ARDS: Therapy and Controversies

Michel Boivin MD
NM Lung Disease Symposium
Objectives

- Review recent data in ARDS
- Discuss the role of pressure versus volume trauma in ARDS
- Understand role of patient ventilator dysynchrony in ARDS
Definition and Epidemiology
What is ARDS

- Acute onset
- Bilateral infiltrates consistent with pulmonary edema
- A ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen (PaO2/FiO2) between 1 and 300 mmHg. (The PaO2 is measured in mmHg and the FiO2 is expressed as a decimal between 0.21 and 1.00.)
- No clinical evidence for an elevated left atrial pressure. If measured, the pulmonary capillary wedge pressure is 18 mmHg or less.
The new “Berlin” classification

OXYGENATION

<300 mmHg  <200 mmHg  <100 mmHg

MILD    MODERATE    SEVERE

ACUTE RESPIRATORY DISTRESS SYNDROME
Epidemiology

• The age-adjusted incidence was:
  – 86 per 100,000 person-years for individuals with a (PaO$_2$/FiO$_2$) ≤300 mmHg and
  – 64 per 100,000 person-years for individuals with a PaO$_2$/FiO$_2$ ≤200 mmHg.

• The incidence increased with patient age from 16 per 100,000 person-years among individuals 15 to 19 years of age to 306 per 100,000 person-years among individuals 75 to 84 years of age.

• There are approximately 190,000 cases of ARDS in the United States each year.
LIPS score >4 predicts ARDS

• The LIPS is the sum of the points assigned for each of the following predisposing conditions:
  – shock (2 points) aspiration (2 points)
  – sepsis (1 point) pneumonia (1.5 points)
  – orthopedic spine surgery (1.5 points) acute abdominal surgery (2 points)
  – cardiac surgery (2.5 points) aortic vascular surgery (3.5 points)
  – traumatic brain injury (2 points) smoke inhalation (2 points)
  – near drowning (2 points) lung contusion (1.5 points)
  – multiple fractures (1.5 points) alcohol abuse (1 point)
  – obesity (BMI >30, 1 point) hypoalbuminemia (1 point)
  – chemotherapy (1 point) fi o2 >0.35 (2 points)
  – tachypnea >30 breaths/min (1.5 points) O2 saturation <95 percent (1 point)
  – acidosis (pH <7.35, 1.5 points) diabetes mellitus (-1 point).
Mortality

![Mortality Bar Graph]

- ARMA-12
- ARMA-6
- FACTT fluid conservative
- ALTA + OMEGA

Mortality (%)
Clinical Manifestations

• Usually present with progressive dyspnea, over a short time frame.

• History more relevant to precipitant and ruling out other conditions than ARDS.

• Exam: Tachypnea, cyanosis, use of accessory muscles, occasional crackles, absence of signs of heart failure.
Respiratory Failure

- Usually hypoxemic except in the patient with pre-existing lung disease, muscle weakness or heavy sedation
Differential Diagnosis

- Cardiogenic Pulmonary Edema
- Diffuse Alveolar Hemorrhage
- Diffuse Pneumonia
- Broncho-Alveolar Carcinoma
- Pulmonary Alveolar Proteinosis
- Hypersensitivity Pneumonitis
- Acute Interstitial Pneumonitis
- Acute Eosinophilic Pneumonia
Bronchoscopy in ARDS

• Potential Causes:
  – Infectious (PJP, viruses, bacterial etc...)
  – Aspiration

• Potential Diagnosis:
  – Pulmonary Hemorrhage, BAC or PAP
  – Acute Eosinophilic Pneumonia
  – HSP
Differentiation of Cardiac vs. Non-Cardiac Pulmonary Edema

- Underlying condition: Myocardial infarction vs. severe infection
- X-ray appearance
- Estimates of Pc (central venous pressure, BNP peptide)
- Measurement of Pc (Swann-Ganz Catheter)
- Measurement of Alveolar protein concentration (estimate of $\pi_i$)
Cardiogenic vs Non-Cardiogenic Pulmonary Edema

Ware et al, NEJM 2005
Other test that may help discriminate:

Measures of Intravascular Volume (CVP, PCWP etc…)

Measurement of Alveolar Protein Concentration

* Data are from Milne et al.²⁸ and Aberle et al.³¹
† The width of the vascular pedicle is determined by dropping a perpendicular line from the point at which the left subclavian artery exits the aortic arch and measuring across to the point at which the superior vena cava crosses the right mainstem bronchus. A vascular-pedicile width greater than 70 mm on a portable digital anteroposterior radiograph of the chest when the patient is supine is optimal for differentiating high from normal-to-low intravascular volume.³²
Cardiogenic vs ARDS
Precipitants of ARDS

- Pulmonary
  - Pneumonia
  - Toxic Inhalation
  - Aspiration of Gastric acid
  - *Negative Pressure Pulmonary Edema*

- Extra-Pulmonary
  - Sepsis
  - Pancreatitis
  - Burns / Trauma
  - TRALI
  - Medications ...
  - Obstetric Catastrophies
  - *Narcotic induced pulmonary edema*
Causes of Non-Cardiogenic Pulmonary Edema (Adult Respiratory Distress Syndrome – ARDS)

• **Rapid Resolution** (24-48 hours)
  – Transfusion associated Acute Lung Injury
  – Narcotic associated pulmonary edema
  – Negative pressure pulmonary edema

• **Usual Resolution** (5 days +)
  – Sepsis
  – Pneumonia
  – Aspiration of acidic gastric contents
  – Pulmonary contusion
  – Pancreatitis
  – Burns
  – Some medications
Pathology

- Influx of inflammatory cells.
- Hyaline membranes
- Proteinaceous fluid
- Hyperplasia of type II pneumocytes
Phases of ARDS
Figure 3
Molecular targets for new therapies that can lead to endothelial and epithelial barrier stabilization and reversal of increased permeability. (A) Disrupted alveolar barrier function, resulting in increased permeability to water, proteins, and other solutes, is a hallmark of clinical and experimental ALI. Intra-alveolar accumulation of neutrophils, other leukocytes, and erythrocytes is also associated with altered endothelial and epithelial barrier function. TNF-α, IL-1, thrombin, and microbes and their toxins — including LPS, noxious agents, and factors generated by neutrophils and platelet-leukocyte interactions — can destabilize and disrupt alveolar barrier function, leading to increased permeability. (B) Disruption of VE-cadherin bonds is a central mechanism of altered endothelial barrier function in experimental ALI and in models of sepsis and systemic vascular destabilization. VE-cadherin is an endothelial-specific adherens junction protein that mediates Ca²⁺-dependent homophilic interactions at the lateral cell membranes of adjacent endothelial cells. VE-cadherin is regulated by cytoplasmic associations with catenins and actin and by cytoskeletal organization, in addition to intracellular signaling by Rho and Rac. Disruption of VE-cadherin bonds also facilitates transendothelial migration of leukocytes and, in some studies, is associated with accumulation of leukocytes and platelets in microvessels. (C) Stabilizing agonists (i) or
Resolution of ARDS

**Figure 4**
Resolution of ALI requires removal of alveolar edema fluid, removal of the acute inflammatory cells, and repair of the injured alveolar epithelium. (A) Alveolar edema fluid reabsorption is driven by vectorial transport of sodium and chloride from the airspaces to the lung interstitium, creating a mini-osmotic gradient. Sodium is transported across apical sodium channels (including epithelial sodium channel [ENaC]) and then extruded basolaterally by sodium-potassium ATPase (NaKATPase). Chloride is transported by transcellular or paracellular pathways. In the presence of endogenous or exogenous cAMP stimulation, the rate of alveolar fluid transport increases substantially, accomplished by increased expression and activity of ENaC, NaKATPase, and opening of the CFTR. For net fluid clearance to occur, however, there needs to be a reasonably intact alveolar epithelial barrier (see C). AQP5, aquaporin 5. (B) The resolution of inflammation in ALI and ARDS requires the removal of neutrophils from the distal airspace of the lung. Neutrophils are normally taken up by alveolar macrophages, a process termed efferocytosis. The rate of neutrophil clearance can be accelerated by regulatory T lymphocytes, in part by release of TGF-β. (C) Restoration of the alveolar epithelial barrier initially occurs by reepithelialization of the epithelial surface by alveolar type II cells. Although it was previously thought that this occurred via proliferation of resident type II cells, new work suggests there may be niches of progenitor cells that also contribute. An α6β4+ progenitor cell has been identified in the mouse lung that is responsible for restoration of the alveolar epithelial barrier after bleomycin-induced lung injury (88). Thus, repair may occur by endogenous stem cell proliferation, not just by epithelial cell migration and proliferation of existing differentiated cells.
Ventilation in ARDS
Pathophysiology of hypoxemia

- Shunt is due to alveoli that are collapsed and perfused but receive no ventilation
- Also – Poor CO due to Cor Pulmonale
- Capillary membrane diffusion block
Pathophysiology of Dead-Space in ARDS

- Dead Space or wasted ventilation in ARDS may be due to several mechanisms:
  - Poor V/Q matching
  - Pulmonary Hypertension
  - Pulmonary Microcirculatory abnormalities

Nuckton et al., NEJM 2002
The Baby Lung and Ventilator-Induced Lung Injury

- Several animal models of ARDS demonstrated that high VT or shearing alveoli lead to increased ARDS and increased generation of pro-inflammatory mediators

Gattinoni, ICM 2005
Baby Lung or Sponge Lung

- Baby Lung is not an anatomical unit, but a result of Lung Edema and compressive forces that are dependant.

Gattinoni, ICM 2005
Open lung hypothesis
Pressure Volume Curves

Albaiceta GM et al. Current Opinion in Critical Care 2008;14:80-86
Recruitment Maneuvers

• Part of Alveoli trial, showed only modest, transient benefit and were dropped afterward.

• More severe ARDS has more recruitable lung.

Gattinoni et al., NEJM 2006
Currently accepted therapies for ARDS
Low tidal volume

- Amato 38 vs 71%
- ARMA 31 vs 40%
- One of the few widely accepted principles of CC.

**Table 1—Randomized Controlled Trials Evaluating Strategies of Mechanical Ventilation for the Treatment of ARDS**

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients, No.</th>
<th>Intervention</th>
<th>Mortality Rates†</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amato et al⁵⁰</td>
<td>53</td>
<td>≤ 6 mL/kg ABW; VT; &lt; 20 cm H₂O Pdriving</td>
<td>38% vs 71%‡</td>
<td>0.001</td>
</tr>
<tr>
<td>Stewart et al⁵¹</td>
<td>120</td>
<td>≤ 8mL/kg IBW; VT; ≤ 30 cm H₂O Pplat</td>
<td>50% vs 47%</td>
<td>0.72</td>
</tr>
<tr>
<td>Brochard et al⁵²</td>
<td>116</td>
<td>6–10 mL/kg IBW; VT; 25–30 cm H₂O Pplat</td>
<td>47% vs 38%§</td>
<td>0.38</td>
</tr>
<tr>
<td>Brower et al⁵³</td>
<td>52</td>
<td>≤ 8 mL/kg PBW; VT; ≤ 30 cm H₂O Pplat</td>
<td>50% vs 46%</td>
<td>0.61</td>
</tr>
<tr>
<td>ARMA⁴⁴</td>
<td>861</td>
<td>≤ 6mL/kg PBW; Vr; ≤ 30 cm H₂O Pplat</td>
<td>31% vs 40%</td>
<td>0.007</td>
</tr>
</tbody>
</table>

*ARDSnet NEJM 2000*
Low Vt protocol

INCLUSION CRITERIA: Acute onset of
1. $\text{PaO}_2/\text{FiO}_2 \leq 300$ (corrected for altitude)
2. Bilateral (patchy, diffuse, or homogeneous) infiltrates consistent with pulmonary edema
3. No clinical evidence of left atrial hypertension

PART I: VENTILATOR SETUP AND ADJUSTMENT
1. Calculate predicted body weight (PBW)
   - Males = $50 + 2.3 \times \text{[height (inches)] - 60}$
   - Females = $45.5 + 2.3 \times \text{[height (inches)] - 60}$
2. Select any ventilator mode
3. Set ventilator settings to achieve initial $V_t = 8 \text{ ml/kg PBW}$
4. Reduce $V_t$ by 1 ml/kg at intervals ≤ 2 hours until $V_t = 6 \text{ ml/kg PBW}$.
5. Set initial rate to approximate baseline minute ventilation (not > 35 bpm).
6. Adjust $V_t$ and RR to achieve pH and plateau pressure goals below.

OXYGENATION GOAL: $\text{PaO}_2$ 55-80 mmHg or $\text{SpO}_2$ 88-95%
Use a minimum PEEP of 5 cm H$_2$O. Consider use of incremental FI02/PEEP combinations such as shown below (not required) to achieve goal.

<table>
<thead>
<tr>
<th>Lower PEEP/higher FI02</th>
<th>FI02</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>
</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>10</td>
<td>12</td>
</tr>
</tbody>
</table>

| FI02 | 0.7 | 0.8 | 0.9 | 0.9 | 0.9 | 1.0 |
| PEEP | 14  | 14  | 14  | 16  | 16  | 18-24 |

<table>
<thead>
<tr>
<th>Higher PEEP/lower FI02</th>
<th>FI02</th>
<th>0.3</th>
<th>0.3</th>
<th>0.3</th>
<th>0.3</th>
<th>0.3</th>
<th>0.4</th>
<th>0.4</th>
<th>0.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEEP</td>
<td>5</td>
<td>8</td>
<td>10</td>
<td>12</td>
<td>14</td>
<td>14</td>
<td>16</td>
<td>16</td>
<td>16</td>
</tr>
</tbody>
</table>

| FI02 | 0.5 | 0.5-0.8 | 0.8 | 0.9 | 1.0 | 1.0 |
| PEEP | 18  | 20       | 22  | 22  | 22  | 24  |

PLATEAU PRESSURE GOAL: ≤ 30 cm H$_2$O
Check Pplat (0.5 second inspiratory pause), at least q 4h and after each change in PEEP or $V_t$.
If Pplat > 30 cm H$_2$O: decrease $V_t$ by 1 ml/kg steps (minimum = 4 ml/kg).
If Pplat < 25 cm H$_2$O and $V_t < 6$ ml/kg, increase $V_t$ by 1 ml/kg until Pplat > 25 cm H$_2$O or $V_t = 6$ ml/kg.
If Pplat < 30 and breath stacking or dys-synchrony occurs: may increase $V_t$ in 1ml/kg increments to 7 or 8 ml/kg if Pplat remains ≤ 30 cm H$_2$O.
Steroids and ARDS – Probably no benefit

Figure 2. Probability of Survival and the Proportion of Patients with Persistent ARDS Who Became Able to Breathe without Assistance during the First 180 Days after Randomization.

At 180 days, 29 patients in the placebo group had died, 58 had been discharged home, and 4 had not been discharged home; the respective values in the methylprednisolone group were 28, 57, and 4. The status was known for all 180 patients at 180 days.
Fluid and ARDS – Keep them even and they get off the vent sooner

Table 1—Pulmonary Outcomes and Physiologic Variables in the FAcCT

<table>
<thead>
<tr>
<th>Variable</th>
<th>Conservative Group</th>
<th>Liberal Group</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventilator-days, No.</td>
<td>14.6 ± 0.3</td>
<td>12.1 ± 0.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PEEP or PIP, cm H₂O</td>
<td>7.5 ± 0.3</td>
<td>6.5 ± 0.2</td>
<td>0.006</td>
</tr>
<tr>
<td>Positive end-expiratory pressure</td>
<td>14.2 ± 0.0</td>
<td>20.7 ± 0.3</td>
<td>0.002</td>
</tr>
<tr>
<td>Fio₂/FracO₂</td>
<td>105 ± 5</td>
<td>103 ± 5</td>
<td>0.07</td>
</tr>
<tr>
<td>Oxygen index</td>
<td>50.2 ± 0.6</td>
<td>13.5 ± 0.7</td>
<td>0.003</td>
</tr>
<tr>
<td>Lung injury score</td>
<td>3.05 ± 0.07</td>
<td>2.07 ± 0.00</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Values are given as the mean ± SE, unless otherwise indicated. PEEP = positive end-expiratory pressure; PIP = positive inspiratory pressure. Up Values for the physiologic variables are for comparison of trends over time using repeated-measures analysis of variance, though only day 7 values are shown for inspiratory. Diagnosis index was calculated as (mean driver pressure × Fio₂/FracO₂) ÷ 100, with a lower number indicating better gas exchange. Lung injury score was calculated as previously described by Murray et al.**

Table 2—Simplified Algorithm for Conservative Management of Fluids in Patients With ALI, Based on Protocol Used in the FAcCT

<table>
<thead>
<tr>
<th>CVP, mm Hg (Recommended)</th>
<th>PAOP, mm Hg (Optional)</th>
<th>MAP ≥ 60 mm Hg and Not Receiving Vasopressors for ≥ 12 h</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Average Urine Output &lt; 0.5 mL/kg/h</td>
</tr>
<tr>
<td>&gt; 8</td>
<td>&gt; 12</td>
<td>Furosemide: resest in 1 h</td>
</tr>
<tr>
<td>4-6</td>
<td>8-12</td>
<td>Fluid bolus as fast as possible; resest in 1 h</td>
</tr>
<tr>
<td>&lt; 4</td>
<td>&lt; 6</td>
<td>Fluid bolus as fast as possible; resest in 1 h</td>
</tr>
</tbody>
</table>

*CVP = central venous pressure; PAOP = pulmonary artery occlusion pressure; MAP = mean arterial pressure. Reprinted with the courtesy of the NHLBI Acute Respiratory Distress Syndrome Network. Patients must have had a MAP of ≥ 60 mm Hg without requiring vasopressors for at least 12 h before this protocol is initiated.

Furosemide dosage: begin with a 20-mg bolus, 3 mg/h infusion, or last known effective dose. Double each subsequent dose until the goal is achieved (oliguria renal or intravascular pressure target), with a maximal dose of 150-mg bolus or 24 mg/h. Do not exceed 620 mg/d. If the patient has heart failure, treatment with diuretics may be considered. Diuretic therapy should be withheld for patients with renal failure, which is defined as dialysis dependence, oliguria with a serum creatinine level of ≥ 3 mg/dL, or oliguria with a serum creatinine level of < 2 mg/dL but with urinary indices indicative of acute renal failure.

Fluid bolus: 15 mL/kg crystalloid (rounded to nearest 250 mL) or 1 unit of packed RBCs or 25 g of albumin.
Prone ventilation improves survival in ARDS

- Patients with P/F ratio less than 150.
- Started within 24h
- 18h a day proned

Guerin et al, NEJM 2013
Neuromuscular Blockade

- 2 studies have shown improved survival and time off ventilator.
- Used cis-atracurium for 48h
- Mechanism unclear, vent parameters didn’t change much.

Papazian et al., NEJM 2010
Case

- 59 yo male (70 kg, 165cm) found down at home with fentanyl patch on.
- Improved mental status with narcan drip
- Developed progressive hypoxia over next 12h and eventually intubated.
What initial mode of ventilation should patient be placed on?

- A) Bivent  P-hi 25 T-Hi 4s
- B) Vol-targeted A/C Vt – 840 Rate 10 Peep 5
- C) Vol-targeted A/C Vt - 420 ml rate 20 Peep 8
- D) Ventilators are for sissies, I’m putting him on ECMO.
Plateau Pressure

- Is close to the pressure the Alveolus “feels”
- Correlates with barotrauma (loosely)
- Should be kept under 30 cm/H2O in ARDS

**Components of Inflation Pressure**

**Plateau Pressure Goal:** ≤ 30 cm H2O

- Check Pplat (0.5 second inspiratory pause), at least q 4h and after each change in PEEP or Vₜ.
- If Pplat > 30 cm H₂O: decrease Vₜ by 1ml/kg steps (minimum = 4 ml/kg).
- If Pplat < 25 cm H₂O and Vₜ < 6 ml/kg, increase Vₜ by 1 ml/kg until Pplat > 25 cm H₂O or Vₜ = 6 ml/kg.
- If Pplat < 30 and breath stacking or dys-synchrony occurs: may increase Vₜ in 1ml/kg increments to 7 or 8 ml/kg if Pplat remains ≤ 30 cm H₂O.
Pressure or Volume

• Studies had previously shown that ventilation at high pressures but low tidal volumes had not caused as much lung damage.
• However these were animal models that did not account for transpulmonary pressure.
• Current standard is to control both ... low Vt and Ppl <30.
Pressure vs Volume

• They are not totally separable. But one can be prioritized over the other.
• It’s not clear which is worse for the lung in ARDS, or even which pressure...
Driving Pressure

Amato et al., NEJM 2015
Transpulmonary pressure

- Atmospheric pressure
- Parietal pleura
- Visceral pleura
- Pleural cavity
- Transpulmonary pressure: 760 mm Hg
  - 756 mm Hg
  - 4 mm Hg
- Intrapleural pressure: 756 mm Hg
  - (−4 mm Hg)
- Intrapulmonary pressure: 760 mm Hg
  - (0 mm Hg)

Thoracic wall
Lung
Diaphragm
Transpulmonary pressure

Transpulmonary Pressure and Lung Volume

\[ P_{tp} = P_{aw} - P_{eso} \]

- \( P_{tp} = 25 \)
- \( P_{tp} = 15 \)
Take home about volume vs pressure

- For now we have insufficient evidence beyond ARDSnet ventilation to adjust ventilator settings for safety.

- But concepts of driving pressure and transpleural pressure may explain some of the benefits of paralysis and possibly proning.
Dyssynchrony

- Patient with ARDS is on low tidal ventilation.
- Volume control at 6 ml/kg
- Patient is making strong respiratory efforts (tracheal tugging, SCM use)
Increased respiratory efforts with insufficient flow in volume control are going to lead to an increase in which pressure?

A) Plateau pressure
B) Peak pressure
C) Trans-pleural pressure
Which of the following is NOT a potential solution for this situation?

- A) Increase flow rate / Decrease i-time
- B) Change to Pressure Control mode
- C) Paralyze / Deeply sedate the patient
- D) Change the Flow pattern to decelerating
- E) Change trigger to pressure-trigger
Downsides to increasing the inspiratory flow rate

- A) increased peak pressures – but not very important
- B) decreased oxygen saturation from lower mean pressures
- C) Double triggering from prolonged inspiration
A patient with ARDS is dysynchronous on low Vt volume control ventilation.

He is switched to Pressure Control, has a PEEP of 12, Fio2 80% but with a delta P of 5 still gets a Vt 9 ml/kg but with high WOB

What is correct ventilation strategy?

A) Accept high Vt
B) Reduce Delta P to 0
C) Extubate patient
D) Paralyze the patient
Dysynchrony is a reason to increase Vt

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**Lower PEEP/higher FiO2**

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<thead>
<tr>
<th>(\text{FiO}_2)</th>
<th>0.3</th>
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<th>0.4</th>
<th>0.5</th>
<th>0.5</th>
<th>0.6</th>
<th>0.7</th>
<th>0.7</th>
</tr>
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<tbody>
<tr>
<td>(\text{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>
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</table>

<table>
<thead>
<tr>
<th>(\text{FiO}_2)</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>
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<tbody>
<tr>
<td>(\text{PEEP})</td>
<td>14</td>
<td>14</td>
<td>14</td>
<td>16</td>
<td>18</td>
<td>18-24</td>
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**Higher PEEP/lower FiO2**

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<th>(\text{FiO}_2)</th>
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<td>14</td>
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<table>
<thead>
<tr>
<th>(\text{FiO}_2)</th>
<th>0.5</th>
<th>0.5-0.8</th>
<th>0.8</th>
<th>0.9</th>
<th>1.0</th>
<th>1.0</th>
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**PLATEAU PRESSURE GOAL:** ≤ 30 cm \(\text{H}_2\text{O}\)

Check \(P_{plat}\) (0.5 second inspiratory pause), at least q 4h and after each change in PEEP or \(V_t\).

If \(P_{plat} > 30 \text{ cm H}_2\text{O}\): decrease \(V_t\) by 1ml/kg steps (minimum = 4 ml/kg).
If \(P_{plat} < 25 \text{ cm H}_2\text{O and V_t} < 6 \text{ ml/kg}\), increase \(V_t\) by 1 ml/kg until \(P_{plat} < 25 \text{ cm H}_2\text{O or V_t} = 6 \text{ ml/kg}\).
If \(P_{plat} < 30\) and breath stacking or dys-synchrony occurs: may increase \(V_t\) in 1ml/kg increments to 7 or 8 ml/kg if \(P_{plat}\) remains ≤ 30 cm \(\text{H}_2\text{O}\).
Dysynchrony is common in ARDSnet ventilation and ARDS patients

- 1. Try to match flow to need in Volume Control modes
- 2. Increase goal Vt to 7-8 ml/kg if plateau is less than 30 and patient has dysynchrony.
- 3. Consider paralysis when appropriate, deep sedation or extubation.
## Dyssynchrony

Table 1 Prevalence of different asynchronies in the different modes studied

<table>
<thead>
<tr>
<th>Modes</th>
<th>PCV</th>
<th>PSV</th>
<th>VCV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hours</td>
<td>692</td>
<td>2.141</td>
<td>2.886</td>
</tr>
<tr>
<td>Aborted inspirations</td>
<td>0.08 [0.000; 0.31]</td>
<td>-</td>
<td>0.06 [0.00; 0.29]</td>
</tr>
<tr>
<td>Short cycling</td>
<td>-</td>
<td>0.27 [0.06; 0.70]</td>
<td>-</td>
</tr>
<tr>
<td>Prolonged cycling</td>
<td>-</td>
<td>0.07 [0.00; 0.24]</td>
<td>-</td>
</tr>
<tr>
<td>Autotriggering</td>
<td>-</td>
<td>1.01 [0.13; 4.60]</td>
<td>-</td>
</tr>
<tr>
<td>Double-triggering (^{b,c})</td>
<td>0.11 [0.00; 0.44]</td>
<td>0.12 [0.00; 0.32]</td>
<td>0.06 [0.00; 0.29]</td>
</tr>
<tr>
<td>Ineffective inspiratory efforts during expiration (^{a,c})</td>
<td>0.98 [0.23; 3.32]</td>
<td>1.18 [0.49; 2.96]</td>
<td>0.91 [0.15; 3.36]</td>
</tr>
<tr>
<td>Asynchrony index (^{a,c})</td>
<td>1.69 [0.54; 4.37]</td>
<td>2.15 [0.90; 4.74]</td>
<td>1.49 [0.32; 4.68]</td>
</tr>
</tbody>
</table>

Data are expressed as medians and interquartile ranges

VCV volume control ventilation, PCV pressure-controlled ventilation, PSV pressure support ventilation

\(^{a}\) \(p\) significant PSV vs PCV

\(^{b}\) \(p\) significant VCV vs PCV

\(^{c}\) \(p\) significant VCV vs PSV
<table>
<thead>
<tr>
<th></th>
<th>AI ≤ 10 % (n = 44)</th>
<th>AI &gt; 10 % (n = 6)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of MV (days)</td>
<td>6 [5.0; 15.0]</td>
<td>16 [9.7; 20.0]</td>
<td>0.061</td>
</tr>
<tr>
<td>Reintubation</td>
<td>9 (20 %)</td>
<td>0 (0 %)</td>
<td>0.57</td>
</tr>
<tr>
<td>Tracheostomy</td>
<td>14 (32 %)</td>
<td>2 (33 %)</td>
<td>0.999</td>
</tr>
<tr>
<td>ICU mortality</td>
<td>6 (14 %)</td>
<td>4 (67 %)</td>
<td>0.011*</td>
</tr>
<tr>
<td>Hospital mortality</td>
<td>10 (23 %)</td>
<td>4 (67 %)</td>
<td>0.044*</td>
</tr>
</tbody>
</table>

Data are expressed as numbers and percentages or as medians and interquartile ranges.

**MV** mechanical ventilation, **ICU** intensive care unit, **AI** asynchrony index

* Significant at $p < 0.05$
Case

- Patient with ARDS has been on low Vt 6 ml/kg volume control and paralyzed.
- His plateau pressure is 30 cmH2O
- Patient remains severely hypoxemic (pO2 55) on 100% FiO2 and 15 PEEP.
Right Heart Dysfunction

Figure 2 – Acute cor pulmonale by a transthoracic approach in a patient ventilated for ARDS. A, Apical four-chamber view demonstrating right ventricular dilatation with an RV bigger than the left. B, Parasternal short-axis view of the LV demonstrating paradoxical septal motion (arrow, d-shape). LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ventricle.
A

RV FUNCTION EVALUATION

B

Pulmonary Vascular Resistance

RECRUITMENT
- Reverse hypoxic pulmonary vasoconstriction
- Unloads the RV
- Increases CO
- Improves hemodynamics

OVERINFLATION
- Overloads the RV
- Decreases CO
- Compromises hemodynamics

Lung stress (TPP)
RV friendly approach

• PEEP control
• Control of driving pressure <18
• iNO?
• Keep PCO2 <60
• Prone positioning
Prone Positioning

- Mechanisms
- Improves lung recruitment
- Improves V/Q matching
- Unloads RV
Conclusions

- ARDSnet low Vt, low plateau ventilation is current standard.
- Paralysis and Proning are appropriate in severely hypoxemic patients.
- Dysynchrony is common in ARDS patients and should be acted upon.
- RV dysfunction is an important cause of refractory hypoxemia in ARDS.