Wet Lungs Dry lungs
Impact on Outcome in ARDS

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Today’s talk

- Pathophysiology of ARDS
- The case for dry
- Targeting EVLW
Disclosures

- Advisor for Pulsion Medical Systems - PiCCO™
Lung is a fairly dry place

- Needed for proper gas exchange
  - Surfactant function
  - Recruitment
  - Diffusion of gases

- Increase EVLW by only 200-300ml - ALI
- In ALI mortality approaches 100% if EVLW > 14.3 ml/kg PBW on day 1
Acute lung injury
Gap formation

Vessel Lumen

Endothelium

Epithelium

Alveoli

Scanning EM

Hypoxia
Platelets
Thrombin
TNF
Reactive Oxygen/Nitrogen Species
Stretch
Cytokines

Cell Activation

Gap formation

LPS

Matthay, et al
Acute lung injury
Animal studies: modest decrease in pulmonary vascular pressure can reduce the quantity of pulmonary edema in oleic acid-induced permeability pulmonary edema.

Reduction in pulmonary capillary wedge pressure has been associated with increased survival in human ARDS patients.
Improved survival in ARDS patients associated with a reduction in pulmonary capillary wedge pressure

H Humphrey, J Hall, I Sznajder, M Silverstein and L Wood

*Chest* 1990;97:1176-1180
DOI 10.1378/chest.97.5.1176

40 pts with ARDS

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (N = 16)</th>
<th>Group 2 (N = 24)</th>
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<tbody>
<tr>
<td>Survived</td>
<td>12 (75%)</td>
<td>7 (29%)*</td>
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<tr>
<td>ICU length of stay (days)</td>
<td>8.9 ± 8</td>
<td>14.8 ± 11.4 days</td>
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*p*<0.02 chi square, Mantel-Haenzel.
Argument for Dry

- Several studies in humans supporting using diuretics and fluid restriction in an attempt to reduce the amount of EVLW in ALI
EVLW goal directed Rx of ALI

- Prospective, randomized study
- 48 subjects in ICU with SBP < 90 felt to require PAC
- Routine vs EVLW driven management
- PAOP, EVLW Q6-8 hours
- Subgroup with ARDS (19): EVLW > 14, PAOP < 19
  - Mortality 33% (3/9) vs. 100% (10/10) (p<0.05)

Eisenberg et al, Am Rev Respir Dis 1987;136
EVLW

Pulmonary Hydrostatic Pressure

Increased Permeability

Normal

Improved Outcome Based on Fluid Management in Critically Ill Patients Requiring Pulmonary Artery Catheterization\textsuperscript{1-3}

JOHN P. MITCHELL, DAN SCHULLER, FRANK S. CALANDRINO, and DANIEL P. SCHUSTER

Am Rev Respir Dis 1992;145

- Prospective, randomized study
- 101 of 302 consecutive patients clinically requiring PAC met eligibility
- EVLW vs PAOP protocol
Diuresis to goal EVLW - management

n=101

Comparison of Two Fluid-Management Strategies in Acute Lung Injury

The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network

- 1000 patients with ALI/ARDS prospectively randomized to fluid conservative vs. fluid liberal
  - Fluid-conservative/CVC: fluids were restricted and diuretics administered to maintain a CVP < 4 mm Hg;
  - Fluid-liberal/CVC: fluids were used to maintain a CVP between 10 and 14 mm Hg
- 60 day mortality primary outcome
- ARDS-net ventilation
- Weaning Protocol as part of Ventilator Management Protocol
FACTT Results

- Difference in outcome between liberal and conservative fluid management arms:
  - improved the oxygenation index
  - improved Lung Injury Score
  - lowered plateau airway pressure
  - increased the number of ventilator-free days (14.6 ± 0.5 vs. 12.1 ± 0.5; \(P = .0002\))
  - Increased ICU-free days (13.4 ± 0.4 vs 11.2 ± 0.4; \(P = .0003\)) to day 28.
- 2.9% reduction in the 60-day mortality rate in the conservative fluid management arm compared with the liberal fluid management arm, 25.5% vs. 28.4%, respectively; \(p = 0.30\)
37 with ALI and serum protein ≤ 5.0 g/dl
Randomized to receive five-day protocolized regimen of 25g albumin every 8 hours with continuous infusion of furosemide vs. dual placebo

- Improved fluid balance
  +5.3 kg more weight loss in treatment group (p = .04)
- Improved oxygenation
  +PaO₂/FiO₂ - 171 to 236 (p = .02)
- Improved hemodynamics
  +MAP increased 80 to 88 mmHg (p = .10)
  +Heart rate decreased 110 to 95 (p = .008)
Make them dry

Evidence strongly suggests for most patients with ALI/ARDS who are not in shock using:

1. Diuretics
2. Fluid restriction
3. Albumin and furosemide in selected patients with hypoproteinemia and ALI

How best to do it

Targeting EVLW
The Case for Measuring EVLW in ARDS

1. Can “drown” with only 200-300 ml extra lung water
2. Want to know precisely what is happening to lung water with resuscitative and therapeutic interventions
3. CXR, oxygen need, severity of injury – LIS, are imprecise determinates of the amount of pulmonary edema
4. No correlation to PaOP, CVP or fluid balance with lung water
The case for measuring EVLW

5. EVLW predicts mortality in ARDS
6. EVLW predicts progression to ALI in patients at risk
7. EVLW driven protocols only approach shown to improve mortality
Large increase in EVLW for small increase CO.
27 year old male with AML developed severe ARDS
- ARDSNet ventilation
  + RR 35, Vt = 5ml/kg PBW
  + plateau pressure ~ 33
  + PaO2/FiO2 62 with 18 PEEP 100% O₂
- APRV
  + PaO2/FiO₂ 86
Fluid balance: + 3.7 liters
Blood Pressure: 135/80 → 82/38
HR: 95 → 128
CVP: 10 mmHg
FiO₂: 1.0
Urine output: 60ml/hr → 0ml
PaO₂/FiO₂: 82

Hypotension, tachycardia, high normal CVP, hypoxemia, fluid long
What would you do?

- Fluid long, decreased urine output, high normal CVP in shock
- Vasopressors?
- Inotropes?
- Fluids?
Transpulmonary thermodilution measurements

- CI = 2.7 L/min/m²
- SVRI = 825 dyne.cm.sec⁻⁵/m²
- GEDVI = 550 ml/m² (800-1000)
- PPV = 18-20% (13%)
- EVLWI = 19 ml/kg

Septic, dry but with severe pulmonary edema
Gave 500 ml bolus of NS

- MAP = 55 mmHg
- CVP = 10 mmHg
- CI = 3.2 L/min/m²
- SVRI = 950 dyne.cm.sec⁻⁵/m²
- GEDVI = 625 ml/m² (800-1000)
- PPV = 16% (13%)
- EVLWI = 19 ml/kg

No change in lung water so given 2 additional boluses
- MAP = 58 mmHg
- CVP = 11 mmHg
- CI = 4.1 L/min/m²
- SVRI = 985 dyne.cm.sec⁻⁵/m²²
- GEDVI = 825 ml/m² (800-1000)
- PPV = 14 - 15% (13%)
- EVLWI = 21 ml/kg

At the time fluid was stopped patient remained fluid responsive and low dose norepinephrine was started.
12 hours later on norepinephrine

- MAP = 76 mmHg
- CI = 4.1 L/min/m²
- SVRI = 1250 dyne.cm.sec⁻⁵/m²
- Fluid balance + additional 3.2 liters in ARF
- GEDVI = 1100 ml/m² (800-1000)
- PPV = 9% (<13%)
- EVLWI = 22 ml/kg PBW

- Diuresis was started with furosemide
Large decrease in EVLW for small decrease preload.
- MAP = 65 mmHg
- CI = 4.1 L/min/m²
- SVRI = 1175
- Fluid balance - 2.5 liters
- GEDVI = 855 ml/m² (800-1000)
- PPV = 13-14% (<13%)
- EVLWI = 15 ml/kg PBW
EVLW ALI

EVLW cc/kg

Days

1 2 3 4 5 6

11 13 15 17 19 21