What’s new in ARDS?

Objectives

• Look for ARDS & recognize it early
• Implement low tidal volume ventilation early
• Approaches to severe hypoxemia
• Conservative fluid management decreases ventilator time and ICU stay
• Limited role for corticosteroids in ARDS

Outline

• Epidemiology & Diagnosis
• Low tidal volume ventilation
  – Implementation & Obstacles
• Mechanical Ventilation
  – Beyond Low Tidal Volume
  – Severe Hypoxemia
• Fluids & Pulmonary artery catheters
• Steroids
• Emerging Therapies

Is this ARDS?

• 55-year-old man admitted to the ICU with respiratory distress progressive over 3 weeks. He was admitted to the hospital 2 days prior with complaints of dyspnea, trace hemoptysis, and fatigue. Decreasing UOP noted prior to ICU transfer.

• Exam notable for tachypnea, tachycardia, and hypoxemia (90% on NRB mask). Ht 5’ 4”, Normal neurological and skin exam. No adenopathy. Bilateral LL rales. HR 120, no murmur or gallop, JVP 7 cm. Abn unremarkable. No edema.

• Labs show WBC 10, Hgb 8.5, Plts 188, Cr 2.5, ABG pH 7.25 PaCO2 38 PaO2 135 FIO2 0.7
Is this ARDS?

Acute Lung Injury & Acute Respiratory Distress Syndrome

- Bilateral infiltrates
- No left atrial hypertension
- \( \frac{\text{PaO}_2}{\text{FiO}_2} \leq 300 \)

Acute Lung Injury
\( \frac{\text{PaO}_2}{\text{FiO}_2} \) 201-300

ARDS:
\( \frac{\text{PaO}_2}{\text{FiO}_2} \leq 200 \)

Clinical Disorders Associated with Acute Lung Injury

- Aspiration
- Major Trauma
- Abdominal Sepsis
- Pneumonia

Acute Lung Injury/ARDS is a common cause of death

<table>
<thead>
<tr>
<th>Disease</th>
<th>Attributable mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute lung injury</td>
<td>74,500</td>
</tr>
<tr>
<td>Breast Cancer</td>
<td>41,528</td>
</tr>
<tr>
<td>HIV disease</td>
<td>14,802</td>
</tr>
<tr>
<td>Asthma</td>
<td>4,657</td>
</tr>
<tr>
<td>Cystic fibrosis</td>
<td>485</td>
</tr>
</tbody>
</table>

Rubenfeld G et al, NEJM, 2005
**ARDS Prognosis**
- Overall mortality rate of 40%
- Oxygenation is a poor predictor of prognosis
- Compliance (volume/pressure) and dead space fraction have some predictive value
- Additional organ failures and comorbidities increase mortality

**ALI/ARDS Risk Factors & Risk of Mortality**

<table>
<thead>
<tr>
<th>Clinical Risk Factor</th>
<th>Risk of Mortality (odds ratio)</th>
</tr>
</thead>
<tbody>
<tr>
<td>sepsis</td>
<td>6</td>
</tr>
<tr>
<td>pneumonia</td>
<td>5</td>
</tr>
<tr>
<td>aspiration</td>
<td>4</td>
</tr>
<tr>
<td>other</td>
<td>3</td>
</tr>
<tr>
<td>trauma</td>
<td>1</td>
</tr>
</tbody>
</table>


**Low Tidal Volume Decreases Mortality**
- Lower Tidal Volume or PEEP if pressure higher
- Mortality (Percent)

<table>
<thead>
<tr>
<th>Tidal Volume (ml/kg)</th>
<th>Mortality</th>
<th>P=0.0054</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>0.5</td>
<td></td>
</tr>
</tbody>
</table>

Eisen et al, NEJM 342: 1301-8, 2000

**Low Tidal Volume-Implementation**

<table>
<thead>
<tr>
<th>Volume &amp; Pressure Goals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tidal Volume ≤ 6 ml/kg PBW</td>
</tr>
<tr>
<td>Plateau Pressure ≤ 30</td>
</tr>
</tbody>
</table>

- Lower tidal volume or PEEP if pressure higher
- PEEP & FiO2 Scale
- Weaning Guidelines

NEJM 342:1301-8, 2000
Low Tidal Volume—Implementation

Ventilator Settings “ARDSNet”

The patient required intubation. Tidal volume set to 390 ml with volume controlled ventilation. Respiratory rate 20. Peak airway pressure 35, plateau pressure 32. ABG 7.34 / 40 / 67 FIO2 0.7 PEEP 12

Do you:
1. Make no changes
2. Lower tidal volume
3. Lower PEEP

Low Tidal Volume—Obstacles

Is the patient better???

- Worse PaO2 for first 2-3 days
- Higher respiratory rate
- Concern for more sedation

- Lower Mortality (by 10%)
- More Ventilator-Free Days (by 7)

Beyond Low Tidal Volume

Higher PEEP or “Open Lung”

- Higher PEEP
  - Higher PaO2
  - No improvement in mortality
  - Possibly fewer ventilator days

  “Open Lung” – PEEP & Recruitment Maneuvers
  - Higher PaO2
  - No improvement in overall mortality
  - Fewer hypoxemia deaths

NEJM 351: 327-38, 2004 “ALVEOLI”
JAMA 299: 646-655, 2008 “EXPRESS”
JAMA 299: 637-45, 2008 “LOV”
ARDS Management – Our 55-year-old patient

Severe Hypoxemia

- Over the first two ICU days the patient developed oliguric renal failure
- Renal biopsy showed vasculitis
- Worsening oxygenation: PaO2 50-55 mmHg on FiO2 1.0 and PEEP 18

Beyond Low Tidal Volume

Non-Pharmacologic Management of Severe Hypoxemia

- Increase Inspiratory Time
- Determine Best PEEP
  - 40/40
  - Stepwise increase in pressure
  - 18/6h intervals for up to 10 days
  - Swimmer position
  - Unclear mortality benefit
- Nitric Oxide (NO)
  - Higher PaO2, no mortality benefit (JAMA 2004, 291: 1603-09)

ARDS Management – Our Patient

Severe Hypoxemia

- Solumedrol/cyclophosphamide started for vasculitis
- Patient initially managed with prone positioning, but remained hypoxemic (PaO2 50 on FiO2 1.0, decreasing to 40s with movement)
- NO started at 10pm with improvement in PaO2 to 80s on FiO2 of 0.6 and PEEP 10
- Extubated two days later and later went home
ARDS Management

**Severe Hypoxemia**

- Measures to improve oxygenation may not improve mortality in ARDS patients
- However, prone positioning, recruitment maneuvers, and NO improve oxygenation, which could be clinically important in some cases

Is this ARDS?

- 67-year-old man with a history of LUL broncholoalveolar cell carcinoma, resected 1 year prior to admission, admitted to the ICU with respiratory distress progressive over 2 weeks. He started oral erlotinib (150 mg) 1 month ago for PET positive mediastinal lymph nodes on CT.
- Exam notable for tachypnea (30s), and hypoxemia (82% on NRB mask). Skin with diffuse pustular rash. Bilateral diffuse rales. HR 90, no murmur or gallop, JVP 5 cm. No edema.
- Labs show WBC 8, Hgb 10, Plts 300, ABG pH 7.44 PaCO2 37 PaO2 75 on NRB 100%

ARDS

**Fluid and catheter management**

- Required intubation
- UOP is 50 ml/hr, Cr. is 1.8 (baseline)
ARDS
Fluid and catheter management

Should this patient with normal CVP and brisk UOP receive diuretics?

1. Yes
2. No
3. Maybe – with appropriate monitoring

Fluids

Yes
No
Maybe – with appropriate monitoring

16%
47%
37%

ARDS
Fluid and catheter management

Should this patient receive a PA catheter to guide fluid management?

1. Yes
2. No
3. Maybe

Fluid Management

FACTT: Factorial trial design

Conservative or Liberal Fluids
• Is fluid restriction beneficial?

Pulmonary Artery vs. Central Venous
• Is use of PA line advantageous?

Conservative
Liberal

CATHETER

PAC

CVC

(n = 500)

(n = 500)

(n = 500)

(n = 500)

250 patients
250 patients
250 patients
250 patients

NEJM 355:1175-1176, 2007
Conservative fluid strategy

Furosemide

- UOP < 0.5 ml/kg/h & CVP or PAOP low
- MAP < 60
- Low flow by exam or CI < 2.5

Favors Perfused KIDNEY (organs)

Liberal fluid strategy

- FIO2 > 0.7
- CI > 4.5

Favors Perfused KIDNEY (organs)

Fluids

CVP: 10-14
PAOP: 14-18

LUNG

Cumulative fluid balance

- Liberal
- Conservative

Fluid balance similar to other recent studies

4000 6000 8000

0 1 2 3 4 5 6 7

ml of fluid

Study Day

-2000
Central Venous Pressure

On study plateau pressure

Oxygenation: PaO$_2$/FiO$_2$

Fluid & Catheter Management in ARDS

Conservative Fluids:
- No difference in survival
- 2 more ventilator-free days
- 1 less ICU day
- Lower plateau pressures
- No increase in renal failure, fewer complications
- No difference in vasopressor use
- Is conservative fluid management beneficial?
  - YES
Evidence the PAC may be harmful in the critically ill

Relative Hazard of Death:

<table>
<thead>
<tr>
<th>Patients (n)</th>
<th>Odds Ratio (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>All (5735)</td>
<td>1.21 (1.09-1.25)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>ARF (1789)</td>
<td>1.30 (1.05-1.61)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>MOF (2480)</td>
<td>1.32 (1.11-1.57)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>CHF (456)</td>
<td>1.02 (0.55-1.89)</td>
<td>ns</td>
</tr>
<tr>
<td>Others* (1010)</td>
<td>1.06 (0.80-1.41)</td>
<td>ns</td>
</tr>
</tbody>
</table>

Connors A. JAMA 1996; 276:889-897
Fluid & Catheter Management in ARDS

**Pulmonary Artery vs. Central Venous**

- No difference in survival
- No difference in vent free days or organ failure
- More arrhythmias in PA line group

Is use of PA line advantageous?  
- NO

Steroids for ARDS

**Corticosteroids in Late ARDS**

- More Ventilator-Free Days (1 day)
- No Difference in Overall Mortality
- Mortality When Treated on Days 14-21 Higher
- No Difference in Infection Rates
- Increased Neuromuscular Complications

_Corticosteroids are NOT recommended unless there is another indication_

N Engl J Med. 2006;354:1671-84

Emerging Therapies for ARDS

**Pharmacologic**

- Beta-adrenergic agonists (albuterol)
- Omega-3, antioxidants
- Activated protein C
- GM-CSF

**Non-pharmacologic**

- Early full nutritional support or trophic feeding
- High frequency oscillatory ventilation

What’s New in ARDS?

Summary

- ARDS is a common cause of death in the ICU
- Recognize ARDS early and use low tidal volume ventilation!
- In general, high PEEP, lung recruitment, & NO improve PaO2, but not outcome
- For severe hypoxemia, may be reasonable to consider prone position, recruitment, NO
- Restrict fluids and diurese ARDS patients to keep fluid balance even
- PA catheters do not improve outcomes
- In the absence of another indication, steroids do not benefit ARDS patients
1. Set alarm clock 2 hours before wake-up time.
2. Wake up at the alarm clock. With a deep breath, the patient will wake up naturally.
3. After waking up, have a light breakfast consisting of a high-protein meal.
4. Drink at least 8 glasses of water per day.
5. Avoid caffeine and sugar before bedtime.
6. Create a relaxing bedtime routine.
7. Maintain a regular sleep schedule.
8. Exercise regularly for at least 30 minutes per day.
9. Keep a sleep journal to track sleep patterns.
10. If sleep problems persist, consult a healthcare professional.