling based on lung compliance
- Still emphasize importance of transpulmonary pressure in determining lung stress

NEJM 2015

EDITORIAL

Acute respiratory distress syndrome and the promise of driving pressure

- Limiting driving pressure may help in preventing ARDS (Blondonnet et al.)
- Caution if spontaneous breathing
- Raising PEEP is not the same as lowering tidal volume even though similar driving pressure
- Tidal recruitment may maximize atelectrauma but could lower driving pressure

Respirology in press
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.
Titrating ventilation based on ventilator pressures does not allow us to take this variability into account.

In Humans

Patient Oxygenation - Repeated Measures

- EP
- conventional

P=0.002

6-Month Survival

- Esophageal pressure guided protocol
- Conventional protocol
Studied high vs. low PEEP and showed no difference

PEEP set based on oxygenation tables which were reasonably arbitrary.

Clinical Trial Oxygenation vs. Mechanics

Oxygenation
ALVEOLI - negative
LOVS - negative

Mechanics
Amato - positive
Villar - positive
EpVent - positive

? Express - equivocal
Prone positioning reduces mortality from acute respiratory distress syndrome in the low tidal volume era: a meta-analysis

Convenience

Debate over mechanism

Likely not just a function of paralytics

Patient ventilator synchrony may be important

It may be the only thing that works!
Effect of Lung Recruitment and Titrated Positive End-Expiratory Pressure (PEEP) vs Low PEEP on Mortality in Patients With Acute Respiratory Distress Syndrome
A Randomized Clinical Trial
Writing Group for the Alveolar Recruitment for Acute Respiratory Distress Syndrome Trial (ART) Investigators, Alexandre Biasi Cavalcanti, MD, PhD, [...] and Carlos Roberto Ribeiro de Carvalho, MD, PhD

Increased mortality using strategy I recommend

Ouch

Maybe some design flaws e.g. best compliance

Rethinking the ARDS Lung
Baby Lung: Implications for Lung Injury

- **Well-aerated regions**
  - Risk of overdistension (volutrauma/barotrauma)

- **Poorly aerated regions**
  - Risk of cyclic atelectasis

- **Collapsed regions**
  - Decrease lung volume available for ventilation

- **Inhomogeneity (border zones)**
  - High shear forces

*Best evidence*: therapies targeting optimal mechanics
Recruitment Maneuver Volume ($V_{RM}$)

Continuous Positive Airway Pressure of 40 cmH$_2$O for 30 seconds

Flow: $AUC = V_{RM}$

Recruitment Maneuver Volume ($V_{RM}$)

Predicting Lung Stress & Mortality

- End-inspiratory stress: \( P_{\text{tp}} = P_{\text{aw}} - P_{\text{pl}} \)

- \( V_{\text{RM}} \) predicts risk of death (OR 0.84, 95% CI 0.71-1.00; \( p = .02 \))

\[ \begin{align*}
\text{Tidal Volume (mL/kg PBW)} & \quad \text{End-Inspiratory Stress (cmH}_2\text{O)} \\
0 & \quad 5 & \quad -5 & \quad 0 & \quad 5 & \quad 10 & \quad 15 & \quad 20 & \quad 25 \\
2 & \quad -2 & \quad 0 & \quad 5 & \quad 10 & \quad 15 & \quad 20 & \quad 25 & \quad 30 \\
\end{align*} \]

\[ \begin{align*}
\text{V}_{\text{RM}} & \quad \text{End-Inspiratory Stress (cmH}_2\text{O)} \\
0 & \quad 5 & \quad 10 & \quad 15 & \quad 20 & \quad 25 & \quad 30 & \quad 35 & \quad 40 \\
0 & \quad 5 & \quad 10 & \quad 15 & \quad 20 & \quad 25 & \quad 30 & \quad 35 & \quad 40 \\
\end{align*} \]

\[ \begin{align*}
\text{V}_{\text{T}/V}_{\text{RM}} & : \text{Scaling} \text{ } \text{V}_{\text{T}} \text{ to Baby Lung Size} \\
\text{V}_{\text{RM}} & = \text{maximum insufflation volume achievable under clinically plausible conditions} \\
& \text{Analogous to relative inspiratory capacity measured beginning from PEEP} \\
\text{V}_{\text{T}/V}_{\text{RM}} & = \text{fraction of the potentially available lung volume that is insufflated with each tidal breath} \\
\end{align*} \]
Summary

- Oxygenation is one of many factors that influences ventilator settings.
- Mechanics may be more important than oxygenation since patients rarely die from low PO2 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.
- Providing tidal volume consistent with the available lung for gas exchange deserves further study.
- EPVENT 2 and ROSE are soon to release.
Disclosures /Funding

Grants PI: Malhotra
- NIH and AHA

Industry (none since May 2012)