Organ dysfunction in AHF

PULMONARY EDEMA

Josep MASIP MD, PhD, FESC

Intensive Care Dept. Consorci Sanitari Integral
Cardiology Dept. Hospital Sanitas CIMA. Barcelona
Associate Professor Cardiology
University of Barcelona. SPAIN

NO CONFLICT OF INTEREST
<table>
<thead>
<tr>
<th>LUNG DYSFUNCTION IN HEART FAILURE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ACUTE</strong></td>
</tr>
<tr>
<td>Pulmonary Edema (Hydrostatic)</td>
</tr>
<tr>
<td>Starling forces imbalance in pulmonary capillaries</td>
</tr>
<tr>
<td>Alveolar fluid reabsorption (NO-dependent)</td>
</tr>
<tr>
<td>Alveolar fluid secretion (Cl⁻ / Na⁺ transport-driven)</td>
</tr>
<tr>
<td>Pulmonary capillary stress failure</td>
</tr>
<tr>
<td>Individual susceptibility and other forms of APE</td>
</tr>
<tr>
<td><strong>CHRONIC</strong></td>
</tr>
<tr>
<td>Restrictive pattern</td>
</tr>
<tr>
<td>Cardiac asthma</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
</tr>
</tbody>
</table>
AHF SYNDROMES

Hypertensive AHF

Acutely Decompensated Chronic HF

PULMONARY OEDEMA

ACS and HF

Cardiogenic shock

Right HF

ESC 2008
Starling forces involved in APE

ALVEOLUS

<table>
<thead>
<tr>
<th>Lymphatic pressure</th>
<th>Surface tension</th>
</tr>
</thead>
</table>

INTERSTITIUM

CAPILLARY

Lymphatic drainage

Hydrostatic pressure

8-10 mmHg

Oncotic pressure

25 mmHg
NO dependence of alveolar fluid reabsorption

4-amino-5-methylamino-2-7-difluorofluorescein diacetate (DAF-FM DA)

N-nitro-L-arginine methyl ester (L-NAME)

Transcellular Na+ and Cl− movement across alveolar epithelial cells

**Diagram:**
- **CFTR:** Cystic fibrosis transmembrane conductance regulator
- **ENaC:** Amiloride-inhibitable epithelial Na+ channel
- **NKCC:** Na-K-Cl cotransporter
- **CL−:** Chloride ions
- **Na+:** Sodium ions
- **K+:** Potassium ions
- **H2O:** Water

**Legend:**
- Normal LAP

**Source:** Londino et al. PNAS 2013
ALVEOLAR FLUID CLEARANCE

65 mechanically ventilated APE patients

Vergheze et al. J Appl Physiol 1999
ALVEOLAR FLUID CLEARENCE

PEEP

Tidal Volume

Verghese et al. J Appl Physiol 1999
Low reabsorption rate was not related to LVEF or PCWP

Table 6. Comparison of outcomes in patients with intact vs. impaired alveolar fluid clearance

<table>
<thead>
<tr>
<th>Outcome Variable</th>
<th>Impaired $(n=16)$</th>
<th>Intact $(n=49)$</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in alveolar-arterial oxygen difference at 4 h</td>
<td>4 ± 100</td>
<td>−40 ± 132</td>
<td>0.19</td>
</tr>
<tr>
<td>Change in alveolar-arterial oxygen difference at 24 h</td>
<td>−167 ± 198</td>
<td>−268 ± 172</td>
<td>0.03</td>
</tr>
<tr>
<td>Days of unassisted ventilation, median (range)</td>
<td>8 (0–27)</td>
<td>23 (0–27)</td>
<td>0.10</td>
</tr>
<tr>
<td>Hospital mortality, %</td>
<td>44%</td>
<td>26%</td>
<td>0.20</td>
</tr>
</tbody>
</table>

Values of change in alveolar-arterial oxygen difference at 4 and 24 h are means ± SD.
High altitude pulmonary edema (HAPE)

Genetic HAPE susceptibility

Defective NO synthesis

↑ ET-1, oxidative stress, sympathetic outflow

Impaired pulmonary vasodilation

Augmented pulmonary vasoconstriction

Exaggerated hypoxic pulmonary hypertension
High altitude pulmonary edema (HAPE)

IMPAIRMENT OF ALVEOLAR FLUID CLEARANCE

Altered transepithelial Na transport
- Genetic
- Induced by hypoxia-hypothermia

Greater hypoxic pulmonary vasoconstriction


U. Scherrer et al. Prog Cardiovasc Dis 2010
To cause APE, the ↑↑↑ PAP has to be transmitted to the capillaries

Inhomogeneous hypoxic pulmonary vasoconstriction

Some capillaries are not protected
Regional overperfusion with ↑ PCP

Hypoxia → pulmonary veno-constriction
Increased vascular resistance downstream to the site of fluid filtration
Further increase in PCP

Impairment of alveolar fluid clearance

Capillary stress failure with altered permeability

BAL: erythrocytes and large molecular weight proteins
Neurogenic pulmonary edema

Spinal cord injury, Severe epileptic grand mal seizure,
Primary spinal cord hemorrhage, Intracerebral bleeding,
Brain trauma, Subdural hematoma, Subarachnoid hemorrhage

Elevation of intracranial pressure
Rapid systemic sympathetic discharge
Peripheral vasoconstriction
Increase in systemic blood pressure
Elevated venous return
Reduction LV compliance

Constriction of the pulmonary veins
Hydrostatic increase in PCP

Damage to the alveolar wall and the leakage of fluid into the interstitium and intraalveolar space, hemorrhage and intra-alveolar accumulation of protein-rich edema fluid
It is likely to occur as a result of overload of the vascular and lymphatic drainage systems because of the high cardiopulmonary demands of intense exercise, resulting in APE
SEVERE ACUTE CARDIOGENIC PULMONARY EDEMA
The increase in capillary pressure or volume disrupts the anatomic configuration of the membrane.

M. Guazzi et al. Chest 2003
ACUTE HEART FAILURE

- Backward hemodynamic effects
- Increasing hydrostatic pressure
- Interstitial and Alveolar fluid filtration

Alveolar-capillary stress failure

NEUROHORMONAL ACTIVATION

- Neurohormonal activation (Angiotensin II, Norepinephrine)
- Inflammatory reaction (Cytotoxic stimuli: IL, TNFα)
- Gene reexpression

Lung capillaries and Tissue membrane REMODELING

- Impaired endothelial permeability
- Loss of active alveolar clearance capacity
- Extracellular matrix thickening

Permanent lung dysfunction

REVERSIBILITY

CHRONIC

Modified from M. Guazzi et al. Chest 2003
DM: Alveolar-capillary membrane gas conductance
DLCO: Diffusion capacity
Vc: Capillary Volume

M. Guazzi. J Cardiac Failure 2008
### Pulmonary function in CHRONIC HF patients according to Peak-VO2

<table>
<thead>
<tr>
<th>Peak VO₂</th>
<th>n</th>
<th>FVC</th>
<th>FEV-1</th>
<th>DLCO</th>
<th>DM</th>
<th>VC</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;12</td>
<td>25</td>
<td>67%</td>
<td>76%</td>
<td>65</td>
<td>27.7</td>
<td>83</td>
</tr>
<tr>
<td>12-16</td>
<td>75</td>
<td>80%*</td>
<td>85%*</td>
<td>80*</td>
<td>30.3</td>
<td>104</td>
</tr>
<tr>
<td>16-20</td>
<td>64</td>
<td>85%*</td>
<td>90%*</td>
<td>80*</td>
<td>31.1</td>
<td>103*</td>
</tr>
<tr>
<td>&gt;20</td>
<td>26</td>
<td>87%*</td>
<td>98%*</td>
<td>90*</td>
<td>42.3*</td>
<td>111*</td>
</tr>
</tbody>
</table>

* p > 0.05 or 0.01

*P. Agostoni. Pulmonary Pharmacology & Therapeutics 2007*
Prevalence asthma syndromes in > 65 years is 6-10%

Elderly with CHF have 35% cardiac asthma (3.5 times greater)
Conclusions

• Hydrostatic pulmonary edema is the common clinical presentation of LV-AHF. An imbalance in the starling forces in the capillaries is the main pathophysiologial mechanism, but NO-dependent alveolar fluid reabsorption, Cl⁻ and Na⁺ transport alveolar fluid secretion and alveolar-capillary stress failure with inflammatory activation are other important contributing factors.

• Individual susceptibility may explain why in different scenarios some patients tend to present severe APE.

• Chronic and severe decompensations may lead to persisting alterations in the lung parenchyma and bronchi with a restrictive pattern, cardiac asthma and finally, pulmonary hypertension.