ECMO for Septic Shock:

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no conflict of interest
Overview

1. Septic Shock: brief pathophysiology

2. ECMO in septic shock: published literature
   - children
   - adults

3. ECMO in septic shock: which indication?
   - right heart failure
   - left heart failure
   - distributive shock

4. ECMO in septic shock: problems (selected)

5. Summary
Sepsis: a deleterious host response to infection

Jean-Louis Vincent

Septic Shock

- shock: „life threatening acute circulatory failure with inadequate oxygen utilization by the cells“

- „septic shock is the most severe manifestation of sepsis with reported case-fatality rates in the range of 40-50 %, reaching as high as 80 %“

  Cecconi M et al, Consensus Conference, ICM 2014;40:1795-1815

Septic shock and MOV:
- vasoplegia
- renal failure
- ARDS
- DIC
- cardiomyopathy
- „cerebral failure“
- rhabdomyolysis
- hepatic failure

and ECMO?

c-MRSA
ECMO in Septic Shock

1. ECMO is not a treatment for sepsis.

2. **veno-venous** ECMO can provide oxygen and carbon dioxide transfer in severe lung failure.

3. **peripheral veno-arterial** ECMO can provide circulatory support (+ some gas transfer).

4. **central atrio-aortal** ECMO can provide circulatory and respiratory support, but needs sternotomy.
Extracorporeal membrane oxygenation for refractory septic shock in children: One institution’s experience

Graeme MacLaren, MBBS, FJFICM, FRACP; Warwick Butt, MBBS, FRACP, FJFICM; Derek Best, RN, RSCN, BN; Susan Donath, BSc, MA; Anna Taylor, BN, RN

- retrospective 1988 – 2006
- n = 45, age 2.5 (0.4-9) yrs
- 22 hours shock before ECMO
- 40 % cardiac arrest
- 91 % ≥ 3 organ failure
- ECMO:
  - 34 peripheral (carotid artery)
  - 11 central (atrio-aortal)
  - time on ECMO 84 (32-135) hours
  - 38 % mechanical problems
  - 24 % bleeding
- outcome:
  47 % survival to hospital discharge

<table>
<thead>
<tr>
<th>Blood cultures</th>
<th>Organism</th>
<th>No. of Patient</th>
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<tbody>
<tr>
<td>Neisseria meningitidis</td>
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<td>Staphylococcus aureus</td>
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<td>Coagulase-negative</td>
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<td>S. aureus</td>
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<tr>
<td>Pseudomonas aeruginosa</td>
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<tr>
<td>Klebsiella species</td>
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<tr>
<td>Enterobacter species</td>
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<td>Burkholderia cepacia</td>
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<tr>
<td>Streptococcus species</td>
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<tr>
<td>S. aureus</td>
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<tr>
<td>P. aeruginosa</td>
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<tr>
<td>Bordetella pertussis</td>
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<tr>
<td>Parainfluenza virus</td>
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<tr>
<td>Mycoplasma species</td>
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<tr>
<td>Klebsiella species</td>
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<tr>
<td>Salmonella species</td>
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Pediatr Crit Care Med 2007;8:447-51
Central extracorporeal membrane oxygenation for refractory pediatric septic shock

Graeme MacLaren, MBBS, FCICM, FRACP; Warwick Butt, MBBS, FRACP, FCICM; Derek Best, RN, RSCN, BN; Susan Donath, BSc, MA

- retrospective 2000 – 2009
- n = 23, age 6 (2.8-12.3) yrs
- 7 hours in ICU before ECMO
- 35% cardiac arrest
- 96% ≥ 3 organ failure
- ECMO:
  - cannulation: sternotomy, atrio-aortal
  - time on ECMO 93 (43-119) hours
  - 9% circuit change
  - 30% sternotomy bleeding
- outcome:
  - 74% survival to hospital discharge

<table>
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<tr>
<th>Parameter</th>
<th>Mean</th>
<th>(Range)</th>
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<tbody>
<tr>
<td>Mean airway pressure, cm H₂O</td>
<td>16.1 (13.4-23)</td>
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<tr>
<td>Positive end-expiratory pressure, cm H₂O</td>
<td>10 (8-10)</td>
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<tr>
<td>PaO₂/FIO₂</td>
<td>99 (50.7-192)</td>
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<tr>
<td>pH</td>
<td>7.11 (7.08-7.2)</td>
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<tr>
<td>Arterial lactate, mmol/L</td>
<td>7.8 (4.1-9.7)</td>
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<tr>
<td>Mean arterial pressure, mm Hg</td>
<td>57 (47-69)</td>
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</tr>
<tr>
<td>Urine output, mL/kg/hr</td>
<td>0 (0-0.9)</td>
<td></td>
</tr>
<tr>
<td>Mean inotrope score</td>
<td>82.2 (sd, 115.6)</td>
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</tr>
</tbody>
</table>

*Pediatr Crit Care Med 2011;12:133-36*
Pediatric and Neonatal Septic Shock: Recommendations 2007

Initial resuscitation: Push boluses of 20 cc/kg isotonic saline or colloid up to & over 60 cc/kg until perfusion improves or unless rales or hepatomegaly develop. Correct hypoglycemia & hypocalcemia. Begin antibiotics.

Fluid refractory shock: Begin isoproterenol IV/IO. Use atropine/ketamine IV/IO/EM to obtain central access & airway if needed. Reverse cold shock by titrating central dopamine or, if resistant, titrate central epinephrine. Reverse warm shock by titrating central norepinephrine.

Catecholamine resistant shock: Begin hydrocortisone if at risk for absolute adrenal insufficiency.

Cold shock with normal blood pressure: 1. Titrate fluid & epinephrine, SevO2 > 70%, Hgb > 10 g/dL. 2. If SevO2 still < 70% Add vasodilator with volume loading (nitrates, norepinephrine, milrinone, inotrope, & others). Consider levosimendan.

Cold shock with low blood pressure: 1. Titrate fluid & epinephrine, SevO2 > 70%, Hgb > 10 g/dL. 2. If still hypotensive consider norepinephrine. 3. If SevO2 still < 70% consider dobutamine, milrinone, epinephrine or levosimendan.

Warm shock with low blood pressure: 1. Titrate fluid & norepinephrine, SevO2 > 70%. 2. If still hypotensive consider vasopressin, terlipressin or angiotensin.
3. If SevO2 still < 70% consider low dose dopamine.

Persistent catecholamine resistant shock: Rule out and correct pericardial effusion, pneumothorax, & intra-abdominal pressure > 12 mm Hg. Consider pulmonary artery, PICCO, or FATD catheter, & or doppler ultrasound to guide fluid, inotrope, vasopressor, vasodilator and hormonal therapies. Goal CI > 3.3 & < 6.0 L/min/m².

Refractory shock: ECMO.
Extracorporeal membrane oxygenation resuscitation in adult patients with refractory septic shock

Chun-Ta Huang, MD, Yi-Ju Tsai, PhD, Pi-Ru Tsai, RN, and Wen-Je Ko, MD, PhD

- retrospective, 6 yrs
- n = 52 adults, age 56.8 yrs
- 75% ≥ 3 organ failure, 40 % CPR pre ECMO

ECMO:
- peripheral cannulation VA
- blood flow 2.7 L/min
- 8 % major bleeding
- 24 % mechanical complications

outcome:
15 % hospital survival

survival and age
extracorporeal membrane oxygenation for refractory septic shock in adults

Taek Kyu Park, Jeong Hoon Yang, Kyeongman Jeon, Seung-Hyuk Choi, Jin-Ho Choi, Hyeon-Cheol Gwon, Chi Ryang Chung, Chi Min Park, Yang Hyun Cho, Kiick Sung and Gee Young Suh

- retrospective, 2005 – 2013
- n = 32 adults, age 55 yrs
- 66 % immunocompromised
- LV-EF 25 % (20-41%)
- ECMO:
  - peripheral cannulation VA
  - blood flow 3.5 L/min
  - 6 % major bleeding
  - 16 % limb ischemia
- outcome:
  - 22 % hospital survival

CPR and survival

Eur J CardioThorac Surg 2015;47:e68-e74
Venoarterial Extracorporeal Membrane Oxygenation Support for Refractory Cardiovascular Dysfunction During Severe Bacterial Septic Shock

Nicolas Bréchot, MD, PhD; Charles-Edouard Luyt, MD, PhD; Matthieu Schmidt, MD; Pascal Leprince, MD, PhD; Jean-Louis Trouillet, MD; Philippe Léger, MD; Alain Pavie, MD; Jean Chastre, MD; Alain Combes, MD, PhD

- retrospective 1/08 – 09/11
- n = 14 adults, age 45 (28 – 66) yrs
- EF 16 %, CI 1.3 L/min/m²
- norepinephrine or epinephrine > 1 µg/kg/min

ECMO:
- peripheral cannulation VA
- blood flow 4 – 5 L/min
- antegrade perfusion
- > 60 % major ECMO related complication: leg ischemia, amputation, bleeding, stroke, wound infection
Venoarterial Extracorporeal Membrane Oxygenation Support for Refractory Cardiovascular Dysfunction During Severe Bacterial Septic Shock*

- outcome: 71% (10 patients) survival to hospital discharge
- 12 patients weaned after 5.5 (2–12) days
- LV-function:

![Diagram showing LV function over time: ECMO implantation, ECMO explantation, and follow-up with statistical significance marked with ***]

- respiratory parameter:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Median (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(P_{aO_2}/F_{iO_2}) ratio, median (range)</td>
<td>87 (28–364)</td>
</tr>
<tr>
<td>Tidal volume, mL/kg of ideal body weight, median (range)</td>
<td>6.4 (4.0–8.5)</td>
</tr>
<tr>
<td>Positive end-expiratory pressure, (cm H_2O), median (range)</td>
<td>10 (4–15)</td>
</tr>
<tr>
<td>Plateau pressure, (cm H_2O), median (range)</td>
<td>26 (21–45)</td>
</tr>
</tbody>
</table>

Crit Care Med 2013;41:1616-26
ECMO: which mode?

- **septic shock**: 1µg/kg/min epineph. or norepi

  - ECHO
    - **RV-failure + ARDS**
      - VV ECMO
    - **persistent RV failure**
      - VVA ECMO
    - **normal EF hyperkinesia**
      - ?
      - central cannulation

  - **LV-failure**
    - ECG Troponin Coro?
    - **LV-failure**
      - **peripheral VA ECMO**
      - **severe ARDS**
        - VAV ECMO

VV-ECMO: Blood Gases and Vasopressors

PaO$_2$/FiO$_2$

PaCO$_2$

pH

NOR
Survival and Norepinephrine-Dosage

n = 439 adults, VV-ECMO
However...

be aware of potentially lethal complications

Rupture of femoral vein

Oclusion of femoral artery
Harlekin - Syndrome
Risk of competitive flow in aortic arch
Circulatory + Respiratory Failure
Bleeding: Platelets and ECMO

**VV-ECMO**

- n = 440

**VA-ECMO**

- n = 312
- ** = p < 0.001
- * = p < 0.05
Summary

- ECMO is not a treatment of sepsis, but may support a failing lung and/or circulation
- mode of ECMO is guided by Echocardiography:
  - acute RV-failure due to ARDS:
    veno-venous
  - acute LV-failure (septic cardiomyopathy):
    veno-arterial
  - vasoplegic (distributive) shock: ?
    (central cannulation)
- consider early in the course of disease, not in late, fully established MOF
- consider upgrade to VVA or VAV ECMO („Harlekin-Syndrome“)
- remember: „expert“ opinion, no randomized prospective data
Circuit Infection in Septic Patients: does it happen?

- prospective pilot study:
- 10 patients with severe sepsis on vv ECMO
- time on ECMO: 13 (9-22) days
- median time to oxy exchange: 9.5 days
- incubation of exchanged oxys for 14 days

- one patient with diffuse systemic bleeding despite substitution of fibrinogen, platelets and stop of heparin;
- rapid improvement after exchange of MO
- detection of enterococci in MO

Müller et al, Artificial Organs 2011,35:E84-90
diffuse bleeding diathesis,
high d-dimers:
consider exchange of oxy
Model 2 (day 1):

- age
- immunocompromised state
- minute ventilation
- pre ECMO Hb
- day 1 $\text{FiO}_2$
- day 1 fibrinogen
- day 1 norepi.
- day 1 CRP
“Harlekin – Syndrome”

be aware of “two circulations”:
1. blood from the heart and native lung
2. blood from the membrane lung

CO₂ is removed both by the ECMO and by the lung