ARDS: AN UPDATE
6th March 2017
A. Hakeem Al Hashim, MD, FRCP
SQUH
Case

- 30M, previously healthy
- Hx: 1 week dry cough
- Gradually worsening SOB
- No travel Hx

BP 130/70, HR 100/min
Temp 39C, O2 sat 84%

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.29</td>
</tr>
<tr>
<td>pCO2</td>
<td>35</td>
</tr>
<tr>
<td>pO2</td>
<td>50</td>
</tr>
<tr>
<td>HCO3</td>
<td>22</td>
</tr>
<tr>
<td>O2 sat</td>
<td>84%</td>
</tr>
</tbody>
</table>

- Acute onset
- B/L lung infiltrate
- PaO2/FiO2 : 50/1.0 = 50
## Berlin Definition of ARDS

<table>
<thead>
<tr>
<th></th>
<th><strong>Acute Onset</strong></th>
<th>within 1 week of clinical insult</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td><strong>Chest imaging</strong></td>
<td>B/L opacities not fully explained by collapse, effusion or nodule</td>
</tr>
<tr>
<td>3</td>
<td><strong>Edema origin</strong></td>
<td>Respiratory failure not fully explained by pulmonary edema or fluid overload</td>
</tr>
</tbody>
</table>

### Oxygenation

- **Mild**: $<300$
- **Moderate**: 200-300
- **Severe**: $<100$ (PEEP $\geq 5$ cmH2O)
30M w b/l pneumonia, ARDS

- 30M, previously healthy
- Hx: 1 week dry cough
- Gradually worsening SOB
- No travel Hx
- WBC 2.9, normal renal and LFT
- Echo: good LV & RV function
Important Management points
Overall treatment strategy

<table>
<thead>
<tr>
<th>Increase oxygen delivery</th>
<th>Decrease oxygen consumption</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduce shunt fraction</td>
<td>Avoid further injury</td>
</tr>
</tbody>
</table>
High-Flow Oxygen through Nasal Cannula in Acute Hypoxemic Respiratory Failure
• **Inclusion criteria (all 4)**
  1) RR ≥ 25/min
  2) PaO2/FiO₂ ≤ 300 mmHg (on high flow O₂)
  3) PaCO₂ < 45 mmHg
  4) Absence of chronic respiratory failure

• **Exclusion criteria**
  • PaCO₂ > 45 mmHg
  • Exacerbation of asthma or chronic respiratory failure
  • Cardiogenic pulmonary edema
  • Severe neutropenia
  • Hemodynamic instability
  • GCS ≤ 12
A. Overall Population

Cumulative Incidence of Intubation

- Noninvasive ventilation
- Standard oxygen
- High-flow oxygen

Days since Enrollment

P = 0.17 by log-rank test

B. Patients with a PaO2/FiO2 ≤ 200 mm Hg

Cumulative Incidence of Intubation

- Noninvasive ventilation
- Standard oxygen
- High-flow oxygen

PaO2/FiO2 < 200

P = 0.009 by log-rank test
30M w b/l pneumonia, ARDS

- 30M, previously healthy
- Hx: 1 week dry cough
- Gradually worsening SOB
- No travel Hx
- BP 170/90, HR 100, temp 38
- WBC 2.9, normal renal and LFT
- Started on NIV (FiO₂: 100%)
- Echo: good LV & RV function

Intubated and mechanically ventilated
### Overall treatment strategy

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<tr>
<th>Increase oxygen delivery</th>
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<td>Reduce shunt fraction</td>
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**Lung protective ventilation**
Question 2

Which of the following represent the mechanisms utilized to achieve open lung ventilation to reduce ventilator induced injury to the lung?

a) Low tidal volume ventilation and PEEP
b) Permissive hypercapnia and PEEP
c) Low VT ventilation and respiratory drive suppression
d) Inverse ratio ventilation and PEEP
Which of the following represent the mechanisms utilized to achieve open lung ventilation to reduce ventilator induced injury to the lung?

a) Low tidal volume ventilation and PEEP
b) Permissive hypercapnia and PEEP
c) Low VT ventilation and respiratory drive suppression
d) Inverse ratio ventilation and PEEP
Why should we use low tidal volume?
Why lung protective ventilation?

<table>
<thead>
<tr>
<th>Opening Pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflated</td>
</tr>
<tr>
<td>Small Airway</td>
</tr>
<tr>
<td>Collapse</td>
</tr>
<tr>
<td>Alveolar Collapse</td>
</tr>
<tr>
<td>(Reabsorption)</td>
</tr>
<tr>
<td>Consolidation</td>
</tr>
</tbody>
</table>
Open lung ventilation occurs between the lower and upper inflection points

- **Prevents:**
  - Collapse-Reopening
  - Over-distension

**PEEP & low V\textsubscript{T}**
**Iatrogenic lung injury**

- High inflation pressure → Barotrauma
- Over distension → Volutrauma
- Repetitive opening & closing of alveoli
  - atelectrauma
  - cytokine release → Biotrauma
Barotrauma / Volumutrauma

Zone of Atelectrauma

Zone of Volutrauma

Upper inflection point

Lower inflection point
How to choose Optimal PEEP at bedside?

1) Imaging: eg. CT
2) Bedside physiology: eg. Pressure volume curves

3) Gas Exchange:
   - PEEP/FiO2 table
   - Adjusting Plateau P, PEEP, FiO2
   - Adequate blood gases (not maximum)
Lung Protective Ventilation

1) Tidal volume 4-6 mL/kg
2) Plateau pressure < 30 cmH2O
3) High PEEP

**Table 4: Main Outcome Variables.**

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>GROUP RECEIVING LOWER TIDAL VOLUMES</th>
<th>GROUP RECEIVING TRADITIONAL TIDAL VOLUMES</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death before discharge home and breathing without assistance (%)</td>
<td>31.0</td>
<td>39.8</td>
<td>0.007</td>
</tr>
<tr>
<td>Breathing without assistance by day 28 (%)</td>
<td>65.7</td>
<td>55.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No. of ventilator free days</td>
<td>12±11</td>
<td>10±11</td>
<td>0.007</td>
</tr>
</tbody>
</table>

NEJM 342, 18: 1301-1308
Timing of Low Tidal Volume Ventilation and Intensive Care Unit Mortality in Acute Respiratory Distress Syndrome
A Prospective Cohort Study

Dale M. Needham¹,²,³,⁴ Ting Yang⁴, Victor D. Dinglas¹,², Pedro A. Mendez-Tellez¹,⁵ Carl Shanholz⁶, Jonathan E. Sevransky⁷, Roy G. Brower², Peter J. Pronovost¹,⁴,⁵, and Elizabeth Colantuoni¹,⁸

Am J Respir Crit Care Med Vol 191, Iss 2, pp 177–185, Jan 15, 2015

![Graphs showing survival probability and time from ARDS onset for patients with first tidal volume ≤ 6.5 ml/kg PBW and > 6.5 ml/kg PBW.](image)
Timing of Low tidal volume

• Prospective study of 520 patients with ARDS (medical, surgical, trauma)
• Compared with 6 mL/kg, absolute ICU mortality was higher by:
  7.2% at 10 mL/kg
  2.7% at 8 mL/kg
• Increasing the initial Vt by 1 mL/kg was associated with:
  23% rise in mortality risk

OXYGENATION GOAL: PaO₂ 55-80 mmHg or SpO₂ 88-95%
Use a minimum PEEP of 5 cm H₂O. Consider use of incremental FiO₂/PEEP combinations such as shown below (not required) to achieve goal.

<table>
<thead>
<tr>
<th>Lower PEEP</th>
<th>Higher FiO₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>FiO₂</td>
<td>0.3 0.4 0.4 0.5 0.5 0.6 0.7 0.7</td>
</tr>
<tr>
<td>PEEP</td>
<td>5 5 8 8 10 10 10 12</td>
</tr>
</tbody>
</table>

| FiO₂       | 0.7 0.8 0.9 0.9 0.9 1.0 |
| PEEP       | 14 14 14 16 18 18-24 |

<table>
<thead>
<tr>
<th>Higher PEEP</th>
<th>Lower FiO₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>FiO₂</td>
<td>0.3 0.3 0.3 0.3 0.3 0.4 0.4 0.5</td>
</tr>
<tr>
<td>PEEP</td>
<td>5 8 10 12 14 14 16 16</td>
</tr>
</tbody>
</table>

| FiO₂       | 0.5 0.5-0.8 0.8 0.9 1.0 1.0 |
| PEEP       | 18 20 22 22 22 24 |
Recruitable lungs
High VS Low PEEP

In-hospital time to death

Patients with ARDS

HR, 0.85 (95% CI, 0.73-0.99); P = .03

Patients without ARDS

HR, 1.32 (95% CI, 0.87-2.00); P = .20

No. at risk
Higher PEEP 949  760  693  666  183  158  148  144
Lower PEEP  939  723  649  619  219  196  186  183

JAMA. 2010;303(9):865-873.
doi:10.1001/jama.2010.218
Lung Protective Ventilation

- Low tidal volume 4-6 mL/kg (IBW)
- High PEEP
- Limit Pplat ≤ 30 cmH2O
Case: 30M w B/L pneumonia

- **Intubated, ventilated:**
  - Mode: PC 14/10, FiO2: 80%, sat 84% RR 12/min
  - Target VT 4-6cc/kg (weight 60 kg)
  - PPlt max: 30 cmH2O

- **Current parameters:**
  - VT: 700mL
  - RR 20/min

What is the next step?
Question: What is the next step?

a) Induction of a coma using pentobarbital
b) Sustained inflation with CPAP 40 cm H$_2$O for 40 seconds
c) Prone positioning maintained for 6 to 12 hours
d) Neuromuscular blockade maintained for 48 hours
Question: What is the next step?

a) Induction of a coma using pentobarbital
b) Sustained inflation with CPAP 40 cm H\textsubscript{2}O for 40 seconds
c) Prone positioning maintained for 6 to 12 hours
d) Neuromuscular blockade maintained for 48 hours
Neuromuscular Blockers in Early Acute Respiratory Distress Syndrome

Laurent Papazian, M.D., Ph.D., Jean-Marie Forel, M.D., Arnaud Gacouin, M.D., Christine Penot-Ragon, Pharm.D., Gilles Perrin, M.D., Anderson Loundou, Ph.D., Samir Jaber, M.D., Ph.D., Jean-Michel Arnal, M.D., Didier Perez, M.D., Jean-Marie Seghboyan, M.D., Jean-Michel Constantin, M.D., Ph.D., Pierre Courant, M.D., Jean-Yves Lefrant, M.D., Ph.D., Claude Guérin, M.D., Ph.D., Gwenaël Prat, M.D., Sophie Morange, M.D., and Antoine Roch, M.D., Ph.D., for the ACURASYS Study Investigators*
Figure 2. Probability of Survival through Day 90, According to Study Group.
Neuromuscular blocking agents in acute respiratory distress syndrome: a systematic review and meta-analysis of randomized controlled trials

Waleed Alhazzani1*, Mohamed Alshahrani2, Roman Jaeschke1,3, Jean Marie Forel4, Laurent Papazian4, Jonathan Sevransky5 and Maureen O Meade1,3
Mortality @ 28 days

ICU mortality

Hospital Mortality (90 days)
Case

• 30 M, with severe ARDS
• Intubated, ventilated with lung protective ventilation, paralyzed
• On high settings (PEEP 18, Fio2: 100%)
• ABG: pH 7.22, pCO2 58, pO2 50, O2 sat 82%

What is your next step?
Rx of refractory hypoxemia

1) Recruitment
2) APRV (airway pressure release ventilation)
3) HFO (high frequency oscillation)
4) NO (nitric oxide)
5) Proning
6) ECLS (extracorporeal life support)
Rx of refractory hypoxemia

1) Recruitment

2) APRV (airway pressure release ventilation)

3) HFO (high frequency oscillation)

4) NO (nitric oxide)

5) Proning

6) ECLS (extracorporeal life support)
Recruitment maneuvers

Deep sedation and paralysis

FiO$_2$ 100%
Pressure Limit 60 cmH$_2$O
PEEP limit 40 cmH$_2$O
Trigger sensitivity to prevent auto-triggering

PC 20
RR 15
I:E 1:1

Repeat recruitment maneuver

Set PEEP 2 cm above noted value

Detrimental PEEP by 1 cm Till PaO$_2$ falls

PEEP 25 x 10 breaths
PEEP 20

PEEP 30 x 10 breaths
PEEP 20

PEEP 35 x 10 breaths
PEEP 20

PEEP 20
Rx of refractory hypoxemia

1) Recruitment
2) APRV (airway pressure release ventilation)
3) HFO (high frequency oscillation)
4) NO (nitric oxide)
5) Proning
6) ECLS (extracorporeal life support)
Airway pressure release ventilation with spontaneous breathing

- **P high**: Mean airway pressure
- **P low**: **T low**
- **T high**: Time (seconds)
Rx of refractory hypoxemia

1) Recruitment
2) APRV (airway pressure release ventilation)
3) HFO (high frequency oscillation)
4) NO (nitric oxide)
5) Proning
6) ECLS (extracorporeal life support)
High-Frequency Oscillation for Acute Respiratory Distress Syndrome

HFO

≈ 800 pts

No. at Risk
Conventional ventilation
HFOV

397 351 312 281 259 243 236

398 349 311 280 253 241 233

HFO: Oscil

High-Frequency Oscillation for Acute Respiratory Distress Syndrome

P=0.004 by log-rank test

Days since Randomization

No. at Risk

<table>
<thead>
<tr>
<th></th>
<th>HFOV</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>275</td>
<td>273</td>
</tr>
<tr>
<td>15</td>
<td>169</td>
<td>181</td>
</tr>
<tr>
<td>30</td>
<td>98</td>
<td>92</td>
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<tr>
<td>45</td>
<td>54</td>
<td>54</td>
</tr>
<tr>
<td>60</td>
<td>26</td>
<td>39</td>
</tr>
</tbody>
</table>

Rx of refractory hypoxemia

1) Recruitment
2) APRV (airway pressure release ventilation)
3) HFO (high frequency oscillation)
4) NO (nitric oxide)
5) Proning
6) ECLS (extracorporeal life support)
Prone positioning

Figure 2. Cumulative Probability of Patient Survival After Randomization

No. at Risk
Supine Position 378 314 273 257 244 234 226 220 219 218
Prone Position 413 346 302 279 258 246 242 237 234 234

Log-Rank P = .84
Prone Positioning in Severe Acute Respiratory Distress Syndrome

Claude Guérin, M.D., Ph.D., Jean Reignier, M.D., Ph.D., Jean-Christophe Richard, M.D., Ph.D., Pascal Beuret, M.D., Arnaud Gacouin, M.D., Thierry Boulin, M.D., Emmanuelle Mercier, M.D., Michel Badet, M.D., Alain Mercat, M.D., Ph.D., Olivier Baudin, M.D., Marc Clavel, M.D., Delphine Chatellier, M.D., Samir Jaber, M.D., Ph.D., Sylvène Rosselli, M.D., Jordi Mancebo, M.D., Ph.D., Michel Sirodot, M.D., Gilles Hilbert, M.D., Ph.D., Christian Bengler, M.D., Jack Richercoeur, M.D., Marc Gainnier, M.D., Ph.D., Frédérique Bayle, M.D., Gael Bourdin, M.D., Véronique Leray, M.D., Raphaëlle Girard, M.D., Loredana Baboi, Ph.D., and Louis Ayzac, M.D., for the PROSEVA Study Group*
Proning

- **Inclusion criteria**
  - PO2/FiO2: < 150 mmHg
    \[ \text{FiO2} > 0.6 \text{ & PEEP} > 5 \]
  - < 36 hours on ventilator
  - 229 pt supine
  - 237 pt prone

- **Proning**
  - Prone within 1 hour of randomization
  - For 16 consecutive hours
Proning

Cumulative Probability of Survival

No. at Risk
Prone group  237  202  191  186  182
Supine group 229  163  150  139  136

P < 0.001

Days
Prone positioning

• Improves oxygenation
• Mortality benefit more in moderate & severe groups if applied early

• Complications:
  - Need for increase sedation
  - Muscle paralysis
  - Hemodynamic instability
  - Device displacement
Rx of refractory hypoxemia

1) Recruitment
2) APRV (airway pressure release ventilation)
3) HFO (high frequency oscillation)
4) NO (nitric oxide)
5) Proning
6) ECLS (extracorporeal life support)
ECMO

Veno-venous ECLS with a double lumen cannula
Extracorporeal Membrane Oxygenation (ECMO)

Survival:
- ECMO 63%
- Conventional 47%

Only 75% transferred to ECMO centre received ECMO

Peel GJ et al., Lancet 2009
Contraindications

- Unlikely to be reversed in 10-14 days
- Multi-organ failure
- Severe Irreversible brain damage
- Significant CPR (>30mins) pre-ECMO
- Uncontrolled metabolic acidosis
- Terminal disease/malignancy
- Chronic lung disease
- Chronic myocardial dysfunction
- Immunosuppression
ECMO complications

- Anticoagulation: Clotting, Bleeding
- Vessel: bleeding, infection, ischemia, dislodgement of cannula
- Air emboli
- Volume management
- Sepsis
- Renal failure
- Decubitus ulcer
- Neurological damage

Refer to ECMO center early
Conservative fluid management

Conservative fluid group had better:
- Lung Function
- More ventilator free days
- Less ICU stay

Once stable, ARDS patients should be kept on conservative fluid balance
Transfusion

- Prospective cohort study
  - PRBC → develop ARDS (OR 1.52)
  - PRBC → dose dependent ↑mortality

- RCT of liberal vs restrictive transfusion
  - Restrictive at least as effective
  - Restrictive improved hospital mortality
  - Restrictive improved mortality in less ill patients

Crit Care Med 2005 Vol. 33, No. 6
Not recommended

- **Surfactant**: Better oxygenation, no outcome benefit
- **Anti-oxidant therapy** (Diet): Mixed data
- **Salbutamol/albuterol**: no proven benefit
- **Statins, NSAIDs, NAC, Glutamine, APC**: no benefit
- **iNO**: no proven benefit (expensive)
- **Steroids**: Controversial (late: cause more harm)
Corticosteroids: meta-analysis

Tang, CCM, 2009 Vol. 37, No. 5
<table>
<thead>
<tr>
<th><strong>Reduce Shunt Fraction</strong></th>
<th><strong>Decrease O2 Consumption</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>✓ Tidal volumes and PEEP</td>
<td>➔ Mechanical Ventilation</td>
</tr>
<tr>
<td>➔ Negative fluid balance</td>
<td>➔ Paralysis</td>
</tr>
</tbody>
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<tr>
<th><strong>Increase Oxygen Delivery</strong></th>
<th><strong>Avoid further injury</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Adequate cardiac filling, Adequate hemoglobin, Inotropic agents, ECMO</td>
<td>✓ Lung protective ventilation ✓ Proning</td>
</tr>
</tbody>
</table>
30M with pneumonia & severe ARDS

- Lung protective ventilation
- Fully sedated and paralyzed x 5 days
- Prone x 3 days
- Methylprednisolone infusion
- +H1N1
- Extubated successfully in 1 week
ARDS management

Lung Protective ventilation: Low VT, Max PPlt < 30

- **Low PEEP**
  - NIV
  - ECMO
  - Prone

- **High PEEP**
  - ECMO
  - Prone

- **Moderate**
  - ECMO
  - Prone

- **Severe**
  - ECMO
  - Prone

**PaO₂/FiO₂**

- **Mild**
  - 300 (40)
  - 250 (33.3)
  - 200 (26.7)

- **Moderate**
  - 150 (20)

- **Severe**
  - 100 (13.3)
  - 50 (6.7)
Questions

ah.alhashim@gmail.com