ECMO for Acute Respiratory Failure

Raghu Seethala, MD, MSc

Medical Director, ECMO Service

Director, Thoracic and Cardiac Surgical Intensive Care Unit

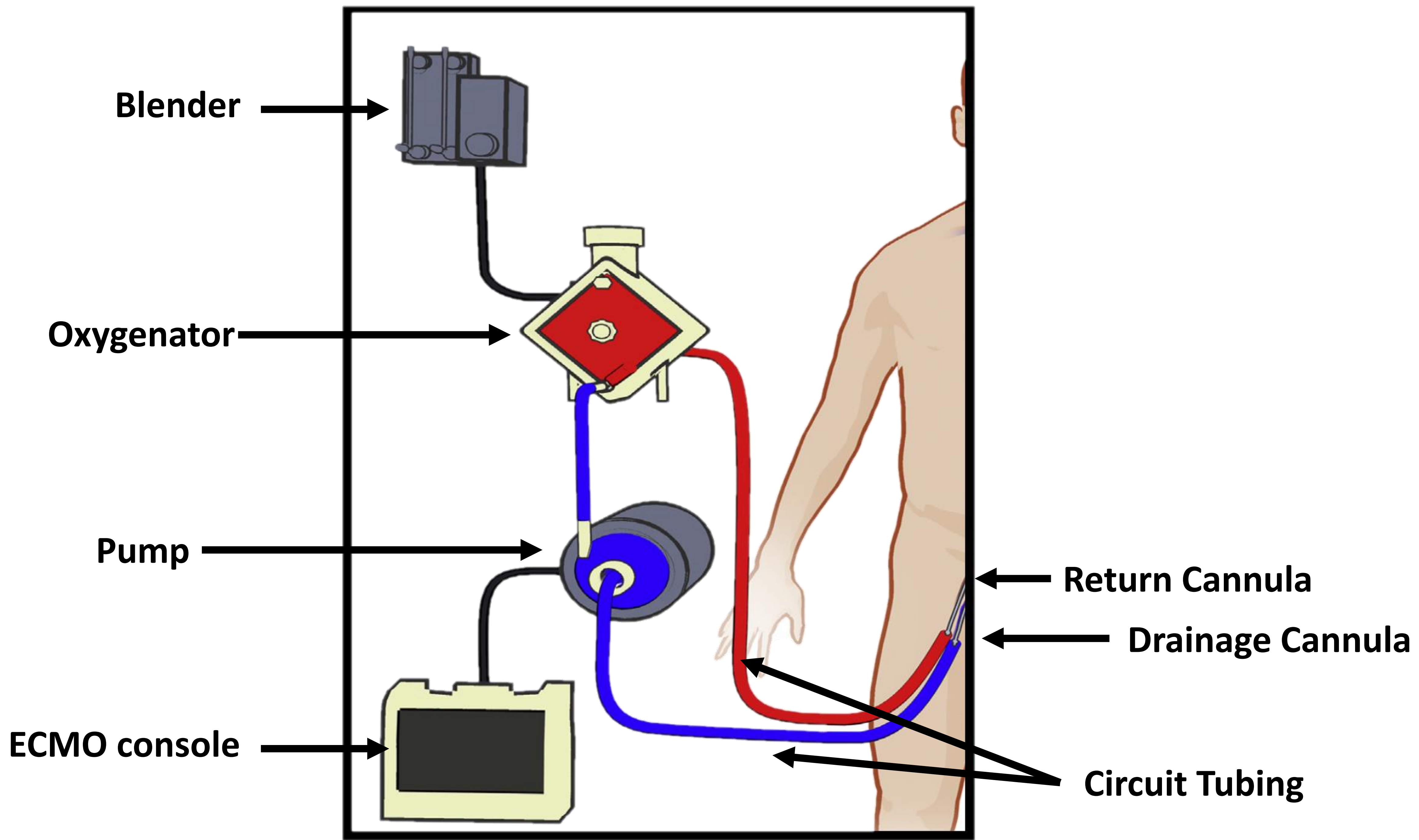
Section Chief of Critical Care, Division of Thoracic and Cardiac Surgery

Disclosures

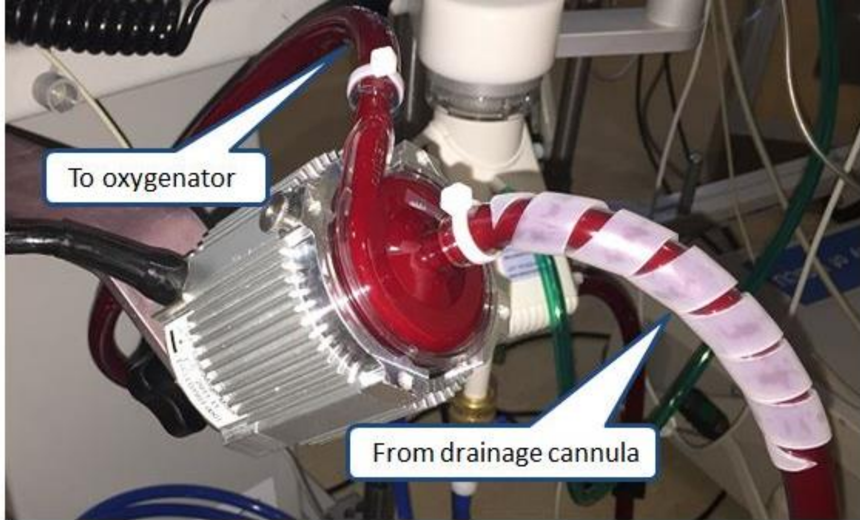
- None

Objectives

- Describe criteria to initiate ECMO in acute respiratory failure
- Recognize common contraindications for ECMO
- Review evidence supporting the use of ECMO in ARDS
- Describe ventilator management on ECMO for ARDS
- Identify common complications that can occur during VV-ECMO



Clin Chest Med 2015; 36:373–384

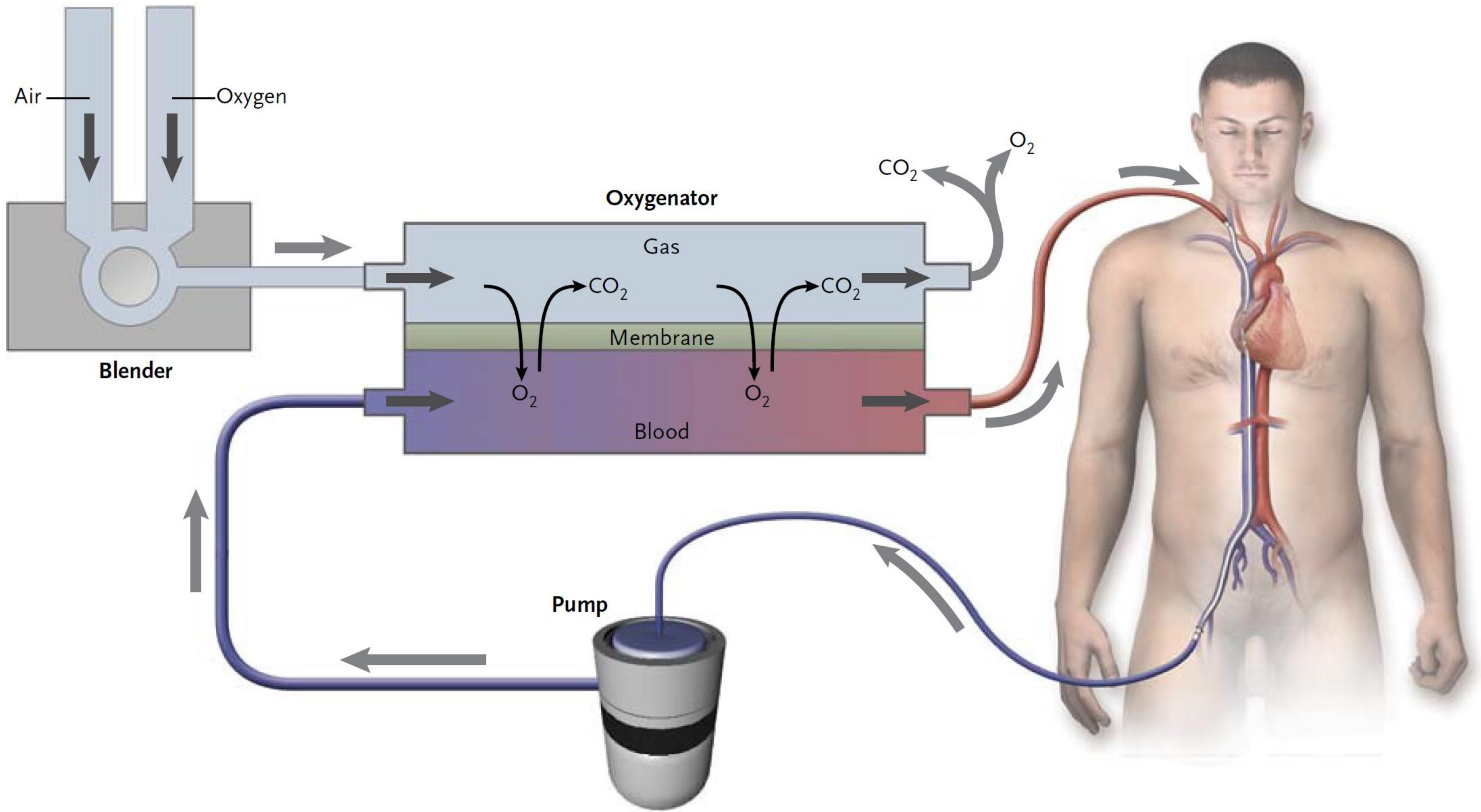


Pump

- Centrifugal
- Generate flow by a spinning rotor which applies suction to the blood inlet and then propels blood outward from the pump housing by generating a positive pressure
- 0 – 4500 RPM
- Preload and afterload sensitive

Oxygenator

- Large thin membrane made of a polymer which allows gas exchange to occur by diffusion
- Oxygenates the patient's blood, and removes carbon dioxide.
- Blood from drainage side is pumped in on one side, gas from the blender is pumped into the other side.



N Engl J Med. 2011 Nov 17;365(20):1905-14

Cannulae

Poiseuille's Law

$$Q = \frac{\Delta P \, \pi \, r^4}{8 \, \eta \, l}$$

Q = volume flux
ΔP = change in pres
r = pipe or vessel
η = viscosity
l = pipe or vessel

- Drainage
  - Multi-stage
  - 19 Fr – 27 Fr

- Return
  - 15 Fr – 21 Fr

Gas Blender / Flowmeter

- O_2 source
- Usually start at 100%, can change the fraction of O_2 during weaning

- Flow of the gas
- Called “sweep”
  - How fast the gas flows

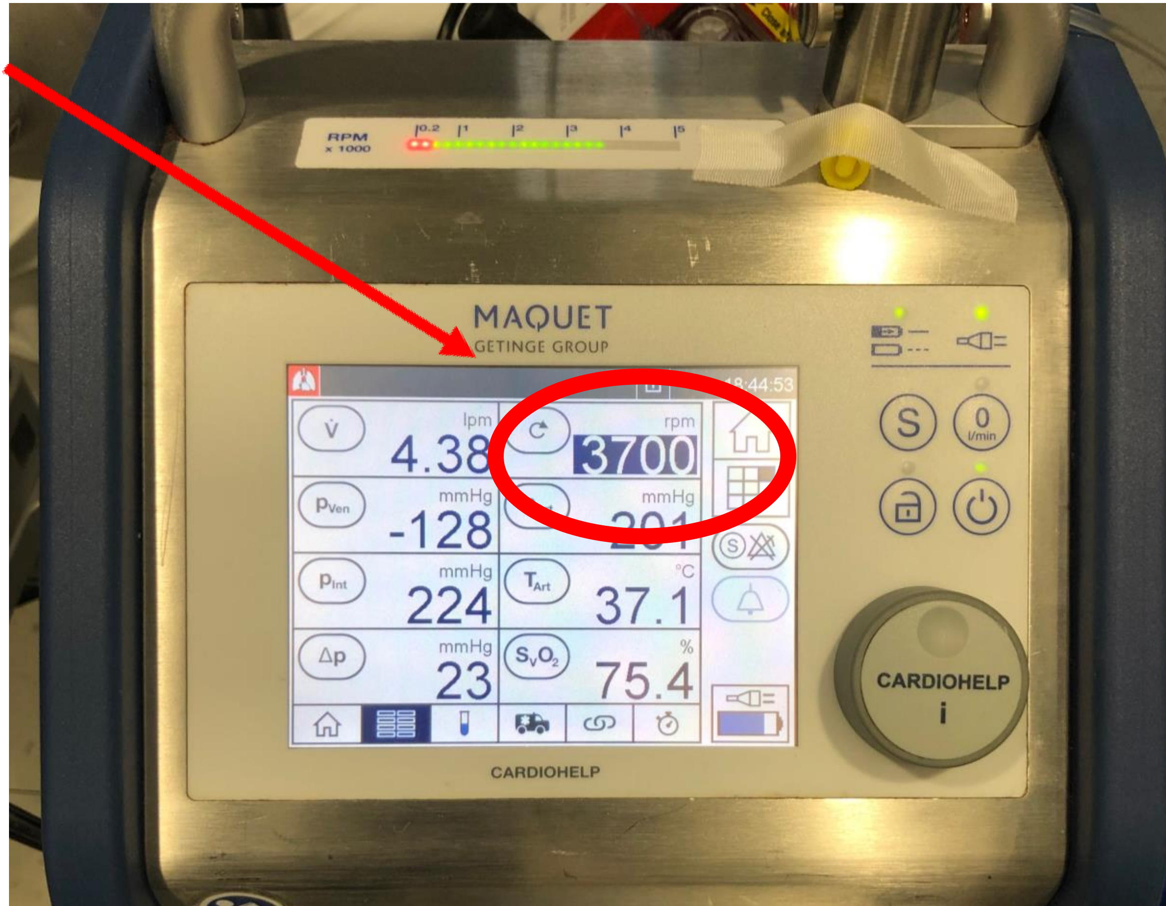
Heat Exchanger

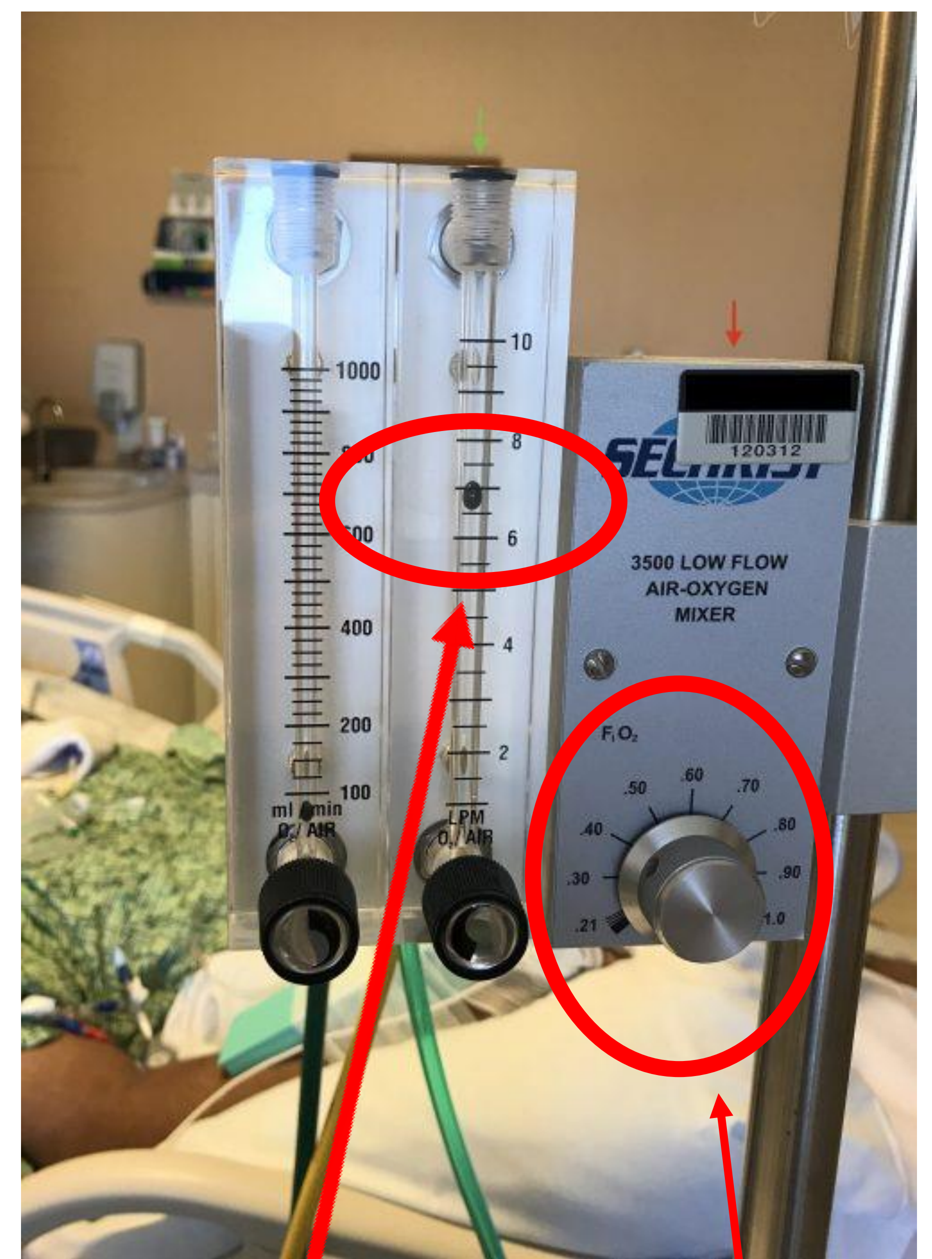
- Maintain body temperature
- Heat loss for many reasons during ECMO
  - Gas flow is cold
  - Blood flow exposed to room air
- Can cool patients as well if clinically indicated

Console

Parameters that can be set

RPM



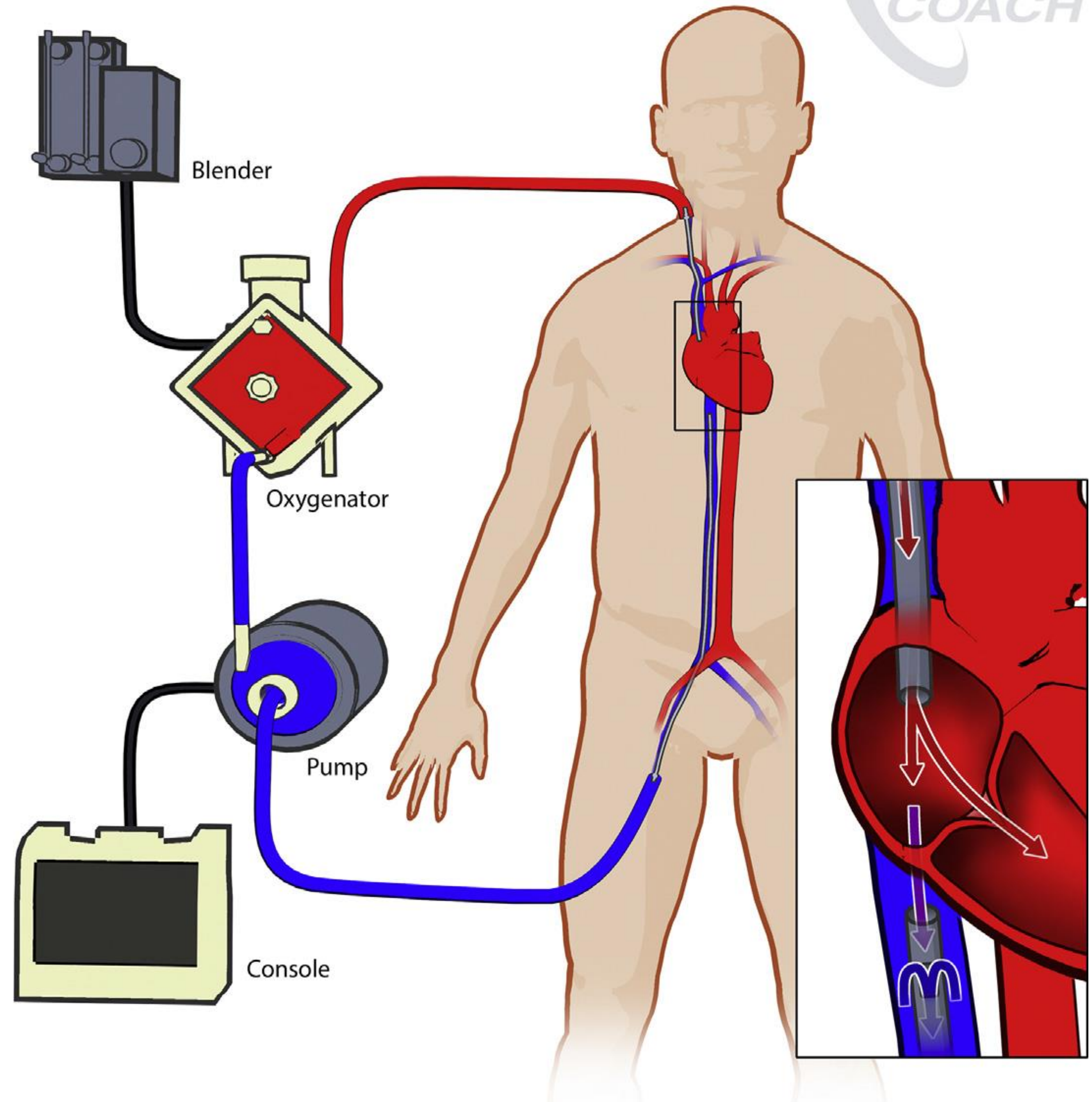


Sweep

FDO_2

VV ECMO

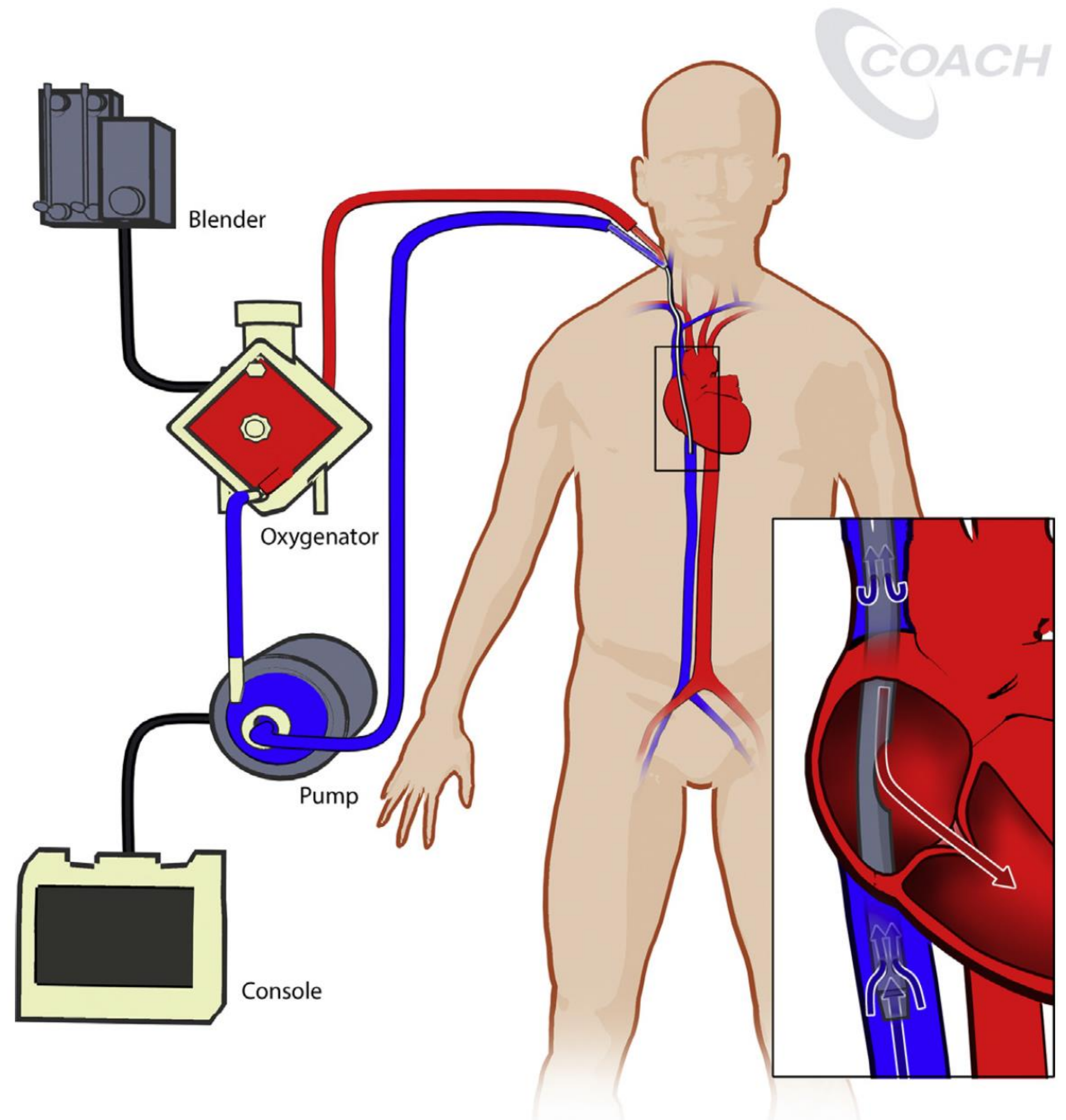
- **Only lung support**



Clin Chest Med 2015; 36:373–384

VV ECMO

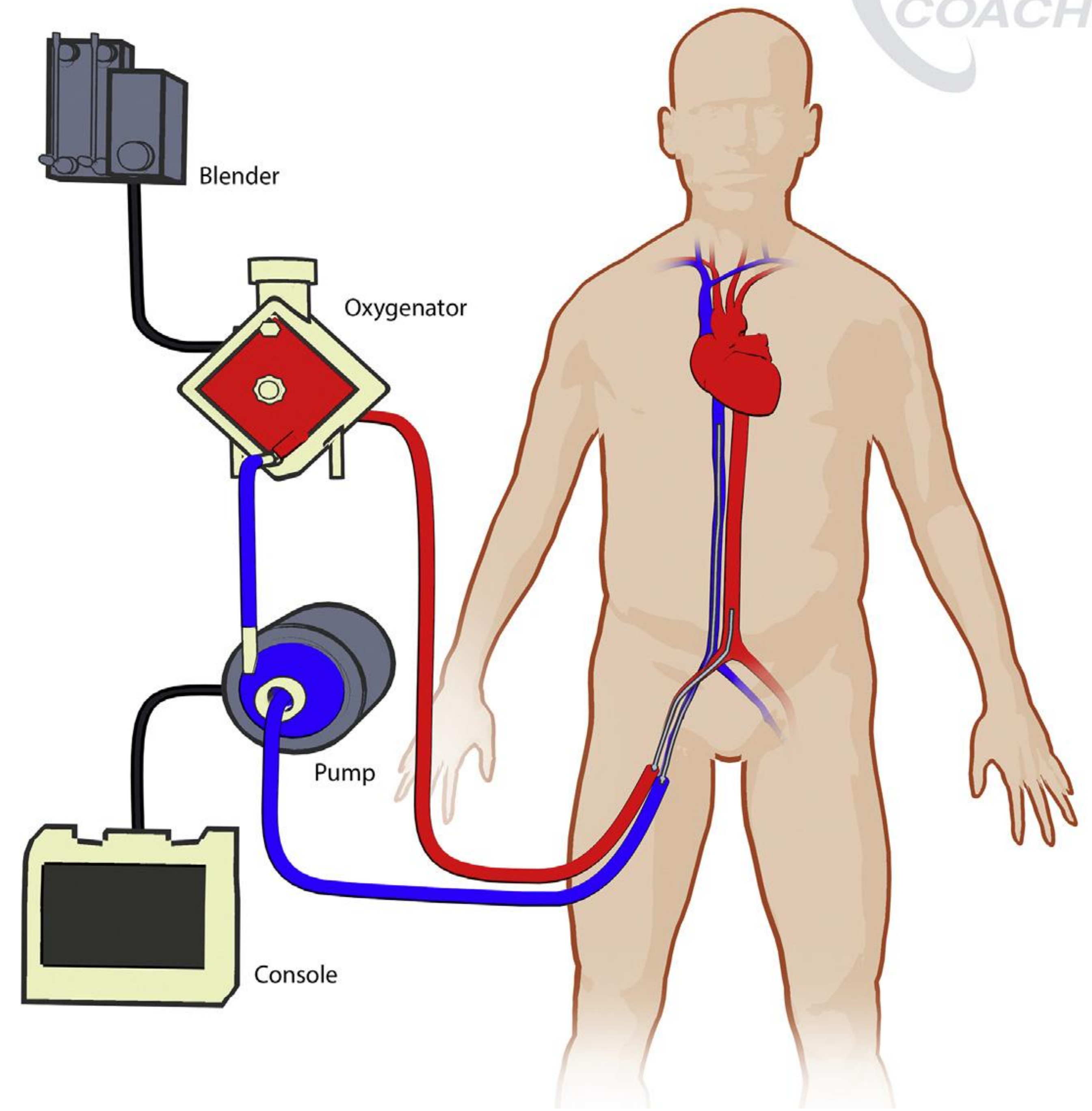
- **Only lung support**



Clin Chest Med 2015; 36:373–384

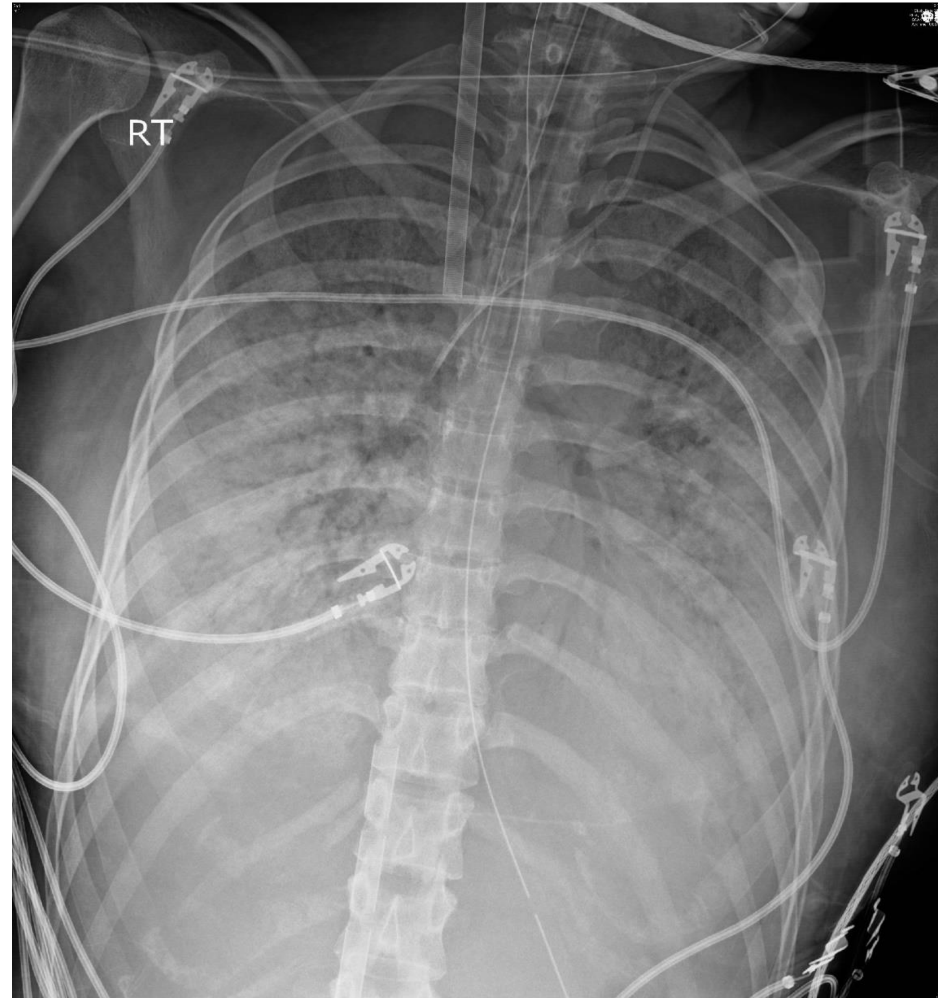
VA ECMO

- **Heart AND lung support**



Clin Chest Med 2015; 36:373–384

Which respiratory failure patients can benefit from ECMO?



Patient Selection

- Severe respiratory failure that is potentially **reversible**, not improving despite **optimal medical management**, AND without major **contraindications**.

Bridge to …

- Recovery
- Transplant
- Decision

ASAIO Journal 2021

Management of Adult Patients Supported with Venovenous Extracorporeal Membrane Oxygenation (VV ECMO): Guideline from the Extracorporeal Life Support Organization (ELSO)

Joseph E. Tonna, MD, MS,*† Darryl Abrams, MD,‡ Daniel Brodie, MD‡ John C. Greenwood, MD,§
Jose Alfonso Rubio Mateo-Sidron, MD,¶ Asad Usman, MD, MPH,|| and Eddy Fan, MD, PhD#

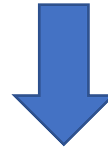


Table 1. Indications/Contraindications for Adult VV ECMO

Common indications for venovenous extracorporeal membrane oxygenation
One or more of the following:

1) Hypoxemic respiratory failure ($PaO_2/FiO_2 < 80$ mm Hg)*, after optimal medical management, including, in the absence of contraindications, a trial of prone positioning.
2) Hypercapnic respiratory failure (pH < 7.25), despite optimal conventional mechanical ventilation (respiratory rate 35 bpm and plateau pressure [P_{plat}] ≤ 30 cm H_2O).
3) Ventilatory support as a bridge to lung transplantation or primary graft dysfunction following lung transplant.

Specific clinical conditions:

- Acute respiratory distress syndrome (*e.g.*, viral/bacterial pneumonia and aspiration)
- Acute eosinophilic pneumonia
- Diffuse alveolar hemorrhage or pulmonary hemorrhage
- Severe asthma
- Thoracic trauma (*e.g.*, traumatic lung injury and severe pulmonary contusion)
- Severe inhalational injury
- Large bronchopleural fistula
- Peri-lung transplant (*e.g.*, primary lung graft dysfunction and bridge to transplant)

ASAIO J. 2021 Jun 1;67(6):601-610.

Management of Adult Patients Supported with Venovenous Extracorporeal Membrane Oxygenation (VV ECMO): Guideline from the Extracorporeal Life Support Organization (ELSO)

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"Currently, the only absolute contraindication for the start of ECMO is anticipated nonrecovery without a plan for viable decannulation"

Relative contraindications for venovenous extracorporeal membrane oxygenation

- Central nervous system hemorrhage
- Significant central nervous system injury
- Irreversible and incapacitating central nervous system pathology
- Systemic bleeding
- Contraindications to anticoagulation
- Immunosuppression
- Older age (increasing risk of death with increasing age, but no threshold is established)
- Mechanical ventilation for more than 7 days with P_{plat} > 30 cm H_2O and F_iO_2 > 90%

ASAIO J. 2021 Jun 1;67(6):601-610.

Study	Factors That Worsen Prognosis
Pappalardo et al[44] (N = 60)	Increased length of hospital stay pre-ECMO Increased creatinine Increased bilirubin Lower MAP Lower haematocrit
Schmidt et al[36] (N = 140)	Age Immunocompromise Length of mechanical ventilation before ECMO > 6 d Pplat > 30 cm H_2O PEEP < 10 cm H_2O Higher SOFA score
Roch et al[34] (N = 85)	Higher age Higher SOFA score
Enger et al[39] (N = 304)	Increased age Immunocompromise Minute ventilation Low pre-ECMO hemoglobin High day 1 F_{IO_2} High day 1 norepinephrine dose Low day 1 fibrinogen
Schmidt et al[32] (N = 2,355)	Increasing age Immunocompromise Increased length of mechanical ventilation prior to ECMO Extrapulmonary infection Higher peak inspiratory pressure Neurologic dysfunction Bicarbonate (HCO_3^-) infusion pre-ECMO Higher Pa_{CO_2} Nitric oxide use pre ECMO Cardiac arrest
Hilder et al[31] (N = 108)	Longer length of hospital stay before ECMO Lower MAP Higher lactate Lower pH Lower platelet concentration

Chest. 2020 Sep;158(3):1036-1045.

Indications for VV-ECMO:

1. Severe hypoxemic respiratory failure

    a. PaO_2:FiO_2 ratio < 80 mm Hg for more than 6 hours, despite optimal management listed below:
    b. Optimized PEEP (Best PEEP trial, esophageal balloon, PV tool)
    c. Neuromuscular blockade
    d. Inhaled pulmonary artery vasodilator
    e. Prone positioning
        i. only contraindication to proning is spinal cord instability (elevated BMI is not a contraindication)

2. Severe hypercarbic respiratory failure

    a. pH < 7.2 and $PaCO_2$ > 80 mm Hg for more than 3 hours

3. Inability to maintain lung protective ventilation for ARDS patients

    a. P_{plat} > 30 cm H_20 on lung protective ventilation

4. To maintain viability as a lung transplant candidate

5. Perioperative support for complex airway/lung surgeries

Absolute contraindications:

1. Non-recoverable multiorgan failure (excluding cardiopulmonary)
2. Receipt of mechanical ventilation for 10 days or longer (7 days if on high ventilatory settings; FiO_2 > 70%, P_{plat} > 30 cm $H_2 0$)
3. Irreversible neurologic injury or unknown neurologic status
4. Expected life expectancy < 6 months
5. Active cardiac arrest
6. Significant baseline comorbidities including but not limited to the following:
   a. Advanced chronic heart failure in a patient that is not a candidate for any destination therapy
   b. Long-term chronic respiratory insufficiency treated with oxygen therapy in a patient that is not a lung transplant candidate
   c. ESRD on hemodialysis
   d. Cirrhosis (MELD ≥ 30)
   e. Severe neurologic disability/dementia
   f. Unable to perform ADL's at baseline

What is the evidence?

PubMed.gov

ECMO and ARDS

Search

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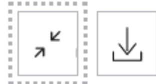
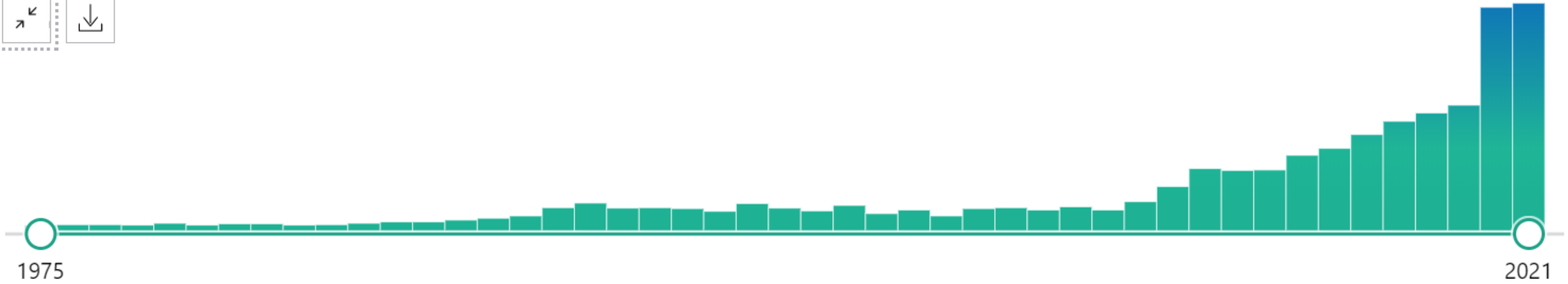
RESULTS BY YEAR

3,205 results





2009
Influenza A
(H1N1)

2020
COVID-19

ECLS Registry Report

International Summary

April, 2021

Report data through 2020

Extracorporeal Life Support Organization
3001 Miller Rd
Ann Arbor, MI 48103 USA

Adult Respiratory (18 years and over)

Annual Respiratory Adult Runs

Cases

8000
6000
4000
2000
0

	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
Cases	20	15	25	35	73	70	95	92	97	83	114	93	93	117	117	151

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Cases	121	155	200	496	538	705	1008	1551	2095	2406	3128	3513	4158	4779	7161

ECMO Registry of the Extracorporeal Life Support Organization (ELSO), Ann Arbor, Michigan, 4/2021.

Studies –RCT’s

- CESAR - 2009
- EOLIA - 2018

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 Thalanany, Clare L Hibbert, Ann Truesdale, Felicity Clemens, Nicola Cooper, Richard K Firmin, Diana Elbourne, for the CESAR trial collaboration

Inclusion

- 18–65 years with severe but potentially reversible respiratory failure
- Murray score ≥ 3
  - PaO2/FiO2 ratio
  - Positive end-expiratory pressure
  - Lung compliance
  - Chest radiograph
- Uncompensated hypercapnia with a pH < 7.2 despite optimum conventional treatment

Exclusion

- PIP > 30 cm H20 or FIO2 > 80% for 7 days
- Signs of intracranial bleeding
- Any other contraindication to limited heparinisation
- Any contraindication to continuation of active treatment

Lancet 2009; 374: 1351–63

CESAR - Results

	ECMO group (n=90)*	Conventional management group (n=90)	Relative risk (95% CI, p value)
Death or severe disability at 6 months	NA	NA	0·69 (0·05–0·97, 0·03)†
No	57 (63%)	41 (47%)‡	NA
Yes	33 (37%)	46 (53%)‡	NA
No information about severe disability	0	3 (3%)§	NA
Died at ≤6 months or before discharge	NA	NA	0·73 (0·52–1·03, 0·07)
No	57 (63%)	45 (50%)	NA
Yes	33 (37%)	45 (45%)	NA

43/68 (63%) survived that actually went on ECMO

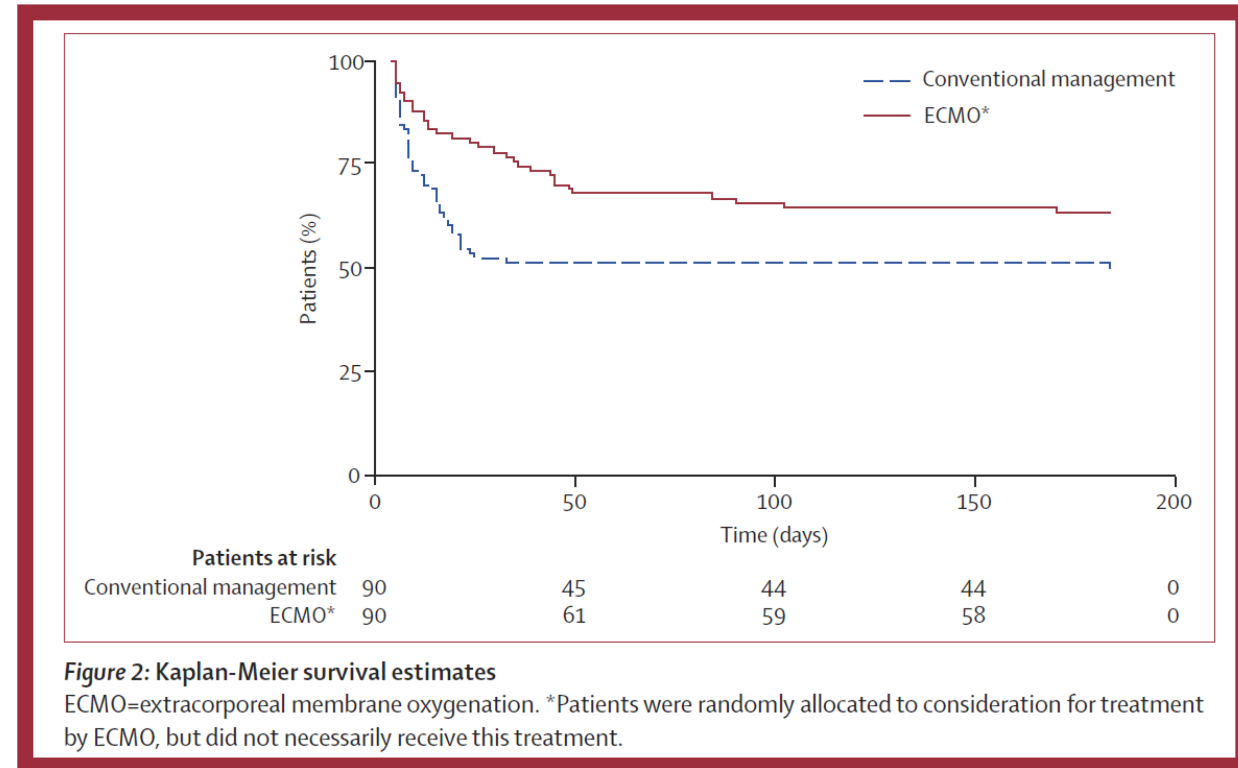


Figure 2: **Kaplan-Meier survival estimates**
ECMO=extracorporeal membrane oxygenation. *Patients were randomly allocated to consideration for treatment by ECMO, but did not necessarily receive this treatment.

Lancet 2009; 374: 1351–63

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

Inclusion

- Pao2:Fio2 of < 50 mm Hg for > 3 hours
- Pao2:Fio2 of < 80 mm Hg for > 6 hours
- pH of < 7.25 with Paco2 of ≥ 60 mm Hg for >6 hours
  - with the respiratory rate increased to 35 breaths per minute on protective mechanical-ventilation settings

Exclusion

- < 18 yr
- Mechanical ventilation for > 7 days
- Pregnancy
- BMI > 45
- Chronic respiratory insufficiency
- Cardiac failure resulting in VA-ECMO
- Hx of HITT
- Cancer with a life expectancy of < 5 years
- A moribund condition or a Simplified Acute Physiology Score (SAPS-II) value of more than 90
- Current non–drug-induced coma after cardiac arrest
- Irreversible neurologic injury
- Decision to withhold or withdraw life-sustaining therapies;
- Expected difficulty in obtaining vascular access

N Engl J Med 2018;378(21):1965-1975

EOLIA – Results

Table 2. End Points.*

End Point	ECMO Group (N=124)	Control Group (N=125)	Relative Risk or Difference (95% CI)†	P Value
Primary end point: mortality at 60 days — no. (%)	44 (35)	57 (46)	0.76 (0.55 to 1.04)	0.09

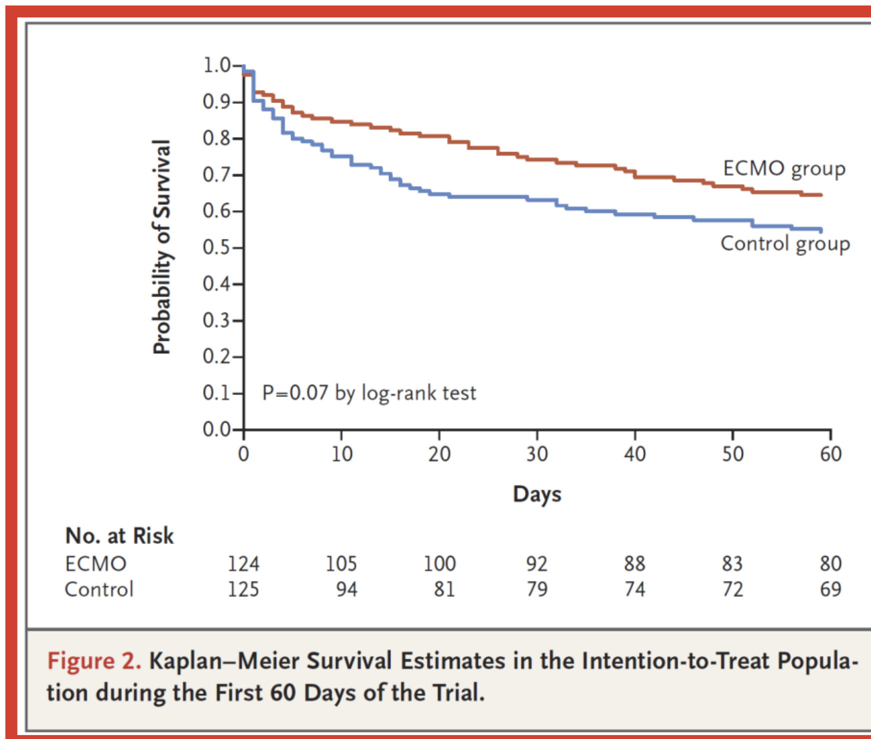


Figure 2. Kaplan–Meier Survival Estimates in the Intention-to-Treat Population during the First 60 Days of the Trial.

N Engl J Med 2018;378(21):1965-1975

ORIGINAL

ECMO for severe ARDS: systematic review and individual patient data meta-analysis

Alain Combes[1,2*], Giles J. Peek[3], David Hajage[4], Pollyanna Hardy[5], Darryl Abrams[6,7], Matthieu Schmidt[1,2], Agnès Dechartres[4] and Diana Elbourne[8]

Table 2 Endpoints

Endpoint	ECMO group (*N* = 214)	Control group (*N* = 215)	Relative Risk or difference (95% CI)	*p* value	I^2 (%)
Primary endpoint					
Day 90 mortality—no. (%)	77 (36)	103 (48)	0.75 (0.6–0.94)	0.013	0

Intensive Care Med (2020) 46:2048–2057

Meta-analysis - Results

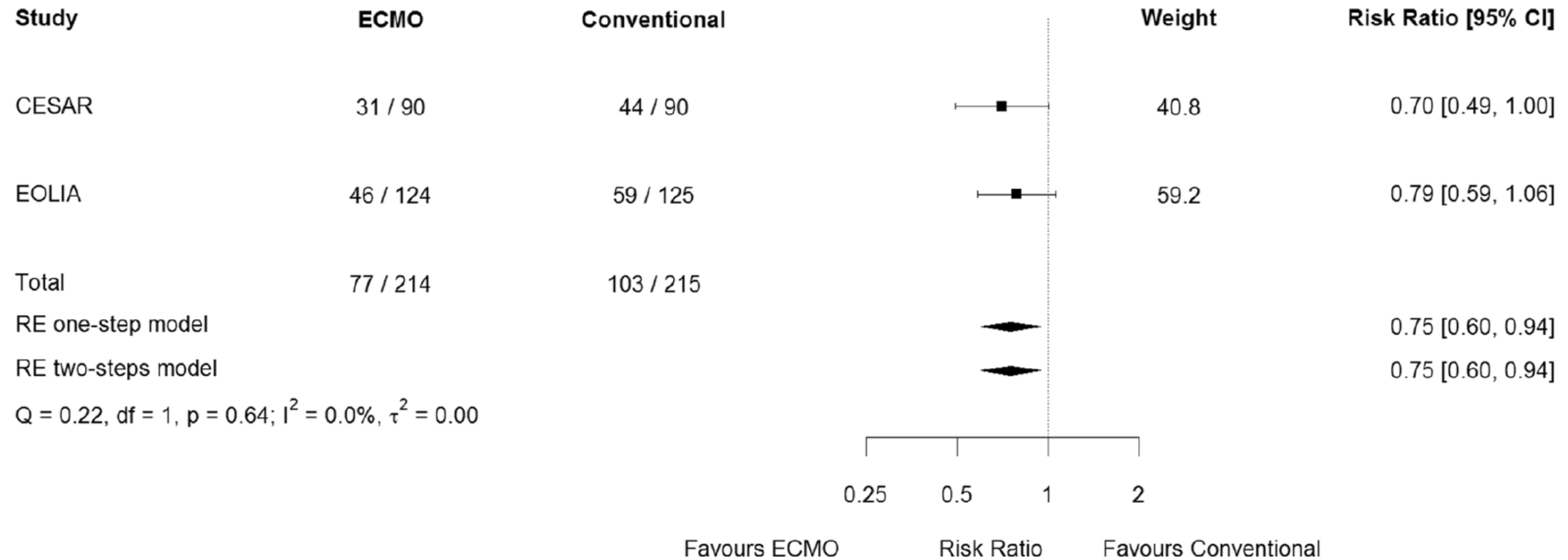


Fig. 1 Forest plot of 90-day mortality in the intention-to-treat population

Intensive Care Med (2020) 46:2048–2057

Meta-analysis - Results

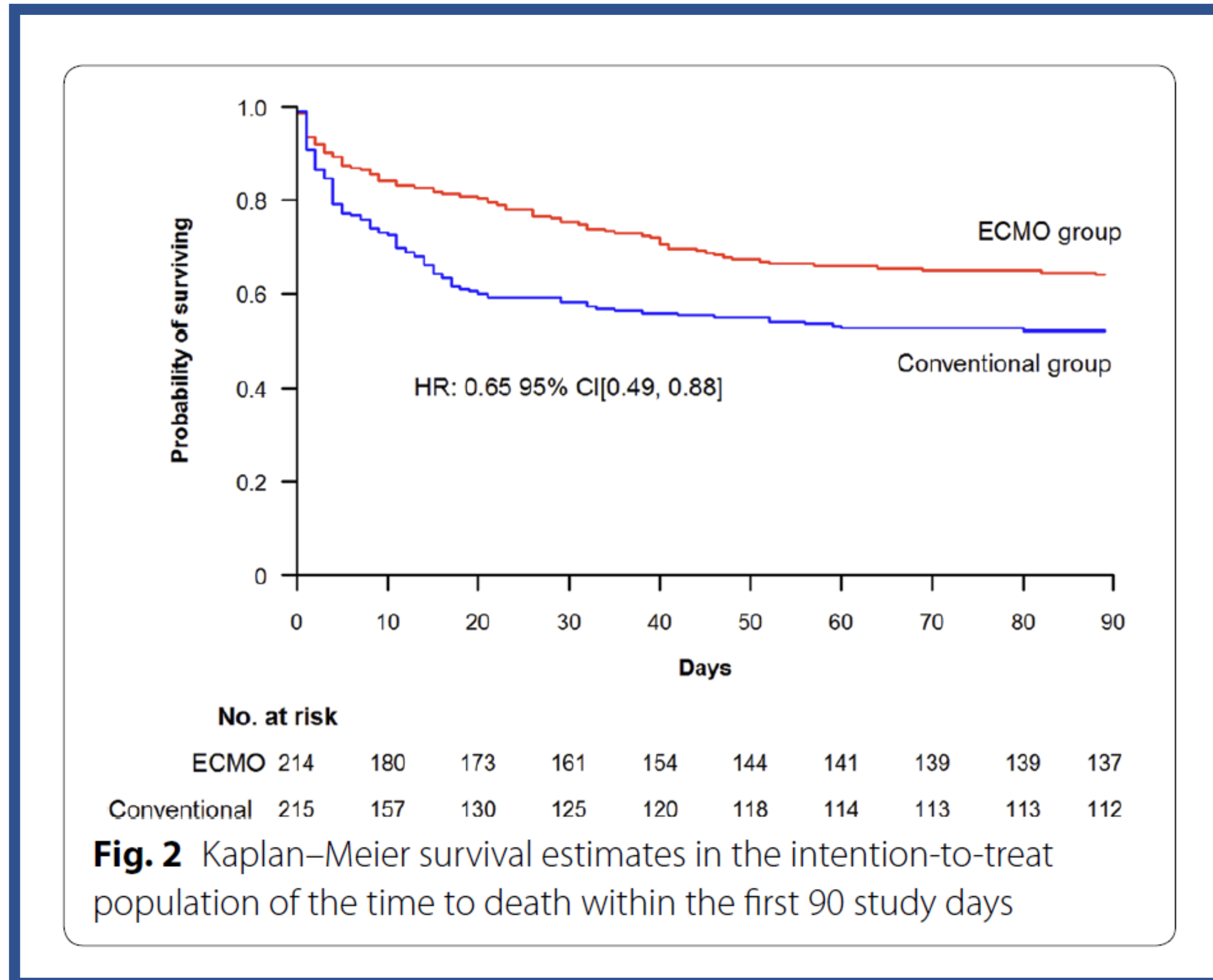


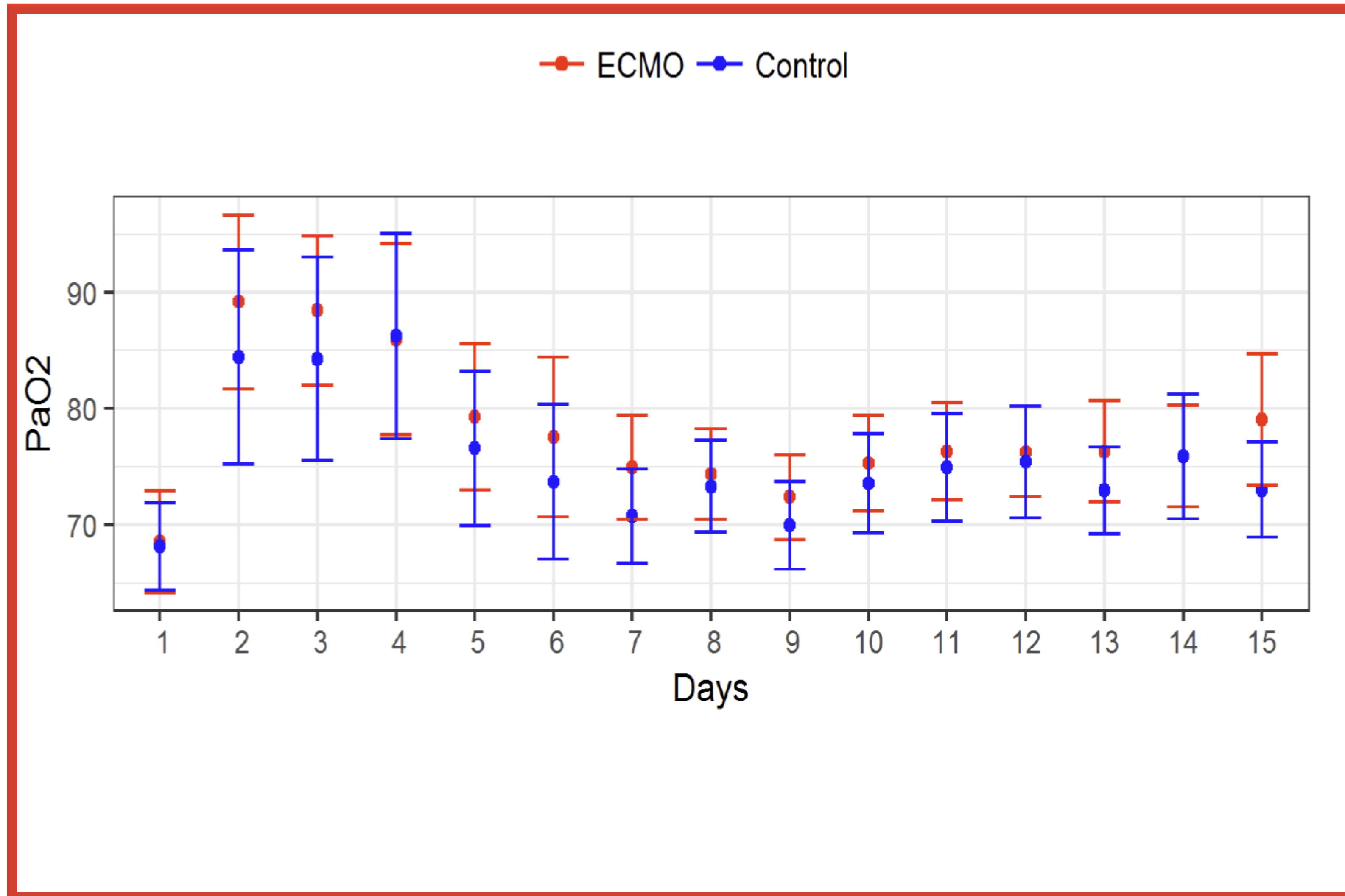
Fig. 2 Kaplan–Meier survival estimates in the intention-to-treat population of the time to death within the first 90 study days

Intensive Care Med (2020) 46:2048–2057

How does VV-ECMO help in ARDS??

- Maintain oxygen delivery
- Remove CO_2
- **Rest lungs**
  - **Allows reductions in the mechanical forces contributing to ventilator-induced lung injury**
  - **Ultra-lung-protective ventilation**

Supplementary data from EOLIA



Supplementary data from EOLIA

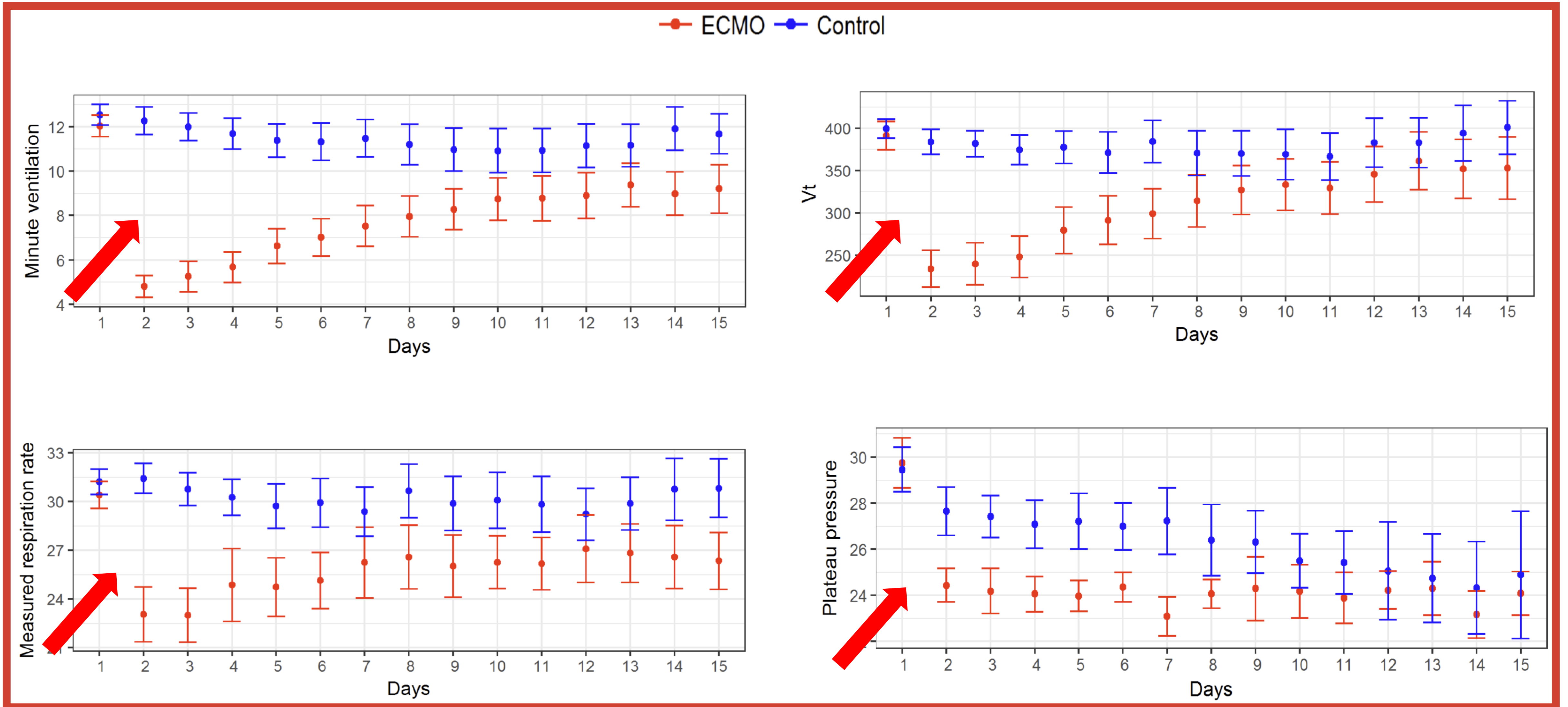


Table 1. Ventilatory Parameters before and after Extracorporeal Life Support Initiation in Studies of ECLS for Acute Respiratory Distress Syndrome

	Retrospective Studies						Prospective Studies							
	Schmidt *et al.* (54)		Marhong *et al.* (55)		Serpa Neto *et al.* (53)		Xtravent (46)		EOLIA (1)		SUPERNOVA (52)		LIFEGARDS (56)	
	Before ECLS	After ECLS*	Before ECLS	After ECLS†	Before ECLS	After ECLS†	Before ECLS	After ECLS†	Before ECLS	After ECLS†	Before ECLS	After ECLS†	Before ECLS	After ECLS‡
V_T, ml/kg PBW	6.3	3.9	6.1	3.9	6.0	4.0	5.9	3.4	6.0	3.4	6.0	4.2	6.4	3.7
RR, breaths/min	22.0	15.0	—	—	21.9	17.8	22.4	22.2	30.4	23.1	27.4	23.5	26	14
$\dot{V}_E$, L/min	8.8	3.6	—	—	9.1	5.0	9.9	5.8	—	—	10.2	5.9	10.2	3.5
PEEP, cm H_2O	13.0	12.0	14.0	12.0	13.7	12.9	16.1	17.1	11.7	11.2	13.6	14	12	11
Pplat, cm H_2O	32.2	26.4	32	25.5	31.1	26.2	29.0	25.1	29.8	24.4	27.7	23.9	32	24
ΔP, cm H_2O	19	13.7	18	13.5	17.7	13.7	12.9	8.0	17.8	13.2	13.2	9.9	20	14
Crs, ml/cm H_2O	23.2	19.9	22.7	19.4	26.8	23.2	34.4	32.2	25.0	20.1	—	—	24	19
F_{IO_2}	0.96	0.60	0.99	0.40	0.90	0.69	0.62	0.54	0.96	0.50	—	—	1.0	0.5
Pa_{CO_2}, mm Hg	66.0	40.5	—	—	58.3	40.3	57.3	53.9	57	38	48	46.7	68	42
pH	7.24	7.41	—	—	7.27	7.39	7.34	7.38	7.24	7.37	7.34	7.39	7.24	7.4
Pa_{O_2}/F_{IO_2}, mm Hg	67.0	—	61.0	—	72.6	152.5	152	154.5	73	—	168	168	71	—
$\dot{Q}_E$, L/min	—	4.5	—	3.0	—	4.3	—	1.3	—	5.0	—	0.4	—	4.2

Am J Respir Crit Care Med Vol 201, Iss 5, pp 514–525

Recommendations from International ECMO Network

Table 2. Suggested Initial Mechanical Ventilation Targets during ECLS for Acute Respiratory Distress Syndrome

Parameter	Target	Notes
Pplat*	⩽24 cm H_2O; may choose to go lower if feasible	
Driving pressure*	⩽14 cm H_2O	
V_T	Adjust for goal Pplat	Typically ⩽4 ml/kg PBW, often much lower
Respiratory rate†	⩽10 breaths/min	Typically only achieved when sedation, with or without NMBAs, is being used. Consider increased sweep flow to achieve, when appropriate
PEEP*	⩾10 cm H_2O	*See* text for circumstances that may warrant particularly high levels of PEEP
$F_{I_{O_2}}$*	0.3–0.5	Higher $F_{I_{O_2}}$ may be necessary if ECLS is inadequate for achieving acceptable levels of oxygenation Adequate oxygen delivery is the primary goal, not a particular Sa_{O_2}

Am J Respir Crit Care Med Vol 201, Iss 5, pp 514–525

Management of ARDS patient while on VV-ECMO

- Good general ARDS management
- Sedation/analgesia
  - Allow for non-injurious breathing/ventilation
- Conservative fluid management
  - Negative fluid balance
- Close attention to hemodynamics
  - Specifically watching for RV dysfunction

Duration of ECMO therapy for ARDS (pre-COVID)

- CESAR – median 9 [6 – 16] days
- EOLIA – mean 15 ± 13 days
- ELSO 2019 Registry data – mean 12 days

ECLS Registry Report

International Summary

April, 2021

Report data through 2020

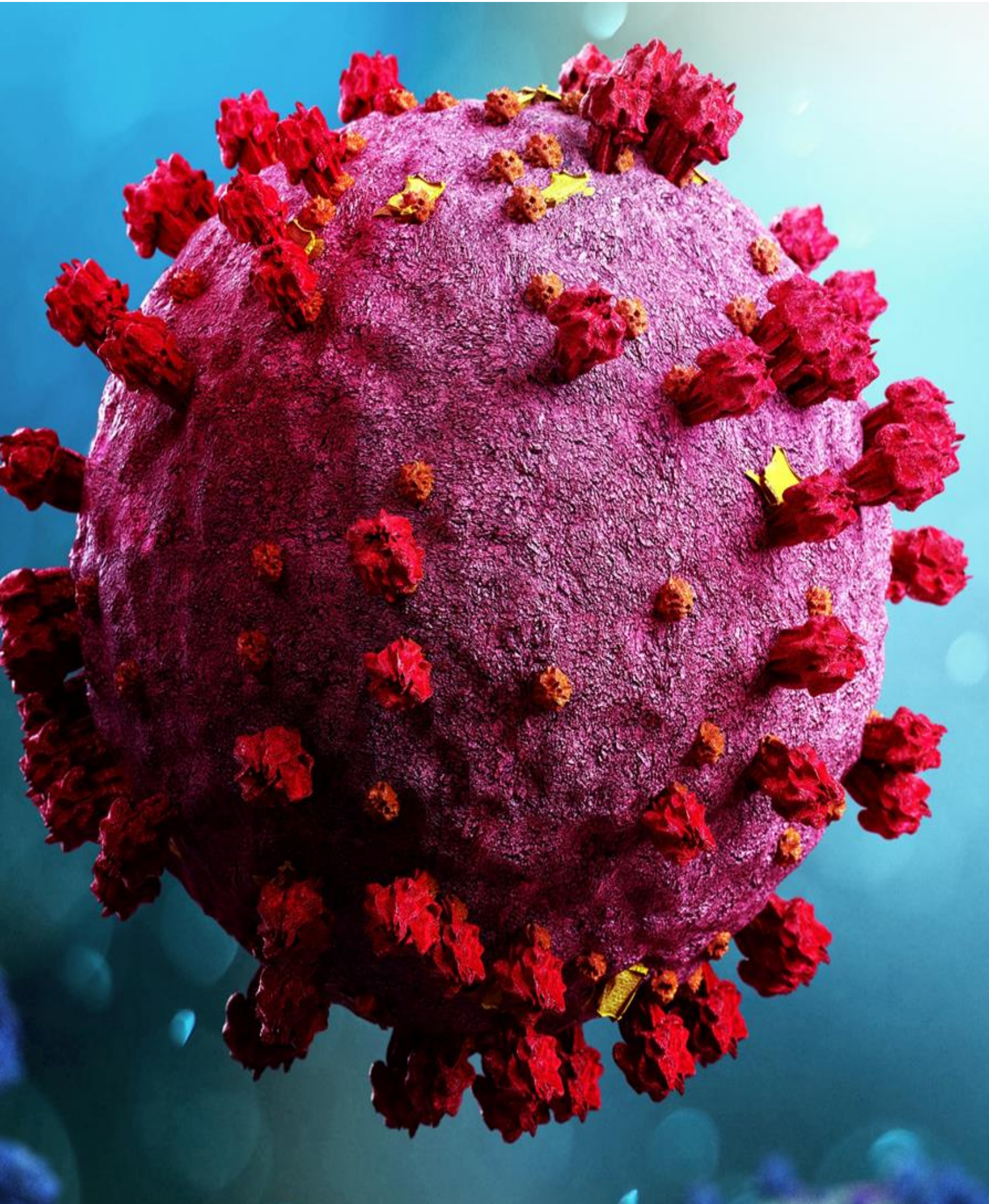
Extracorporeal Life Support Organization
3001 Miller Rd
Ann Arbor, MI 48103 USA

Adult Respiratory Complications from 2016 to 2020

Complication	%
Mechanical: Oxygenator failure	8.3%
Mechanical: Cannula problems	5.5%
Mechanical: Circuit change	10.6%
Mechanical: Clots and Air Emboli	0.1%
Mechanical: Thrombosis/Clots: circuit component	6.6%
Hemorrhagic: GI hemorrhage	5.6%
Hemorrhagic: Cannulation site bleeding	2.4%
Hemorrhagic: Surgical site bleeding	6.2%
Hemorrhagic: Hemolysis (hgb > 50 mg/dl)	2.3%
Hemorrhagic: Disseminated intravascular coagulation (DIC)	0.6%
Hemorrhagic: Peripheral cannulation site bleeding	2.9%
Neurologic: Brain death	1.2%
Neurologic: Seizures:	0.7%
Neurologic: CNS Infarction	1.4%
Neurologic: CNS hemorrhage	1.7%
Neurologic: Intraventricular CNS hemorrhage	0.7%
Neurologic: CNS diffuse ischemia (CT/MRI)	0.4%
Neurologic: Neurosurgical intervention performed	0.1%

Complication	%
Renal: Renal Replacement Therapy Required	26.9%
Cardiovascular: Inotropes on ECLS	6.9%
Cardiovascular: CPR required	4.7%
Cardiovascular: Cardiac arrhythmia	8.5%
Cardiovascular: Tamponade (blood) 218 1% 98 45%	1%
Pulmonary: Pneumothorax requiring treatment	7%
Pulmonary: Pulmonary hemorrhage	3.4%
Infectious: Culture proven infection	3.3%
Metabolic: Hyperbilirubinemia	5.2%
Metabolic: Moderate hemolysis	1.9%
Metabolic: Severe hemolysis	1.2%
Limb: Ischemia	1.1%

Extracorporeal membrane oxygenation for COVID-19: evolving outcomes from the international Extracorporeal Life Support Organization Registry



ECMO for COVID-19

- Initially (first wave) high-volume ECMO centers reported outcomes similar to non-COVID ARDS patients that underwent ECMO
  - 90-day survival -> 63%
- As pandemic progressed …..
- **Mortality significantly worsened** (May 2020 – December 2020)
  - 90-day survival -> 49%
- **Duration of ECMO support increased**
  - Median duration of ECMO (May 2020 – December 2020)
  - 20.0 days IQR [9.7–35.1]

Lancet 2021; 398: 1230–38

- Consider VV-ECMO for patients with severe respiratory failure of a potentially reversible etiology that has failed optimal medical management **and** are without significant comorbidities/contraindications
  - Severe hypoxemia -> p:f < 80
  - Severe hypercapnia -> pH < 7.25 with elevated pcO2
  - Inability to maintain lung protective ventilation
- Greatest body of evidence supporting VV-ECMO is for ARDS
- VV-ECMO as a bridge to recovery for ARDS:
  - Supports patient oxygenation/ventilation
  - Allows for ultra-protective ventilation thereby decreasing on-going ventilator induced lung injury

Question

A 45-year woman with ARDS is cannulated for ECMO due to severe hypoxemia despite optimized PEEP, neuromuscular blockade, inhaled veletri, and proning.

Pre-cannulation ventilator settings: ACVC: Vt: 340 (6 cc/kg/IBW), RR: 28 PEEP 18 cm H20, FIO2 100%. Pplat: 30 cm H20

Post cannulation O2 saturation is 98%

Which of the following are appropriate post-ECMO cannulation ventilator settings?

a) ACPC: PC 10, PEEP 10, RR 10, FIO2 21%
b) ACVC: Vt: 230 (4 cc/kg/IBW), RR: 10, PEEP 16 cm H20, FIO2 30%. Pplat: 24 cm H20
c) CPAP: 15 cm H20, FIO2 30%
d) APRV: P_{high} 20 P_{low} 5, T_{high} 5.5 s, T_{low} 0.5 s, FIO2 40%
e) All of the above