SESSION II:
PERSPECTIVES IN ISCHEMIC HEART DISEASE (PART II)

R. Hubmayr (Rochester—MN—USA)

Lecture
Management of the critically ill cardiac patient: a Critical Care Specialist’s perspective
Management of the Critically Ill Cardiac Patient:
An Intensivist’s Perspective

Rolf D Hubmayr, MD
Mayo Clinic College of Medicine

http://mayoresearch.mayo.edu/mayo/research/hubmayr/index.cfm
Ventilator-Induced Lung Injury
The Real Culprit ?
Effects of CPAP on the distribution of lung water

Benefits of CPAP in Heart Failure

Kaneko et al. NEJM 348 (13): 1233, 2003
Under which circumstances are the lungs a Ventilatory Assist Device?


<table>
<thead>
<tr>
<th>Variable</th>
<th>Standard Oxygen Treatment (N=367)</th>
<th>CPAP or NIPPV (N=702)</th>
<th>Odds Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death within 7 days (% of patients)</td>
<td>9.8</td>
<td>9.5</td>
<td>0.97 (0.63 to 1.48)</td>
<td>0.87</td>
</tr>
<tr>
<td>Death within 30 days (% of patients)</td>
<td>16.4</td>
<td>15.2</td>
<td>0.92 (0.64 to 1.31)</td>
<td>0.64</td>
</tr>
<tr>
<td>Intubation within 7 days (% of patients)</td>
<td>2.8</td>
<td>2.9</td>
<td>1.05 (0.49 to 2.27)</td>
<td>0.90</td>
</tr>
<tr>
<td>Admission to critical care unit (% of patients)</td>
<td>40.5</td>
<td>45.2</td>
<td>1.21 (0.93 to 1.57)</td>
<td>0.15</td>
</tr>
<tr>
<td>Myocardial infarction (% of patients)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WHO criteria</td>
<td>24.9</td>
<td>27.0</td>
<td>1.12 (0.84 to 1.49)</td>
<td>0.46</td>
</tr>
<tr>
<td>Universal criteria</td>
<td>50.5</td>
<td>51.9</td>
<td>1.06 (0.82 to 1.36)</td>
<td>0.66</td>
</tr>
<tr>
<td>Difference between Means (95% CI)†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean length of hospital stay (days)</td>
<td>10.5</td>
<td>11.4</td>
<td>0.9 (−0.2 to 2.0)</td>
<td>0.10</td>
</tr>
<tr>
<td>Mean change at 1 hr after start of treatment‡</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyspnea score §</td>
<td>3.9</td>
<td>4.6</td>
<td>0.7 (0.2 to 1.3)</td>
<td>0.008</td>
</tr>
<tr>
<td>Pulse rate (beats/min)</td>
<td>13</td>
<td>16</td>
<td>4 (1 to 6)</td>
<td>0.004</td>
</tr>
<tr>
<td>Blood pressure (mm Hg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>34</td>
<td>38</td>
<td>3 (−1 to 8)</td>
<td>0.17</td>
</tr>
<tr>
<td>Diastolic</td>
<td>22</td>
<td>22</td>
<td>0 (−3 to 3)</td>
<td>0.95</td>
</tr>
<tr>
<td>Respiratory rate (breaths/min)</td>
<td>7.1</td>
<td>7.2</td>
<td>0.2 (−0.8 to 1.1)</td>
<td>0.74</td>
</tr>
<tr>
<td>Peripheral oxygen saturation (%)</td>
<td>3.5</td>
<td>3.0</td>
<td>−0.4 (−1.4 to 0.6)</td>
<td>0.41</td>
</tr>
<tr>
<td>Arterial pH</td>
<td>0.08</td>
<td>0.11</td>
<td>0.03 (0.02 to 0.04)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Arterial PaO2 (kPa)</td>
<td>0.7</td>
<td>−0.6</td>
<td>−1.2 (−2.6 to 0.1)</td>
<td>0.07</td>
</tr>
<tr>
<td>Arterial PaCO2 (kPa)</td>
<td>0.8</td>
<td>1.5</td>
<td>0.7 (0.4 to 0.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Serum bicarbonate level (mmol/liter)</td>
<td>1.7</td>
<td>1.8</td>
<td>0.1 (−0.7 to 1.0)</td>
<td>0.77</td>
</tr>
</tbody>
</table>
Noninvasive Ventilation in Acute Cardiogenic Pulmonary Edema

No. at Risk
<table>
<thead>
<tr>
<th></th>
<th>CPAP or NIPPV</th>
<th>Standard therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. at Risk</td>
<td>667</td>
<td>348</td>
</tr>
</tbody>
</table>

No. at Risk
<table>
<thead>
<tr>
<th></th>
<th>CPAP</th>
<th>NIPPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. at Risk</td>
<td>325</td>
<td>342</td>
</tr>
</tbody>
</table>

Ventilator Management:
Physical Therapy of Injured Lungs

Overdistension

Collapse

TLC
CV
FRC

IC
Injury is associated with a large variability in regional impedance.
Open the lung and keep it open

**Critical Assumptions**

- $\Delta P$ is the critical VILI determinant
- There is no Pplat safety threshold
- Preventing opening and collapse is more important than avoiding high transpulmonary pressure
- Measures of Gas Exchange Efficiency are acceptable surrogate efficacy endpoints
The Meaning of Overdistension?
Electrical Impedance Tomography

FUZZY MODELING OF ELECTRICAL IMPEDANCE TOMOGRAPHY IMAGES OF THE LUNGS

Patients on invasive mechanical ventilation ≥48h (n=482)

Excluded

Neuromuscular disease (n=12)
Pneumonectomy (n=11)
Home ventilatory support (n=6)
Palliative care only (n=6)

Cohort patients (n=447)

ALI present at the onset of mechanical ventilation (n=115)

PaO2/FiO2 <300, diffuse infiltrates and PAOP<18 or no clinical evidence of left atrial hypertension

Y

ALI not present at the onset of mechanical ventilation (n=332)

PaO2/FiO2 <300, diffuse infiltrates and PAOP<18 or no clinical evidence of left atrial hypertension

N

Late-onset ALI (n= 80)

No worsening (n=177)

VAP (n=34)

Cardiogenic pulmonary edema (n=41)

Mayo Ventilator Practice 2001

Probability of late-onset Acute Lung Injury (%)


VALI & TRALI: CAN WE PREVENT IATROGENIC ARDS?
Better Lung Protection

Noisy Ventilation

High Frequency Oscillatory Ventilation

ARDS-NET Approach

Better Synchrony

Proportional Assist Ventilation

Neurally Adjusted Ventilatory Assist

Patient knows best
Neurally Adjusted Ventilation Assist

Efficacy of HFO

- Adults
- Neonates

Henderson-Smart DJ, Cools F, Bhuta T, Offringa M

Am J Respir Crit Care Med  Vol 166. pp 801–808, 2002

Copyright © 2008 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd
Bridge to Lung Transplantation With the Extracorporeal
Membrane Ventilator Novalung in the Veno-Venous Mode:
The Initial Hannover Experience

Stefan Fischer,* Marius M. Hoepf,+ Sandra Tomaszek,* Andre Simon,* Jens Gottlieb,+ Tobias Welte,+ Axel Haverich,*
and Martin Striebel*

Table 1. Patient Characteristics Before Novalung Implantation

<table>
<thead>
<tr>
<th></th>
<th>Patient 1</th>
<th>Patient 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>35</td>
<td>38</td>
</tr>
<tr>
<td>Gender (m/f)</td>
<td>F</td>
<td>F</td>
</tr>
<tr>
<td>Indication for LTx</td>
<td>Alveolitis</td>
<td>CF</td>
</tr>
<tr>
<td>Pre v-v Novalung ventilation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FIO₂</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Peak inspiratory pressure (mm Hg)</td>
<td>45</td>
<td>51</td>
</tr>
<tr>
<td>PEEP (mm Hg)</td>
<td>15</td>
<td>6</td>
</tr>
<tr>
<td>Tidal volume (ml)</td>
<td>214</td>
<td>185</td>
</tr>
<tr>
<td>PaO₂ at Novalung insertion (mm Hg)</td>
<td>38</td>
<td>37</td>
</tr>
<tr>
<td>PaCO₂ at Novalung insertion (mm Hg)</td>
<td>89</td>
<td>173</td>
</tr>
<tr>
<td>pH in arterial blood</td>
<td>7.22</td>
<td>6.95</td>
</tr>
<tr>
<td>Time of pre-Novalung ventilation (days)</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>Secondary organ failure (yes/no)</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Hemodynamics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean arterial pressure (mm Hg)</td>
<td>67</td>
<td>75</td>
</tr>
<tr>
<td>Central venous pressure (mm Hg)</td>
<td>15</td>
<td>10</td>
</tr>
<tr>
<td>Mean pulmonary artery pressure (mm Hg)</td>
<td>32</td>
<td>n/a</td>
</tr>
<tr>
<td>Inotrop support (yes/no)</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Infection status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sepsis (yes/no)</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Positive blood cultures (yes/no)</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Test results</td>
<td>Neg.</td>
<td>Neg.</td>
</tr>
<tr>
<td>Other positive cultures (yes/no)</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Test results</td>
<td>Neg.</td>
<td>Pseud aer in lung</td>
</tr>
</tbody>
</table>

CF, cystic fibrosis; Pseud aer, Pseudomonas aeruginosa; n/a, not assessed.
Hypercapnic Acidosis

Effects of CO$_2$ on Pulmonary Vascular Barrier Properties

Weight Gain (g)

- Uninjured Control
- Normo-capnic Injury
- Hypo-capnic Injury
- Hyper-capnic Injury

Permissive Hypercapnia and VILI

Scott E. Sinclair, Am. J. Respir. Crit. Care Med. 166: 403-408
Bicarbonate buffers generate CO₂

<table>
<thead>
<tr>
<th>Case</th>
<th>pHₐ Pre-NaHCO₃</th>
<th>pHₐ Post-NaHCO₃</th>
<th>PₐCO₂ Pre-NaHCO₃ (mm Hg)</th>
<th>PₐCO₂ Post-NaHCO₃ (mm Hg)</th>
<th>Base Deficit Pre-NaHCO₃ (mEq/L)</th>
<th>Base Deficit Post-NaHCO₃ (mEq/L)</th>
<th>NaHCO₃ Dose (mEq)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD</td>
<td>7.21 ± 0.06</td>
<td>7.10 ± 0.04*</td>
<td>53 ± 19</td>
<td>62 ± 24*</td>
<td>-6.4 ± 9.5</td>
<td>-9.7 ± 11.3</td>
<td>82.5 ± 64.5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Case</th>
<th>pHₐ Pre-THAM</th>
<th>pHₐ Post-THAM</th>
<th>PₐCO₂ Pre-THAM (mm Hg)</th>
<th>PₐCO₂ Post-THAM (mm Hg)</th>
<th>Base Deficit Pre-THAM (mEq/L)</th>
<th>Base Deficit Post-THAM (mEq/L)</th>
<th>THAM dose (mmol/kg/h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD</td>
<td>7.14 ± 0.05</td>
<td>7.26 ± 0.08†</td>
<td>63 ± 19</td>
<td>50 ± 16†</td>
<td>-8.1 ± 8.0</td>
<td>-4.4 ± 7.6†</td>
<td>1.07 ± 1.23</td>
</tr>
</tbody>
</table>

Kallet et al. AJRCCM 161: 1149, 2000
Effects of Hypercapnic Acidosis on Myocardial Contractility

Weber et al. AJRCCM 162: 1361; 2000
Cardiogenic or Non-Cardiogenic Edema

The heart is NOT the problem! It’s the LUNGS

The lungs are NOT the problem! It’s the HEART
The Swan and the Zone 1 Misconception

There is Nothing Magic about a Wedge of 18

Arterial and Capillary Resistance = 0.6 PVR

Venous Resistance = 0.4 PVR

The Wedge Pressure is NOT equal to the capillary hydrostatic pressure!!!
The Starling Equation does NOT tell the Whole Story

• Endothelial and Epithelial Barrier Properties are actively controlled

• Compliance and Hydration of the Lung Interstitium is regulated by matrix metalloproteinases

• Edema Clearance from the Alveolar Space is accomplished by active Ion Transport
Figure 2

Actin/Myosin Contraction ↔ Cellular Adhesion

Thrombin | Sph 1-P

PAR-1 | Occludin

Gelsolin | hsp27 | p38

Cofilin | MLC phosphatase | MLCK

Rho Kinase | Ca²⁺-CaM | SRC

Myosin | Actin Stress Fibers

Myosin | Actin Stress Fibers

PECAM-1 | Integrin

Zona Occludins

Adherens Junction

β/γ cat | SHP2

β/γ cat | SHP2

αA

Vin | Pax | Talin

FAK

Cortical Actin

Barrier Dysfunction

Barrier Integrity

Dudek & Garcia JAP. 91(4):1487-1500, 2001
Integrating acute lung injury and regulation of alveolar fluid clearance

David M. Guidot,¹ Hans G. Folkesson,² Lucky Jain,¹
Jacob I. Sznajder,³ Jean-François Pittet,⁴ and Michael A. Matthay⁴

First published May 12, 2006; doi:10.1152/ajplung.00153.2006.
Nitric oxide-dependent inhibition of alveolar fluid clearance in hydrostatic lung edema

![Graph A](image)
P<sub>LA</sub>, cmH<sub>2</sub>O

![Graph B](image)

Negative-Feedback Loop Attenuates Hydrostatic Lung Edema via a cGMP-Dependent Regulation of Transient Receptor Potential Vanilloid 4

(Circ Res. 2008;102:966-974.)
Stimuli of Na Transport

• Dopamine
• Catecholamines
• Glucocorticoids
• Aldosterone
• Thyroid Hormone
• Cytokines and Growth Factors (HGF, KGF, TNFα)

NHLBI Workshop Summary: Alveolar Epithelial Transport. AJRCCM
Vol 162 pp 1021, 2001
Normal Lung

Edematous Lung

Hubmayr; Am J Respir Crit Care Med, 2002; 165:1647-1653
Crackles and the Sounds of VILI
Patient on Ventilator