Opportunities for minimizing cerebral

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  - Ontario Neurotrauma Foundation
Cerebral morbidity with ECLS

- It’s frequent
- It’s either caused by or associated with ECLS
- If you’re not seeing it…your not looking close enough…
- It’s continues to be associated with death and disability among survivors
- There’s a huge potential for
Outline

• Nomenclature and definitions
• Preclinical evidence: mechanisms
• Epidemiological evidence & clinical risk factors
  • Which risk factors are modifiable?
• Now & Novel:
  • Diagnosis & Management
  • Prognosis
Nomenclature

- **ECLS**: Extracorporeal Life Support
- **ECMO**: Extracorporeal Membrane Oxygenation
- **E–CPR**: ECMO in cardiopulmonary resuscitation
- **VAD**: Ventricular Assist Device e.g., Berlin Heart®, Heart Mate®
- **iLA**: Interventional Lung assist device
Cerebral morbidity

• Cerebral morbidity (cerebral nervous system) which occurs during the interval of care on ECMO or during index hospitalization
  • Excludes peripheral neuromuscular morbidity, retinal, spinal cord related injuries

• Clinical reporting is framed by classifications used in registries
  • ELSO Extracorporeal Life Support
Types of cerebral morbidity

• Structural anomalies
  • Hemorrhage* (7–10%)
  • Infarction*/Stroke (5–10%)
  • Edema

• *Neurologic complications in ELSO on CT or Ultrasound
Types of cerebral morbidity

- Functional anomalies
  - Coma
  - Seizures (clinical, EEG non clinical)* (2–12%)
  - Clinical brain death* (1–4%)
- Delirium
- Pain/Anxiety
- Cognitive or behavioral changes
ELSO Registry 1990–2011 46,509 total

Cases reported
- Survived ECLS
- Survived to Discharge

<table>
<thead>
<tr>
<th></th>
<th>Total N</th>
<th>24,770</th>
<th>4,375</th>
<th>694</th>
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<tbody>
<tr>
<td>Respiratory</td>
<td>0</td>
<td>0</td>
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<td>0</td>
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<tr>
<td>Cardiac</td>
<td>25</td>
<td>21</td>
<td>5</td>
<td>1</td>
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<tr>
<td>ECMO</td>
<td>50</td>
<td>44</td>
<td>2</td>
<td>14</td>
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<tr>
<td>Total</td>
<td>75</td>
<td>65</td>
<td>7</td>
<td>15</td>
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</table>
ELSO Registry 1990–2011 46 509 total

cases reported

Survived ECLS
Survived to Discharge

<table>
<thead>
<tr>
<th></th>
<th>Survived ECLS</th>
<th>Survived to Discharge</th>
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<tbody>
<tr>
<td>Total</td>
<td>5009</td>
<td>5423</td>
</tr>
<tr>
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Total N | 5009 | 5423 | 1347
ELSO Registry 1990–2011 46 509 total

cases reported

<table>
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<tr>
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<th>Survived ECLS</th>
<th>Survived to Discharge</th>
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<tr>
<td>Respiratory</td>
<td>2620</td>
<td></td>
</tr>
<tr>
<td>Cardiac</td>
<td>1680</td>
<td></td>
</tr>
<tr>
<td>ECMO</td>
<td>591</td>
<td></td>
</tr>
</tbody>
</table>

Total N | 2620 | 1680 | 591
Preclinical models

• Mechanisms: subject factors
  • Neurobiology/Neurodevelopment: apoptotic & necrotic pathways
• Injury
  • Ischemia/Hypoxia
  • Cerebral emboli
  • Cerebral vascular disregulation
    – Arterial relative hypo-hypertension
    – Venous drainage
• Inflammation, cytokines
Pathophysiology

• Mechanisms: ECMO vs. CPB?
  • Differences and similarities
• Vascular access: VA > VV
  • Neck > peripheral – Thoracic
• Vessel reconstruction
  • vs ligation?

Impaired cerebral autoregulation in the newborn lamb during recovery from severe, prolonged hypoxia, combined with carotid artery and jugular vein ligation

Billie L. Short, MD, FAAP; L. Kyle Walker, MD; Richard J. Traystman, PhD, FCCM
Supportive management

• Temperature
  • Normothermia? Mild hypothermia?
  • THAPCA NIH funded RCT for cardiopulmonary arrest children

• pH Management
• Pulsatile vs non–pulsitile support
• Anticoagulation /DIC
Modifiable/ Non-modifiable – Factors

- Patient
  - Modifiable: length of support, monitoring, cannulation
  - Non-modifiable: indication
- Technology
- Pharmacological
  - Hemorrhage vs. thrombosis balance
Risk factors

- Neonatal – ELSO
  - Prematurity < 34 w
  - Sepsis
  - Acidosis < 7.20 before initiation
  - Epinephrine use before initiation

- Pediatric
  - E–CPR or cardiac arrest

- Adult
  - Female, renal failure, thrombopenia Kasirajan
ECMO Subjects Q4th 2007-2011
111

Subjects Analysed
102 (100%)

Confirmed Cerebral Hemorrhage

Died
27 (27%)

Survived
8 (8%)

No Cerebral Hemorrhage
67 (66%)

Died
31 (30%)

Survived
36 (35%)

Outcome Not Assessed with Neuro-Imaging or Likely No Cerebral Hemorrhage

Died
7 (6%)

Survived
8 (7%)

Factors:
- E-CPR
- 50% Hemorrhage occurred by day 5
Extracorporeal Membrane Oxygenation for 2009 Influenza A(H1N1) Acute Respiratory Distress Syndrome

ANZ ECMO Influenza Investigators
Figure 1. Flow Diagram of Patients Receiving Mechanical Ventilation for Suspected 2009 Influenza A(H1N1) Infection at ECMO Centers

201 Patients given mechanical ventilation for confirmed or suspected influenza

68 Received ECMO

61 Confirmed 2009 influenza A(H1N1) or influenza A not subtyped

53 Confirmed 2009 influenza A(H1N1)
42 Alive
4 Still in ICU
11 Died

8 Confirmed influenza A not subtyped
6 Alive
1 Still in ICU
2 Died

7 Had suspected but unconfirmed influenza

6 Alive
1 Still in ICU
1 Died

133 Confirmed 2009 influenza A(H1N1) or influenza A not subtyped

133 Confirmed 2009 influenza A(H1N1) or influenza A not subtyped

116 Alive
11 Still in ICU
17 Died

ECMO indicates extracorporeal membrane oxygenation; ICU, intensive care unit.
<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>2009 Influenza A(H1N1)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Confirmed Infection (n = 53)</td>
</tr>
<tr>
<td>Length of stay, median (IQR), d ICU</td>
<td>26 (16-35)</td>
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<tr>
<td></td>
<td>35 (24-45)</td>
</tr>
<tr>
<td>Hospital</td>
<td></td>
</tr>
<tr>
<td>Duration, median (IQR), d</td>
<td>24 (13-31)</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td></td>
</tr>
<tr>
<td>ECMO support</td>
<td>10 (7-14)</td>
</tr>
<tr>
<td>Survival at ICU discharge</td>
<td>38 (72)</td>
</tr>
<tr>
<td>Still in ICU</td>
<td>4 (8)</td>
</tr>
<tr>
<td>Survival at hospital discharge</td>
<td>22 (42)</td>
</tr>
<tr>
<td>Still in hospital</td>
<td>14 (26)</td>
</tr>
<tr>
<td>Ambulant at hospital discharge</td>
<td>21 (95)</td>
</tr>
<tr>
<td>SaO₂ on room air at hospital discharge, median (IQR), %</td>
<td>97 (95-98)</td>
</tr>
<tr>
<td>Discharge destination</td>
<td></td>
</tr>
<tr>
<td>Died</td>
<td>11 (21)</td>
</tr>
<tr>
<td>Home</td>
<td>18 (34)</td>
</tr>
<tr>
<td>Other hospital</td>
<td>0</td>
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<tr>
<td>Rehabilitation facility</td>
<td>4 (8)</td>
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<tr>
<td>Cause of death d</td>
<td></td>
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<tr>
<td>Hemorrhage</td>
<td>3 (27)</td>
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<tr>
<td>Intracranial hemorrhage</td>
<td>4 (36)</td>
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<tr>
<td>Infection</td>
<td>1 (9)</td>
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<tr>
<td>Intractable respiratory failure</td>
<td>3 (27)</td>
</tr>
</tbody>
</table>

Abbreviations: ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; IQR, interquartile range; SaO₂, arterial oxygen saturation.

Data are presented as No. (%) unless otherwise specified.

Not including patients still in the ICU.

For survivors only.

Data are shown as No. (% of deaths) and patients could have more than 1 cause contributing to death.
Available for Diagnosis –

• Clinical examination
  • Practice of supporting patients awake
    • VV mode > VA
Impaired pressure regulation during CPB rewarming using TCD

Joshi 2010
Available for diagnosis

- Diagnostic imaging:
  - Ultrasound
  - CT – portable CT imaging

Cranial CT for Diagnosis of Intracranial Complications in Adult and Pediatric Patients During ECMO: Clinical Benefits in Diagnosis and Treatment

Marika K. Lidegran, Mikael Mosskin, Hans G. Ringertz, Björn P. Frenckner, Viveka B. Lindén
Elevated S100B protein as an early indicator of intracranial haemorrhage in infants subjected to extracorporeal membrane oxygenation

D Gazzolo¹, P Masetti², M Meli², D Grutzfeld³ and F Michetti⁴

Department of Neonatology¹, G. Gaslini Children’s University Hospital, Genoa, Italy; Department of Pediatric Cardiac Surgery², Hesperia Hospital, Modena, Italy; Department of Neonatology³ Pompik-Centrum Zdrowia Dziecka, University Hospital, Warsaw, Poland; Institute of Anatomy⁴, Catholic University, Rome, Italy

S100 B glial cell marker of injury
Biomarkers

GFAP: glial fibrillar acidic protein in blood

p=0.04

Bembea PCCM 2011
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Acknowledgements

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