Are Long-Term Outcomes Impacted by ECMO?

A/Prof Carol Hodgson PhD, FACP, M(Phil), BAppS(PT)
Deputy Director, Australian & New Zealand Intensive Care Research Centre
Disclosures:

- National Heart Foundation Fellow

- Project funding from NHMRC National Partnership Grant including funding from national ECMO centers, National Heart Foundation & International ECMONet
ECMO Survivorship

More Centers, more ECMO, more Patients, more Technology

= more survivors
= more complex health issues

Are ECMO survivors different to other ICU survivors?

Barbaro 2015; Combes (2008); Hodgson (2012); Kahn (2015); Mirabel (2011)
Is survival different following ECMO for ARDS?

- 1 RCT & 5 Observational studies
- 3 studies compared ECMO to CMV
- Overall quality of studies high

Wilcox, Hodgson, Ferguson, Fan et al, JICM, 2017
Systematic Review: QoL after ECMO in ARDS survivors

A

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>ECLS Mean</th>
<th>ECLS SD</th>
<th>ECLS Total</th>
<th>CMV Mean</th>
<th>CMV SD</th>
<th>CMV Total</th>
<th>Weight</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Luyt et al 2012</td>
<td>91.1</td>
<td>8.8</td>
<td>12</td>
<td>88</td>
<td>11.05</td>
<td>25</td>
<td>3.8%</td>
<td>3.10 [-3.50, 9.70]</td>
<td></td>
</tr>
<tr>
<td>Peek et al 2009</td>
<td>63.57</td>
<td>3.84</td>
<td>90</td>
<td>58.07</td>
<td>5.06</td>
<td>90</td>
<td>96.0%</td>
<td>5.50 [4.19, 6.81]</td>
<td></td>
</tr>
<tr>
<td>Stoll et al 1998</td>
<td>69.75</td>
<td>42</td>
<td>42</td>
<td>72</td>
<td>45</td>
<td>14</td>
<td>0.2%</td>
<td>-2.25 [-34.49, 29.99]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>116</td>
<td>129</td>
<td>129</td>
<td>109.9%</td>
<td>5.40</td>
<td>100.0%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Heterogeneity: Tau^2 = 0.00; Chi^2 = 0.71, df = 2 (P = 0.70); I^2 = 0%
| Test for overall effect: Z = 8.22 (P < 0.00001) |

Outcome: SF-36 PCS

Favours CMV
Favours ECLS

B

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>ECLS Mean</th>
<th>ECLS SD</th>
<th>ECLS Total</th>
<th>CMV Mean</th>
<th>CMV SD</th>
<th>CMV Total</th>
<th>Weight</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Luyt et al 2012</td>
<td>47.1</td>
<td>5.6</td>
<td>12</td>
<td>44.7</td>
<td>10.9</td>
<td>25</td>
<td>1.7%</td>
<td>2.40 [-2.92, 7.72]</td>
<td></td>
</tr>
<tr>
<td>Peek et al 2009</td>
<td>30.38</td>
<td>2.03</td>
<td>90</td>
<td>27.23</td>
<td>2.7</td>
<td>90</td>
<td>98.3%</td>
<td>3.15 [2.45, 3.85]</td>
<td></td>
</tr>
<tr>
<td>Stoll et al 1998</td>
<td>60.51</td>
<td>51</td>
<td>14</td>
<td>66.75</td>
<td>42.5</td>
<td>14</td>
<td>0.0%</td>
<td>-6.75 [-41.53, 28.03]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>116</td>
<td>129</td>
<td>129</td>
<td>100.0%</td>
<td>3.13</td>
<td>[2.44, 3.83]</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Heterogeneity: Tau^2 = 0.00; Chi^2 = 0.39, df = 2 (P = 0.82); I^2 = 0%
| Test for overall effect: Z = 8.88 (P < 0.00001) |

Outcome: SF-36 MCS

Favours CMV
Favours ECLS

Wilcox, Hodgson, Ferguson, Fan et al, JICM, 2017
Less psychological morbidity in ECMO survivors compared to CMV

2 studies; Luyt et al, 2012 and Peek et al, 2009

N=217 [ECMO - CMV] assessed with the HADS
MWD -1.31 [CI, -1.98, -0.64] for depression
MWD -1.60 [CI, -1.80, -1.39] for anxiety

Schmidt et al, ICM, 2013 (no comparator)
N = 140, follow-up in 80% survivors
Poor physical function
Anxiety, depression, PTSD in 34%, 25%, 16%
HRQoL did not improve over time (to 12M)
Acute Skeletal Muscle Wasting in Patients Requiring ECMO

Hayes et al, JCC 2018

Senior ICU Physiotherapist, Alfred Health

Figure 1. Cross section of quadricep muscle of a 23 year old patient showing 43% reduction of muscle mass from Day 1 in ICU (top) to Day 7.
Acute Skeletal Muscle Wasting in Patients Requiring ECMO

Eligible
n = 48

Included
n = 25

Baseline measures
n = 25

Day 10 measures
n = 23

Day 20 measures
n = 19

Alive at Hospital DC
n = 18

Excluded n = 23

Deceased
n = 2

Deceased
n = 4

Deceased
n = 1
<table>
<thead>
<tr>
<th>Ultrasound muscle parameter</th>
<th>Baseline/Day 1 (n = 25)</th>
<th>Day 10 (n = 23)</th>
<th>Day 20 (n = 19)</th>
<th>% change Day 1 – Day 20 (n = 19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RF CSA (cm²)</td>
<td>4.2 ± 1.3</td>
<td>3.4 ± 1.1</td>
<td>2.9 ± 1.0</td>
<td>-30.5 ± 13.3**</td>
</tr>
<tr>
<td>RF Thickness (cm)</td>
<td>1.1 ± 0.3</td>
<td>0.7 (0.6 – 1.0)</td>
<td>0.6 ± 0.2</td>
<td>-34.9 ± 25.9**</td>
</tr>
<tr>
<td>VI Thickness anterior view (cm)</td>
<td>0.9 ± 0.3</td>
<td>0.8 ± 0.2</td>
<td>0.7 ± 0.2</td>
<td>-31.0 (-42.5 to -27)**</td>
</tr>
<tr>
<td>VL Thickness (cm)</td>
<td>1.6 ± 0.3</td>
<td>1.4 ± 0.3</td>
<td>1.1 ± 0.3</td>
<td>-32.5 ± 15.5**</td>
</tr>
<tr>
<td>VI Thickness lateral view (cm)</td>
<td>1.2 ± 0.4</td>
<td>1.1 ± 0.5</td>
<td>0.9 ± 0.4</td>
<td>-26.7 ± 23.9**</td>
</tr>
<tr>
<td>Total muscle thickness anterior view = (RF + VI)</td>
<td>2.1 ± 0.6</td>
<td>1.7 ± 0.5</td>
<td>1.4 ± 0.4</td>
<td>-30.3 ± 20.1**</td>
</tr>
</tbody>
</table>
Physical Function following ECMO for Lung Transplant

Physical function in ECMO patients pre or post lung transplantation

- 2 year retrospective study comparing ECMO to non-ECMO
- 17 ECMO matched patients v 28 non-ECMO lung transplant patients
  - ECMO patients - 82% survival to hospital discharge
  - Leg complications reported in 50% of ECMO survivors
  - 79% were readmitted to hospital within 12 months

Hayes, Hodgson, Pellegrino et al, Resp Care, 2018
<table>
<thead>
<tr>
<th></th>
<th>ECMO</th>
<th>No ECMO</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>41.8 ± 12.8</td>
<td>41.2 ± 13.4</td>
<td>0.9</td>
</tr>
<tr>
<td><strong>Female</strong></td>
<td>8 (57.1)</td>
<td>16 (57.1)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td><strong>APACHE II</strong></td>
<td>16.5 (14.0 – 20.0)</td>
<td>14.0 (12.0 – 20.0)</td>
<td>0.16</td>
</tr>
<tr>
<td><strong>Ventilation (days)</strong></td>
<td>5.0 (3.5 – 14.0)</td>
<td>1.0 (1.0 – 1.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>ICU LOS</strong></td>
<td>15.0 (8.0 – 26.0)</td>
<td>5.0 (3.0 – 7.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Hospital LOS</strong></td>
<td>40.1 ± 20.1</td>
<td>19.2 ± 5.8</td>
<td>0.002</td>
</tr>
<tr>
<td><strong>Diagnosis - CF</strong></td>
<td>5 (35.7)</td>
<td>18 (64.3)</td>
<td>0.07</td>
</tr>
<tr>
<td><strong>IMS - Hospital discharge</strong></td>
<td>10 (9 – 10)</td>
<td>10 (10 – 10)</td>
<td>0.006</td>
</tr>
<tr>
<td><strong>6MWD Hospital discharge</strong></td>
<td>285 ± 112</td>
<td>384 ± 93</td>
<td>0.004</td>
</tr>
<tr>
<td><strong>Discharge to home</strong></td>
<td>541 ± 133</td>
<td>584 ± 67</td>
<td>0.11</td>
</tr>
<tr>
<td><strong>6MWD 3 months</strong></td>
<td>285 ± 112</td>
<td>384 ± 93</td>
<td>0.32</td>
</tr>
</tbody>
</table>

Matched for age and gender

Physical function at 3 months - no difference

BUT

79% ECMO survivors required hospital readmission within 12 months

Hayes, Hodgson, Pellegrino et al, Resp Care, 2018
LL Complications following ECMO in 50% of survivors

<table>
<thead>
<tr>
<th>Patient</th>
<th>ECMO Type</th>
<th>Leg Complication</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>VA</td>
<td>L femoral artery thrombectomy and vein patch repair of false aneurysm</td>
</tr>
<tr>
<td>2</td>
<td>VA</td>
<td>R femoral artery multiple surgeries, ischaemic R foot with ongoing infection leading to amputation of toes</td>
</tr>
<tr>
<td>3</td>
<td>VA</td>
<td>L groin seroma with long-term drain insitu. Dense paraesthesia L thigh.</td>
</tr>
<tr>
<td>4</td>
<td>VA</td>
<td>R groin haematoma and infection. R femoral artery reconstruction and vein patch repair</td>
</tr>
<tr>
<td>5</td>
<td>VA</td>
<td>Stenosis of external iliac vein resulting in significant L leg oedema, managed conservatively</td>
</tr>
<tr>
<td>6</td>
<td>VV</td>
<td>R leg paraesthesia and neurogenic pain</td>
</tr>
<tr>
<td>7</td>
<td>VA</td>
<td>R groin seroma and R thigh numbness, bilateral pins and needles</td>
</tr>
</tbody>
</table>

Hayes, Hodgson, Pellegrino et al, Resp Care 2018
Survival Outcomes Following the Use of Extracorporeal Membrane Oxygenation as a Rescue Technology in Critically Ill Patients: Results From Pennsylvania 2007-2015.

Huesch M, Foy A, Brehm, C.

Retrospective analysis of clinical data

Statewide (Pennsylvania)

2948 ECMO patients

Over the 9-year period, the mortality rate was 51.7%

Of all survivors

- 15% went home to self care
- 43.8% were readmitted within 1 month
- 60.6% within 1 year
Cognitive function analyses

- Neuropsychologist tests in median 9 years after ECMO, N=28
- Three cognitive domains (index, normal=100, 1SD = 15)
  - Full-scale IQ (global function)
  - Memory index (memory function)
  - Executive index (executive function)

von Bahr et al 2018, Crit Care Med
Cognitive function

N=13

N=8

N=5

N=3
Socio-economic Recovery

Tramm et al, 2016

Work Status Before ECMO in %

Work Status One Year After ECMO in %

- Working: 54%
- Not working: 30%
- Not working and no in-patient rehab: 23%

Before ECMO:
- Working: 70%
- Not working: 30%
- Not working and no in-patient rehab: 23%
Interviews with Patients

3 themes:
• Threat of serious injury & death
• Hallucinations during ICU
• Deconditioning, immobility and dependency

“The thing that I probably dreaded the most was the physio, because my legs ... I couldn't even do a simple thing ... I couldn't move my ankles or anything”
Family members experienced several stressors:

- Unexpected deterioration and crisis
- Prolonged risk of death and uncertainty during ECMO
- Role Conflicts: Decision Maker, Carer, Manager, Recorder
- Multiple transitions after discharge:
  - Negative: No care plan, no one in charge, incomplete recovery
  - Positive: Major life milestones – marriage, building homes, travel
The evidence gap

Disability Assessment

cognitive / physical / psych

Interventions to reduce disability?

Physical and mental / cognitive baseline status

Acute illness

Organ function - impairment

Activity - functional limitation

Participation - disability

Quality of life

Iwashyna and Netzer, 2012
<table>
<thead>
<tr>
<th>International ECMO Network</th>
<th>National Heart Foundation</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANZICS</td>
<td>Intensive Care Foundation (ANZ)</td>
</tr>
<tr>
<td>ANZIC-RC</td>
<td>Alfred Health</td>
</tr>
<tr>
<td>Royal Prince Alfred</td>
<td>St Vincent’s Sydney</td>
</tr>
<tr>
<td>The Prince Charles Hospital</td>
<td>Fiona Stanley</td>
</tr>
</tbody>
</table>
INDEX / EXCEL International Research Program
2015 – 2018

E-DATM – Evidence synthesis of ECMO outcomes, complications and definitions – lead Aidan Burrell

SCOPE – Systematic development of a Core Outcome Set for ECMO – lead Carol Hodgson

INDEX – International Database for ECMO research – lead Eddy Fan
Core outcome set: a minimum data set to be reported in every trial of ECMO

The OMERACT Framework 2.0 - used to structure domains within Core Areas
Conclusions & Limitations of the Research

- Mostly small cohort studies, minimal RCT data
- Pooled data of VA ECMO and VV ECMO – heterogeneity
- Current data mostly incudes groups who may have substantial differences in response to treatment & outcomes
  - VV-ECMO: acute (ARDS) v chronic (CF) patients
  - VA-ECMO: heart failure v cardiac arrest
- Loss to follow-up