Rescue Ventilation Strategies for ARDS

Susan Bose Stempek, MMSc, PA-C
Chief Critical Care Advanced Practitioner
Lahey Health, Burlington, MA
Objectives

Use current evidence to define Acute Respiratory Distress Syndrome (ARDS)

Describe conventional therapy for ARDS

Describe the evidence based role for prone positioning in ARDS in 2016

Describe the evidence based role for oscillatory ventilation (HFOV) in ARDS in 2016

Discuss other strategies for management of severe ARDS
ARDS - Identification

- Acute respiratory distress syndrome
- An acute, diffuse inflammatory lung injury resulting in increased pulmonary vascular permeability
- Characterized by hypoxemia and bilateral infiltrates
- Causes severe hypoxemic respiratory failure
- Initially defined by the American-European Consensus Conference in 1994, widely used definition now updated in 2012
ARDS – The Berlin Definition
(Ranieri et al, 2012)

• Onset within one week of a known clinical insult or new respiratory symptoms

• Bilateral opacities on chest imaging (CT or CXR) not fully explained by effusions, lung/lobar collapse or nodules

• Respiratory failure not fully explained by cardiac failure or volume overload
  – Echocardiogram needed in absence of ARDS risk factor
ARDS – The Berlin Definition
(Ranieri et al, 2012)

Oxygenation categories

• Mild
  - $\text{PaO}_2/\text{FIO}_2 > 200 \text{ to } \leq 300 \text{ mm Hg with PEEP } \geq 5 \text{ cm H}_2\text{O}$

• Moderate
  - $\text{PaO}_2/\text{FIO}_2 > 100 \text{ to } \leq 200 \text{ mm Hg with PEEP } \geq 5 \text{ cm H}_2\text{O}$

• Severe
  - $\text{PaO}_2/\text{FIO}_2 < 100 \text{ mm Hg with PEEP } \geq 5 \text{ cm H}_2\text{O}$
## ARDS – The Berlin Definition
(Ranieri et al, 2012)

<table>
<thead>
<tr>
<th>Direct</th>
<th>Indirect</th>
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<tbody>
<tr>
<td>Pneumonia</td>
<td>Non-pulmonary sepsis</td>
</tr>
<tr>
<td>Aspiration of gastric contents</td>
<td>Major trauma*</td>
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<tr>
<td>Inhalation injury</td>
<td>Pancreatitis</td>
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<tr>
<td>Pulmonary contusion</td>
<td>Severe burns</td>
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<tr>
<td>Pulmonary vasculitis</td>
<td>Non-cardiogenic shock</td>
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<tr>
<td>Drowning</td>
<td>Drug overdose</td>
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<td></td>
<td>Multiple transfusions</td>
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</table>
ARDS – Treatment
(The Acute Respiratory Distress Syndrome Network, NEJM 2000)

- Mechanical Ventilation with lung protective strategy, goal 6cc/kg of PBW (predicted body weight) for set tidal volume in volume control mode
  - PBW male = 50+0.91(cm of height – 152.4)
  - PBW female = 45.5+0.91(cm of height – 152.4)
- A helpful link so you don’t have to do the math
ARDS – Treatment
(The Acute Respiratory Distress Syndrome Network, NEJM 2000)

• Plateau pressure $\leq 30cm H_2O$
  • Measure this in volume control with inspiratory hold; it is measurement taken with no flow
  – Can decrease the tidal volume as low as 4cc/kg PBW to achieve appropriate plateau pressure
  – Sometimes requires permissive hypercapnia
    • Due to need for low tidal volumes and increased physiologic dead space
    • goal pH $>7.15$
      – Of course should maximize respiratory rate to increase minute ventilation
ARDS – Treatment
(The Acute Respiratory Distress Syndrome Network, NEJM 2000)

- Volume control is the preferred mode
- PEEP should be titrated based on oxygenation and compliance
- Keep plateau pressure less than 30
ARDS – Treatment
(The Acute Respiratory Distress Syndrome Network, NEJM 2000)

FiO$_2$ should be titrated for an oxygen saturation $\geq 88\%$, but following other measures of oxygen delivery also makes sense

- Central venous saturation
- Lactate
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 Boulain, 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 Richecoeur, M.D., Marc Gainnier, M.D., Ph.D., Frédérique Bayle, M.D., Gael Bourdin, M.D., Véronique Leray, M.D., Raphaèle Girard, M.D., Loredana Baboi, Ph.D., and Louis Ayzac, M.D., for the PROSEVA Study Group*
Prone Ventilation

Supine

Prone

1 G

Lahey Hospital & Medical Center
ARDS – Rescue Ventilation
Prone Positioning

• Prone Positioning (PROSEVA, Guerin NEJM 2013)
  – Prospective, multicenter randomized controlled trial
    • Inclusion criteria:
      – ARDS as defined by the AECC ("old" definition)
      – Intubation/mechanical ventilation for <36 hours
      – Severe ARDS
        » PaO$_2$/FiO$_2$ < 150 with an Fio$_2$ of ≥0.6
        » a PEEP of ≥5 cm of water
        » tidal volume of about 6 cc/kg PBW
      – Criteria were confirmed after 12 to 24 hours of mechanical ventilation
ARDS – Rescue Ventilation
Prone Positioning

Protocol

• After randomization patients were placed in prone position within 1 hour
• They had to have at least 16 consecutive hours
• Standard beds were used
• Volume control, PEEP/FiO$_2$ table, goal plateau <30cm water, goal pH 7.20-7.45
ARDS – Rescue Ventilation
Prone Positioning

• PROSEVA Criteria for stopping prone treatment:
  – improvement in oxygenation (defined as a Pao2:Fio2 ratio of ≥150 mm Hg, with a PEEP of ≤10 cm of water and an Fio2 of ≤0.6; in prone group this had to be met after 4 hours supine after the last proning session
  
  – a decrease in the Pao2:Fio2 ratio of more than 20%, relative to the ratio in the supine position, before two consecutive prone sessions
  
  – complications occurring during a prone session and leading to its immediate interruption
    • Nonscheduled extubation,
    • main-stem bronchus intubation
ARDS – Rescue Ventilation

Prone Positioning

PROSEVA Criteria for stopping prone treatment (continued):

- Endotracheal tube obstruction
- Hemoptysis
- Oxygen saturation of less than 85% on pulse oximetry or a Pao2 of less than 55 mm Hg for more than 5 minutes when the Fio2 was 1.0,
- Cardiac arrest
- A heart rate of less than 30 beats per minute for more than 1 minute
- A systolic blood pressure of less than 60 mm Hg for more than 5 minutes
- Any other life threatening reason
ARDS – Rescue Ventilation
Prone Positioning

• Prone Positioning was continued for 28 days and then was up to clinician discretion as to whether to continue or not

• Patients could only cross over from the supine to prone group if the following were in place
  – \( \text{PaO}_2/\text{FiO}_2 \) ratio was 55 or less with \( \text{FiO}_2 \) of 1.0 on maximal PEEP
  – Administration of nitric oxide at 10 ppm
  – infusion of intravenous almitrine bismesylate at a dose of 4 \( \mu \text{g/kg/min} \)
  – Recruitment maneuvers had been done
ARDS – Rescue Ventilation
Prone Positioning - PROSEVA

- Primary endpoint 28 day mortality

- Secondary endpoints
  - 90 day mortality
  - Rate of successful extubation
    - No reintubation or use of non-invasive ventilation within 48 hours of extubation
    - In the case of patients with tracheotomy this was defined as ability to breathe through the cannula for 24 hours unassisted
  - Time to successful extubation
  - Length of stay in the ICU
  - Complications
  - Use of non-invasive ventilation
Secondary Endpoints (continued)

- Tracheotomy rate
- Days free from organ dysfunction
- Ventilator settings
- Measurements of ABGs
- Respiratory system mechanics during the first week after randomization
Characteristics between prone and supine groups were statistically similar except for:

- Use of vasopressors (higher in supine group)
- Use of neuromuscular blockers (higher in prone group, but duration was similar in both groups when used)
- SOFA score (higher in supine group)
  - Higher scores indicate more severe organ failure
ARDS – Rescue Ventilation
Prone Positioning - PROSEVA

Ventilator Settings and Lung Function

• Pao2:Fio2 recorded in the supine position was significantly higher in the prone group on day 3 and 5
• PEEP and Fio2 were significantly lower
• Pplat was 2cm of water lower in the prone group on day 3
ARDS – Rescue Ventilation
Prone Positioning

Primary Outcome, Mortality at day 28 was significantly lower in the prone group than the supine group (16% vs. 32.8%, $P < 0.001$)

- The significance in the difference persisted at 90 days
- After adjusting for the significance in the difference in use of vasopressors, neuromuscular blockers and SOFA score the mortality difference remained significant
Figure 2. Kaplan–Meier Plot of the Probability of Survival from Randomization to Day 90.
ARDS – Rescue Ventilation
Prone Positioning - PROSEVA

Secondary Outcomes:
• Successful extubation was higher in prone group
• Other measures did not differ

Complications
• 31 cardiac arrests in the supine group, 16 in the prone group, P = 0.02
ARDS – Rescue Ventilation
Prone Positioning - PROSEVA

• Should we prone?
  – Proning helps with recruitment while decreasing overinflation (Galiatsou et al., 2006)
    • Hopefully preventing ventilator induced lung injury
  – This study showed a mortality benefit in severe ARDS when used early (after confirming diagnosis in the first 12-24 hours) and in relatively long sessions
  – System familiarity is not to be discounted as an important factor in success and low complications
    • NEJM videos
ARDS – Rescue Ventilation
High Frequency Oscillation (HFOV)

What is HFOV?

• Patients lungs are held inflated to maintain oxygenation
• Small volumes of gas are moved in and out of the respiratory system at 3 to 15 Hz
• This is supposed to minimize damage from opening and collapsing alveoli
High-Frequency Oscillation for Acute Respiratory Distress Syndrome

ARDS – Rescue Ventilation
High Frequency Oscillation (HFOV)

OSCAR 2013 (Young, et. al)

• Primary outcome was 30 day mortality
• Patients with Pao2/FiO2 of 200mmHg or less and an expected need for mechanical ventilation for at least 2 days were randomized to HFOV or usual ventilatory care
• Bilateral infiltrates without evidence of left atrial hypertension
• PEEP of at least 5 cm H₂O
ARDS – Rescue Ventilation
High Frequency Oscillation (HFOV)

• OSCAR 2013 exclusion criteria
  – Ventilation greater than 7 days
  – Under 16
  – Weight less than 35 kg
  – If they are participating in other studies
  – Airway disease
    • Airway narrowing
    • Air trapping
    • Recent lung surgery
ARDS – Rescue Ventilation
High Frequency Oscillation (HFOV)

OSCAR 2013

- HFOV patients had titration guidelines for achieving PaO2 goals and maintaining pH 7.25
- Sites were encouraged to use pressure control ventilation on conventional ventilation patients
ARDS – Rescue Ventilation
High Frequency Oscillation (HFOV)

OSCAR 2013

• Primary outcome all cause mortality 30 days after randomization
• Secondary outcomes:
  - All cause mortality at the time of discharge from the ICU and the hospital
  - Duration of mechanical ventilation
  - Use of antibiotics, sedatives, vasoactive medications and neuromuscular blockers
ARDS – Rescue Ventilation
High Frequency Oscillation (HFOV)

• OSCAR 2013
  – No difference in mortality when using HFOV vs. conventional ventilation at 30 days
    • (conventional ventilation group was treated at the upper end of the accepted 6-8cc/kg PBW)
  – HFOV initially associated with increased use in neuromuscular blockers
  – HFOV did not increase use of vasopressors/inotropes despite thought that it reduces cardiac output
Figure 3. Kaplan–Meier Survival Estimates during the First 30 Study Days.
ARDS – Rescue Ventilation
High Frequency Oscillation (HFOV)

OSCAR 2013

- Given findings; recommends that HFOV not be used for routine care
High-Frequency Oscillation in Early Acute Respiratory Distress Syndrome

ARDS – Rescue Ventilation
High Frequency Oscillation (HFOV)

OSCILLATE 2013 (Ferguson et. al)

• Previous studies limited by using outdated comparator ventilation strategies and small sample sizes
• Study Characteristics
  • Moderate to severe ARDS randomized to HFOV with lung recruitment or control ventilation targeting lung recruitment with low tidal volumes and high PEEP
  • Primary outcome was the rate of in hospital death from any cause
• Inclusion Criteria
  - 2 weeks or less of pulmonary symptoms
  - PaO2/FiO2 of ≤ 200mmHg on ≥ 0.50 FiO2
  - Bilateral airspace opacities on CXR
  - Age 16-85
ARDS – Rescue Ventilation
High Frequency Oscillation (HFOV)

– Exclusion Criteria
  • Left atrial hypertension
  • Pulmonary hemorrhage
  • Neuromuscular disorders
  • Severe chronic respiratory disease
  • Another condition contributing to 6 month mortality >50%
  • Not committed to life support
  • Already met criteria for 72 hours
  • Vent duration expected <48 hours
  • Weight <35kg or more than 1kg per cm of height
  • Risk for intracranial hypertension
ARDS – Rescue Ventilation
High Frequency Oscillation (HFOV)

OSCILLATE 2013

• After randomization a recruitment maneuver was done - 40cm of water pressure for 40 seconds
  - HFOV protocol
  - Conventional ventilation protocol with pressure control, tidal volume goal 6cc/kg and high PEEP
ARDS – Rescue Ventilation
High Frequency Oscillation (HFOV)

• OSCILLATE 2013
  – Trial stopped early; intention to enroll 1200 patients to power for primary endpoint with expectation of 45% mortality in the control group
  – Only 571 patients enrolled and 548 randomized
  – Mortality higher in the HFOV group
  – Use of vasopressors higher in HFOV group within 4 hours of initiation
  – Use of neuromuscular blockers also higher after on HFOV
**Figure 2.** Probability of Survival from the Day of Randomization to Day 60 in the HFOV and Control Groups.

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

P = 0.004 by log-rank test
ARDS – Rescue Ventilation
High Frequency Oscillation (HFOV)

OSCILLATE 2013

- Refractory hypoxemia developed in significantly more patients in the control group, but number of deaths after refractory hypoxemia were similar
- Doses of midazolam were higher in HFOV group
ARDS – Rescue Ventilation
High Frequency Oscillation (HFOV)

OSCILLATE 2013

• Raises significant concern about using HFOV early in moderate to severe ARDS as compared with conventional ventilation with low tidal volume and high PEEP
Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial

Giles J Peek, Miranda Mugford, Rovindranath Tiruvoipati, Andrew Wilson, Elizabeth Allen, Mariamma M Thalaparambil, Clare L Hibbert, Ann Truesdale, Felicity Clemens, Nicola Cooper, Richard K Firmin, Diana Elbourne, for the CESAR trial collaboration
ARDS – Rescue Ventilation
ECMO

CESAR 2009 (Peek et. al)

Adults with

- severe, but potentially reversible respiratory failure
- Murray score > 3.0 (PaO2/FiO2, PEEP, CXR involvement and compliance)
- pH <7.20 on maximal conventional management

SHOULD be transferred to a center that can provide ECMO to improve survival without severe disability
Figure 2: Kaplan-Meier survival estimates
ECMO=extracorporeal membrane oxygenation. * Patients were randomly allocated to consideration for treatment by ECMO, but did not necessarily receive this treatment.
ARDS – Rescue Ventilation

APRV

Not much evidence regarding APRV in ARDS

It can be helpful in refractory hypoxemia, but should not be used routinely in ARDS (Maxwell, 2010)
ARDS – Rescue Ventilation
Nitric Oxide (Vasodilator)


- No mortality benefit or ventilator days
- Transient oxygenation benefit (24-96 hours)
- Can contribute to AKI (acute kidney injury)
- Should not be used routinely

Consider as bridge to Prone positioning or ECMO
Case Study

A 24 year old male presented to the emergency department with 3 days of shortness of breath. He also had fevers and a cough.

- Vitals: HR 110, RR 22, oxygen saturation 92% on RA, blood pressure 120s/70s
- CXR with minimal right infiltrate
Case Study

He is admitted to the hospital on ceftriaxone. He is allergic to macrolides and quinolones, so he did not receive additional antibiotics.

He clinically worsened 16 hours following hospitalization requiring initially face mask oxygen, quickly progressing to respiratory failure requiring intubation.
Case Study

• Question #1: **Initial** ventilator settings should include the following criteria EXCEPT:

1. Low tidal volume (6cc/kg IBW)
2. High PEEP
3. He should be put directly on the oscillator
4. His saturation goal should be \( \geq 88\% \)
Case Study

The ventilator is set on assist control/volume control with the following settings:
24/400/1.0/10 (RR/Vt/FiO2/PEEP)

His ABG shows:
7.20/55/78/20

His lactic acid is 4.5

He is requiring norepinephrine at 30mcg/min and vasopressin at 0.03 units/min
Case study

Question #2:

Which of the following is true assuming his clinical state remains stable without much improvement in her oxygen requirements in the 12 hours post-intubation?

1) **proning should be initiated**

2) **HFOV should be initiated**

3) both should be initiated
Case Study

• The patient is maintained on ACVC with uptitration of the respiratory rate to treat the respiratory component of his acidosis. His plateau pressure is 40 cm of water.

• Question #3: You should:
  1) decrease the tidal volume
  2) try diuresis
  3) accept this plateau pressure
  4) decrease PEEP
Case Study

- You decrease the tidal volume so the patient is on the maximal respiratory rate with the highest tidal volume to keep plateau pressure less than 30. His PEEP has been uptitrated to optimize oxygenation and facilitate decreasing the FiO2. An acceptable pH is:
  - 1) anything greater than 7.0
  - 2) $\geq 7.15$
  - 3) $\geq 7.20$
  - 4) both 2 and 3
Case Study

The patient is undergoing the proning protocol with conventional ventilation, but his oxygenation is worsening despite maximal FiO2 and PEEP. He should:

1) Be placed on HFOV with proning
2) The proning protocol with conventional ventilation should be continued
3) The proning protocol should be stopped and HFOV initiated
ARDS – Treatment
Other Considerations (Outside the Scope of this Talk)

Fluid management (FACTT trial, NEJM 2006)

- Conservative fluid management
- Off vasopressors for >12 hours
  - d/c maintenance fluid
  - goal CVP </= 4
  - For 7 days goal negative fluid balance with diuretics; withhold for evidence of acute kidney injury

Paralytics, Steroids, beta-2 agonists
References


• FACTT


References, continued


