ECMO: In the setting of liver failure & transplantation?

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What I am going to discuss …

- What is ECMO
- The literature
- International registry data from ELSO
- King’s College Hospital data
- ECMO & liver disease
- Case studies
- What does the future hold
What is ECLS

VA-ECMO

VV-ECMO

Femoral Artery

Internal Jugular Vein

Returning Oxygenated Blood

De-oxygenated Blood
ECMO – Overview

- ECLS = Extracorporeal Life support
- MCS = Mechanical circulatory support
- ECMO = Extracorporeal membrane oxygenation

- ECMO Basics (VV,VA)
  - Veno-Venous = respiratory support – AKA lung bypass
  - Veno-Arterial = cardiorespiratory support – AKA heart-lung bypass

- eCPR = Initiation of ECMO during CPR
ECMO - indications

- **Respiratory failure**
  - Reversible cause
  - National respiratory centres
  - Specialist populations

- **Refractory cardiogenic shock**
  - Bridge to …
  - … recovery, destination therapy, transplant, decision …
  - Unavailable outside of specialist centres

- **Refractory cardiac arrest**
  - eCPR
Respiratory ECMO

CESAR TRIAL – Peek et al

H1N1 & ECMO

NHSE National specification

To fulfil the CESAR eligibility criteria the patient will have severe but potentially reversible severe respiratory failure, defined as a Murray score ≥ 3.0, or uncompensated hypercapnoea with a pH < 7.20 despite optimal conventional treatment. Reversibility will be based on expert clinical opinion.

The Murray score uses four variables to assess the acuity of lung injury:
- oxygenation
- radiographic findings Chest X-ray changes
- level of positive end expiratory pressure (PEEP) used in mechanical ventilation
- lung compliance.
Cardiac ECMO

- INTERMACS
- Between INTERMACS 0 & 1 – levels of cardiogenic shock
  - Level 2 advanced cardiogenic shock (profound shock)
    - CI < 2.2 & lactate > 3 despite 2 inotropes/vasopressors
  - Level 3 deep cardiogenic shock (deep shock)
    - Two of: lactate > 8, anuric, MV, RHF, escalating inotropes/vasopressors

<table>
<thead>
<tr>
<th>INTERMACS® Profile Descriptions</th>
<th>Time Frame for Intervention</th>
</tr>
</thead>
</table>
| PROFILE 1: Critical cardiogenic shock  
 Patients with life threatening hypotension despite rapidly escalating inotropic support, critical organ hypoperfusion, often confirmed by worsening acidosis and/or lactate levels. “Crash and burn.” | Definitive intervention needed within hours |
| PROFILE 2: Progressive decline  
 Patient with declining function despite intravenous inotropic support, may be manifest by worsening renal function, nutritional depletion, inability to restore volume balance “Sliding on inotropes.” Also describes declining status in patients unable to tolerate inotropic therapy. | Definitive intervention needed within few days |
eCPR – cardiac arrest is bad for you …

- Survival post OHCA neurologically intact is 6 - 10 %
- 90 % of these survivors have ROSC within 16 minutes
- Significant global variation but …
Relevant literature
– ECLS in general

- NICE guidelines on acute heart failure
  - Adequate evidence
  - Uncertainty on selection
  - Serious complications

- Combes et al
  - Position paper on acute respiratory failure
  - Restrict to high volume centres (> 20 cases)

- Barbaro et al
  - ELSO registry analysis on outcomes
  - High volume centres & mortality

- The Cheer Trial
  - eCPR

**Extracorporeal membrane oxygenation (ECMO) for acute heart failure in adults**
Issued: March 2014
guidance.nice.org.uk/ipg482

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

Barbaro et al

Association of Hospital-Level Volume of Extracorporeal Membrane Oxygenation Cases and Mortality
Analysis of the Extracorporeal Life Support Organization Registry

The Cheer Trial

ecPR
The evidence base

- Cohort studies
- Historical comparisons
- Scores
- Review papers, letters
- Position papers
- RCT ...

MANAGEMENT OF CARDIAC SHOCK

The Patients - Survivors & Non-Survivors
Complications …

- e.g. Harlequin syndrome
- There are lots …
- Not to be entered into lightly …

SPO2 & ARTERIAL LINE ON RIGHT SIDE

NOT FOR THE FAINT-HEARTED
Modern ECMO - Technology

- Easier to use
- Portable
- Centrifugal pumps
- Stable oxygenators
- Less anti-coagulation
- Single circuit
- Cannulation can be percutaneous or surgical
The UK national problem?

- Major acute admitting hospitals
- Super-specialist centres
- Commissioning support required

There’s a gap … what about the patients that need both and cannot wait to be transferred for treatment … or that need super-specialist care such as liver transplantation
King’s College Hospital ECLS

- **Background**
  - 4 years, registered with ELSO, cost effective service

- **Caseload: (1/3 ECLS are within liver patients)**
  - 80 runs in 73 patients
  - 1/3 eCPR for refractory cardiac arrest (IHCA, OHCA)
  - 1/3 VA ECMO for refractory cardiovascular failure
  - 1/3 VV ECMO for specialist populations
King’s College Hospital ECLS

- Staff, education & training
  - Dedicated team across critical care
  - Eight consultants, sixteen nursing, perfusion support

- Governance
  - Meets international (ELSO) & national standards

- External validation
  - ELSO award holder for new centres
  - National Peer Review Programme: clinical case review
  - CQC: innovation
Look after where? How long?

| Liver (All) |  |  |  |  |
|------------|-----------------|----------------|----------------|----------------|----------------|
| ECMO run (days) | Years | Units | 2012 | 2013 | 2014 | 2015 | 2016 Grand Total |
| CB |  |  |  |  |  |  |  |
| FS |  |  |  |  |  |  |  |
| JS |  |  |  |  |  |  |  |
| LITU |  |  |  |  |  |  |  |
| Grand Total |  |  |  |  |  |  |  |
| 32 | 108 | 178 | 213 | 109 | 640 |

Note: ECMO run (days) refers to the number of days the ECMO (Extracorporeal Membrane Oxygenation) was used.
SOFA & MORTALITY

Jones et al Crit Care Med 2009
### The ELSO registry data 2015

**Cumulative outcomes – what can you expect from international registry data**

<table>
<thead>
<tr>
<th>Adult</th>
<th>Total</th>
<th>Weaned</th>
<th>% weaned</th>
<th>Survived</th>
<th>% survived</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac</td>
<td>7,850</td>
<td>4,394</td>
<td>56%</td>
<td>3,233</td>
<td>41%</td>
</tr>
<tr>
<td>Respiratory</td>
<td>9,102</td>
<td>5,989</td>
<td>66%</td>
<td>5,254</td>
<td>58%</td>
</tr>
<tr>
<td>eCPR</td>
<td>2,379</td>
<td>948</td>
<td>40%</td>
<td>707</td>
<td>30%</td>
</tr>
</tbody>
</table>
# King’s ECMO – absolute outcomes

<table>
<thead>
<tr>
<th>Cumulative outcomes</th>
<th>n = 73</th>
<th>ECMO survival</th>
<th>% ECMO survival</th>
<th>Survival or 90 day</th>
<th>% Survival or 90 day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac (non-eCPR)</td>
<td>23</td>
<td>17</td>
<td>74 %</td>
<td>15</td>
<td>65 %</td>
</tr>
<tr>
<td>(International)</td>
<td></td>
<td></td>
<td>(41 %)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Predicted – risk adjusted)</td>
<td></td>
<td></td>
<td>SAVE</td>
<td>(21 %)</td>
<td></td>
</tr>
<tr>
<td>Respiratory</td>
<td>25</td>
<td>18</td>
<td>72 %</td>
<td>15</td>
<td>60 %</td>
</tr>
<tr>
<td>(International)</td>
<td></td>
<td></td>
<td>(58 %)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Predicted – risk adjusted)</td>
<td></td>
<td></td>
<td>RESP</td>
<td>(31 %)</td>
<td></td>
</tr>
<tr>
<td>eCPR</td>
<td>25</td>
<td>14</td>
<td>56 %</td>
<td>12</td>
<td>48 %</td>
</tr>
<tr>
<td>(International)</td>
<td></td>
<td></td>
<td>(30 %)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Predicted – risk adjusted)</td>
<td></td>
<td></td>
<td>eCPR score</td>
<td>(&lt; 10 %)</td>
<td></td>
</tr>
</tbody>
</table>
King’s College Hospital VA ECMO

**Figure 3** Individual observed survival regarding the survival after veno-arterial-extracorporeal membrane oxygenation score within 95% confidence interval. Each dot represents the observed survival proportion at each score value in the study population (n = 3846) used to derive the survival after veno-arterial-extracorporeal membrane oxygenation score. Curved black lines represent 95 and 99% confidence intervals for predicted survival at each score level.
King’s College Hospital VV ECMO

Figure 2. Individual observed survival regarding the Respiratory Extracorporeal Membrane Oxygenation Survival Prediction (RESP) score within 95% confidence interval. Each dot represents the observed survival percentage in the study population (n = 2,355) used to derive the RESP score. Curved dotted gray lines and curved black lines represent 95 and 99% confidence intervals, respectively, for predicted survival at each score level.
ECMO in a liver intensive care

- All Liver
- ALF
- ALF with OLT
- Elective OLT
- Pre/peri/post

REALLY ... ???
OLT outcomes

Figure 7: Outcomes for elective liver transplantation
ALF/OLT outcomes

Figure 24: Risk-adjusted 1 year patient survival rates for adult super-urgent first liver transplants, 1 April 2010 - 31 March 2014

Figure 8: Outcomes for acute liver failure & super-urgent liver transplantation
## ECMO & liver disease

### LIVER NEEDING ECMO

<table>
<thead>
<tr>
<th></th>
<th>N =</th>
<th>ECMO survival</th>
<th>%</th>
<th>Survival to discharge (or 90 days)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALL liver patients</td>
<td>20</td>
<td>16</td>
<td>80</td>
<td>13*</td>
<td>65</td>
</tr>
<tr>
<td><strong>11 ALF, 7 elective OLT, 2 CLD</strong></td>
<td></td>
<td></td>
<td></td>
<td>* of which 12 VV, 8 VA with being 5 eCPR</td>
<td></td>
</tr>
<tr>
<td>ALL elective liver transplants</td>
<td>7</td>
<td>6</td>
<td>86</td>
<td>6</td>
<td>86</td>
</tr>
<tr>
<td><strong>3 VV, 4 VA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALL liver transplants</td>
<td>15</td>
<td>11</td>
<td>73</td>
<td>8</td>
<td>53</td>
</tr>
<tr>
<td><strong>9 VV, 6 VA</strong></td>
<td></td>
<td></td>
<td></td>
<td>* of which 4 eCPR</td>
<td></td>
</tr>
</tbody>
</table>

* One late death from HAT at 5 months

**ELSO REGISTRY:** 99 adult OLT, 26 survived, 8 at King’s, survival elsewhere 21 %
### ALF & ECMO - Demographics

<table>
<thead>
<tr>
<th></th>
<th>Aetiology</th>
<th>Age</th>
<th>Gender</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>SALF†</td>
<td>23</td>
<td>F</td>
</tr>
<tr>
<td>2</td>
<td>Avascular*</td>
<td>29</td>
<td>M</td>
</tr>
<tr>
<td>3</td>
<td>POD</td>
<td>17</td>
<td>F</td>
</tr>
<tr>
<td>4</td>
<td>PPOD‡</td>
<td>26</td>
<td>F</td>
</tr>
<tr>
<td>5</td>
<td>HH**</td>
<td>29</td>
<td>M</td>
</tr>
<tr>
<td>6</td>
<td>Status/POD</td>
<td>44</td>
<td>M</td>
</tr>
<tr>
<td>7</td>
<td>Wilsons</td>
<td>11</td>
<td>M</td>
</tr>
</tbody>
</table>

†Sub-acute liver failure  
*Penetrating trauma, HA ligated, prolonged Pringle manoeuvre  
‡Polypharmacy OD  
‡‡Polypharmacy OD  
**Suspected myocarditis and hepatitis
ALF & ECMO - Severity of liver disease

<table>
<thead>
<tr>
<th></th>
<th>AST IU/L</th>
<th>INR</th>
<th>Lactate</th>
<th>Bilirubin</th>
<th>HE III-IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>8531</td>
<td>6</td>
<td>13.1</td>
<td>282</td>
<td>6</td>
</tr>
<tr>
<td>SALF</td>
<td>57</td>
<td>5.4*</td>
<td>8</td>
<td>312</td>
<td>I</td>
</tr>
<tr>
<td>Avascular</td>
<td>6000</td>
<td>3*</td>
<td>12</td>
<td>159</td>
<td>I</td>
</tr>
<tr>
<td>POD</td>
<td>9966</td>
<td>9.7</td>
<td>11</td>
<td>325</td>
<td>I</td>
</tr>
<tr>
<td>PPOD</td>
<td>12650</td>
<td>5.35*</td>
<td>18</td>
<td>227</td>
<td>I</td>
</tr>
<tr>
<td>HH</td>
<td>12200</td>
<td>6.1*</td>
<td>15</td>
<td>219</td>
<td>unknown</td>
</tr>
<tr>
<td>Status HH</td>
<td>18180</td>
<td>5*</td>
<td>13.2</td>
<td>94</td>
<td>I</td>
</tr>
<tr>
<td>Wilsons</td>
<td>667</td>
<td>7.36*</td>
<td>14.4</td>
<td>636</td>
<td>I</td>
</tr>
</tbody>
</table>

*INR supported

6/7 (86%) pts fulfilled KCH criteria for ELT
# Extra-hepatic organ failure

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>VV</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOFA</td>
<td>22 (20-24)</td>
<td></td>
</tr>
<tr>
<td>CPR</td>
<td>5 (71%)</td>
<td></td>
</tr>
<tr>
<td>RRT</td>
<td>7 (100%)</td>
<td></td>
</tr>
<tr>
<td>ICH</td>
<td>6 (86%)</td>
<td></td>
</tr>
<tr>
<td>Plt</td>
<td>40 (20-77)</td>
<td></td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>1.02 +</td>
<td>37 (32-40)</td>
</tr>
<tr>
<td>μg/kg/min</td>
<td>other</td>
<td></td>
</tr>
<tr>
<td>PPlat</td>
<td></td>
<td>3.8 (3-4)</td>
</tr>
<tr>
<td>Murray</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Outcomes – ALF & ECMO

<table>
<thead>
<tr>
<th></th>
<th>ECLS duration</th>
<th>Weaned ECLS</th>
<th>Discharge or 90d survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>8d (1-20)</td>
<td>6/7 (86%)</td>
<td>5/7 (71%)</td>
</tr>
<tr>
<td>VV ECMO</td>
<td>11d (5-20)</td>
<td>4/5 (80%)</td>
<td>3/5 (60%)</td>
</tr>
<tr>
<td>VA ECMO</td>
<td>5d (4-6)</td>
<td>2/2 (100%)</td>
<td>2/2 (100%)</td>
</tr>
<tr>
<td>ECMO pre ELT</td>
<td>8d (3-21)</td>
<td>3/4 (75%)</td>
<td>2/4 (50%)*</td>
</tr>
</tbody>
</table>

- 86% wean rate
- 71% 90 day survival off ECMO
- All patients transplanted (n = 4) survived OLT procedure
- 100% had excellent early graft function – normal D1 lactate
- One died at 5 months from HAT
ECLS in ALF – the edge of reason?

Acute Liver Failure and ECMO support: The edge of reason?


1 Liver Intensive Care Unit, KCH London, UK
2 Department of Transplant Surgery, KCH London, UK

AASLD

INTRODUCTION

The use of extracorporeal membrane oxygenation (ECMO) in ALF has increased exponentially over the last 5 years. In parallel, indications for ECMO in acute liver failure have broadened considerably. Despite that, there is no level of evidence to support the use of ECMO in ALF. The high rates of complications associated with ECMO in ALF are a significant concern. Therefore, we performed a systematic review of the literature to assess the potential benefits and complications of ECMO in ALF.

AIM

Review of all AF patients supported with veno-venous (VV) or veno-arterial (VA) ECMO since introduction of an adult ECMO service in our hospital. Description of indications and outcome of VV versus VA ECMO patients and dependent on timing of initiation of extracorporeal support in relation to ACFL.

MATERIAL & METHODS

Retrospective cohort of our ECMO database. All patients supported with ECMO were included. The definition of ALF was based on diagnostic criteria. Presentation with severe liver failure, potentially reversible in nature, and with signs of hepatic encephalopathy within 3 weeks of the first symptoms in the presence of pre-existing liver disease.

RESULTS

Of 52 patients supported on ECMO over 8 years, 3 patients presented with acute liver failure. Mortality of patients with acute liver failure are shown in Table 1. Physical benefits and complications associated with ECMO are shown in Table 2.

CONCLUSION

ECMO support in adult ALF is technically feasible. Excluding a young patient with ALF induced ALF who survived with ECMO support, all patients were successfully bridged to LT. Only 1 patient survived to hospital discharge. A patient admitted to orthotopic liver transplantation (OLT) for 2 patients presenting but not diagnosed prior to ECMO and LT. Two patients who underwent ECMO without being transplant candidates (after all 1 of their failed KIT) died after 2 patients were treated with ECMO without complications. ECMO may offer a viable bridge to recovery or emergency LT in ALF.

ACKNOWLEDGEMENTS

We are very grateful to our ECMO coordinators and nurses as well as the KIT perfusion team for their tireless efforts and dedication.

REFERENCES


DISCLOSURES

None of the authors have anything to disclose or declare conflicts of interest in relation to the presented data.

Contact Information

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Examples of rescue ECMO

- 45 year OLT for HPS (VV)
  - Refractory hypoxaemia
- 26 year old liver transplant recipient (VA)
  - FTW from CPB after aortic surgery
- 44 year old hyper-acute liver failure (VV)
  - AST > 18000 meeting transplant criteria
- 52 year old post OLT (VV)
  - In another hospital in extremis
- 17 year old with POD hyper-acute (VV)
  - Transplanted on ECMO
- 34 year old with ALF secondary to eclampsia (VV)
  - Transplanted on ECMO
A tale of a new mother …

- 34 yr new mother referred post partum
- Pre-eclampsia & E. Coli sepsis
- Emergency LSCS
- MOF associated with ALF
- Transferred to King’s College Hospital
- Investigations suggest pregnancy related liver disease with HELLP & eclampsia
- Established MOF
… meets transplant criteria

- Despite ‘fulminant’ standard of care …
  - Biochemical and imaging correlates with unrecoverable ALF
  - Unremitting hyperlactataemia 8.2 despite HV CVVHDF & optimisation
  - Peak AST 4156 INR(supported) 5.87 Bilirubin 316 PLT 43

- Meets criteria for emergency OLT
  - Super-urgently listed but continues to deteriorate
  - SOFA 19 – without scoring for CNS …
  - RESP score is – ve 9
… considered for ECMO as bridge

- Intra-cranial hypertension
- Refractory hypoxaemia on 100 % Oxygen
  - P/F 67 mmHg Murray score 3.75
- On high dose vasopressors
- Acute liver failure
- HV CVVHDF
- Coagulopathic
- Sepsis – on broad spectrum abx
- Low platelets

Deemed untransplantable due to severity of illness and risk of graft loss in the setting of refractory hypoxaemia and severe MOF
What to do …

- Patient versus Organ availability
- 100 % mortality without transplantation
  - Realistically
- Shared decision making
  - Surgeons, hepatology
- Offered ECMO as rescue therapy
  - TOE guided cannulation
  - 29 Fr bicaval Avalon 4/4.5L ECMO flow
- Transplanted on VV ECMO heparin free
  - 9 days on ECMO, open abdomen, 33 days on ICU
  - Discharged to her family and new baby
A tale of two children

- 11 yr girl with hepatoblastoma
- Re-do ELT for graft failure
- Refractory ARDS D43
  - PF 75 Murray 4 HFOV iNO
- Refused ECLS by GOSH/Leicester
- 26 days on VV ECMO
- Home with her family

- 11 yr boy with acute Wilson’s
- Refractory MOF
- Untransplantable
  - Refractory MOF
- VV ECMO – ELT
- 8 days on VV ECMO
- Home with his family

EXTENDING THE REACH OF LIVER TRANSPLANTATION
Conclusion

• The ‘mortally ill’ can survive … but they need our help

• Even in the worst sub-groups …

• Even in untried groups …

• Youth is on their side but …

• Overall, the KCH_{ECMO} SMR 0.574 (CI 0.35-0.82)
  ◦ SAVE & RESP scores
  ◦ p = 0.00004

• ECMO & liver disease – go to a centre that does both

• Thank you
Questions

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