ECMO: a breakthrough in care for respiratory failure?

PD Dr. Thomas Müller
Regensburg
no conflict of interest
Overview

- Mortality of severe ARDS
- Indication for ECMO
- Efficiency of ECMO: gas transfer, ventilation, outcome
- Problems of ECMO
- Conclusion
ARDS - Mortality

Phua et al, Am J Respir Crit Care Med 2009;179:220-27
These results highlight the need for future effective therapeutic interventions in this highly lethal syndrome"
Epidemiology, Patterns of Care, and Mortality for Patients With Acute Respiratory Distress Syndrome in Intensive Care Units in 50 Countries

Giacomo Bellani, MD, PhD; John G. Laffey, MD, MA; Tài Pham, MD; Eddy Fan, MD, PhD; Laurent Brochard, MD, HDR; Andres Esteban, MD, PhD; Luciano Gattinoni, MD, FRCP; Frank van Haren, MD, PhD; Anders Larsson, MD, PhD; Daniel F. McAuley, MD, PhD; Marco Ranieri, MD; Gordon Rubenfeld, MD, MSc; B. Taylor Thompson, MD, PhD; Hermann Wrigge, MD, PhD; Arthur S. Slutsky, MD, MASC; Antonio Pesenti, MD; for the LUNG SAFE Investigators and the ESICM Trials Group

- 459 ICUs from 50 countries
- 3022 patients (10.4 %) with ARDS
- Hospital mortality 40 %: 34.9 % - 40.3 % - 46.1 % mild – moderate - severe
LUNG SAFE: Mortality and Driving/Plateau Pressure

Driving Pressure

Plateau Pressure

A Driving pressure quintiles and risk of hospital death

B Plateau pressure quintiles and risk of hospital death

JAMA 2016;315:788-800
Case Presentation

- 49 yr, female, past history empty
- 30.01: dry cough, fatigue, flu-like symptoms, diarrhoea, temp 38.5°C
- 01.02.: admission to external hospital,
  - progressive dyspnoe
  - PCT 20 µg/l, CRP 177 mg/l, lactate 113 mg/l,
    WBC 2.2/µl, Platelets 78/µl, INR 1.63, aPTT 54 sec
  - Ampicillin, Sulbactam, Clarithromycin
  - CT-Scan:
    - intubation
    - referral
- broad spectrum antibiotic coverage

expected mortality?
Case Presentation

02.02: septic shock and MOF:
- + 11 liters volume
- PCT 177 ng/ml, CK 3475 U/l, troponin I 22.6 ng/ml, platelets 77/ nl, INR 1.84, aPTT 87 sec, AT-III 19 %, D-Dimers > 35 mg/l
- PaO$_2$/FiO$_2$ 98 mmHg, PaCO$_2$ 40 mmHg
- PEEP/PIP 14/27 → 17/31 cm H$_2$O
- noradrenaline 6 mg/h, epinephrine 0.5 mg/h
- lactate 90 mg/dl
- ECHO: septic cardiomyopathy

12:00 o´clock decision for ECMO:
veno-arterial cannulation, blood flow 3.8 l/min
plasma exchange

expected mortality?
Case Presentation

➢ 18:00 o’clock:
  – noradrenaline 1.8 mg/h, epinephrine 0.3 mg/h
  – lactate 110 mg/dl
  – PaO₂/FiO₂ 50 mmHg, PaCO₂ 45 mmHg
  – PEEP/PIP 17/31 → 24/38 cm H₂O

➢ decision for additional venous cannula: VAV ECMO; blood flow 2.8 + 2.2 l/min

➢ chest X-ray: expected mortality?

**diagnosis:** streptococcal toxic shock syndrome group A streptococci

**expected mortality?**
Extracorporeal Gas Transfer

1. **O₂ Transfer**
   - **efficiency** depends on blood flow and blood sat
   - **effects:**
     – avoid hxpoxemia
     – protective ventilation: VILI ↓, right heart strain ↓
     – gain of time

2. **CO₂ Elimination**
   - **efficiency** depends on blood flow, gas flow and \( \text{PvCO}_2 \) (recirculation!)
   - **effects:**
     – protective ventilation ↑
     – over-inflation ↓
     – work of breathing ↓
     – facilitation of extubation ?
     – avoidance of intubation?
Gas-transfer Capacity of MOs

PLS-System

Rank 326 Eqn 531 Cosine Series Bivariate Order 2
$r^2=0.2977707$ DF Adj $r^2=0.29151011$ FitStdErr=50.636245 Fstat=57.16009
$a=214.62472 \ b=-38.939241 \ c=-44.98047$
$d=-18.781239 \ e=4.3347906 \ f=0.43219192$

HL-System

Rank 322 Eqn 531 Cosine Series Bivariate Order 2
$r^2=0.54707572$ DF Adj $r^2=0.53611787$ FitStdErr=29.146825 Fstat=60.152153
$a=151.42229 \ b=-57.51453 \ c=-18.233638$
$d=-6.6921931 \ e=7.5423673 \ f=4.7339263$

Lehle K et al, ICM 2014;40:1870-77
# Indication: ELSO

1. In hypoxic respiratory failure due to any cause (primary or secondary) ECLS should be considered when the risk of mortality is 50% or greater, and is indicated when the risk of mortality is 80% or greater.
   
   a. 50% mortality risk is associated with a \( \frac{\text{PaO}_2}{\text{FiO}_2} < 150 \) on \( \text{FiO}_2 > 90\% \) and/or Murray score 2-3.
   
   b. 80% mortality risk is associated with a \( \frac{\text{PaO}_2}{\text{FiO}_2} < 100 \) on \( \text{FiO}_2 > 90\% \) and/or Murray score 3-4 despite optimal care for 6 hours or more.

2. \( \text{CO}_2 \) retention on mechanical ventilation despite high Pplat (>30 cm H\(_2\)O)

3. Severe air leak syndromes

4. Need for intubation in a patient on lung transplant list

5. Immediate cardiac or respiratory collapse (PE, blocked airway, unresponsive to optimal care)
Indication for VV ECMO

1. **Rescue**
   Vital gas exchange can not be secured by conventional means, and rapidly progressive hemodynamic instability
   
   \[(P/F < 60 \text{ mm Hg}, \text{ and pH} < 7.2, \text{ and PIP} > 35 \text{ cm H}_2\text{O}, \text{ and Nor} > 1.5 \text{ mg/h})\]

2. **Semielektive**
   Lung protective ventilation not possible to secure vital gas exchange;
   no improvement after 12 – 24 hours

3. **Given that:**
   - treatable cause
   - all conventional therapeutic methods optimized
   - no contraindication

   \[
   \begin{align*}
   &\text{• PaO}_2/\text{FiO}_2 < 80 \text{ mm Hg with PEEP} > 15 \text{ cm H}_2\text{O} \\
   &\text{• uncompensated respiratory acidosis: pH} < 7.15
   \end{align*}
   \]

Vv-ECMO: PaO$_2$/FiO$_2$, PaCO$_2$ and TV

Müller et al, Dtsch Arztebl Int 2013;110:159-66
Ventilation on ECMO

- **FiO₂**
  - Pre: [Box plot]
  - Day 1: [Box plot]

- **MV**
  - [Box plot]

- **TV**
  - Pre: [Box plot]
  - Day 1: [Box plot]

- **PEEP**
  - Pre: [Box plot]
  - Day 1: [Box plot]

- **n = 375**

- **PIP**
  - Pre: [Box plot]
  - Day 1: [Box plot]
# Survival with modern ECMO

<table>
<thead>
<tr>
<th>Study</th>
<th>Literature</th>
<th>Number</th>
<th>Age</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANZ ECMO</td>
<td>JAMA 2009;302:online Oct 12</td>
<td>68</td>
<td>34.4</td>
<td>75 %</td>
</tr>
<tr>
<td>Italian ECMOnet</td>
<td>Intensive Care Med 2011;37:1447</td>
<td>60</td>
<td>40</td>
<td>68 %</td>
</tr>
<tr>
<td>ELSO H1N1 registry (adults &gt; 20 yrs)</td>
<td><a href="http://www.elso.med.umich.edu/">www.elso.med.umich.edu/</a> April 13, 2011</td>
<td>218</td>
<td>?</td>
<td>70 %</td>
</tr>
<tr>
<td>CESAR</td>
<td>Lancet 2009;374:1351-63</td>
<td>68</td>
<td>39.9</td>
<td>63 %</td>
</tr>
<tr>
<td>UK ECMO for H1N1</td>
<td>JAMA 2011;306:online Oct 5</td>
<td>69</td>
<td>36.5</td>
<td>71 %</td>
</tr>
<tr>
<td>REVA Research Network</td>
<td>Am J Respir Crit Care Med 2013;187:276-85</td>
<td>123</td>
<td>42</td>
<td>64 %</td>
</tr>
</tbody>
</table>
Extracorporeal membrane oxygenation: evolving epidemiology and mortality

Christian Karagiannidis, Daniel Brodie, Stephan Strassmann, Erich Stoelben, Alois Philipp, Thomas Bein, Thomas Müller and Wolfram Windisch

- Incidence VV-ECMO 2014: 2.4/100,000 (n = 1944)
- In-hospital mortality 2014: 58%
Survival RESP-Score Population

N = 2355
Age (years) 41 (28-54)

Schmidt M et al, AJRCCM in press 02.April 2014
Prediction of mortality in adult patients with severe acute lung failure receiving veno-venous extracorporeal membrane oxygenation: a prospective observational study


Table 4 Novel mortality prediction models for ALF-patients receiving ECMO support

<table>
<thead>
<tr>
<th>Model 1 (pre-ECMO)</th>
<th>Coefficient</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per 5 years)</td>
<td>0.176</td>
<td>1.193</td>
<td>(1.148-1.239)</td>
</tr>
<tr>
<td>Immunocompromised state</td>
<td>0.958</td>
<td>2.605</td>
<td>(1.316-5.158)</td>
</tr>
<tr>
<td>Minute ventilation (L/min)</td>
<td>0.098</td>
<td>1.103</td>
<td>(1.014-1.199)</td>
</tr>
<tr>
<td>Pre-ECMO haemoglobin (g/dL)</td>
<td>-0.182</td>
<td>0.834</td>
<td>(0.728-0.954)</td>
</tr>
<tr>
<td>Pre-ECMO lactate (mmol/L)</td>
<td>0.013</td>
<td>1.013</td>
<td>(1.004-1.023)</td>
</tr>
<tr>
<td>Intercept</td>
<td>-2.083</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Model 2 (day 1):

age day 1 FiO₂
immunocompromised state day 1 fibrinogen
minute ventilation day 1 norepi.
pre ECMO Hb day 1 CRP

TB Enger...T Müller, Crit Care 2014;18:R67
Outcome according to age (n = 551)
Long-Term Survival in Adults Treated With Extracorporeal Membrane Oxygenation for Respiratory Failure and Sepsis*

Viktor von Bahr, MD¹; Jan Hultman, MD, PhD¹,²; Staffan Eksborg, PhD³; Björn Frenckner MD, PhD²,⁴; Håkan Kalzén MD¹,²

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total</th>
<th>Pneumonia, Bacterial</th>
<th>Pneumonia, Viral</th>
<th>Pneumonia, Aspiration</th>
<th>Nonpulmonary Infection</th>
<th>Severe Inflammatory Response</th>
<th>Traumatic Chest/Lung Contusion</th>
<th>Other Respiratory Etiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>255²</td>
<td>134</td>
<td>31</td>
<td>19</td>
<td>24</td>
<td>23</td>
<td>9</td>
<td>15</td>
</tr>
<tr>
<td>Age at treatment (yr)</td>
<td>46 (33–58)</td>
<td>49</td>
<td>(37–59)</td>
<td>44</td>
<td>(29–53)</td>
<td>46</td>
<td>(32–57)</td>
<td>55</td>
</tr>
<tr>
<td>Sex, male, n (%)</td>
<td>160 (63)</td>
<td>83</td>
<td>(62)</td>
<td>19</td>
<td>(61)</td>
<td>11</td>
<td>(58)</td>
<td>18</td>
</tr>
<tr>
<td>ICU (d)</td>
<td>135 (53)</td>
<td>78</td>
<td>(58)</td>
<td>14</td>
<td>(45)</td>
<td>10</td>
<td>(53)</td>
<td>9</td>
</tr>
<tr>
<td>Cannulation, VV² n (%)</td>
<td>70 (27)</td>
<td>29</td>
<td>(22)</td>
<td>10</td>
<td>(32)</td>
<td>5</td>
<td>(26)</td>
<td>12</td>
</tr>
<tr>
<td>Converted to VV, n (%)</td>
<td>13 (5)</td>
<td>7</td>
<td>(5)</td>
<td>3</td>
<td>(10)</td>
<td>0</td>
<td>(0)</td>
<td>0</td>
</tr>
<tr>
<td>Converted to VA, n (%)</td>
<td>37 (15)</td>
<td>20</td>
<td>(15)</td>
<td>4</td>
<td>(13)</td>
<td>4</td>
<td>(21)</td>
<td>3</td>
</tr>
<tr>
<td>PaO₂/FiO₂ ratio at referral (mmHg)</td>
<td>54 (47–60)</td>
<td>54</td>
<td>(47–60)</td>
<td>51</td>
<td>(44–58)</td>
<td>56</td>
<td>(48–62)</td>
<td>52</td>
</tr>
<tr>
<td>Follow-up time in survivors (yr)</td>
<td>4.4 (2.1–9.3)</td>
<td>5.2</td>
<td>(2.2–10.7)</td>
<td>4.2</td>
<td>(1.4–4.4)</td>
<td>5.4</td>
<td>(4.4–6.8)</td>
<td>2.0</td>
</tr>
<tr>
<td>Follow-up time in diseased (d)</td>
<td>48 (14–427)</td>
<td>56</td>
<td>(33–544)</td>
<td>4/502</td>
<td>(n = 2)</td>
<td>21/157/334/727</td>
<td>5/14/15/60</td>
<td>1/3/15/870</td>
</tr>
</tbody>
</table>

*See Crit Care Med. 2017 Feb;45(2):164-170
Long-Term Survival in Adults Treated With Extracorporeal Membrane Oxygenation for Respiratory Failure and Sepsis*

Viktor von Bahr, MD¹; Jan Hultman, MD, PhD¹,²; Staffan Eksborg, PhD³; Björn Frenckner MD, PhD²,⁴; Håkan Kalzén MD¹,²
Risks of ECMO

- Rupture of femoral vein
- Tamponade
- Broken cannula
Risk of Technical Failure

- LDH [U/l]
- Free hemoglobin [mg/dl]

Graph showing changes in LDH and free hemoglobin over time:
- Pre 24 hrs
- Exchange
- +12 hrs
- +24 hrs
- +36 hrs
- +48 hrs

Legend:
- Red: LDH [U/l]
- Blue: Free hemoglobin [mg/dl]
Avoid unnecessary interventions

- risk of bleeding:
  platelets 173,000 → 105,000 day 4 (61%)
  (n = 440)

- no unnecessary blood transfusions
  ✓ Hb transfusion threshold 8.0 g/dL
  ✓ RBCs/day on ECMO:
    0.31 (0.00;0.78)
VV-ECMO and Cerebral Complications: preliminary results

- 04/2006 – 10/2015

495 vv ECMO runs

- CCT n=290

- no pathology n = 226 (78 %)
  - survival n = 142 (63 %)

- ICB n = 53 (18 %)
  - survival n = 27 (51 %)

- ischemia n = 11 (4 %)
  - survival n = 8 (73 %)
Requirements for an ECMO Center

Position Paper for the Organization of Extracorporeal Membrane Oxygenation Programs for Acute Respiratory Failure in Adult Patients

1. experience in the treatment of severe ARDS: tertiary care ICU
2. transport possible with ECMO: mobile team
3. experience with ECMO:
   - > 10 (20) cases per year
   - 24/7 trained personnel: intensivists, nurses, (perfusionists)
4. management of complications:
   - blood bank, lab, CT 24/7
   - ECMO replacement equipment
   - vascular surgery, (abdominal-, thoracic surgery)
5. quality management:
   - regular training
   - data base
   - M + M conference
   - participation in national or international registry

Am J Respir Crit Care Med. 2014 Sep 1;190(5):488-96.
Conclusion: ECMO: a breakthrough in care for respiratory failure?

1. ECMO saves lives.

2. Indications:
   - relatively sure: severe refractory ARDS
   - uncertain: CO₂ elimination (avoidance of intubation? facilitated weaning?)

3. Balance benefits versus risks

4. Costs!

5. Experience necessary: ECMO Center
EuroELSO 2017
6th EuroElso Congress on ECMO-ECLS

4 - 7 MAY 2017
SAVE THE DATE
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THE NETHERLANDS
WWW.EUROELSO.NET