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

Medicine Grand Rounds
April 14, 2021

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No Disclosures or Conflicts of Interest

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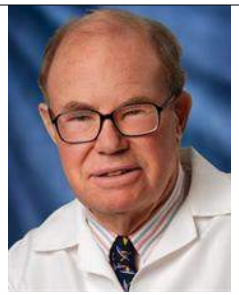
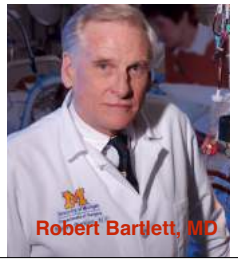
George Crawford, MD



Richard Hyde, MD

Forrest Bird, MD

John Stapp, MD



Robert Bartlett, MD

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A 50 yr old female with COVID-19 is intubated for rapidly progressive hypoxemia despite 12 hours of HFNC O_2. After 3 days of lung protective ARDSNet mechanical ventilation, prone positioning, cisatracurium, diuresis, dexamethasone, and iNO 40 ppm, she continues to worsen. On FiO_2 100% and PEEP 22 cm H_2O, her PaO_2 is now 48 mmHg, SaO_2 74%, $PaCO_2$ 72 mmHg, and pH 7.14.

What should be done next?

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The Past….

"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)

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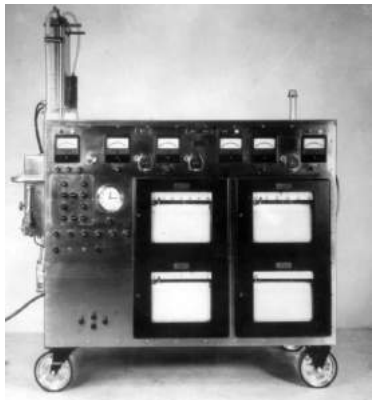
John Gibbon's first heart-lung machine…1952



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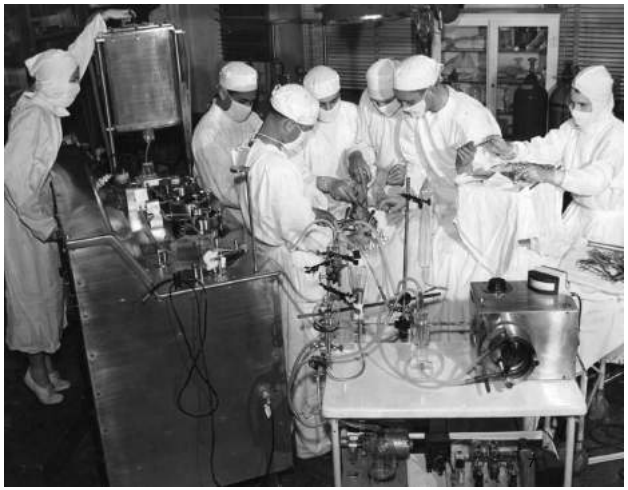
1952 Bernard Miller tests John Gibbons experimental Heart-Lung Machine on dogs - 90% survive



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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 Dontigny, M.D., M. L. Bramson, A.C.G.I., J. J. Osborn, M.D., and F. Gerbode, M.D.

Abstract A 24-year-old man sustained subadventitial transection of the thoracic aorta and multiple orthopedic injuries resulting from blunt trauma. The aortic injury was repaired. Because respiratory failure 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 appropriate membrane lung.

NEJM Mar 23, 1972

75 hours on heart-lung machine (V_F-A_F ECMO) started in ICU
By-pass Flow 3-3.5 lpm
PaO_2 from 38 to 75 mmHg
Ventilator pressure reduced 60 to 35 cm H_2O

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Dr Hill's first adult ECMO patient 1972

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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)

ELSO 1989

2009

H1N1 Epidemic
Adult V-V ECMO

Pediatric ECMO

ECCO2R
ECOS
PMP oxygenators
Centrifugal pumps

2010

ER V-A ECPR
for OHCA

2020

COVID-19 ECMO
Community V-A ECPR

V-A, V-AV 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

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

Extracorporeal Membrane Oxygenation in Severe Acute Respiratory Failure

A Randomized Prospective Study

Warren M. Zapol, MD; Michael T. Snider, MD, PhD; J. Donald Hill, MD; Robert J. Fallat, MD; Robert H. Bartlett, MD; L. Henry Edmunds, MD; Alan H. Morris, MD; E. Converse Peirce II, MD; Arthur N. Thomas, MD; Herbert J. Proctor, MD; Philip A. Drinker, PhD; Philip C. Pratt, MD; Anna Bagniewski, MA; Rupert G. Miller, Jr, PhD

JAMA. 1979;242(20):2193-2196

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

Randomized clinical trial of pressure-controlled inverse ratio ventilation and extracorporeal CO_2 removal for adult respiratory distress syndrome

A H Morris [1], C J Wallace, R L Menlove, T P Clemmer, J F Orme Jr, L K Weaver, N C Dean, F Thomas, T D East, N L Pace, M R Suchyta, E Beck, M Bombino, D F Sittig, S Böhm, B Hoffmann, H Becks, S Butler, J Pearl, B Rasmusson

AJRCCM 1994; 149:295-305

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

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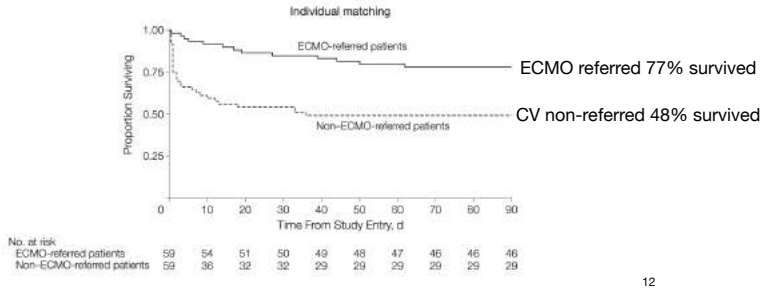
ONLINE FIRST

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

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Noah MA, Peek GJ, et al. JAMA 2011;306(15):1659-1668

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The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 MAY 24, 2018 VOL. 378 NO. 21

Extracorporeal Membrane Oxygenation for Severe Acute Respiratory Distress Syndrome (EOLIA)

A. Combes, D. Hajage, G. Capellier, A. Demoule, S. Lavoué, C. Guervilly, D. Da Silva, L. Zafrani, P. Tirot, B. Veber, E. Maury, B. Levy, Y. Cohen, C. Richard, P. Kalfon, L. Bouadma, H. Mehdaoui, G. Beduneau, G. Lebreton, L. Brochard, N.D. Ferguson, E. Fan, A.S. Slutsky, D. Brodie, and A. Mercat, for the EOLIA Trial Group, REVA, and ECMONet*

- RCT N = 249 (planned was 331, stopped early)
- Inclusion: Severe ARDS (PaO_2/FiO_2 < 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)

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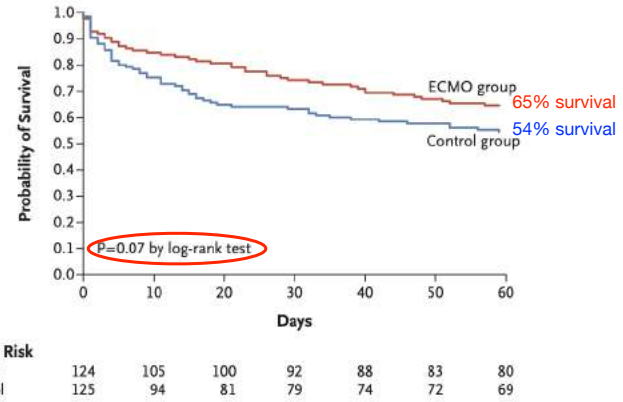
EOLIA Trial Survival Trend favored ECMO, but study stopped early (slow enrollment)



Combes, NEJM 2018

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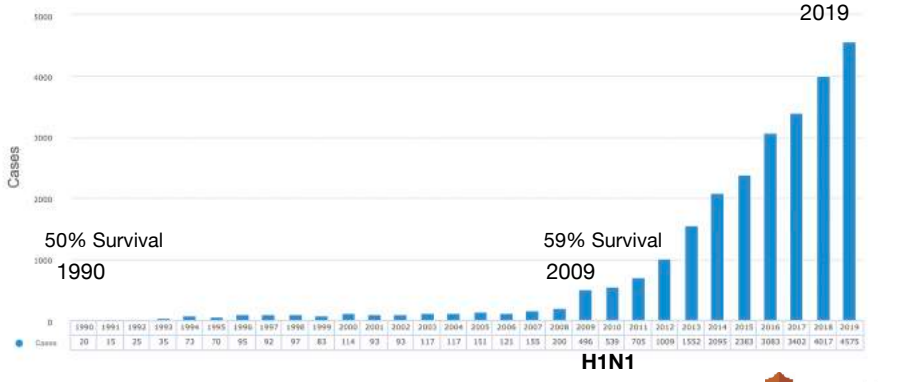
V-V ECMO Annual Respiratory Adult Runs (pre-COVID)



ELSO Registry accessed Apr 2, 2021

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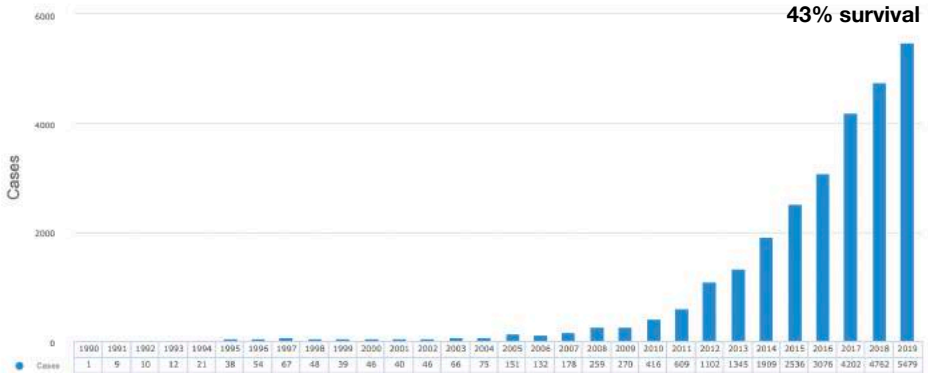
V-A ECMO Annual Cardiac Adult Runs



ELSO Registry accessed Apr 2, 2021

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Worldwide COVID-19 Patients in ELSO Registry

	COVID-19 Suspected or Confirmed	COVID-19 Confirmed Cases
Total COVID-19 Cases	5532	5513

Total counts of COVID-19 confirmed patients and count of COVID-19 suspected but not confirmed by testing.

	COVID-19 Confirmed	COVID-19 In-hospital Mortality
Patients who initiated ECMO at least 90 days ago	4187	49%

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

ELSO Registry accessed Mar 23, 2021

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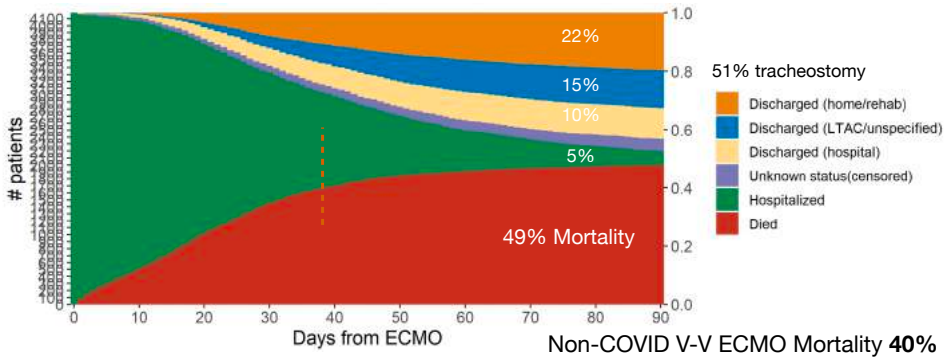
ECMO Outcomes for COVID-19 Patients N=4,214



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

ELSO Registry accessed Mar 23, 2021

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Extracorporeal Life Support Organization COVID-19 Interim Guidelines

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

ELSO.org accessed Mar 25, 2021

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Conventional Capacity

System is running within capacity, judicious ECMO case selection

Capacity exists
Judicious patient selection
Offer V-V, V-A ECMO in selected COVID-19 patients based on usual criteria
Offer ECMO for non COVID-19 indications
ECPR only in expert centres

Contingency Capacity Tier 1

System is running within expanded capacity: triage to maximize ECMO capacity to outcome

Expanded capacity
Triage to maximise resource:benefit ratio
V-V, V-A ECMO in younger COVID-19 patients with single organ failure
Judicious ECMO use for non COVID-19 indications
ECPR not offered

Contingency Capacity Tier 2

Expanded capacity close to saturation, restrictive ECMO selection criteria

Capacity Saturated
Restrictive ECMO criteria for all indications
Prioritise non COVID-19 indications with better chance of survival
V-V ECMO in younger, single organ failure COVID-19 patients
V-A ECMO and ECPR not offered

Crisis Capacity

System is overwhelmed, ECMO may no longer be appropriate, concentrate resources to usual care

Capacity overwhelmed
ECMO not feasible in both COVID-19 and non-COVID-19 patients
Triage ICU admissions
Consider ceasing all futile care to create capacity in the system

COVID-19: Triage ECMO Based On Capacity

ELSO COVID-19 Guidelines 2021

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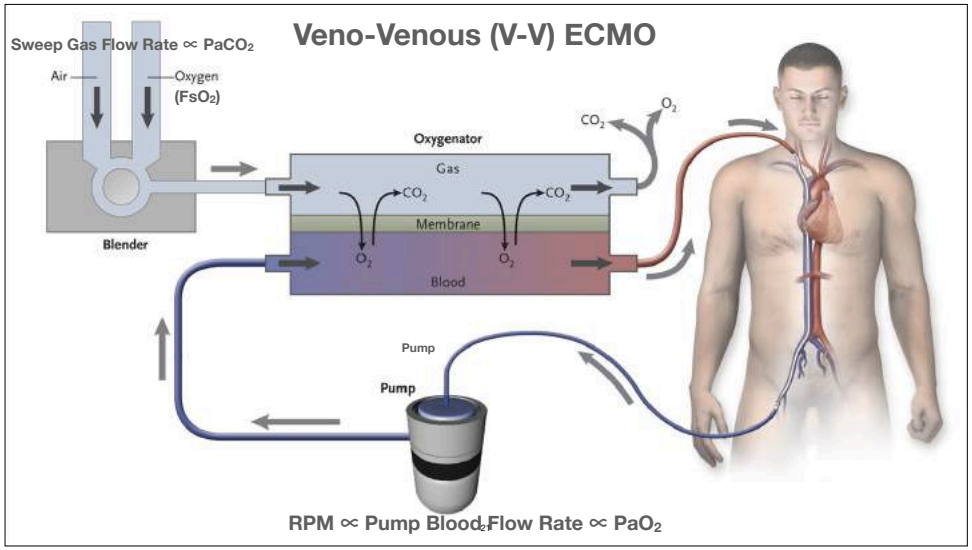

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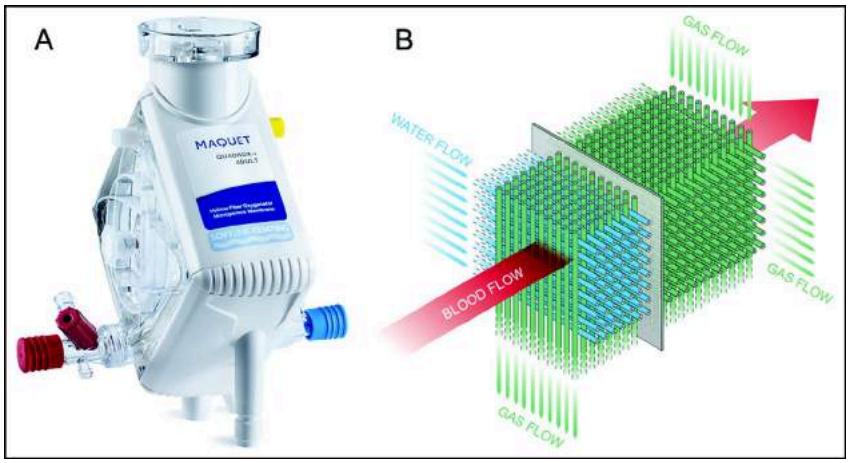

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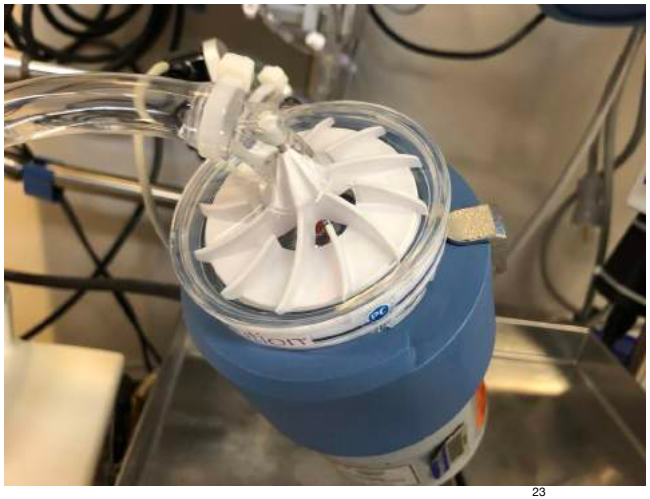

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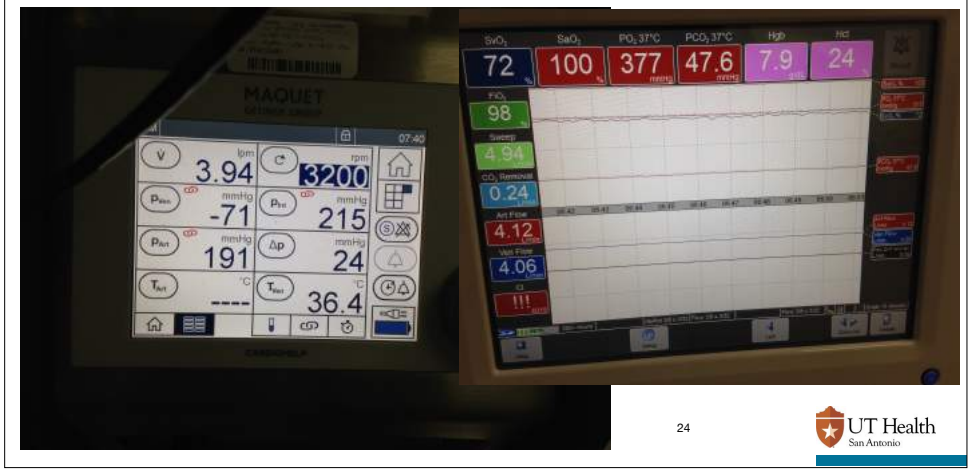
ECMO Situational Awareness



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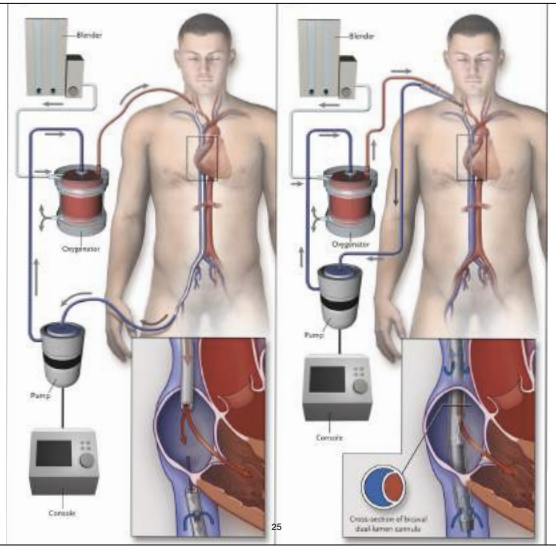
V-V ECMO
Dual Cannula
(Single Lumen)



V-V ECMO
Single Cannula
(Dual Lumen)

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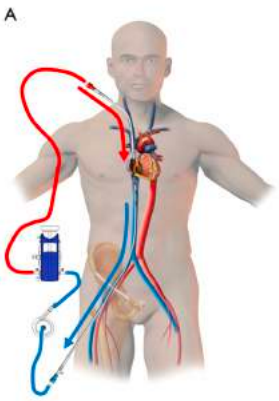
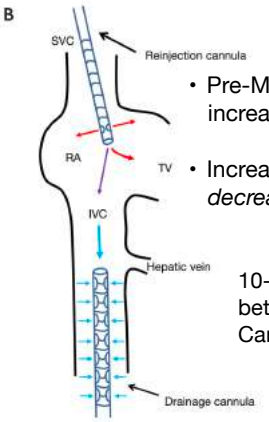
Vf-Vij ECMO



V-V Recirculation (dual site)



Clues

- Pre-Mem SvO_2 > 80% that increases with ECMO Pump Flow
- Increase ECMO Pump Flow *decreases* patient SaO_2

10-12 cm separation ideal between **Return** and **Drain** Cannulas

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

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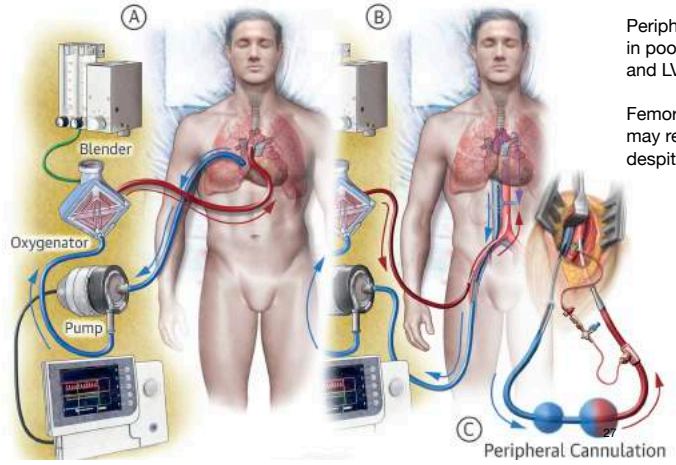
RA-Aorta Central Cannulation

V_f-A_f Peripheral Cannulation



Peripheral V-A may result in poor brain oxygenation and LV distention, clots

Femoral Artery cannulation may result in leg ischemia despite placement of DPC

Keebler, JACC 2018

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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, SaO_2 improves
- Long runs (months)

V-A ECMO

- Primarily for *circulation* (BP) support
- Increases MAP and LV afterload
- May *not* support brain oxygenation
- *No recirculation* (parallell cannulation)
- Risk of stroke, LV thrombus, ischemic leg
- *Wean ECMO pump flow* as native CO improves (BP, pulse pressure, SvO_2)
- Short runs (days-weeks)

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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-V_{ij})
- fem, fem, ij (V_f-$A_f V_{rij}$)

Bi-caval dual lumen cannulas

- (Crescent, Avalon)
- bc V_{ij}-RA
- bc V_{sc}-RA

RA-PA dual lumen cannulas

- ProTek Dual Lumen (V_{ij}-Pa)
- V_{ij}-V_{pa} Single Lumen

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Single Site Dual Lumen Cannulas

- Avalon Cannula (31 cm)
- Crescent Cannula (34 cm)

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ECMO Cannula Security is Essential
(agitated delirium can be a disaster)

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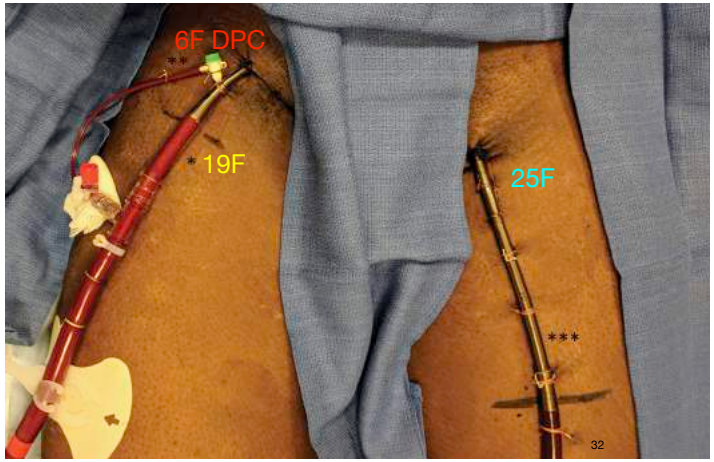
Cannula Security (4-5 suture points) and Position Markers



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VA-ECMO: distal perfusion catheter right superficial femoral artery

Distal Perfusion Cannula in SFA

Somatic oximetry sensor (NIRS)

Somatic oximetry sensor (NIRS)

Rupprecht, 2015

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V_f-A_f should *always* have DPC, somatic oximetry

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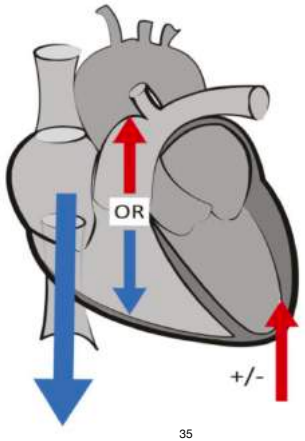
V-A ECMO with PA Cannulation (V-APa): Support for **RV bypass** or **LV unloading**

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



Lorusso, Interactive CardioVascular and Thoracic Surgery 2020

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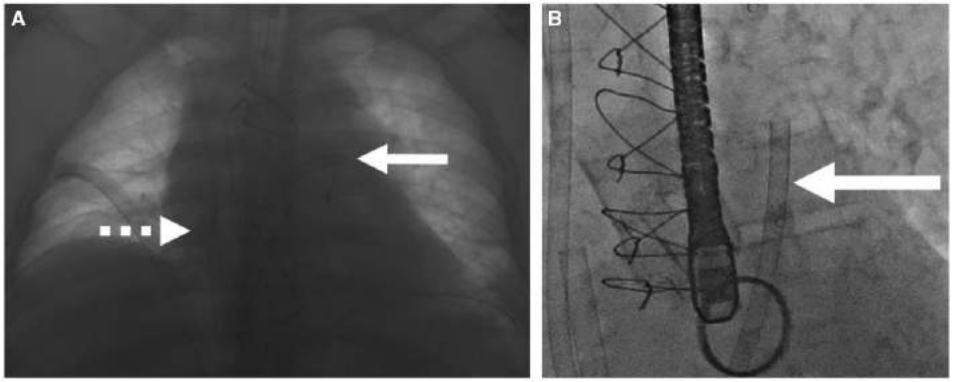

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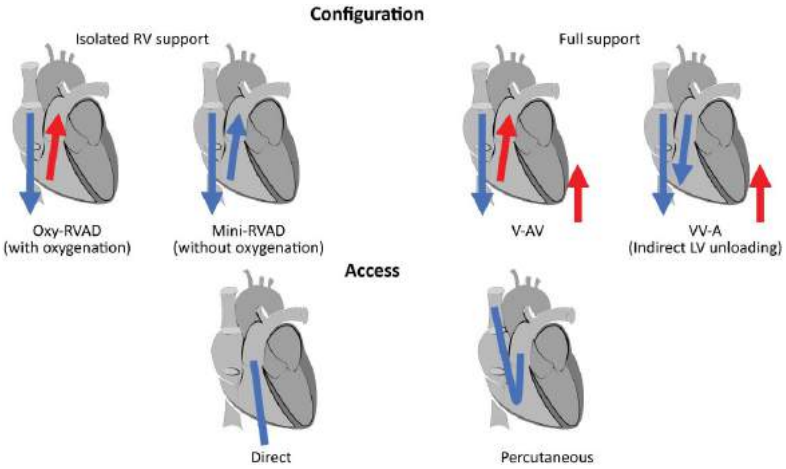

Lorusso, Interactive CardioVascular and Thoracic Surgery 2020

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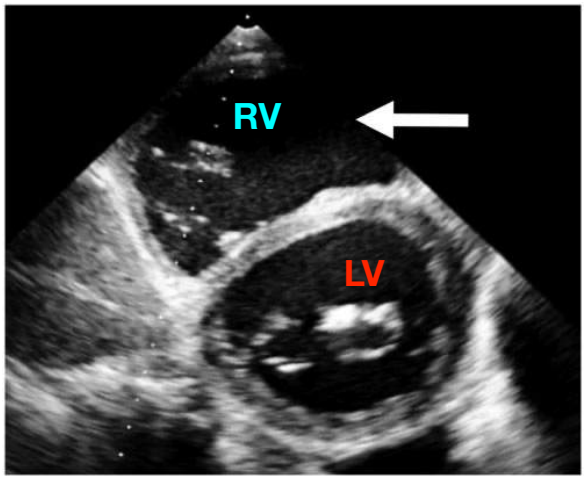

Lorusso, Interactive CardioVascular and Thoracic Surgery 2020

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

Drainage
Indirect LV unloading (poor LV function with LV or LA stasis/acute pulmonary 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

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V-A ECMO Indications

Refractory Cardiogenic Shock

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

ECPR

Absolute Contraindicatons

- 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)

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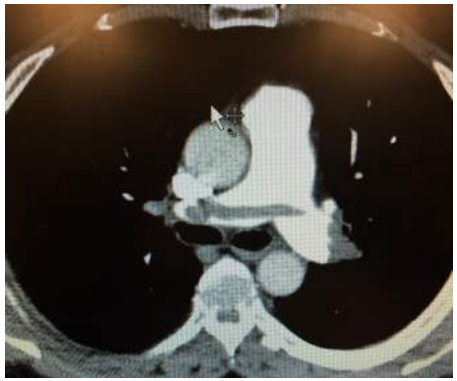
High Risk PE: put V-A ECMO place holders



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

EkoSonic TPA Catheter

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

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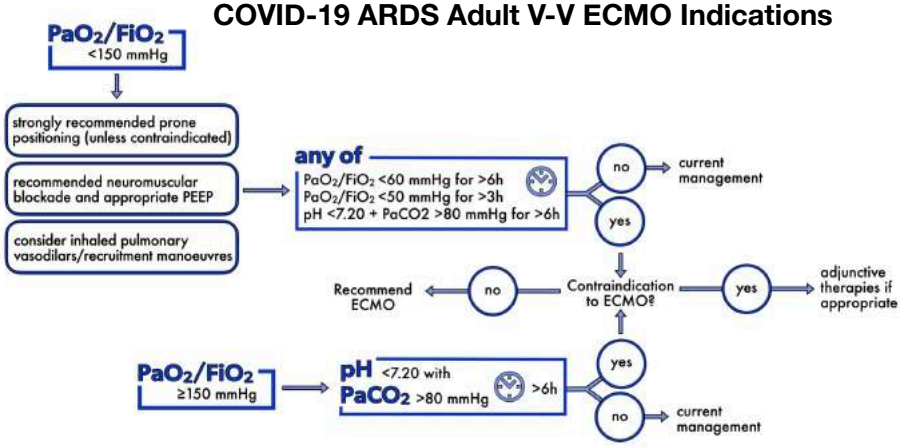
COVID-19 ARDS Adult V-V ECMO Indications



ELSO Guidelines Feb 2021

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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)

Go PH et al, Perfusion 2021

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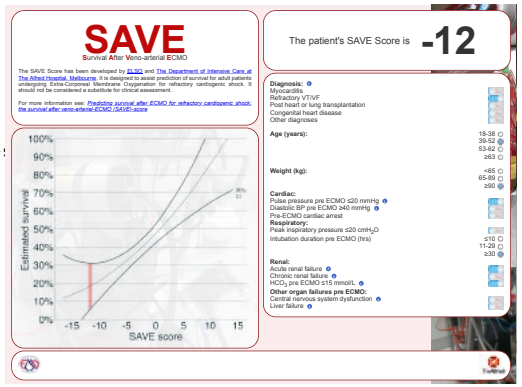
Outcome Prediction on ECMO: Scoring Systems

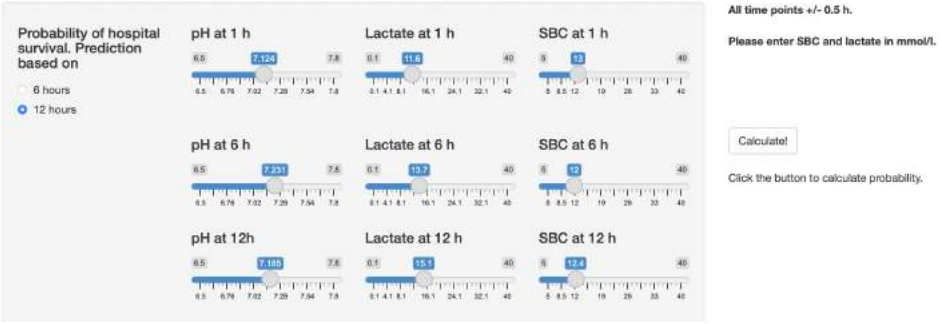
- SAVE Score (V-A)
- PREDICT Score (V-A ECPR, CS)
- RESP Score (V-V)
- NPi (V-A ECPR)

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



PREDICT Scoring for V-A ECPR and Cardiogenic

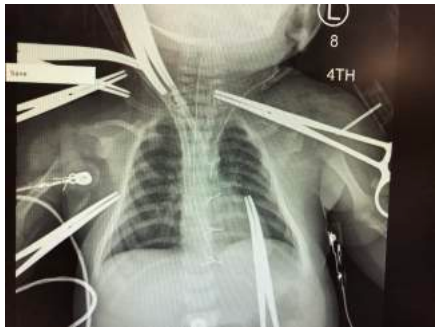
Development and validation of a prognostic model for survival in patients treated with venoarterial extracorporeal membrane oxygenation: the PREDICT VA-ECMO score



https://www.predict-va-ecmo.org

The Present….

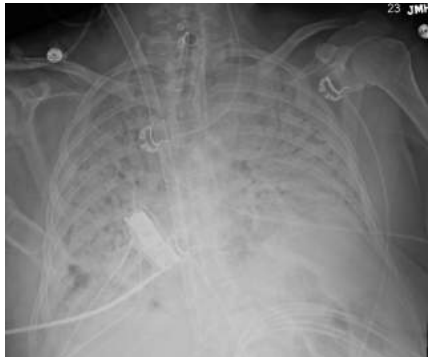
3 month old Tricuspid Atresia
V-A ECMO D#2



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

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CARDIOHELP ECMO SYSTEM (integrated pump+oxygenator+console)

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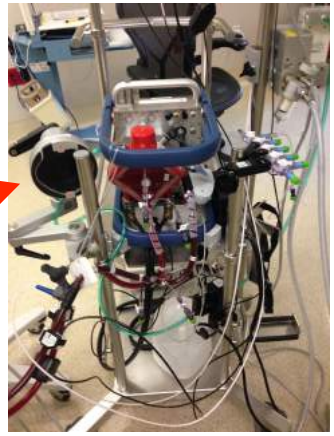
Backside of the CardioHelp System

Emergency Hand Crank



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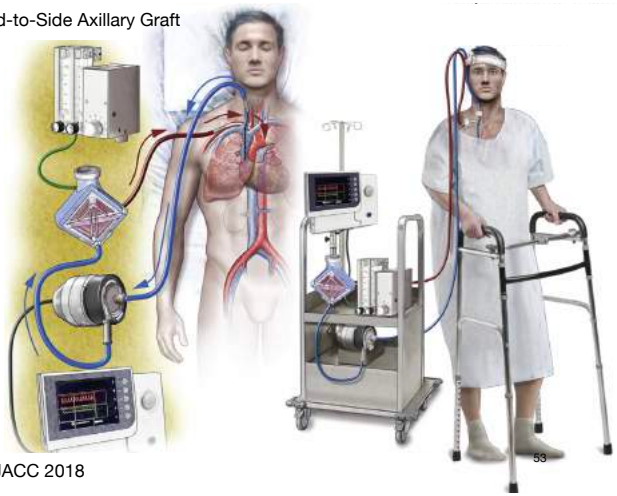
V_f-A_f conversion to V_{ij}-A_{ax} Improves Brain Oxygenation and Facilitates Ambulation

End-to-Side Axillary Graft



Keebler, JACC 2018

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Tilt Table Platform

Total Lift Bed

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The UH ECMO Physical Therapy Team Rocks!

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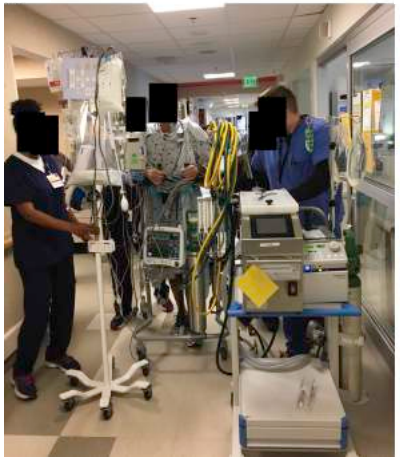
ECMO goal: Awake, Alert, and Walking as soon as hemodynamically stable



V-A ECMO D#42

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V-A ECMO D#13

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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

Pasrija et al, Ann Thorac Surg 2019;107:1389–94

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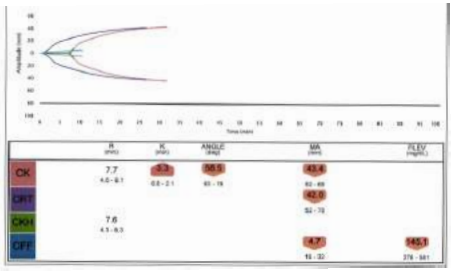
ECMO Bio-Injury (ECBI)

- 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



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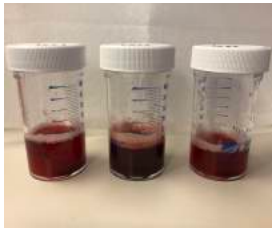
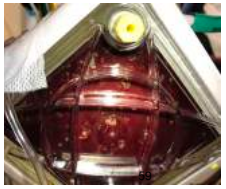
ECMO Complications





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ECMO + Critical Care Situational Awareness






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Cerebral and Somatic Oximetry

Pupillometer

BIS

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ECMO Simulation Training - on the stopwatch…

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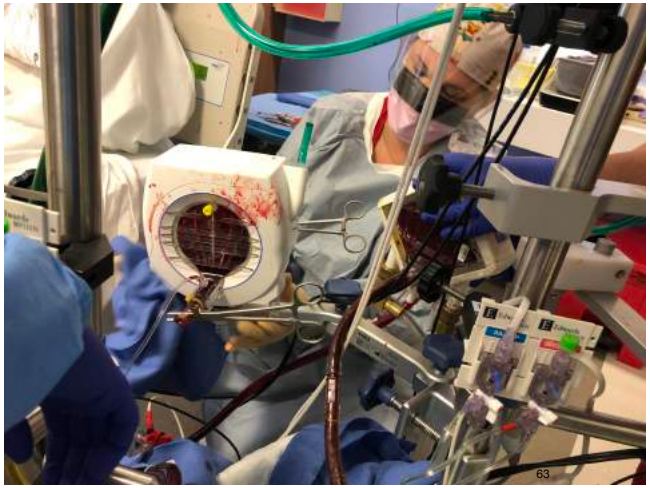

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Changing out a failing ECMO oxygenator…fast is better

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Multi-Disciplinary ECMO Rounds

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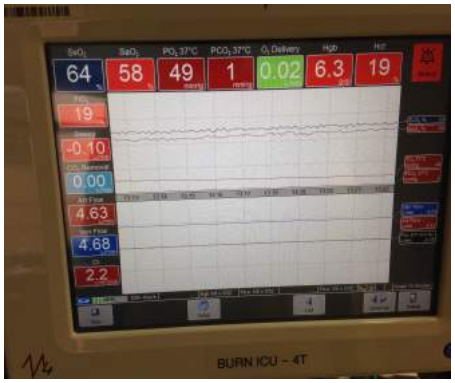
End of Life Care on ECMO

- 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)



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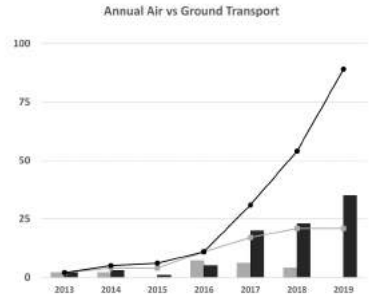
Evolution of the United States Military Extracorporeal Membrane Oxygenation Transport Team

Matthew D. Read, MD, Maj, USAF; Jason J. Nam, MD, MAJ, USA†; Mauer Biscotti, MD, LCDR, USN*; Lydia C. Piper, MD, CPT, USA*; Sarah B. Thomas, MD, Cpt, USAF*; Valerie G. Sams, MD, Ltc, USAF*; Bernadette S. Elliott, RN*; Kathryn A. Negaard, RN*; James H. Lantry III, MD, Maj, USAF‡; Jeffry D. DellaVolpe, MD, Maj, USAF§; Andriy 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%

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Military Medicine 2020; 185:2055-2060

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Intrahospital ECMO Patient Transport MICU to OR…

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Ramstein AFB, Germany to Kelly AFB on V-V ECMO (longest nonstop transport on ECMO)

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The Future….

- 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

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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, $ETCO_2$ > 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

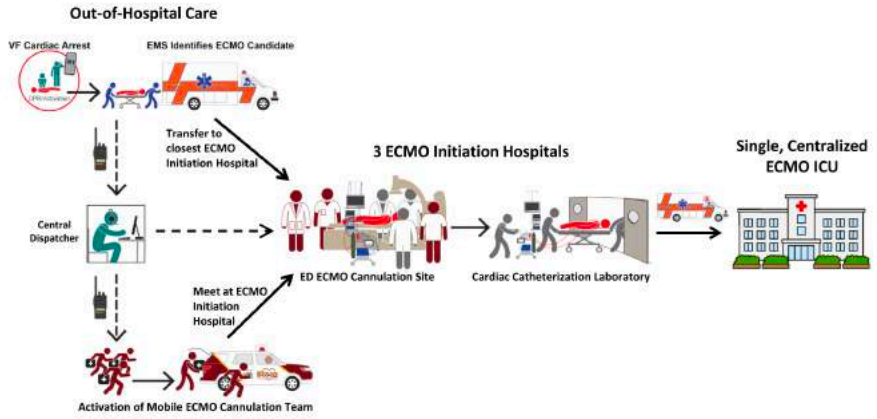
Cath-Lab Based ECPR or V-A for Cardiogenic Shock

Components:

Team Roles Pre-rehearsed
Simulation Practice

LUCAS compressor
Primed ECMO Circuit
Cannulation Trays
Medications
Fluoroscopy
TTE/TEE

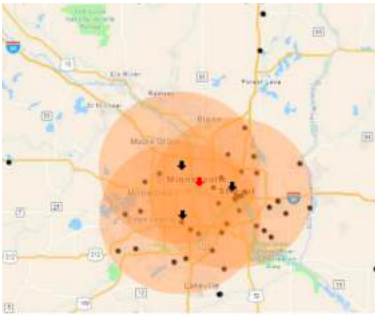
Same-side cannulation
SFA DPC or placeholder
Cerebral and Somatic Oximetry
NPi
cEEG or BIS



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

Minneapolis-St Paul



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)

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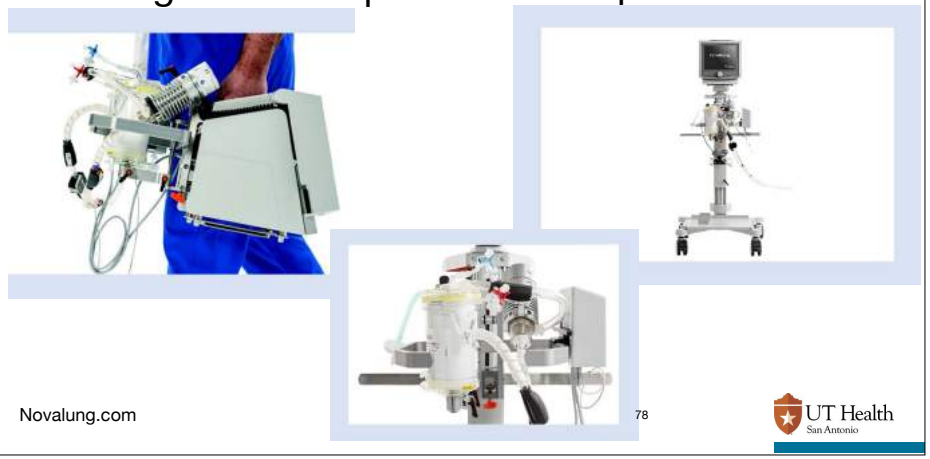
ECMO systems are continuing to evolve and becoming more compact and transportable…



Novalung.com

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$ECCO_2R$ VENT-AVOID Trial

- $ECCO_2R$
- 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

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ALung.com

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Integration of ECCO2R Oxygenator Module into CRRT Devices

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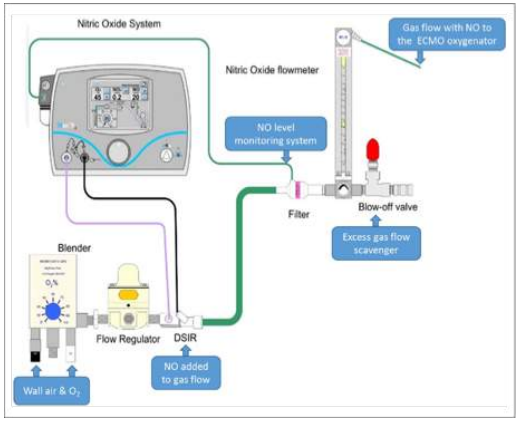
Nitric Oxide added into ECMO Sweep Flow



Chiletti, Perfusion 2018

How long does a previously normal lung take to recover?

50 yr old COVD-19 ARDS
80 days on $V_{ij}V_f$-V_{ij} ECMO

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

Continue Rehab and Ambulation

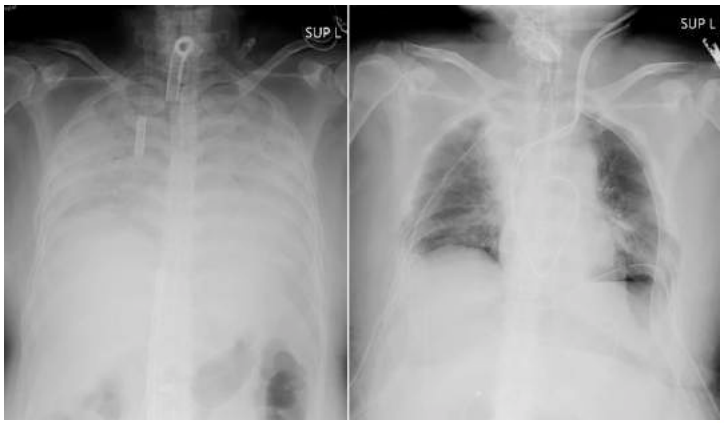
Some will become Lung Transplant candidates

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)



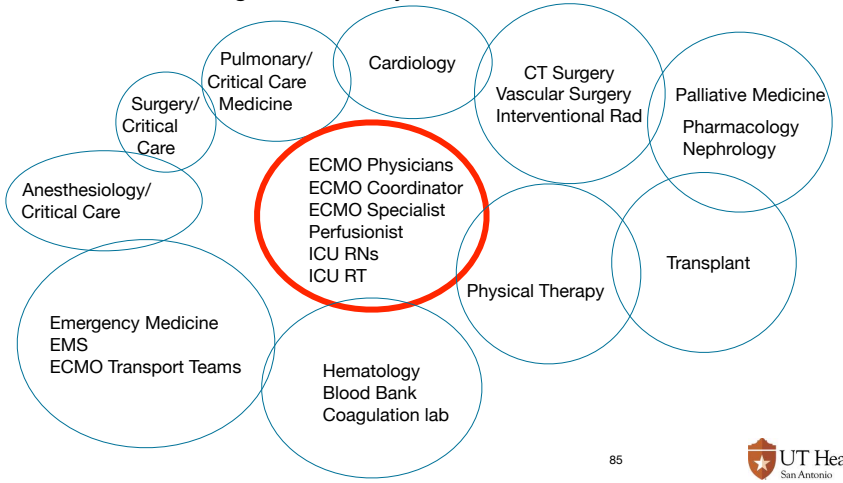
Kyoto University Hospital, Japan April 9, 2021

ECMONet Research

- REVERSE (Impella CP + V-A ECMO Cardiogenic Shock)
- NOVICE (iNO + V-A ECMO)
- REST Trial ($ECCO_2R$)
- VENT-AVOID Trial ($ECCO_2R$)
- 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…



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

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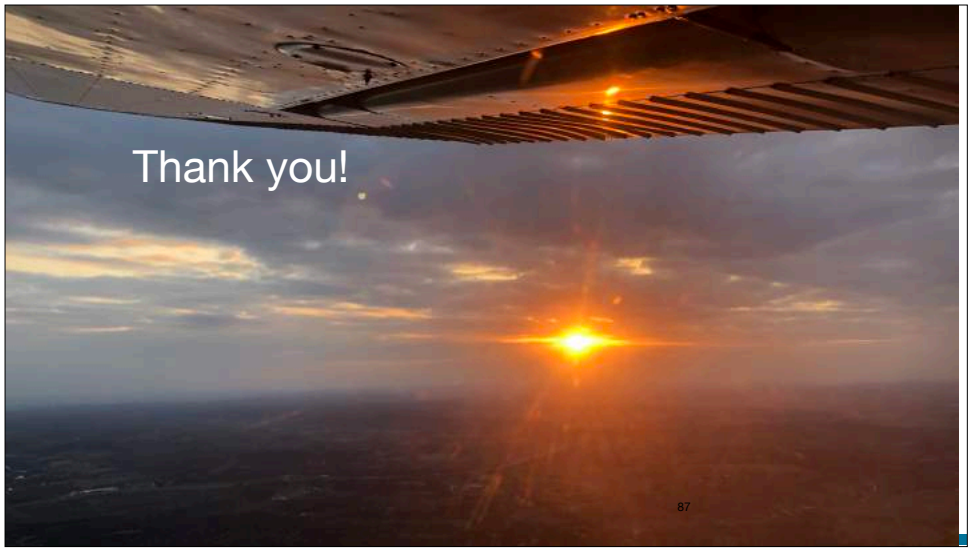

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