ARDS & Rescue Therapies

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Objectives

• Learn to recognize the Acute Respiratory Distress Syndrome “ARDS”
• Understand the pathogenesis of ARDS
• Review key components of the ARDS.net study
• Understand how to properly ventilate ARDS patients
• Discuss some novel therapeutic approaches to treatment
HPI

- A 54 year-old AAM with hx of chronic pancreatitis 2/2 ETOH s/p multiple procedures was brought to Wishard ED by his daughter. Pt was noted to be hypoxemic 64% on RA. Pt seen in ED with cough and hypoglycemia days prior but suddenly worse again this am. Had subjective fever, scant sputum, and abdominal pain c/w pancreatitis.
PMHx

1. Chronic Pancreatitis secondary to alcoholism s/p Whipple
2. DM secondary to chronic pancreatitis
3. h/o Alcoholism
4. h/o Duodenal Ulcers
5. HTN
6. Depression
7. Anxiety
8. Chronic Pain Syndrome
Meds

1. insulin NPH 14 units AM, 10 units PM
2. insulin R 3 units with each meal
3. gabapentin 300mg TID
4. sertraline 200mg daily
5. valsartan 80mg daily
6. pancrealipase 4 pills with meals
7. omeprazole 20mg daily
PSHx

1. Whipple
2. Puestow (lateral pancreatojejunostomy)
3. Roux-enY Revision and repair (last repair done 12/2008)
4. Recent exp lap and lysis of adhesions with resection of pancreaticojejunostomy with removal of intraductal pancreatic stones 12/2008
Additional hx

• ALL: NKDA
• FAM: DM2 and HTN in father and mother
• SOC:
  – Denies any current alcohol (quit 16 yrs ago), heavy in the past, No Tobacco or IV drug use
    Was a chef but currently unemployed
    lives with wife and children
  – No recent travel
  – No sick contacts
  – No history of any STD’s
  – No known TB exposures, prison, homeless, etc…
Exam

97.0 108-125 20-22 111-158/66-103  SpO2 64% on presentation, then 97% on 50% VM

GEN: moderate distress, AAOX3
HEENT: pale conjunctiva, no scleral icterus, PERRLA, EOMI, no JVD, no carotid bruit, no LAD
CV: sinus tachycardia, no m/r/g
PULM: moderate resp distress on venturi mask with tachypnea, using accessory muscles, some costal retractions, crackles at bases
ABD: midline incision scar, tender LUQ, BSx4, no HSM
EXT: WWP, no c/c/e
SKIN: Skin graft L arm, no rash
Admission Labs

141 101 13  
------------------
< 55

3.2 30 0.9  

11.4

13.8 >-----< 491

N 84%

ABG: 7.48/39/41 on RA
ABG: 7.47/40/82 on 100% NRB

UA: WNL  TROP: 0.32 → 0.13  EKG: STach
EKG
CXR 3 days prior (ED hypoglycemia)
Admission CXR
Admission CT
Based on information presented to this point does this patient meet criteria to be diagnosed with ARDS?

What is the potential etiology?
“Adult Respiratory Distress Syndrome”

- “The acute onset of severe respiratory distress and cyanosis that was refractory to oxygen therapy and associated with diffuse CXR abnormality and decreased lung compliance.”

– Asbaugh, Bigelow, Petty  Lancet 1967
The ARDS Definition Task Force: The Draft Berlin Definition, ESICM 24th Annual Congress Berlin, October 2011

- P:F 201-300 w/ PEEP > 5 = MILD
- P:F 100-200 w/ PEEP > 5 = MODERATE
- P:F <100 w/ PEEP > 10 = SEVERE
- Bilateral Infiltrates
- Resp failure not from cardiac overload
ARDS

- PaO2:FiO2 = 82:100
- Acute onset
- ? R/O CHF
  - Echo
  - BNP
  - CVP
  - Swan
ECHO

- Cardiac Echo:
  - Mild concentric left ventricular hypertrophy
  - Normal global left ventricular systolic function
  - No regional wall motion abnormalities
- Otherwise all chambers are normal in size and function.
  - No obvious valvular abnormality
  - No pericardial effusion
- EF: 69%
- BNP = 126
### ARDS: Causes

**Table 2. CLINICAL DISORDERS ASSOCIATED WITH ACUTE RESPIRATORY DISTRESS SYNDROME**

<table>
<thead>
<tr>
<th>Direct Lung Injury</th>
<th>Indirect Lung Injury*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspiration of gastric contents</td>
<td>Severe sepsis</td>
</tr>
<tr>
<td>Severe thoracic trauma</td>
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<tr>
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<tr>
<td><em>Pneumocystis carinii</em></td>
<td>Drug overdose</td>
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<tr>
<td>Toxic gas (smoke) inhalation</td>
<td>Reperfusion injury</td>
</tr>
<tr>
<td>Near-drowning</td>
<td>Post-lung transplantation</td>
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<td>Post-cardiopulmonary bypass</td>
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*Caused by activation of an acute, systemic inflammatory response with hematogenous delivery of inflammatory mediators to the lungs.*
# ARDS: Causes

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*Caused by activation of an acute, systemic inflammatory response with hematogenous delivery of inflammatory mediators to the lungs.*
Pathogenesis

- Activation of inflammatory mediators and cellular components resulting in damage to capillary endothelial and alveolar epithelial cells
- Increased permeability of alveolar capillary membrane
- Influx of protein rich edema fluid and inflammatory cells into air spaces
- Dysfunction of surfactant
Mortality

• Up to 50% for patients diagnosed with ARDS!
Clinical course

Pt started on ceftriaxone and azithromycin
Became increasingly hypoxic and tachypneic, desat’s on 100% NRB.

Transferred to the ICU….

ABG: 7.47/43/65 on 100% NRB
Day #2

- INR 1.2  Albumin 3.1  T. Bili 1.0  AST 26  ALT 24  Alk Phos 105  Tot Prot 6.6
- Mag 2.1  Phos 1.9
- HIV: Negative
- Blood Cultures: No Growth at 24 hours
- UDS: Negative
- Lipase 190
- ESR 109
- CRP 26.40
Do you diurese?

- What is the optimum fluid management strategy in ARDS?
When in doubt…dry em’ out

• It’s a FACTT!
• ARDS.net 2005
• Conservative fluid management was associated with improved lung function and shortened the duration of mechanical ventilation and intensive care.
• Hypotensive pts on pressors excluded
  — (NEJM June 15, 2006; Vol 354, No. 24, pp 2564-75)
CXR day #2
Day #3

- **Day 3 Plan:** Considering intubation for Bronch and BAL.
- 94% on 100% NRB
- Pt does not tolerate NIPPV
- Labs: Creatinine bumps to 2.2. Prerenal secondary to diuresis.
- CVP’s 3-8
Day #4

- **Day 4:** Pt became tachypnic and O2 saturation dropped to 80% on 100% NRB
- Intubated and started on mechanical ventilation
- What considerations do you need to make in ventilating this patient?
True or False?

• In the ARDS.net study patients were placed on mechanical ventilation with tidal volumes of 6ml/kg of actual body weight ("low tidal volume ventilation")
True or false? -- FALSE

- Predicted body weight was used.
- The lungs don’t get fat!

Ventilation with Lower Tidal Volumes as Compared with Traditional Tidal Volumes for Acute Lung Injury and the Acute Respiratory Distress Syndrome
ARDSnet protocol

Calculated predicted body weight (pbw)
  male: 50+2.3[height(inches)-60]
  female: 45.5+2.3[height(inches)-60]

Mode: Volume assist-control, tidal volume (6ml/kg pbw),
  adjust rate to optimize pH, higher peeps….

Plateau press <30cm H2O (end inspiratory pressure)

FiO2/PEEP combination to achieve oxygenation goal
### ARDS Network Study

<table>
<thead>
<tr>
<th>Parameter</th>
<th>6ml/kg</th>
<th>12ml/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>PaCO₂</td>
<td>43 ± 12</td>
<td>36 ± 9</td>
</tr>
<tr>
<td>Respiratory rate</td>
<td>30 ± 7</td>
<td>17 ± 7</td>
</tr>
<tr>
<td>PaO₂/F /FIO₂</td>
<td>160 ± 68</td>
<td>177 ± 81</td>
</tr>
<tr>
<td>Plateau pressure</td>
<td>25 ± 6</td>
<td>33 ± 8</td>
</tr>
<tr>
<td>PEEP</td>
<td>9.2 ± 3.6</td>
<td>8.6 ± 4.2</td>
</tr>
<tr>
<td>Mortality</td>
<td>31%</td>
<td>40% (p = 0.007)</td>
</tr>
</tbody>
</table>
ARDS.net
How to select PEEP

- PEEP/FiO$_2$ relationship to maintain adequate PaO$_2$/SpO$_2$
- FiO2/PEEP combs to achieve oxygenation goals

<table>
<thead>
<tr>
<th>FiO$_2$</th>
<th>0.3</th>
<th>0.4</th>
<th>0.4</th>
<th>0.5</th>
<th>0.5</th>
<th>0.6</th>
<th>0.7</th>
<th>0.7</th>
<th>0.7</th>
<th>0.8</th>
<th>0.9</th>
<th>0.9</th>
<th>0.9</th>
<th>1.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEEP</td>
<td>5</td>
<td>5</td>
<td>8</td>
<td>8</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>12</td>
<td>14</td>
<td>14</td>
<td>14</td>
<td>16</td>
<td>18</td>
<td>20-24</td>
</tr>
</tbody>
</table>
High PEEP or Low PEEP?

• ARDS network study = **ALVEOLI**
• 549 patients with ARDS.net ventilation
• Mean PEEP values were 13 vs 8 in two groups
• No significant outcome benefits seen
• ? Could we be overdistending the “good” alveoli while opening the closed ones?
• ? Will esophageal pressure monitoring become the way to resolve the issue….
Esophageal pressure monitoring
(used to estimate pleural pressure)

• Transpulmonary pressure = airway pressure - pleural pressure
• The transpulmonary pressure can then be adjusted by titrating applied PEEP, since airway pressure is related to applied PEEP. Titrating applied PEEP to an end-expiratory transpulmonary pressure between 0 and 10 cmH2O may reduce cyclic alveolar collapse, while maintaining an end-inspiratory transpulmonary pressure ≤25 cmH2O may reduce alveolar overdistension
Day #4 CXR
Day #4 CXR
Day #4 -- Intubated

- BAL: No organisms. 70% PMN’s, 10% Eos, 17% Lymphs. No biopsy. Cultures pending.
- Start thinking about “rescue” therapies!

- ? Start High Dose Steroids
- ? Start paralytic
- ? Prone
- ? HFOV
- ? ECMO
Steroids for ARDS?

- If?
- When?
- How?
Steroids for ARDS?

Use of corticosteroids in acute lung injury and acute respiratory distress syndrome: A systematic review and meta-analysis*

Benjamin M. P. Tang, PhD; Jonathan C. Craig, PhD; Guy D. Eslick, PhD; Ian Seppelt, MBBS; Anthony S. McLean, MBBS

![Graph showing the use of corticosteroids in ARDS](image-url)
Steroids for ARDS?

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Paralytic?

• If?
• When?
• How?
Figure 2. Probability of Survival through Day 90, According to Study Group.
Day #5-6

- Paralyzed, steroids going
- CXR: Increasing Bibasilar Infiltrates
- BAL data all negative
- ARDS protocol continued w/ difficulty – given pH and pressures
- What did we do next?
Day #7

• Was it the right decision?
1000 words...

Supine

Prone

1. Improve V/Q matching
2. Recruit compressed lung units
3. Improve hemodynamics
1000 words…

1. Improve V/Q matching
2. Recruit compressed lung units
3. Improve hemodynamics
1. Improve V/Q matching
2. Recruit compressed lung units
3. Improve hemodynamics
To prone or not to prone?

A Multicenter Trial of Prolonged Prone Ventilation in Severe Acute Respiratory Distress Syndrome


136 patients (60 supine, 76 prone) → goal was 20 hours/day prone!

Mortality: Supine 58%, Prone 43%

![Graph showing PaO2/FiO2 and PaCO2 over time](image)

(4) hrs

*Am J Respir Crit Care Med Vol 173. pp 1233–1239, 2006*
Prone Positioning in Severe Acute Respiratory Distress Syndrome

### Table 3. Primary and Secondary Outcomes According to Study Group.*

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Supine Group (N = 229)</th>
<th>Prone Group (N = 237)</th>
<th>Hazard Ratio or Odds Ratio with the Prone Position (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality — no. (% [95% CI])</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At day 28</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not adjusted</td>
<td>75 (32.8 [26.4–38.6])</td>
<td>38 (16.0 [11.3–20.7])</td>
<td>0.39 (0.25–0.63)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Adjusted for SOFA score†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At day 90</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not adjusted</td>
<td>94 (41.0 [34.6–47.4])</td>
<td>56 (23.6 [18.2–29.0])</td>
<td>0.44 (0.29–0.67)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Adjusted for SOFA score†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Successful extubation at day 90 — no./total no. (% [95% CI])</td>
<td>145/223 (65.0 [58.7–71.3])</td>
<td>186/231 (80.5 [75.4–85.6])</td>
<td>0.45 (0.29–0.70)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
**Rock and Ro11 Protocol**

*For prone position therapy in patients with ARDS.*

**Inclusion Criteria:**
1. Invasive Ventilation for ≥ 12 hours with:
   a. PaO2:FiO2 < 150
   b. PEEP ≥ 5
   c. FiO2 of ≥ 0.6
   d. Tidal volume of about 6ml/kg/pbw or APRV mode ventilation (bivent)
2. Bilateral infiltrates on CXR
3. Hypoxemia not fully explained by cardiac failure or fluid overload
4. Attending physician approval for initiation

**Order set:** Prone Method

a. Select manual prone protocol (suggested if <100kg) or rotoprone (suggested if ≥100kg)

b. Prone process:
   i. Prone patient as soon as possible
   ii. Supinate patient at 1100 daily unless:
      1. SpO2 <90% on 100% FiO2
      2. If RN/RT discomfort then discuss with MD
      3. If initial prone occurs less than 10 hours from 11am
   iii. Re-prone patient after supination within 4 hours if:
      1. Inability to maintain SpO2 > 90% in supine position
      2. Patient continues to meet inclusion criteria after supinated ABG performed
   iv. Do not re-prone patient if PaO2:FiO2 is better in supine position on identical ventilator settings
   v. Prone procedure:
      1. Ensure endotracheal tube secured
      2. Prone patient (3 RNs, 1 RT at head of bed) via roll (maintain arms at sides)
Rotoprone

- ~$1500/day
- Difficult exam
- Pressure sores
- Line/Ett safety
- High sedation
- Obesity
What next?

- 54 year old male at hospital day #7 with severe ARDS secondary to pancreatitis who is proned on ARDS.net ventilation and is receiving empiric steroids and paralytics.
Stages of ARDS

- 1. Exudative (acute) phase - 0- 4 days
- 2. Proliferative phase - 4- 8 days
- 3. Fibrotic phase - >8 days

Is there *anything* else that can be done to prevent progression of the inflammatory cascade???
Is it too late for High Frequency Oscillatory Ventilation?
Table 1—Comparison of Published Clinical Studies Evaluating the Use of HFOV in Adult Patients With ARDS

<table>
<thead>
<tr>
<th>Study/Year</th>
<th>Study Design</th>
<th>Patients, No.</th>
<th>Baseline Characteristics</th>
<th>Mortality Rate</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fort et al\cite{25}/ 1997</td>
<td>Prospective</td>
<td>17</td>
<td>Mean age, 35 yr; PaO₂/FiO₂ ratio, 56.6; OI, 45.6; APACHE II score, 23.3</td>
<td>30-d, 53%</td>
<td>Greater number of days receiving CMV (p &lt; 0.0009) and OI &gt; 47 were associated with mortality; 3 patients (17.6%) were withdrawn from HFOV because of hypotension</td>
</tr>
<tr>
<td>Claridge et al\cite{26}/ 1999</td>
<td>Prospective</td>
<td>5</td>
<td>Trauma patients; mean age, 36.6 yr; PaO₂/FiO₂ ratio, 52.2; APACHE II score, 25.5</td>
<td>20%</td>
<td>No complications reported</td>
</tr>
<tr>
<td>Mehta et al\cite{27}/ 2001</td>
<td>Prospective</td>
<td>24</td>
<td>Mean age, 45.5 yr; PaO₂/FiO₂ ratio, 96.8; OI, 32.5; APACHE II score, 21.5</td>
<td>30-d, 66%</td>
<td>Small increases in PAOP and CVP and a small decrease in CO were documented during HFOV, with no significant change in systemic BP; two patients (8.3%) had a pneumothorax</td>
</tr>
<tr>
<td>Cartotto et al\cite{28}/ 2001</td>
<td>Retrospective</td>
<td>6</td>
<td>Burn patients; mean age, 45.5 yr; PaO₂/FiO₂ ratio, 96.8; OI, 32.5; APACHE II score, 21.5</td>
<td>30-d, 53.3%</td>
<td>No complications reported</td>
</tr>
<tr>
<td>Dendak et al\cite{29}/ 2002</td>
<td>RCT</td>
<td>16</td>
<td>Mean age, 49.5 yr; PaO₂/FiO₂ ratio, 11.2; OI, 25.2; APACHE II score, 22</td>
<td>30-d: while receiving HFOV, −57%; while receiving CMV, 52% (p = 0.102)</td>
<td>First RCT comparing HFOV to CMV; similar complication rate in both groups</td>
</tr>
<tr>
<td>Andersen et al\cite{30}/ 2002</td>
<td>Retrospective</td>
<td>16</td>
<td>Mean age, 39.2; PaO₂/FiO₂ ratio, 92; OI, 29.1; SAPS II score, 40.3</td>
<td>3-mo, 31%</td>
<td>One patient (6.9%) had a pneumothorax</td>
</tr>
<tr>
<td>Mehta et al\cite{31}/ 2003</td>
<td>Prospective</td>
<td>20</td>
<td>Mean age, 44.9 yr; PaO₂/FiO₂ ratio, 75; APACHE II score, 28.5</td>
<td>ICU, 61%</td>
<td>This study demonstrated that iNO can be used successfully as rescue therapy in patients with severe ARDS and high O₂ requirements (mean increase in PaO₂/FiO₂ ratio at 30 min, 35%); five patients (21.7%) had a pneumothorax</td>
</tr>
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<td>Davol et al\cite{32}/ 2003</td>
<td>Prospective</td>
<td>42</td>
<td>Median age, 49 yr; PaO₂/FiO₂ ratio, 94; OI, 29; APACHE II score, 28.5</td>
<td>30-d, 43%</td>
<td>One patient (2.4%) had a pneumothorax</td>
</tr>
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<td>Mehta et al\cite{33}/ 2004</td>
<td>Retrospective</td>
<td>156</td>
<td>Median age, 47.8 yr; PaO₂/FiO₂ ratio, 91; OI, 31.2; APACHE II score, 23.5</td>
<td>30-d, 62%</td>
<td>34 patients (21.9%) had a pneumothorax</td>
</tr>
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<td>Ferguson et al\cite{34}/ 2005</td>
<td>Prospective</td>
<td>25</td>
<td>Median age, 50 yr; PaO₂/FiO₂ ratio, 94; APACHE II score, 24</td>
<td>ICU, 44%</td>
<td>This pilot study demonstrated the safety and efficacy of combining early BMIs with HFOV for rapid and sustained improvements in oxygenation; 9% of patients had a chest tube inserted for haemothorax; 3.3% of BMIs were aborted because of hypotension</td>
</tr>
<tr>
<td>Papazian et al\cite{35}/ 2005</td>
<td>RCT</td>
<td>39</td>
<td>Mean age, 52 yr; PaO₂/FiO₂ ratio, 103; SOFA score, 9.5</td>
<td>ICU: supine HFOV, 38.4%; prone CV, 30.8%; prone HFOV, 23.1%</td>
<td>This randomized study compared HFOV, prone positioning, or their combination in patients with severe ARDS (12 patients in each arm); patients in the supine HFOV group had no improvement in oxygenation; 1 patient (2.5%) had naso-plugging necessitating a change of ETT</td>
</tr>
<tr>
<td>Bollen et al\cite{36}/ 2005</td>
<td>RCT</td>
<td>61</td>
<td>Mean age, 55 yr; HFOV, 37 patients; CMV, 24 patients; study prematurely stopped; OI, 42; APACHE II score, 28.5</td>
<td>30-d: with HFOV, 43%; with CMV, 39% (p = 0.59)</td>
<td>HFOV group: four patients (10.8%) had hypotension and one patient (2.7%) had an air leak; CMV group: one patient (4.3%) had hypotension and one patient (4.3%) had an air leak; baseline OI was higher in HFOV group (25 vs 18, respectively); 19% of HFOV group crossed over to CMV, and 17% of CMV group crossed over to HFOV</td>
</tr>
<tr>
<td>Paclt et al\cite{37}/ 2006</td>
<td>Prospective</td>
<td>30</td>
<td>Mean age, 55 yr; PaO₂/FiO₂ ratio, 121; SOFA score, 9.6</td>
<td>48%</td>
<td>This study showed that HFOV might be more effective in extrapulmonary forms of ARDS, compared to pulmonary forms of ARDS; complications were not reported</td>
</tr>
<tr>
<td>Finkelman et al\cite{38}/ 2006</td>
<td>Retrospective</td>
<td>14</td>
<td>Mean age, 56 yr; APACHE II score, 23; SOFA score, 11.5</td>
<td>ICU, 57%</td>
<td>HFOV was discontinued in one patient for refractory hypotension</td>
</tr>
</tbody>
</table>
3 RCT’s

11 case control

<table>
<thead>
<tr>
<th>Study Year</th>
<th>Study Design</th>
<th>Patients No</th>
<th>Baseline Characteristics</th>
<th>Mortality Rate</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1997</td>
<td>Prospective</td>
<td>17</td>
<td>Mean age, 35 yr; (P_{O_2}/FIO_2) ratio, 68.6; OI, 45.6; APACHE II score, 23.3</td>
<td>30-4, 53%</td>
<td>Greater number of days receiving CMV (p &lt; 0.009) and OI &gt; 47 were associated with mortality; 3 patients (17.6%) were withdrawn from HFOV because of hypotension</td>
</tr>
<tr>
<td>1999</td>
<td>Prospective</td>
<td>5</td>
<td>Trauma patients; mean age, 36.6 yr; (P_{O_2}/FIO_2) ratio, 52.2; APACHE II score, 25.5</td>
<td>20%</td>
<td>No complications reported</td>
</tr>
<tr>
<td>2001</td>
<td>Prospective</td>
<td>24</td>
<td>Mean age, 45.5 yr; (P_{O_2}/FIO_2) ratio, 96.8; OI, 32.5; APACHE II score, 21.5</td>
<td>30-4, 66%</td>
<td>Small increases in PAOP and CVP and a small decrease in CO were documented during HFOV, with no significant change in systemic BP; two patients (8.3%) had a pneumothorax</td>
</tr>
<tr>
<td>2001</td>
<td>Retrospective</td>
<td>6</td>
<td>Burn patients; mean age, 45.5 yr; (P_{O_2}/FIO_2) ratio, 96.8; OI, 32.5; APACHE II score, 21.5</td>
<td>30-4, 53.3%</td>
<td>No complications reported</td>
</tr>
<tr>
<td>2002</td>
<td>RCT</td>
<td>48</td>
<td>Mean age, 49.5 yr; (P_{O_2}/FIO_2) ratio, 112.5; OI, 25.2; APACHE II score, 25.5</td>
<td>30-4; while receiving HFOV, -57%; while receiving CMV, 52%; (p = 0.102)</td>
<td>First RCT comparing HFOV to CMV; similar complication rate in both groups</td>
</tr>
<tr>
<td>2002</td>
<td>Retrospective</td>
<td>16</td>
<td>Mean age, 33.2; (P_{O_2}/FIO_2) ratio, 92; OI, 25.1; APACHE II score, 40.3</td>
<td>3-mo, 31%</td>
<td>One patient (6.5%) had a pneumothorax</td>
</tr>
<tr>
<td>2003</td>
<td>Prospective</td>
<td>23</td>
<td>Mean age, 44.9 yr; (P_{O_2}/FIO_2) ratio, 75; APACHE II score, 25.6</td>
<td>ICU, 61%</td>
<td>This study demonstrated that tNO can be used successfully as a rescue therapy in patients with severe ARDS and high (O_2) requirements (mean increase in (P_{O_2}/FIO_2) ratio at 30 min, 39%); five patients (21.7%) had a pneumothorax</td>
</tr>
<tr>
<td>2003</td>
<td>Prospective</td>
<td>42</td>
<td>Median age, 49 yr; (P_{O_2}/FIO_2) ratio, 94; OI, 23; APACHE II score, 25.8</td>
<td>30-4, 43%</td>
<td>One patient (2.4%) had a pneumothorax</td>
</tr>
<tr>
<td>2004</td>
<td>Retrospective</td>
<td>156</td>
<td>Median age, 47.8 yr; (P_{O_2}/FIO_2) ratio, 91; OI, 31.2; APACHE II score, 23.5</td>
<td>30-4, 62%</td>
<td>34 patients (21.9%) had a pneumothorax</td>
</tr>
<tr>
<td>2005</td>
<td>RCT</td>
<td>25</td>
<td>Median age, 50 yr; (P_{O_2}/FIO_2) ratio, 92; APACHE II score, 24</td>
<td>ICU, 44%</td>
<td>This pilot study demonstrated the safety and efficacy of combining early RMs with HFOV for rapid and sustained improvements in oxygenation; 5% of patients had a chest tube inserted for hemothorax; 3.5% of RMs were aborted because of hypotension</td>
</tr>
<tr>
<td>2005</td>
<td>RCT</td>
<td>39</td>
<td>Mean age, 52 yr; (P_{O_2}/FIO_2) ratio, 103; SOFA score, 9.5</td>
<td>ICU; supine HFOV, 38.4%; prone CV, 30.8%; prone HFOV, 23.1%</td>
<td>This randomized study compared HFOV, prone positioning, or their combination in patients with severe ARDS (13 patients in each arm); patients in the prone HFOV group had no improvement in oxygenation; 1 patient (2.5%) had major plugging necessitating a change of ETT</td>
</tr>
<tr>
<td>2005</td>
<td>Prospective</td>
<td>30</td>
<td>Mean age, 55 yr; (P_{O_2}/FIO_2) ratio, 121; SOFA score, 9.6</td>
<td>46%</td>
<td>HFOV group: four patients (10.5%) had hypotension and one patient (2.7%) had an air leak; CMV group: one patient (4.9%) had hypotension and one patient (4.2%) had an air leak; baseline OI was higher in HFOV group (25 vs 18, respectively); 19% of HFOV group crossed over to CMV, and 17% of CMV group crossed over to HFOV</td>
</tr>
<tr>
<td>2006</td>
<td>RCT</td>
<td>61</td>
<td>Mean age, 51 yr; HFOV, 37 patients; CMV, 24 patients; study prematurely stopped; OI, 22; APACHE II score, 23</td>
<td>30-4; with HFOV, 43%; with CMV, 52%; (p = 0.159)</td>
<td>This study showed that HFOV might be more effective in extrapulmonary forms of ARDS, compared to pulmonary forms of ARDS; complications were not reported</td>
</tr>
<tr>
<td>2006</td>
<td>Prospective</td>
<td>30</td>
<td>Mean age, 55 yr; (P_{O_2}/FIO_2) ratio, 121; SOFA score, 9.6</td>
<td>46%</td>
<td>HFOV was discontinued in one patient for refractory hypotension</td>
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</tbody>
</table>

**Table 1**—Comparison of Published Clinical Studies Evaluating the Use of HFOV in Adult Patients With ARDS

_High-Frequency Oscillatory Ventilation for Adult Patients With ARDS_ by Kenneth P. W. Chan, Thomas E. Stewart and Sangeeta Mehta

_Chest_ 2007;131;1907-1916
DOI 10.1378/chest.06-1549

[Image of CHEST journal cover]
The Problem of HFOV

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High-Frequency Oscillation in Early Acute Respiratory Distress Syndrome

ORIGINAL ARTICLE

High-Frequency Oscillation for Acute Respiratory Distress Syndrome
The Problem of HFOV

![Graph showing survival probability over days since randomization. The graph compares Control and HFOV groups, with HFOV showing a lower survival probability. P = 0.004 by log-rank test.]
ECMO

• Extracorporeal Membrane Oxygenation
It is all about risk vs. benefit
CO2 Removal
Adjust Sweep gas flow (The SWEEP)

Oxygenation
Adjust FdO2
Adjust Blood Flow
History of ECMO

- **1970**: Hill et al.
  - 24 yo male for 75hrs.
  - NIH randomized prospective study
  - Survival ~ 10%

- **1980**
  - Gattinoni 1986
  - Survival 50-60%

- **1990**
  - Brunet 1994
  - Lewandowski 1997

- **2000**
  - Bartlett 2000
  - Survival ~ 75%

- **2009**
  - CESAR
  - Davies 2009 (H1N1) flu pandemic
  - Survival ~ 75%

**Retrospective Studies**
Problems with earlier studies…

• Delayed initiation of ECMO therapy
• Device malfunctions
• Higher bleeding rates
• Did not use lung-protective ventilatory strategies!
Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial

- 180 patients ARDS < 7 days
- 1° outcome: ECMO 37% vs CV 53%
  - RR 0.69 (CI 95% 0.05 – 0.97; p= 0.03)

However...
Extracorporeal Membrane Oxygenation for 2009 Influenza A(H1N1) Acute Respiratory Distress Syndrome

- 68 patients with H1N1 who received ECMO
- Mean PaO2:FiO2 ratio = 56 at inclusion, PEEP 18
- Non-randomized
- Mortality = 21%
Extracorporeal Membrane Oxygenation for Pandemic Influenza A(H1N1)–induced Acute Respiratory Distress Syndrome
A Cohort Study and Propensity-matched Analysis

- February 2013
- 52 ECMO pts matched to non-ECMO patients
- No mortality difference
- 51 non matched ECMO patients had a significantly lower mortality rate
  - Younger
  - Lower P:F and higher pplat
3 ECMO Indications

ARDS

1. Severe hypoxemia (P:F <100) despite 6 hours of ARDS appropriate ventilation
2. Refractory acidemia (pH <7.15) from ARDS
3. Excessively high inspiratory plateau pressures caused by ARDS
ECMO Risk : Benefit

– Which patients with ARDS are best candidates?

– What is the most favorable time to initiate ECMO?

– Does ECMO therapy provide true mortality benefit compared to standard management?

– Transport issues!
Portable ECMO
Conclusion

• Patient remained on ventilation in rotoprone for 11 days. No improvements were seen. Family decided to withdraw care. An autopsy was performed....
Fibrotic stage
Questions?