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Dr. Farmer is President of the Society of Critical Care Medicine (SCCM) and has served as SCCM Council Member and Treasurer; Program Chair, SCCM Congress; Founding Editor-in-Chief, Multidisciplinary Critical Care Knowledge Assessment Program (MCCKAP); Supplements Editor, Critical Care Medicine; and, textbook editor, Fundamental Critical Care Support (FCCS) and Fundamental Disaster Management (FDM) programs. He is the editor and author of numerous books related to critical care, education, and disaster medical response.

Dr. Farmer is a retired Air Force Colonel and Professor of Medicine and Surgery, Uniformed Services University of the Health Sciences, F. Edward Hébert School of Medicine. He also served as a senior physician executive in the hospital, health plans-insurance, supply chain management, and homeland security sectors. He is one of the founders of the Department of Defense Critical Care Aeromedical Transport Team (CCATT) program, the largest critical care transport system in the world. While in the Air Force, Doctor Farmer served as Chief of Inpatient Services at Wilford Hall Medical Center, and as Chief Medical Officer for TRICARE Southwest, a multi-state Federal HMO. Doctor Farmer also served as the Special Assistant to the Air Force Surgeon General for Homeland Defense and Medical Preparedness.

OBJECTIVES:
Participants should be better able to:

1. Better understand and implement this concept.
Extracorporeal Life Support

Who Benefits?

J. Christopher Farmer
Case Vignette

• A 41-year-old woman presents with severe community-acquired pneumococcal pneumonia.

• Chest radiography reveals diffuse bilateral infiltrates, and hypoxemic respiratory failure develops despite appropriate antibiotic therapy.

• She is intubated and mechanical ventilation is initiated with a volume- and pressure-limited approach for the acute respiratory distress syndrome (ARDS).

• Over the ensuing 24 hours, her partial pressure of arterial oxygen (PaO₂) decreases to 40 mm Hg, despite ventilatory support with a fraction of inspired oxygen (FIO₂) of 1.0 and a positive end-expiratory pressure (PEEP) of 20 cm of water.

• She is placed in the prone position and a neuromuscular blocking agent is administered, without improvement in her PaO₂.

• An intensive care specialist recommends the initiation of extracorporeal membrane oxygenation (ECMO).

ELSO

*Look here first for information...*

- Maintains international data base
- Provides educational resources
- Provides guidelines for practice
- Provides guidelines for training of ECMO Specialists
First generation ECMO devices

• Complex teamwork required
• Difficult (high risk) safety profile
• Focused on neonatal support

Have ECMO...will cannulate!
Ease of use (?)

Required operator skill sets are very high

How hard can it be, anyway?
**Veno-Arterial ECMO**

- Patient Venous Blood
- Native Heart/Lung
- Artificial Heart/Lung
- Patient Arterial Blood

**Veno-Venous ECMO**

- Patient Venous Blood
- Artificial Lung
- Native Lung
- Patient Arterial Blood

**Veno-Veno ECMO**

- Provides gas exchange support only
- Blood drained from venous system and returned to venous system
- e.g., jugular and femoral veins

Veno-Arterial ECMO

- Partial or total cardiopulmonary support
- Heart and lungs are largely bypassed
- Ventilator settings and inotropic support can be minimized, as long as ECMO support is adequate
- Higher risk of stroke from thrombotic /air embolism due to cannulation site

ECMO goals:
- Rest the heart/lungs
- Maintain a ECMO blood flow index of 2.2-2.6 L/kg/min
- Provide adequate oxygenation/ventilation of “ECMO blood”
- Adequately anticoagulate the blood, when appropriate (ACT = 160-200)

Central Cannulation (RA to Ascending Aorta)        Peripheral Cannulation (Fem Vein to Fem Artery)
What can we directly control?

V-A ECMO

<table>
<thead>
<tr>
<th>Control</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sweep</td>
<td>$\downarrow$ PCO2</td>
</tr>
<tr>
<td>FiO2</td>
<td>$\uparrow$ PaO2</td>
</tr>
<tr>
<td>RPM</td>
<td>$\uparrow$ Blood Flow</td>
</tr>
</tbody>
</table>

Patient Systemic Circulation

Right Heart

Patient Lungs

Left Heart

V-A ECMO
Avalon Bi-Caval Dual Lumen Cannula

• Advantages
  – Single stick percutaneous insertion under fluoroscopy or TEE
  – Matches natural flow ratios
  – Potential for patient to be ambulatory

• Disadvantages
  – Potential flow limitations
  – High pressure drop - hemolysis

Hazardous Terrain

WHEN FLOODED TURN AROUND DON’T DROWN
Perils of ECMO cannulation

- Goal: flow sufficient to achieve Cardiac Index of 2.5L/min/m²
- Potential distal limb ischemia with femoral arterial cannulation
  - SFA cannula / graft
- Hemolysis, protein denaturation with excessive pressure drop
  - Pressure drop vs. flow
- Potential hypo-perfusion to cerebral, coronary, limb vessels (V-A)
  - Femoral arterial cannulation
- De-cannulation with massive bleeding

Perils of ECMO cannulation in the ICU

Unstable, dynamic, technically challenging procedure

- Maintain control of personnel in room
- Maintain integrity of sterile field
- Be prepared for:
  - Code
  - Mass transfusion
  - Heparin Administration
  - Rapid blood draws
    - ABG
    - VBG
    - ACT
    - Coagulation profile
Perils of anticoagulation in the ICU

- Heparin drip / bolus
- Argatroban – HIT
- ACT vs. aPTT
- ACT 160 – 220*
  - Hepcon
  - Exceptions
  - Blood product administration
- TEG
  - provides a complete picture of the formation and dissolution of the clot, showing the balance or imbalance of the two systems

Resource requirements

ECMO RN Specialist

- Role developed to provide an efficient, scalable, and sustainable staffing model for expert and competent care of ECMO patients
  - Perfusion staffing limitations
  - Other institutional models
- Training
  - Following ELSO Guidelines for Specialist training
  - Critical Elements:
    - bedside experience
    - didactic learning
    - skills competency
Resource requirements

**ECMO Perfusionist**

- “In-house”
- Maintains and “troubleshoots” ECMO device and circuit
- Monitors ECMO catheter(s)
- Monitors anticoagulation
- Monitors hemodynamic performance

Resource requirements

**ECMO Workgroup**

- **Members (minimum):**
  - ICU nurse manager
  - ICU nurse educator
  - ICU clinical nurse specialist
  - Lead ICU ECMO RN specialist
  - Lead perfusionist
  - ICU medical director

- **Initiatives:**
  - Develop and implement ICU ECMO Practice Guidelines
  - Develop and implement ICU ECMO Order Set
  - Develop and implement ICU RN ECMO Specialist Training Course
  - Develop and implement ICU documentation guidelines
  - Provide platform for Perfusion / Nursing cooperation, collaboration, and communication with the goal of providing the best possible care for our ECMO patients
Risk of adverse events with ECMO

<table>
<thead>
<tr>
<th>Event</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Directly related to the ECMO circuit</td>
<td></td>
</tr>
<tr>
<td>Oxygenator failure</td>
<td>17.5</td>
</tr>
<tr>
<td>Bleed clots</td>
<td></td>
</tr>
<tr>
<td>Oxygenator</td>
<td>12.2</td>
</tr>
<tr>
<td>Other circuit</td>
<td>17.8</td>
</tr>
<tr>
<td>Cannula-related problems</td>
<td>8.4</td>
</tr>
<tr>
<td>Other mechanical complications</td>
<td>7.9</td>
</tr>
<tr>
<td>Not directly related to the ECMO circuit</td>
<td></td>
</tr>
<tr>
<td>Bleeding</td>
<td></td>
</tr>
<tr>
<td>Surgical site bleeding</td>
<td>19.9</td>
</tr>
<tr>
<td>Cannula-site bleeding</td>
<td>17.1</td>
</tr>
<tr>
<td>Pulmonary hemorrhage</td>
<td>8.1</td>
</tr>
<tr>
<td>Gastrointestinal hemorrhage</td>
<td>5.1</td>
</tr>
<tr>
<td>Intracranial hemorrhage</td>
<td>3.8</td>
</tr>
<tr>
<td>Hemolysis</td>
<td>6.9</td>
</tr>
<tr>
<td>Disseminated intravascular coagulation</td>
<td>3.7</td>
</tr>
<tr>
<td>Culture-confirmed infection at any site</td>
<td>21.3</td>
</tr>
</tbody>
</table>

Data are from the Extracorporeal Life Support Organization (ELSO). Rates of adverse events reported by ELSO include events associated with the use of both modern and outdated ECMO technology as well as events occurring at centers with and those without experience in ECMO. These data are inclusive of all adult patients with respiratory failure, not just ARDS alone.

Adverse events not related to the ECMO circuit are prioritized to those that are most clinically significant and potentially related to the use of ECMO.

The event rate for culture-confirmed infection includes infection at the ECMO cannula site and all other infections. The rate of infection at the ECMO cannula site was 10% in one observational study.

WHO BENEFITS?

Applying technology is simply finding the right wrench to pound in the correct screw
Anonymous

ECMO is a bridge to something...
RESCUE vs. RESURRECTION therapy

Potential benefits of ECMO over optimal conventional treatment

- **Rest the heart**
  - Allows decreased use of inotropes
- **Rest the lungs**
  - Allows decreased ventilator settings
- **Improve end-organ and tissue perfusion**
  - Cardiac Index > 2.5
- **Improve oxygen saturation and ventilation**
  - > PaO₂, > SaO₂, > CO₂ removal
- **Allows time for medications and medical therapy to work**
  - e.g., “steroids”
- **Actively control core temperature**

**DESIGN:** first contemporary randomized controlled trial of ECMO referral for respiratory failure in adults compared to conventional supportive critical care

**INTERVENTION:** referral to an ECMO center not treatment with ECMO

**OUTCOME:**

- 75% of ECMO-referred patients actually received ECMO
- Increased 6-month survival without severe disability compared to conventional management
- Criticized because non-ECMO pts did not reliably receive lung protective MV strategies


**DESIGN:** observational study of all patients (n = 68) with 2009 influenza A(H1N1)–associated ARDS treated with ECMO in 15 intensive care units (ICUs) in Australia and New Zealand

**INTERVENTION:** Retrospective case series of ECMO patients with severe respiratory failure

**OUTCOME:**

- 23.7% of the ECMO-treated patients died in-hospital, compared to ~50% of the matched conventionally treated patients
- ECMO patients: 80% had F\textsubscript{O\textsubscript{2}} of 1.0; 50% had failed low-tidal ventilation and were being vented with alternate strategies (which was likely why they were referred for ECMO)
- 86% of patients referred for ECMO were treated with ECMO
- 70% survival ARDS due to H1N1 treated with ECMO
- Hemorrhagic complications were associated with 74% of deaths in the ECMO group.
- “Baked-in” selection bias precluded any strong conclusion of ECMO’s independent benefit
COMPARISON OF RESULTS

68 versus 30 H1N1-associated ARDS patients

MULTICENTER versus SINGLE CENTER

Median age 34 in both studies

56 versus 61 median P/F ratio

YES ECMO versus NO ECMO

75% versus 73% reported survival

SLIDE CONCEPT: Dr. Eddy Fan
Is it the ECMO or is it the provider expertise that makes a difference?

Berlin ARDS definition

1. Improve clarity of definition
2. Link severity to mortality
3. Link severity to aggressiveness of treatment
4. Better separation of prognosis and treatment selection

<table>
<thead>
<tr>
<th>Timing</th>
<th>Acute onset within 1 week of a known clinical insult or new/worsening respiratory symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyponxia</td>
<td>(\text{PaO}_2/\text{FiO}_2\ &gt; 300) with PEEP/CAP (\geq 5) (\text{PaO}_2/\text{FiO}_2\ &lt;= 200) with PEEP (\geq 5) (\text{PaO}_2/\text{FiO}_2\ &lt;= 100) with PEEP (\geq 10)</td>
</tr>
<tr>
<td>Origin of Edema</td>
<td>Respiratory failure associated to known risk factors and not fully explained by cardiac failure or fluid overload. Need objective assessment of cardiac failure or fluid overload if no risk factors are present</td>
</tr>
<tr>
<td>Radiological Abnormalities</td>
<td>Bilateral opacities* (\text{VfCO}<em>2 &gt; 10\ \text{L/min}) or (C</em>{O_{2}} &lt; 40\ \text{ml} / \text{min} / \text{cmH}_2\text{O})</td>
</tr>
</tbody>
</table>

*Not fully explained by effusions, edema, masses, or rebound collapse. Use training set of ARDS: \(\text{VfCO}_2 = \text{Vf} \times \text{PaCO}_2/\text{HR}\) (corrected for body surface area)
Indications and Contraindications for ECMO in Severe Cases of ARDS.

### Indications

- Severe hypoxemia (e.g., ratio of \(P_{A\text{o}_2}\) to \(F_{I\text{O}_2}\) < 80, despite the application of high levels of PEEP [typically 15–20 cm of water] for at least 6 hr in patients with potentially reversible respiratory failure)
- Uncompensated hypercapnia with acidemia (pH < 7.15) despite the best accepted standard of care for management with a ventilator
- Excessively high end-inspiratory plateau pressure (>35–45 cm of water, according to the patient’s body size) despite the best accepted standard of care for management with a ventilator

### Relative contraindications

- High-pressure ventilation (end-inspiratory plateau pressure >30 cm of water) for >7 days
- High \(F_{I\text{O}_2}\) requirements (>0.8) for >7 days
- Limited vascular access

### Any condition or organ dysfunction that would limit the likelihood of overall benefit from ECMO, such as severe, irreversible brain injury or untreated metastatic cancer

### Absolute contraindication

- Any condition that precludes the use of anticoagulation therapy

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*ARDS denotes the acute respiratory distress syndrome, ECMO extracorporeal membrane oxygenation, \(F_{I\text{O}_2}\) fraction of inspired oxygen, \(P_{A\text{o}_2}\) partial pressure of arterial oxygen, and PEEP positive end-expiratory pressure.

† ECMO may be considered after a shorter interval if the ratio of \(P_{A\text{o}_2}\) to \(F_{I\text{O}_2}\) is less than 50. The threshold for the initiation of ECMO varies considerably across studies and guidelines.

‡ In patients with severe bleeding, anticoagulation may be withheld for limited periods of time.
• A 38-year-old man presents with severe H1N1 pneumonia.

• Chest radiography reveals diffuse bilateral infiltrates, and hypoxemic respiratory failure.

• He is intubated and mechanical ventilation is initiated with a volume- and pressure-limited approach for the acute respiratory distress syndrome (ARDS).

• Over the ensuing 12 hours, and despite ventilatory support with a fraction of inspired oxygen (FIO₂) of 1.0 and a positive end-expiratory pressure (PEEP) of 20 cm of water, SpO₂ is 82%.

• The patient is anticoagulated and VV ECMO is initiated.

• Focal neurological findings develop 8 hours later. Non-contrast head CT demonstrates major intracranial hemorrhage

• H1N1 can be associated with encephalitis and myocarditis—screen patients to determine VV versus VA ECMO as well as the safe use of anticoagulation

Whither ECMO?

• Injurious settings on mechanical ventilation?
• The longer you wait, the worse the outcome (> 7-10 days)?
• ECMO facilitates lung protection?
• Does facilitation of “low intensity” MV improve outcomes?
Whither ECMO?

Day 1 Plateau Pressure (cm H\textsubscript{2}O)

Mortality dose response curve to changes in V\textsubscript{T}

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Dale M Needham et al. BMJ 2012;344:bmj.e2124
“PROOF OF CONCEPT”

What are the optimal MV strategies for ECMO patients?

ECMO: An even greater lung protective strategy?

“Healing” ventilation, not just protective

Reducing $V_T$ to very low levels, or even CPAP...

LOW lung tissue pressure exposure

LOW $F_{O_2}$

LITTLE alveolar cycling
Extracorporeal life support for adults with severe acute respiratory failure

Contraindications to VV-ECMO
- Mechanical ventilation >7 days
- Irreversible CNS disease
- Decision to limit therapeutic interventions

Unable to cannulate: intracranial bleeding or other major contraindications to anticoagulation
- Poor prognosis because of underlying disease

The Lancet Respiratory Medicine 2014 2, 154-164. DOI: (10.1016/S2213-2600(13)70197-8)
Today’s reality...

- There are not established data that validate this concept of ECMO versus MV flow to prevent lung injury
- All of this is “extrapolated” from other work
- Studies are underway in Canada and from the ESICM to address this concept

Summary

In the sea there are countless gains,
But if thou desirest safety, it will be on the shore.
The Gulistan of Saadi
Summary

• SOONER IS BETTER THAN LATER?
• TEAM WORK MATTERS
• YOU HAVE TO KNOW WHERE YOU ARE ON THE ARDS “SEVERITY” CONTINUUM
• MV FLOW ← ECMO FLOW?