Extracorporeal Membrane Oxygenation (ECMO): The Past, Present, and Future

Medicine Grand Rounds
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Steve Derdak, DO, FCCP
Adult ECMO Program
Divisions of Cardiology and Pulmonary/Critical Care Medicine
Department of Medicine
Heart and Vascular Institute

No Disclosures or Conflicts of Interest

A 50 yr old female with COVID-19 is intubated for rapidly progressive hypoxemia despite 12 hours of HFNC O₂. After 3 days of lung protective ARDSNet mechanical ventilation, prone positioning, cisatracurium, diuresis, dexamethasone, and iNO 40 ppm, she continues to worsen. On FiO₂ 100% and PEEP 22 cm H₂O, her PaO₂ is now 48 mmHg, SaO₂ 74%, PaCO₂ 72 mmHg, and pH 7.14.

What should be done next?
“If only we could remove the blood from her body by bypassing the lungs, and oxygenate it, then return it to her heart, we could almost certainly save her life.”

John Gibbon MD 1930
(upon watching a patient die of shock from a post-op PE during attempted surgical embolectomy)

John Gibbon’s first heart-lung machine…1952

1952 Bernard Miller tests John Gibbons experimental Heart-Lung Machine on dogs - 90% survive

PROLONGED EXTRACORPOREAL OXYGENATION FOR ACUTE POST-TRAUMATIC RESPIRATORY FAILURE (SHOCK-LUNG SYNDROME)
Use of the Bramson Membrane Lung

J. DONALD HILL, M.D., THOMAS G. O’BRIEN, M.D., JAMES J. MURRAY, M.D., LEON DONTIENY, M.D., M. L. BEAMSON, A.C.G.I., J. J. OSBORN, M.D., AND F. GERRIDE, M.D.

Abstract A 24-year-old man sustained subadventi-
tial transection of the thoracic aorta and multiple orthopedic injuries resulting from blunt trauma. The aortic injury was repaired. Because respiratory fail-
ure occurred four days later and worsened despite maximal conventional supportive therapy, partial venoarterial perfusion with peripheral cannulation, with use of the Bramson membrane heart-lung machine, was initiated and continued for 75 hours. At a by-pass flow of 3.0 to 3.6 liters per minute, oxygen tension increased from 38 to 75 mm of mercury, inspired oxygen concentration was reduced from 100 to 60 per cent, and peak airway pressure decreased from 60 to 35 cm of water. The shock-
lung syndrome was reversed, and the patient recovered. End-stage shock lung may be reversible if the patient receives adequate gas exchange through partial extracorporeal circulation with an appropri-
ate membrane lung.

NEJM Mar 23, 1972
75 hours on heart-lung machine (Vr-Af ECMO) started in ICU
By-pass Flow 3-3.5 lpm
PaO₂ from 38 to 75 mmHg
Ventilator pressure reduced 60 to 35 cm H₂O
An ECMO Timeline

1953
1st use of CPB for open heart surgery
Central Cannulation
Roller pumps
Limit "Pump Time"

1972
1st successful Neonatal ECMO (Bartlett, 1975)

2009
H1N1 Epidemic
Adult V-V ECMO

2010
ER V-A ECPR for OHCA

2020
COVID-19 ECMO
Community V-A ECPR
V-A, V-A Cardiogenic Shock
V-V, V-A Adjunct for MCS
Pre-Hospital V-A ECPR
Massive PE (PERT)
Lung Transplant prehab
“Awake Extubated ECMO”
Single-site Dual Lumen Cannulas
ECMO DCD Organ Support

Why didn’t Adult ECMO become widespread?
(compared with neonatal and pediatric)

Extracorporeal Membrane Oxygenation
in Severe Acute Respiratory Failure
A Randomized Prospective Study

N = 90
No difference in survival p=0.80
CV 4/48 (8%) survival
ECMO 4/42 (2%) survival

N = 40
No difference in survival p=0.80
CV 42% survival
ECMO 33% survival

Referral to an Extracorporeal Membrane Oxygenation Center and Mortality Among Patients With Severe 2009 Influenza A(H1N1)

ECMO referred 77% survived
CV non-referred 48% survived
Extracorporeal Membrane Oxygenation for Severe Acute Respiratory Distress Syndrome (EOLIA)

- RCT N = 249 (planned was 331, stopped early)
- Inclusion: Severe ARDS (Pao2/Fio2 < 50 X 3 hr or < 80 X 6 hr)
- ECMO mortality 44/124 (35%)
- CV mortality 57/125 (46%) p=0.7
  - 35 (28%) CV crossed over to ECMO group, these had 57% mortality
- Overall: No sig difference in mortality by intention to treat but, if crossovers included, ECMO favored (p=0.01)

EOLIA Trial Survival Trend favored ECMO, but study stopped early (slow enrollment)

No. at Risk
ECMO    124    105    100   92   88   83   80
Control 122    94     81    79   74   72   69

P=0.67 by log-rank test

Combes, NEJM 2018

V-V ECMO Annual Respiratory Adult Runs (pre-COVID)

- 50% Survival 1990
- 59% Survival 2009
- 73% Survival 2019

V-A ECMO Annual Cardiac Adult Runs

- 43% survival

ELSO Registry accessed Apr 2, 2021
### Worldwide COVID-19 Patients in ELSO Registry

<table>
<thead>
<tr>
<th>Total COVID-19 Cases</th>
<th>COVID-19 Confirmed Cases</th>
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<tbody>
<tr>
<td>5532</td>
<td>5513</td>
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*Total counts of COVID-19 confirmed patients and count of COVID-19 suspected but not confirmed by testing.*

### COVID-19 Mortality

- **Non-COVID V-V ECMO Mortality**: 40%
  - N=25,631

### ECMO Outcomes for COVID-19 Patients

![Graph showing ECMO outcomes for COVID-19 patients](image)

- **Non-COVID V-V ECMO Mortality**: 40%
  - N=25,631

### Extracorporeal Life Support Organization COVID-19 Interim Guidelines

A consensus document from an international group of interdisciplinary ECMO providers.

### COVID-19: Triage ECMO Based On Capacity

- **Contingency Capacity Tier 1**: System is running within expanded capacity: triage to maximize ECMO capacity to outcome.
- **Contingency Capacity Tier 2**: Expanded capacity.
- **Crisis Capacity**: System is overwhelmed, ECMO may no longer be appropriate, concentrate resources to usual care.

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ELSO Registry accessed Mar 23, 2021

ELSO.org accessed Mar 25, 2021

ELSO COVID-19 Guidelines 2021

Derdak, ECMO GR April 14, 2021 edited copy - May 11, 2021
Sweep Gas Flow Rate $\propto$ PaCO$_2$ 

RPM $\propto$ Pump Blood Flow Rate $\propto$ PaO$_2$
Peripheral ECMO: V-V vs V-A Differences

**V-V ECMO**
- Primarily for lung support
- No direct hemodynamic effects
- Supports brain oxygenation
- Recirculation occurs (series cannulation)
- Can run off anti-coagulation
- Wean ECMO gas sweep as native lung volume, PetCO2, SaO2 improves
- Long runs (months)

**V-A ECMO**
- Primarily for circulation (BP) support
- Increases MAP and LV afterload
- May not support brain oxygenation
- No recirculation (parallel cannulation)
- Risk of stroke, LV thrombus, ischemic leg
- Wean ECMO pump flow as native CO improves (BP, pulse pressure, SvO2)
- Short runs (days-weeks)

**Clues**
- Pre-Mem SvO2 > 80% that increases with ECMO Pump Flow
- Increase ECMO Pump Flow decreases patient SaO2
- 10-12 cm separation ideal between Return and Drain Cannulas

Banfi, J Thorac Dis 2016; 8:3762-3773

Keebler, JACC 2018

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ECMO Cannulation Configurations

**Single lumen cannulas**
- fem-fem (V_f-V_f or V_f-A_f)
- fem-ij (V_f-i_j)
- fem, fem, ij (V_f-A_i_j)

**Bi-caval dual lumen cannulas**
- (Crescent, Avalon)
  - bc V_f-RA
  - bc V_sc-RA

**RA-PA dual lumen cannulas**
- ProTek Dual Lumen (V_f-Pa)
- V_f-V_pa Single Lumen

Cannula Security (4-5 suture points) and Position Markers

ECMO Cannula Security is Essential
(agitated delirium can be a disaster)
VA-ECMO: distal perfusion catheter right superficial femoral artery

Vt-A should always have DPC, somatic oximetry

**V-A ECMO with PA Cannulation (V-APa): Support for RV bypass or LV unloading**

- RV Bypass for severe RVF
  - Lung Transplant
- LV Unloading for LV shock
  - Cardiogenic shock with LV distention

Lorusso, Interactive CardioVascular and Thoracic Surgery 2020
V-A ECMO Indications

**Table 3: Indications and advantages of pulmonary artery cannulation for VA ECMO or RV support**

<table>
<thead>
<tr>
<th>Indication</th>
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<tr>
<td>Drainage</td>
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| Indirect LV unloading (poor LV function with LV or LA stasis/acute pul-
  monary oedema/LV distension)                                           |
| Pulmonary haemorrhage                                                     |
| Biventricular failure                                                    |
| Acute pulmonary hypertension                                             |
| Perfusion                                                                 |
| Harlequin (or: North/South) syndrome in VA ECMO                          |
| Isolated RV failure                                                      |
| Acute pulmonary embolism                                                 |
| Biventricular failure                                                    |
| Pulmonary contusion                                                      |
| VV ECMO with RV failure                                                 |
| VV ECMO with high recirculation                                          |

**Refractory Cardiogenic Shock**

- AMI
- ADCHF
- Fulminant myocarditis
- Massive PE
- Electrical Storm
- Post-cardiotomy
- Primary graft failure
- Toxins overdose
- Procedural support
- ECPR

**Absolute Contraindications**

- Unwitnessed asystole
- Irreversible disease (terminal cancer)
- Severe non-cardiac organ failure

**Relative Contraindications**

- Uncontrollable bleeding or contraindication to AC
- Severe peripheral vascular disease
- Aortic dissection
- Severe AI
- Adverse Prognostic Score (SAVE, PREDICT)
High Risk PE: put V-A ECMO place holders

systolic BP 110 = V-A placeholders
systolic BP 80 = V-A ECMO

EkoSonic TPA Catheter

Massive Pulmonary Embolism with Shock: Initiation V-A ECMO prior to IR thrombectomy

COVID-19 ARDS Adult V-V ECMO Indications

Non-ARDS indications for V-V ECMO

- Bridge to Lung Transplant
- Iatrogenic tracheal injury
- Severe tracheal obstruction
- Severe inhalation injury
- TENS with airway sloughing
- Whole lung lavage (PAP)
Outcome Prediction on ECMO: Scoring Systems

- SAVE Score (V-A)
- PREDICT Score (V-A ECPR, CS)
- RESP Score (V-V)
- NPi (V-A ECPR)

https://www.predict-va-ecmo.org
http://www.save-score.com
http://www.respscore.com

The RESP Score

The RESP Score has been developed by ELSO and The Department of Intensive Care at The Alfred Hospital, Melbourne. It is designed to assist prediction of survival for adult patients undergoing Extra-Corporeal Membrane Oxygenation for respiratory failure. It should not be considered for patients who are not on ECMO or as substitute for clinical assessment.

For more information see:


Immunocompromised
Central nervous system dysfunction
Acute associated (non-pulmonary) infection
Neuro-muscular blockade before ECMO
Nitric oxide use before ECMO
Bicarbonate infusion before ECMO
Cardiac arrest before ECMO

18-49
50-59
≥60
<48 hours
48 hours - 7 days
>7 days

Viral pneumonia
Bacterial pneumonia
Asthma
Trauma/burn
Aspiration pneumonitis
Other acute respiratory diagnosis
Non-respiratory and chronic respiratory diagnoses

PaCO$_2$ ≥75 mmHg / 10kpa
Peak inspiratory pressure ≥42cmH$_2$O

The patient's RESP Score is -4

SAVE Score

Survival After Veno-arterial ECMO (SAVE) Score

The SAVE Score has been developed by ELSO and The Department of Intensive Care at The Alfred Hospital, Melbourne. It is designed to assist prediction of survival for adult patients undergoing Extra-Corporeal Membrane Oxygenation for refractory cardiogenic shock. It should not be considered as a substitute for clinical assessment.

For more information see:

Predicting survival after ECMO for refractory cardiogenic shock: the survival after veno-arterial-ECMO (SAVE)-score

Age (years):
18-38
39-52
53-62
≥63

Weight (kg):
<65
65-89
≥90

Pulse pressure pre ECMO ≤20 mmHg
Diastolic BP pre ECMO ≥40 mmHg
Pre-ECMO cardiac arrest
Peak inspiratory pressure ≤20 cmH$_2$O
Intubation duration pre ECMO (hrs) ≤10
11-29
≥30

Acute renal failure
Chronic renal failure
HCO$_3$ pre ECMO ≤15 mmol/L
Central nervous system dysfunction
Liver failure

The patient's SAVE Score is -12

Diagnosis:
Myocarditis
Refractory VT/VF
Post heart or lung transplantation
Congenital heart disease
Other diagnoses

Cardiac:
Respiratory:
Renal:
Other organ failures pre ECMO:

3 month old Tricuspid Atresia V-A ECMO D#2
50 yr old COVID-19 ARDS V-VV ECMO D#83

University Hospital ECMO 2020 to present...

- 7 COVID-19 ARDS (2 died, one currently on VV-V 82 days; one discharged after 73 days on ECMO)
- 3 post-lung transplant (2 fibrosis, 1 post-covid) 1 died
- 1 snake bite died

Data courtesy of Casey Howard
CARDIOHELP ECMO SYSTEM (integrated pump+oxygenator+console)

15-19 F Arterial Return Cannulas

21-27 F Venous Drain Cannulas

7 LPM Adult Oxygenator

Backside of the CardioHelp System

Emergency Hand Crank
V̇\textsubscript{f}-A\textsubscript{r} conversion to V̇\textsubscript{f}-A\textsubscript{ax} Improves Brain Oxygenation and Facilitates Ambulation

Keebler, JACC 2018

End-to-Side Axillary Graft

53

Tilt Table Platform

Total Lift Bed

54

The UH ECMO Physical Therapy Team Rocks!

55

ECMO goal: Awake, Alert, and Walking as soon as hemodynamically stable

56

V-A ECMO D#13

V-A ECMO D#42

56

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Criteria for Ambulation on ECMO

- Cognition to follow directions
- Cardiovascular:
  - no femoral artery IABP or VAD (femoral vein or arterial cannula ok)
  - stable or decreasing inotropes/vasopressors
- Respiratory:
  - extubated or on trach collar
- Heme:
  - no active bleeding (< 4 UPRCs per 24 hr)
- Musculoskeletal:
  - tolerates vertical positioning (total lift bed)
  - physical strength appropriate for ambulation


ECMO Bio-Injury (ECBI)

- blood-circuit interaction
- activation of systemic fibrinolysis
- RBC injury (hemolysis)
- platelet activation and mediator release
- acquired Von-Willebrands Factor deficiency
- inflammatory response (WBC activation, cytokines)
- immunosuppression

ECMO Complications

ECMO + Critical Care Situational Awareness
ECMO Simulation Training - on the stopwatch…

Changing out a failing ECMO oxygenator…fast is better
Multi-Disciplinary ECMO Rounds

End of Life Care on ECMO

- Transition to full comfort care
- may be a fully awake patient talking with family
- it is a hard, no matter how well you think you’ve prepared or how many times you’ve seen it
- Palliative Medicine is integral to care
- Determination of Brain Death on ECMO
- ECMO for Organ Donation after Cardiac Death (DCD)

Evolution of the United States Military Extracorporeal Membrane Oxygenation Transport Team

Matthew D. Read, MD, Maj, USAF; Jason J. Nare, MD, MAJ, USAF; Mauer Bliscotti, MD, LCDR, USN*;
Lydia C. Piper, MD, CPT, USAF; Sarah B. Thomas, MD, Cpt, USAF; Valerie G. Sarms, MD, Lt, USAF*;
Bernadette S. Elliott, RN*; Kathryn A. Nagard, RN*; James H. Lantry III, MD, Maj, USAF*;
Jeffry D. DellaVolpe, MD, Maj, USAF; Andry Batchinsky, MD*; Jeremy W. Cannon, MD, Col, USAF*;
Phillip E. Mason, MD, Col, USAF*

N = 97 transports 2012-2019
Cannulation on site
81% V-V
12% V-A
7% V-AV
Age 42 yr (19-68 yr)
ECMO Duration 19 d (1- 94 d)
Survival to discharge 66%

Intrahospital ECMO Patient Transport MICU to OR...
Ramstein AFB, Germany to Kelly AFB on V-V ECMO (longest nonstop transport on ECMO)

- Community ECPR
- Regional Coordination for ECMO Availability (Trauma Model)
- Advances in circuits, pumps, oxygenators
- Integration of ECMO and Lung Transplant
- Wearable ECMO (destination therapy)
- Translational and Clinical ECMO Research

The Future....
ECPR (peripheral V-A ECMO) success depends on patient selection and pre-positioned equipment, pre-rehearsed team roles, frequent simulation practice

- witnessed arrest
  - VF, pVT, PEA (PE?)
  - CPR started within 2-4 min
  - Effective CPR (diastolic > 40 mmHg, ETCO₂ > 20)
- no sustained ROSC within 20 min
  - put place holders (fem a-line, fem v introducer or TLC)
- on V-A ECMO within 60 min
- reversible etiology
  - STEMI → PCI, Impella
  - PE → Embolectomy
- Neurologic prognostication after 72 hours

Cath-Lab Based ECPR or V-A for Cardiogenic Shock

**Components:**
- Team Roles Pre-rehearsed
- Simulation Practice
- LUCAS compressor
- Primed ECMO Circuit
- Cannulation Trays
- Medications
- Fluoroscopy
- TTE/TEE
- Same-side cannulation
  - SFA DPC or placeholder
  - Cerebral and Somatic Oximetry
- NP or cEEG or BiS

**OHCA ECPR ECMO Timing Benchmarks**

- 911 OHCA to EMS arrival < 15 min
- EMS transport to ED < 15 min
- Cannulation team arrives < 15 min
- V-A on PUMP < 15 min
- CPR to on PUMP < 60 min
- 911 to Cath Lab < 120 min

Bartos, EClinicalMedicine Nov 26, 2020
The Future…next 5 years

- Regional coordination for ECMO and ECPR center referrals
- ECMO as an alternative to intubation?
- ECMO as destination therapy (wearable, ambulatory lung and heart support)
- ECMO to improve transplant outcomes (heart, lung, liver)
- Improved biocompatibility of circuits and oxygenators (need for anticoagulation?)
- ECMO support to improve organ donor suitability (DCD)

ECMO systems are continuing to evolve and becoming more compact and transportable…

ECMO systems are continuing to evolve and becoming more compact and transportable…

ECCO₂R VENT-AVOID Trial

- ECCO₂R
- 15.5 French Dual Lumen Cannula
- Blood Flow 350-550 ml/min
- Target Enrollment N = 180
- DSMB continuation 2020
- FDA EUA for COVID-19 April 2020

Integration of ECCO2R Oxygenator Module into CRRT Devices
Nitric Oxide added into ECMO Sweep Flow

Chiletti, Perfusion 2018

How long does a previously normal lung take to recover?

50 yr old COVID-19 ARDS
80 days on VjVj-Vj ECMO

Shifting paradigm to longer ECMO support
(7 d, 14 d, 30 d, 60 d, ???)

Continue Rehab and Ambulation

Some will become Lung Transplant candidates

Longest case reported 605 days (11 yr old burn patient)

Personal longest adult ECMO run 105 days and walked out of hospital
(Disseminated Coccidiomycosis ARDS)

COVID-19 ARDS on ECMO > 3 months

Lung Transplant Donation from Husband (left) and Son (right)

Kyoto University Hospital, Japan
April 9, 2021

ECMONet Research

• REVERSE (Impella CP + V-A ECMO Cardiogenic Shock)
• NOVICE (iNO + V-A ECMO)
• REST Trial (ECCO₂R)
• VENT-AVOID Trial (ECCO₂R)
• BIV-ECMO2 (Bivalirudin)
• REDEEM Trial (early ECMO for COVID-19)
• ASAP (Analgesic, Sedative, Antibiotics Pharmacokinetics on ECMO)
• ECMO PT Trial (early < 48 PT)

www.internationalecmonetwork.org
www.clinicaltrials.gov
A successful ECMO Program has many team members and stakeholders:

- Pulmonary/Critical Care Medicine
- Cardiology
- CT Surgery/Vascular Surgery/Interventional Rad
- Palliative Medicine
- Pharmacology
- Nephrology
- Emergency Medicine
- EMS
- ECMO Transport Teams
- Hematology
- Blood Bank
- Coagulation lab
- CT Surgery/Interventional Rad
- Physic Therapy
- Transplant
- Palliative Medicine
- Pharmacology
- Nephrology
- Cardiology
- Pulmonary/Critical Care Medicine
- ECMO Physicians
- ECMO Coordinator
- ECMO Specialist
- Perfusionist
- ICU RNs
- ICU RT

Thanks to the many ECMO and Advanced Therapy Specialists past and present at University Hospital - the core of the UH ECMO Program!

Thank you!

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