APPROACH TO ACUTE LUNG INJURY AND ARDS

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Rocky Mountain Hospitalist Symposium
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DISCLOSURES:

• I have no actual or potential conflict of interest in relation to this presentation

LEARNING OBJECTIVES:

• Define the latest diagnostic criteria for ARDS and identify the most common risk factors for development of ARDS

• Implement an evidence-based approach to the treatment of ARDS

• Describe the current clinical practice of care for patients with ARDS
A Case:

- 62 y/o man POD#3 s/p colectomy with diverting ileostomy for colorectal CA, complicated by post-operative nausea and emesis, develops acute onset dyspnea and hypoxemia.
- HR 120, BP 160/70, RR 24,
  - 87% on 6LNC→
  - 90% on 15LNRB→
  - 95% on BIPAP 12/5, 100% FiO2
- 7.45/32/58/22 on 100% FiO2
- Diagnosis??

Diagnostic Criteria for Acute Respiratory Distress Syndrome (ARDS):

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Timings</td>
<td>Acute Onset</td>
<td>Within 1 week of known clinical insult or new worsening respiratory symptoms</td>
<td>Within 1 week of known clinical insult or new worsening respiratory symptoms</td>
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<tr>
<td>Oxygenation</td>
<td>P/F ≤ 200</td>
<td>P/F ≤ 200</td>
<td>P/F ≤ 200</td>
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<tr>
<td></td>
<td>Mild: F/F &gt; 300</td>
<td>Mild: F/F &gt; 300</td>
<td>Mild: F/F &gt; 300</td>
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<td></td>
<td>Moderate: F/F &gt; 200</td>
<td>Moderate: F/F &gt; 200</td>
<td>Moderate: F/F &gt; 200</td>
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<tr>
<td></td>
<td>Severe: F/F &lt; 100</td>
<td>Severe: F/F &lt; 100</td>
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<tr>
<td>Mortality</td>
<td>27%</td>
<td>27%</td>
<td>46%</td>
</tr>
<tr>
<td>PEEP Requirement</td>
<td>None</td>
<td>Minimum 5 cmH2O PEEP required by mechanical ventilation (noninvasive mechanical ventilation as OK for mild ARDS)</td>
<td>None</td>
</tr>
<tr>
<td>Chest Imaging</td>
<td>Bilateral infiltrates on CXR</td>
<td>Bilateral infiltrates, not fully explained by effusions, edema, or fluid overload on CT or US</td>
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<tr>
<td>Origin of Edema</td>
<td>PCWP ≤ 18</td>
<td>Respiratory failure not fully explained by cardiac failure or fluid overload</td>
<td>Respiratory failure not fully explained by cardiac failure or fluid overload</td>
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**The Lancet · Saturday 12 August 1967**

**ACUTE RESPIRATORY DISTRESS IN ADULTS**

David C. Angus

ASSOCIATE PROFESSOR OF SURGERY

D. Scott Shorr

M.D. Columbia

Consultant in Medicine and an Associate Professor of Surgery at the University of Colorado School of Medicine, Denver, Colorado, U.S.A.
Risk Factors for ARDS:

- Direct lung-injury
  - Pneumonia (bacterial, viral, fungal or opportunistic)
  - Aspiration of gastric contents
  - Pulmonary contusion
  - Inhalation injury
  - Near drowning

- Indirect-lung-injury
  - Sepsis (non-pulmonary source)
  - Non-thoracic trauma or hemorrhagic shock
  - Pancreatitis
  - Major burn injury
  - Drug overdose
  - Transfusion of blood products
  - Cardiopulmonary bypass
  - Reperfusion edema after lung transplantation or embolectomy

Pathophysiology

1. Direct or indirect injury to the alveolus causes alveolar macrophages to release pro-inflammatory cytokines

2. Cytokines attract neutrophils into the alveolus and interstitium, where they damage the alveolar-capillary membrane (ACM).

3. ACM integrity is lost, interstitial and alveolus fills with proteinaceous fluid, surfactant can no longer support alveolus

Pathophysiology

- Consequences of lung injury include:
  - Impaired gas exchange
  - V/Q mismatch (due to alveolar filling)
  - Increased dead space
  - Decreased compliance
    - Requiring higher pressures to deliver set tidal volume
  - Increased pulmonary arterial pressure
  - Hypoxic vasoconstriction (25% of patients with ARDS)
Next Steps.... Management:

- The patient is transferred to the ICU. Diuresis with furosemide is initiated. The following morning, the patient remains on BIPAP 12/5 with oxygen saturation of 90% on 100% FiO2 with tidal volumes ranging from 550-600 (He is 5’8” tall). ABG 7.36/44/58/24. Echocardiogram reveals preserved LV function.

- You recommend:
  A. Intubation and low tidal volume mechanical ventilation
  B. Continue non-invasive ventilation via facemask
  C. Switch to heated high-flow nasal cannula
  D. Continue non-invasive ventilation but use a Helmet mask

Evidence-Based Management of ARDS:

- Recognition of ARDS and treatment of the underlying cause
- Low Tidal Volume Mechanical Ventilation
- Use of PEEP (High vs. Low PEEP)
- Strategies to prevent Mechanical Ventilation in mild ARDS
- Prone positioning
- Fluid management in ARDS
- Controversial Therapies and Therapies to avoid

ARDS Recognition/ Treatment of underlying cause

- 10.4% of ICU admissions with ARDS
- Under recognized: 51.3% mild ARDS to 78.5% of cases of severe ARDS
- Undertreated: less than 2/3rd of patients received appropriate tidal volume ventilation

Belani et al. JAMA, 2016
• When compared to larger tidal volumes (12ml/kg), Vt of 6ml/kg of ideal body weight:
  • Decreased mortality (31% vs. 39.8% (p=0.007))
  • Increased number of ventilator free days (12 vs 10 (p=0.007))
  • Decreased extra-pulmonary organ failure

• Mortality reduction despite these patients having:
  • Worse oxygenation
  • Increased pCO2 (permissive hypercapnia)
  • Lower pH

**ARDSnetwork. NEJM 2000**

**Why does Low Tidal Volume Ventilation reduce mortality?**

ARDS affects the lung in a heterogeneous fashion

- Normal alveoli
- Injured alveoli can potentially participate in gas exchange, susceptible to damage from opening and closing
- Damaged alveoli filled with fluid, do not participate in gas exchange

Low tidal volumes prevent over distention of normal alveoli and PEEP maintains alveolar recruitment to prevent atelectotrauma (opening/closing)

Reduces further lung injury!

**What about PEEP? Is higher PEEP better?**

No difference in mortality, ventilator-free days, organ failure

No difference in outcomes

No difference in mortality but PEEP titrated to reach plateau 28-30 cm H2O decreased ventilator-free days

Improved survival among patients with mod/severe ARDS (P:F<200)
What about PEEP? Is higher PEEP better?

**NO**

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

<table>
<thead>
<tr>
<th>Study or Registry</th>
<th>High</th>
<th>Low</th>
<th>Risk Ratio</th>
<th>Risk Ratio</th>
<th>Minimum</th>
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<tbody>
<tr>
<td>Moderate to Severe ARDS (P:F &lt;200) - high PEEP was associated with increased mortality!</td>
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**Strategies to prevent mechanical ventilation in ARDS**

**High-Flow Oxygen through Nasal Cannula in Acute Hypoxemic Respiratory Failure**

- **Standard Oxygen**
  - Non-rebreather face mask of 10LPM
  - Goal sat >92%

- **High-flow Oxygen**
  - Oxygen through heated humidifier, gas flow rate 50LPM with FIO2 1.0 at initiation
  - Goal sat >92%

- **Noninvasive-ventilation**
  - Pressure-support level adjusted to tidal volume of 4-10cc/kg
  - PEEP 2-10cm H2O
  - FIO2/PEEP adjusted to goal sat >92%
  - 8hr/day for 2 calendar days (sessions of at least 1 hour)

**PRIMARY OUTCOME - INTUBATION RATE**

- **Intubation rate day 28**:
  - 38% high flow
  - 47% oxygen
  - 50% NIV

  *(P=0.18)*

- **Intubation rate day 28 for patients with P:F<200**:
  - 35% high flow
  - 53% oxygen
  - 58% NIV

  *(P=0.009)*

Kaplan–Meier Plots of the Cumulative Incidence of Intubation from Randomization to Day 28
**Secondary Outcome: Mortality Reduction with HHFNC**

![Graph showing survival probability over days with various ventilation methods.

- **Hazard Ratio:** Standard Oxygen vs. HHFNC 1.85 (0.84-4.09)
- NIV vs. HHFNC 2.55 (1.21-5.35)

*Caveat* - Not all pts had ARDS (83% w/pneumonia)

Intubation Rate:
- Helmet: 18.2%
- Nasal Mask: 61.5%

Mortality (90D):
- Helmet: 34%
- Nasal Mask: 56.4%

Patel et al. JAMA 2016

**Effect of Noninvasive Ventilation Delivered by Helmet vs Face Mask on the Rate of Endotracheal Intubation in Patients With Acute Respiratory Distress Syndrome: A Randomized Clinical Trial**

- NIV failure occurred in:
  - Mild ARDS (22%)
  - Moderate ARDS (42%)
  - Severe ARDS 47%

- Hospital mortality: NIV success: 16% vs. NIV failure: 45%


**ORIGINAL ARTICLE**

Noninvasive Ventilation of Patients with Acute Respiratory Distress Syndrome

Insights from the LUNG SAFE Study

- NIV failure occurred in:
  - Mild ARDS (22%)
  - Moderate ARDS (42%)
  - Severe ARDS 47%

- Hospital mortality: NIV success: 16% vs. NIV failure: 45%

- In propensity matched analysis, ICU mortality was higher in NIV than invasively ventilated patients with P:F <150
Next Steps.... Management:

• The patient is transferred to the ICU. Diuresis with furosemide is initiated. The following morning, the patient remains on BIPAP 12/5 with oxygen saturation of 90% on 100% FiO2 with tidal volumes ranging from 550-600 (He is 5'8" tall). ABG 7.36/44/58/24. Echocardiogram reveals preserved LV function.

• You recommend:
  A. Intubation and low tidal volume mechanical ventilation
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Explanations

A. Intubation and low tidal volume mechanical ventilation
   This patient has severe ARDS and is failing non-invasive ventilation, the evidence-based strategy of greatest benefit is mechanical ventilation with lung protective strategy

B. Continue non-invasive ventilation via facemask
   His current tidal volumes are >8cc/kg ideal body weight and therefore he is at risk for lung injury with ongoing use of non-invasive via facemask which as suggested by the FLORAL study is harmful (NEJM 2015). Furthermore, per the recent LUNG SAFE study patients with severe ARDS who are managed with NIV have higher mortality.

C. Switch to heated high-flow nasal cannula
   Although HHFNC therapy reduces intubation rates, there is limited data with regards to efficacy in severe ARDS. Clinically, his disease is likely to severe to benefit but a monitored trial would not be unwarranted.

D. Continue non-invasive ventilation but use a Helmet mask
   Although Helmet mask reduces intubation in ARDS compared to nasal face mask, this was shown in a single-center study and should be repeated in a multicenter study prior to adoption.

Other Therapeutic Strategies:

The patient is intubated and mechanically ventilated. While receiving FiO2 of 0.7, his pH is 7.32, PCO2 is 48mmHg and PO2 is 60mmHg. His tidal volume is 6ml/kg, PEEP is 16cm H2O and plateau pressure is 27cm H2O. You are considering placing the patient in a prone position. The most recent trial would suggest that to improve outcomes, this maneuver will require:

A. A reduction in PEEP
B. A regimen that requires at least 16 h/d in the prone position
C. A regimen that requires continuous rotation
D. A 25% increase in set minute ventilation
Physiologic Benefits of Prone Positioning

• Improves V/Q matching
  • Weight of heart is off posterior lung regions \(\rightarrow\) less alveolar collapse but dorsal lung perfusion is maintained
• Improves compliance of chest wall which improves distribution of tidal volume and PEEP

Other Therapeutic Strategies:

The patient is intubated and mechanically ventilated. While receiving FiO2 of 0.7, his pH is 7.32, PCO2 is 48mmHg and PO2 is 60mmHg. His tidal volume is 6ml/kg, PEEP is 16cm H2O and plateau pressure is 27cm H2O. You are considering placing the patient in a prone position. The most recent trial would suggest that to improve outcomes, this maneuver will require:

A. A reduction in PEEP  
B. A regimen that requires at least 16 h/d in the prone position  
C. A regimen that requires continuous rotation  
D. A 25% increase in set minute ventilation
Explanation

A. A reduction in PEEP
   Applied PEEP does not change based on position

B. A regimen that requires at lease 16 h/d in the prone position
   One potential explanation for the mortality benefit seen in the PROSEVA trial was the extended duration in the prone position which was longer than previous trials

C. A regimen that requires continuous rotation
   The RCT that demonstrated benefit to proning compared the prone position to supine and elaborate beds (rot prone) actually place patients in multiple degrees of relative proning and have not been demonstrated beneficial

D. A 25% increase in set minute ventilation
   The minute ventilation does not need to change based on position

Fluid Management- Fluid and Catheter Treatment Trial (FACTT):

• Conservative (CVP<4) as compared to liberal (CVP 10-14) fluid management strategy

• reduced mechanical ventilation time and ICU days without increasing non-pulmonary organ failures


ACURASYS: Neuromuscular blockers in early ARDS

• ARDS with P:F<150, randomized to 48 hours of continuous neuromuscular blockade with cisatracurium
• Reduction in 90 day mortality (31.6% vs 40.7%; P=0.04, NNT=11)
• Increased ICU free days (47 vs 39 (p=0.03)

Papazian, L, et al. NEJM 2010;
Therapies of Limited Benefit and/or Potential Harm

- Corticosteroids
  - No benefit, associated with increased mortality when initiated >2 weeks after the onset of ARDS (NEJM, 2006)
- High-Frequency Oscillation in Early Acute Respiratory Distress Syndrome
  - OSCAR study group: no difference
  - OSCILLATE study group: early HFOV associated with increased mortality
- Pulmonary vasodilators (epoprostenol or inhaled nitrous oxide)
  - Improve oxygenation, no effect on mortality

Current Care and Potential for Improvement, Lessons from LUNG SAFE:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean arterial pressure</th>
<th>Mean arterial oxygen content</th>
<th>Mean arterial pH</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recruitment</td>
<td>3.0 (0.2)</td>
<td>55.0 (0.2)</td>
<td>7.38 (0.1)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Prone positioning</td>
<td>5.5 (0.5)</td>
<td>65.5 (0.5)</td>
<td>7.21 (0.1)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>LUMO</td>
<td>2.0 (0.2)</td>
<td>50.0 (0.2)</td>
<td>7.27 (0.1)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Inhaled vasodilators</td>
<td>6.0 (1.6)</td>
<td>65.0 (1.6)</td>
<td>7.07 (1.6)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>HFOV</td>
<td>2.0 (0.2)</td>
<td>55.0 (0.2)</td>
<td>7.25 (0.1)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Mean arterial pressure</td>
<td>2.0 (1.6)</td>
<td>50.0 (1.6)</td>
<td>7.20 (1.6)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>P value</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
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Summary:

- Early recognition of ARDS is imperative as well as identification and treatment of factor driving lung injury
- Low tidal volume ventilation remains the most important intervention
- Heated high-flow nasal cannula and perhaps Helmet ventilation may be beneficial in early ARDS
- Use caution when using non-invasive ventilation for ARDS as there is no clear benefit and potential harm
- Prone positioning and paralytics are beneficial therapies to consider early
- Avoid corticosteroids and HFOV!
References:


• Higher vs Lower Positional End-Expiratory Pressure in Patients With Acute Lung Injury and Acute Respiratory Distress Syndrome | Critical Care Medicine | The JAMA Network.