Consequences of Heart-Lung Interactions During Ventilation

John J. Marini
University of Minnesota
Minneapolis/ St. Paul
USA
Cardio-Pulmonary Interactions

- A Few Basics
- Left Ventricle
- Right Ventricle
- Cardiopulmonary Effects
  - Dead Space
  - Proning
  - Increased Abdominal Pressure
- Vascular Pressures & Flows on VILI
Transmural Pressure

High Pleural Pressure

Normal

Low Myocardial Compliance
Compartments and Vascular Pressures

Mean Systemic Pressure

Venous Return

VR = (MSP - Pra) / R_{ven}
Hemodynamic Effects of Lung Inflation With Positive Pressure
Cardio-Pulmonary Interactions

- A Few Basics
- *Left Ventricle*
- Right Ventricle
- Cardiopulmonary Effects
  - Proning
  - Increased Abdominal Pressure
- Vascular Pressures & Flows on VILI
Does PEEP Impair LV Function?

- Prevailing Theory 1980: Stiffened Myocardium Mediated By Ventricular Interdependence
  - Pericardial Space
  - Circumferential Muscle Fibers
  - Interventricular Septum
- Other Reported Mechanisms
  - ‘Depressant’ Factors From Lung Stretch
  - Coronary Ischemia
Ventricular Coupling During Lung Inflation

Shared Pericardium Septum
Interlocking Circumferential Muscle Fibers
Does PEEP Impair \textit{Left} Ventricular Contractility?
Pleural Surface Pressure Sensor

Diagram showing a pleural surface pressure sensor, which consists of a water-filled flexible plastic component connected to a transducer.
CLOSED CHEST
N = 10

Juxta-Cardiac Pressure Explains Slope Change with PEEP
Three Methods to IVC Return:

- PEEP
- Phlebotomy
- IVC Balloon

Am Rev Respir Dis 1985; 131(4):A146
Vagal Braking of Heart Rate by PEEP
Effects of PEEP on Hemodynamics

- Impeded Venous Return
- Increased Pulmonary Vascular Resistance
- Increased Venous Resistance
- Diminished Left Ventricular Compliance and Afterload
- *Restrained Heart Rate Increase (??)
- Coronary Ischemia (??)
Cardio-Pulmonary Interactions

• A Few Basics
• Left Ventricle
• Right Ventricle
• Cardiopulmonary Effects
  • Proning
  • Increased Abdominal Pressure
• Vascular Pressures & Flows on VILI
Two Views of the Right Ventricle

X. REPESSE 1, 2, C. CHARRON 1, A. VIEILLARD-BARON 1, 2

(Minerva Anestesiol 2012;78:941-8)
Ventricular Filling Curves

- **Right ventricle**
- **Left ventricle**

**Axes:**
- Ventricular output (L/min)
- Atrial pressure (mm Hg)
Respiratory Cycle Changes in Preload Drive Most PP Variation

\[ \Delta \text{ Pulse pressure (PP)} = PP_{\text{max}} - PP_{\text{min}} \]

\[ \Delta \text{ Systolic pressure (SP)} = SP_{\text{max}} - SP_{\text{min}} \]

Teboul, Pinsky
HEMODYNAMIC FAILURE

SIGNIFICANT PPV

YES

Hemodynamic effect of MV

NO

No hemodynamic effect of MV (consider norepinephrine)

RELATIVE, ABSOLUTE HYPOVOLEMIA

- Non-dilated RV
- SVC respiratory variations
- Low CVP
- Small IVC

FURTHER FLUID EXPANSION (benefits/risks balance)

RV OVERLOAD

- Dilated RV +/- ACP
- No SVC respiratory variations
- Elevated CVP
- Large IVC

FURTHER NO FLUID EXPANSION
- NOREPINEPHRINE
- RESPIRATORY SETTINGS ADAPTATION
  (Driving pressure, Pplateau, PEEP?)
- LIMIT HYPERCAPNIA
- PRONE POSITION?
Right Ventricle Centered Rules

1. Central venous pressure is only elevated in disease.
   Normally, central venous pressure is zero or slightly higher than intrathoracic pressure.

2. If central venous pressure rises and remains elevated following a fluid challenge: STOP!
   Make sure the patient is not slipping into acute cor pulmonale before proceeding.

3. For cardiac output to increase the RV must dilate.
   There is a physical limit to which fluid resuscitation alone can increase cardiac output.

4. Right ventricular hypertrophy has consequences
   Increased filling must be associated with increased filling pressure that limits venous return & impairs LV diastolic compliance.

Pinsky 2014
Zone of ↑ Risk
High *Vascular* Stresses Also Occur Within the ‘Baby Lung’
PEEP is a *Two-Edged Sword*

*For the Right Heart as well as for VILI*

Re-Opened Vascular Bed
Better Oxygenation
Less Hypercapnia

Stable Recruitment

Increased PVR

Increased Stress
PEEP Without Offsetting Recruitment Strains The Right Ventricle

Figure 2.—Pressure gradient between diastolic pulmonary artery pressure (PAP) and pulmonary capillary wedge pressure (PCWP) induced by application of a high PEEP.

(Minerva Anestesiol 2012;78:941-8)
PEEP-Induced Impairment Of Right Ventricular Ejection

X. REPESSÉ 1, 2, C. CHARRON 1, A. VIEILLARD-BARON 1, 2

(Minerva Anestesiol 2012;78:941-8)
Alveolar and Interstitial Forces During *Passive* Expansion

**Expiration**
- Alveolar pressure = 0 cmH₂O
- Interstitial pressure = -10 cmH₂O

**Inspiration**
- Alveolar pressure = 30 cmH₂O
- Interstitial pressure = -56 cmH₂O
Interstitial Pressures Differ With Breathing Effort

Vascular Transmural Pressures?

Int Care Med 2016
Higher Abdominal Pressure Gradient Translocates Vascular Volume

Spontaneous breathing / increased abdominal pressure
Oleic Acid Injury

Paw [cmH₂O]

0

20

40

I.A.P. [cmH₂O]

0

20

Translocation of Blood and Collapse

Quintel,Gattinoni
Experts’ opinion on management of hemodynamics in ARDS patients: focus on the effects of mechanical ventilation

A. Vieillard-Baron¹,²,³*, M. Matthay⁴, J. L. Teboul⁵,⁶, T. Bein⁷, M. Schultz⁸, S. Magder⁹ and J. J. Marini¹⁰
Cardio-Pulmonary Interactions

- A Few Basics
- Left Ventricle
- Right Ventricle
- **Cardiopulmonary Effects in ARDS**
  - Dead Space
  - Cor Pulmonale
- Vascular Pressures & Flows on VILI
Deadspace Parallels ARDS Severity

Mortality

Dead-Space Fraction

0.18–0.50
0.51–0.57
0.57–0.61
0.61–0.69
0.69–0.83

Nuckton NEJM 2004
Vascular Lesions of ARDS

What Causes High *Dead Space & Ventilation Requirements of ARDS*?

- Vascular occlusion
- Shunting (bypass) of CO$_2$ containing blood
- Lung hypoperfusion
- Excessive PEEP & mean airway pressure
- *Excessive demands on the ‘Baby Lung’*
Effect of inhaled CO$_2$ on hemorrhagic consolidation due to unilateral pulmonary arterial ligation

L. HENRY EDMUNDS, JR. AND JESS C. HOLM
Department of Surgery and Cardiovascular Research Institute, University of Washington

FIG. 1. Inflated left lungs of animals from group C-5 (left) and group CO$_2$-5 (right). Left lung of the CO$_2$-treated animal had only small peripheral areas of hemorrhagic consolidation.
Acute Cor Pulmonale

Apical 4-Chamber

Short Axis
Acute respiratory distress syndrome (ARDS)-associated acute cor pulmonale and patent foramen ovale: a multicenter noninvasive hemodynamic study

Annick Legras¹, Agnès Caille²,³, Emmanuelle Begot⁴,⁵, Gwenaëlle Lhéritier⁴,⁵, Thierry Lherm⁶, Armelle Mathonnet⁷, Jean-Pierre Frat⁸, Anne Courte⁹, Laurent Martin-Lefèvre¹⁰, Jean-Paul Gouëllo¹¹, Emmanuelle Mercier¹² and on behalf of the ARCO and CRICS network

Results: ACP was present in 36 patients, PFO in 21 patients, both PFO and ACP in 8 patients and the 130 remaining patients had neither PFO nor ACP. Patients with ACP exhibited a restricted left ventricle (LV) secondary to RV dilatation and had concomitant RV dysfunction, irrespective of associated PFO, but preserved LV systolic function. Despite elevated systolic pulmonary artery pressure (sPAP), patients with isolated PFO had a normal RV systolic function. sPAP and PaCO₂ levels were significantly correlated.

Conclusions: In patients under protective mechanical ventilation with moderate-to-severe ARDS, ACP was associated with LV restriction and RV failure, whether PFO was present or not. Despite elevated sPAP, PFO shunting was associated with preserved RV systolic function.
‘Oscillate’ Trial
Essentially, **Very High PEEP & Very Low VT**

![Graph showing survival probability over days since randomization](NEJM 2/28/2013)

- Control
- HFOV

*P = 0.004 by log-rank test*
What happened in the Oscillate Trial?

ARDSnet
Aerated Lung Size & RV Strain
Parallel Mean Airway Pressure
Right Ventricular Protection

Key points

- Acute cor pulmonale (ACP) occurs in 25% of cases of ARDS.
- ACP worsens prognosis when not taken into account to adapt respiratory settings.
- RV function assessment can be used to estimate the balance between lung recruitment and lung overdistension resulting from the respiratory strategy.
- The RV protective approach includes a plateau pressure below 27–28 cmH₂O, the absence of intrinsic PEEP, controlled $P_{a\text{CO}_2}$, a ‘low’ PEEP, and routine use of prone positioning of patients with the most severe ARDS.
Prone Positioning Relieves Lung Compression by the Heart

Albert & Hubmayr, *AJRCCM* 2000
Preload Reserve & Proning Response

Non-Responders

Responders

Jozwiak, Teboul, Anguel, et al.
Hemodynamic Responders To Prone Positioning Usually Have Preload Reserve

Jozwiak, Teboul, Anguel, et al.

Am J Respir Crit Care Med Vol 188, Iss. 12, pp 1428–1433, Dec 15, 2013
Experts’ opinion on management of hemodynamics in ARDS patients: focus on the effects of mechanical ventilation

A. Vieillard-Baron¹,²,³*, M. Matthay⁴, J. L. Teboul⁵,⁶, T. Bein⁷, M. Schultz⁸, S. Magder⁹ and J. J. Marini¹⁰

---

**HEMODYNAMIC FAILURE**

**SIGNIFICANT PPV**

**YES**

- Hemodynamic effect of MV
  - RELATIVE, ABSOLUTE HYPOVOLEMIA
    - Non-dilated RV
    - SVC respiratory variations
    - Low CVP
    - Small IVC
  - DISCUSS FLUID EXPANSION (benefits/risks balance)

**NO**

- No hemodynamic effect of MV (consider norepinephrine)
  - RV OVERLOAD
    - Dilated RV +/- ACP
    - No SVC respiratory variations
    - Elevated CVP
    - Large IVC
  - NO FLUID EXPANSION
    - NOREPINEPHRINE
    - RESPIRATORY SETTINGS ADAPTATION
      (Driving pressure, Pplateau, PEEP?)
    - LIMIT HYPERCAPNIA
    - PRONE POSITION?
Fig. 3 Proposed algorithm regarding indications for ECMO/ECCO$_2$R and hemodynamic management during ECMO/ECCO$_2$R in patients with severe ARDS at risk of hemodynamic instability. Readers have to be cautioned that this algorithm was not previously validated. $V_t$ tidal volume, $P_{plat}$ Inspiratory plateau pressure, MAP mean arterial pressure, NOR norepinephrine, $SvO_2$ central venous oxygen saturation. Asterisk as re-emphasized in the text, this is currently not evidence-based data.
Hemodynamic Management ARDS

<table>
<thead>
<tr>
<th>Hemodynamic failure</th>
<th>Incidence</th>
<th>Causes</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>60–70%</td>
<td>Sepsis</td>
<td>++++</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PH</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>MV</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HL Interactions</th>
<th>Increase in Ppi&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Increase in PT, mPaw</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Decrease in VR</td>
<td>Increase in RV afterload</td>
</tr>
<tr>
<td></td>
<td>Decrease in LV afterload</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Decrease in Lung edema</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hemodynamic monitoring</th>
<th>PPV</th>
<th>CVP/RAP</th>
<th>ECHO</th>
<th>PAC/TPT device</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Is mandatory</td>
<td>Should be used</td>
<td>Is mandatory</td>
<td>Could be considered</td>
</tr>
<tr>
<td></td>
<td>May indicate preload responsiveness</td>
<td>High when RV failure</td>
<td>May detect ACP</td>
<td>PAP</td>
</tr>
<tr>
<td></td>
<td>May indicate RV afterload dependency</td>
<td>Of limited value due to transmitted pressure (Ppi)</td>
<td>May measure IVC size</td>
<td>Transmural PAOP when high PEEP</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Transmural pressure (RAP-Peso) is more accurate</td>
<td></td>
<td>MPAP – PAOP</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>RV support</th>
<th>Fluids</th>
<th>Catecholamines</th>
<th>Respiratory strategy</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>NE is the drug of choice</td>
<td>Optimize P/F</td>
<td>Selective pulmonary vasodilators could be considered</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Calcium sensitizer improves RV coupling but cannot be recommended</td>
<td>Limit $\text{Paco}_2 &lt; 48 \text{ mmHg}$</td>
<td>$\text{ECCO}_2$R has to be evaluated to prevent VILI and protect the RV</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Limit driving pressure $&lt; 18 \text{ cmH}_2\text{O}$</td>
<td>The RV</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Adapt PEEP (recruit without overdistend)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Consider PP</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Avoid HFOV with high PEEP baseline</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Avoid vigorous SB</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> Ppi: Pulmonary Thromboembolism Index
Cardio-Pulmonary Interactions

• A Few Basics
• Left Ventricle
• Right Ventricle
• Cardiopulmonary Effects
  • Proning
  • Increased Abdominal Pressure

• *Vascular Pressures & Flows on VILI*
Regional Hemorrhagic Edema From Mechanical Stresses
Vascular Gradient Dependence
Phasic Systemic Gas Embolism
Microvascular Fractures in ARDS
Portals for Gas and Bacteremia?

Hotchkiss et al
CCM Oct 2002
Bacterial Dissemination Depends on Ventilatory Strategy

But Why Vascular Gradient Dependence?
Zone 2 Waterfall Phenomenon
Static Mean Pressure Condition

- Upstream River (Pulmonary Artery pressure)
- Dam
- (Alveolar pressure)
- Downstream River (Pulmonary venous pressure)

Dynamic Instantaneous Pressure Condition

- P_{pas}
- P_{pad}
- Respiratory Dam
Higher Vascular Pressures and Ventilating Frequency Worsen VILI

Epithelial and Endothelial Power?
Could Endothelial Injury Be Another ‘Motor’ For MOSF?

Figure 7 — Acute endothelial injury. Early separation of endothelial cell (E) from capillary basement membrane (B) with interposition of fibrin and cellular debris. Mitochondria (M) and cisternae (C) are swollen, but intercellular junctions are still intact (arrows). Platelets (P), fibrin (F), and membrane-bound debris lie within capillary lumen on right (biopsy, Day 10, toxic inhalation). (x 6580)
• Energy dissipation
• **Endothelial** shear
• Mediator *generation*
Upstream Gas Exchange
Patient-Ventilator Interactions & VILI

Hemodynamic Clinical Interventions

- Inotropes and Pulmonary Vasoactive Drugs. (Nitric Oxide/Prostaglandin)
- “Wet” vs “Dry” Approach to Fluid Management
- Metabolic Rate Control and Ventilation Targets
- Breathing Pattern Modification (NMBA)
- Redirection of Blood Flow
  - PEEP
  - Prone Position
- Recruitment
- Extra-Pulmonary Gas Exchange