Research in ECMO: A revolution is coming

Daniel Brodie

Critical Care Canada Forum
Toronto, Ontario
October 27th, 2015
Research in ECMO: A revolution is coming???

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Faculty Disclosures
Daniel Brodie

Maquet Cardiovascular
  Research support
  Research consulting

ALung Technologies
  Medical Advisory Board

Kadence
  Medical Advisory Board

International ECMO Network
  Chairman, Executive Committee

ECMO is off label
Advances in technology

Pumps
Oxygenators
Biocompatible circuits
Catheters
Rapid growth of ECMO
2009 to present
2009 Influenza A (H1N1) pandemic
Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial

Giles J Peek, Miranda Mugford, Ravindranath Tiruvoipati, Andrew Wilson, Elizabeth Allen, Mariamma M Thalananey, Clare L Hibbert, Ann Truesdale, Felicity Clemens, Nicola Cooper, Richard K Firmin, Diana Elbourne, for the CESAR trial collaboration

CESAR Trial
Adult Cardiac Cases
ELSO Registry January 2015

Annual Cardiac Runs (16 years old and over)
But wait...
Where’s the evidence?
**Pubmed search:**
Extracorporeal membrane oxygenation OR Extracorporeal carbon dioxide OR Extracorporeal CPR

*9,192 references* dating back to 1960

*Spike 2010* to ~650 (from 300 in ‘09)

*2015 annualized to 800* (same as 2014)
What is the quality of the literature in ECMO?
<table>
<thead>
<tr>
<th>Indications</th>
<th>Evidence Level</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Respiratory</strong></td>
<td></td>
</tr>
<tr>
<td>ARDS</td>
<td>Randomized controlled trials</td>
</tr>
<tr>
<td>Hypercapnic respiratory failure</td>
<td>Prospective feasibility studies</td>
</tr>
<tr>
<td>Bridge to lung transplantation</td>
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<td>Primary graft dysfunction after lung transplantation</td>
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<tr>
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<td>Cohort studies with propensity analyses</td>
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<td>Cohort studies</td>
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<tr>
<td>Primary graft failure after heart transplantation</td>
<td>Cohort studies</td>
</tr>
<tr>
<td>Bridge to VAD implantation or heart transplantation</td>
<td>Cohort studies</td>
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<tr>
<td>Prevention of acute right ventricular failure after LVAD implantation</td>
<td>Cohort studies</td>
</tr>
</tbody>
</table>
**Table 1**  Indications and Highest Level of Evidence for ECMO in Cardiopulmonary Disease

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*Randomized controlled trials*  
*Prospective feasibility studies*  
*Cohort studies*  
*Case series*  
*Cohort studies with propensity analyses*

*Cohort study with propensity analysis*
RCTs
for ECMO in ARDS
Zapol 1979
Morris 1994
Advances in technology. . .
Modern RCT in ECMO
Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial

Giles J Peek, Miranda Mugford, Ravindranath Tiruvoipati, Andrew Wilson, Elizabeth Allen, Mariamma M Thalanyi, Clare L Hibbert, Ann Truesdale, Felicity Clemens, Nicola Cooper, Richard K Firmin, Diana Elbourne, for the CESAR trial collaboration

CESAR Trial

Figure 2: Kaplan-Meier survival estimates
Where should we go from here?
Collaboration
Why is collaboration so important to the future of ECMO research?
ECMO is... Complex
High risk
Expensive
Wide variations in technique
We need to settle the most basic questions

Does it work?
Who might benefit?
How to use it?
How do our patients do long term?
Need to advance the science of ECMO

Basic
Translational
Clinical questions
How are we doing?
ECMO Research

Fragmented across centers, countries, continents
What should we do?
First...
Build top quality ECMO centers

Perform quality ECMO
Why build top quality clinical centers before we even know ECMO works?
To participate meaningfully in high quality research

Zapol
Morris

Combes A, et al. AJRCCM 2014
Call for research centers
Do we need “top quality” centers
Or just more centers?
Volume-outcome in ECMO?
Retrospective review of ELSO database 1989-2013

290 centers

56,222 patients (30k neonatal, 15k peds, 11k adult)
Higher age group-specific ECMO volume associated with lower odds of mortality in neonatal & adult populations

2008-2013 only held in adults

≥ 30 adult ECMO cases/y
OR mortality 0.61 (compared with < 6 cases/y)
Not every center should be doing ECMO in 2015

Regionalization
Highest quality, best practices
Next...
Drive collaboration

Across centers, countries & continents
We need a research network in ECMO
ECMOnet
INTERNATIONAL ECMO NETWORK

www.internationalecmonetwork.org
ECMOnet Vision
To serve the ECMO research community
Foster & support
High-quality, high-impact research ideas by investigators throughout the world
International ECMO Network

Ongoing & Upcoming Studies
ECMO to rescue Lung Injury in severe ARDS EOLIA

International RCT
PI: Alain Combes

Enrolling December 2011
ECCO$_2$R for Lung-protection

Moderate to severe ARDS

SUPERNova

Pilot Study
International, multicenter, RCT

PI: Alain Combes, Marco Ranieri
LIFEGARDS

ventilation management of patients with Extracorporeal membrane oxygenation for Acute Respiratory Distress Syndrome

An international observational study

Steering committee

• Matthieu Schmidt (Paris, Melbourne) = PI
• Carol Hodgson (Melbourne)
• Vincent Pellegrino (Melbourne)
• Alain Combes (Paris)
• Eddy Fan (Toronto)
• Daniel Brodie (New York)
Low-dose heparin in critically ill patients undergoing ECMO – Single center, unblinded, randomized, feasibility study

The HELP-ECMO Study Investigators:
C Aubron, V Pellegrino, D Pilcher, J Sheldrake, D Murphy, J Board, L Hockings, J Cooper
What percentage of ICU patients may be candidates for gas eXchange eXtracorporeal techniques?

The XXL study

PI: Laurent Brochard & Eddy Fan
ASAP ECMO

Antibiotic, Sedative and Analgesic Pharmacokinetics during ECMO

PI: Kiran Shekar

Multicentre study of population PK models in ECMO
250 subjects
Develop evidence-based guidelines
International ECMO Network

Proposed Studies
Protective ventilation with venovenous lung assist
in respiratory failure

REST Study

UK collaborative
Multicentre, RCT
PI: Danny McAuley & James McNamee

ECCO$_2$R for acute hypoxemic respiratory failure
Not just ARDS
P:F < 150

1,120 subjects
28 day mortality
ANCHOR

Assessment of ECMO in acute myocardial infarction with Non-reversible, Cardiogenic shock to Halt Organ failure & Reduce mortality

Prospective, open-label, multicenter, randomized, controlled trial

PI: Alain Combes
ECMO PT
ECMO early staged physical training

Carol Hodgson

ANZIC-RC
ACTION CRE

240 subjects
Multicentre, assessor-blinded, RCT
Physical rehab within 48 hours of ECMO vs. no rehab
Outcomes: functional status & muscle strength
ImmunoDeficiency and ECMO for Acute respiratory failure IDEA study

Multicenter, retrospective cohort study

Matthieu Schmidt, Vincent Pellegrino, Carol Hodgson, Alain Combes, Eddy Fan, Daniel Brodie
Multiple other high quality research efforts beyond ECMONet
ECCO$_2$R for COPD?

Need RCTs

Multiple planned international, multicenter RCTs
Is a revolution coming?
Certainly an evolution
Active ECLS Centers
ELSO Registry January 2015

Centers by Year

<table>
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<tr>
<th>Year</th>
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Need for high quality research