



ECMO for Acute Respiratory Failure

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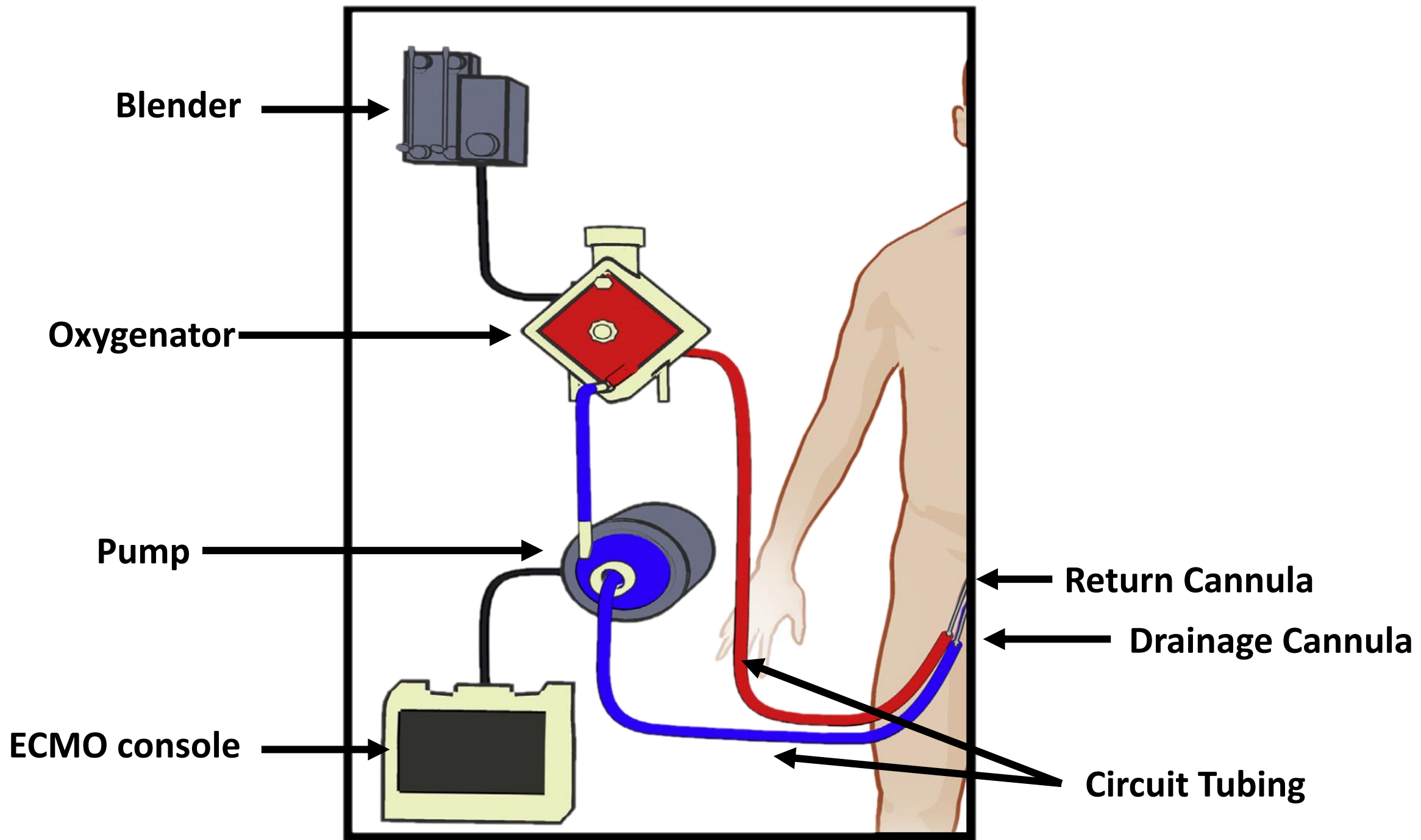
Disclosures

- BD - Consulting

Objectives

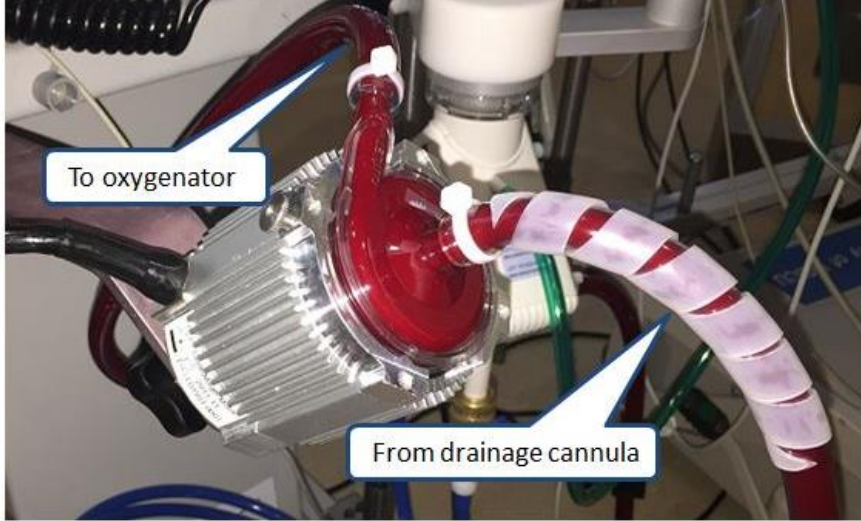
- Describe criteria to initiate ECMO in acute respiratory failure
- Recognize common contraindications for ECMO
- Review evidence supporting the use of ECMO in ARDS
- Describe ventilator management on ECMO for ARDS
- Identify common complications that can occur during VV-ECMO





Pump

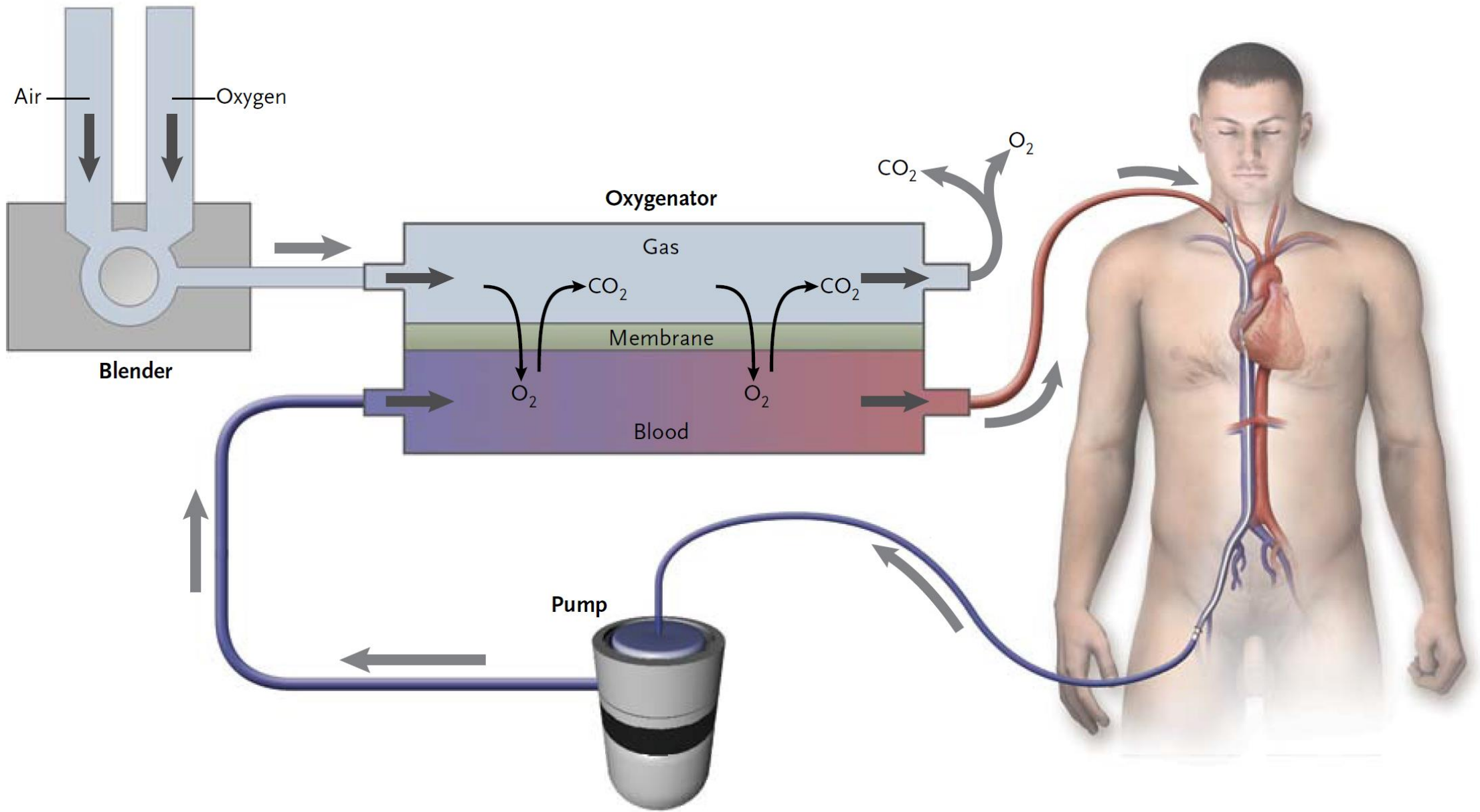
- Centrifugal
- Generate flow by a spinning rotor which applies suction to the blood inlet and then propels blood outward from the pump housing by generating a positive pressure
- 0 – 4500 RPM
- Preload and afterload sensitive



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.





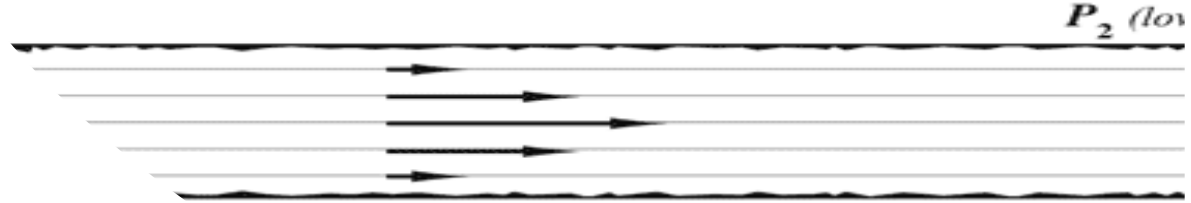
Poiseuille's Law

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

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

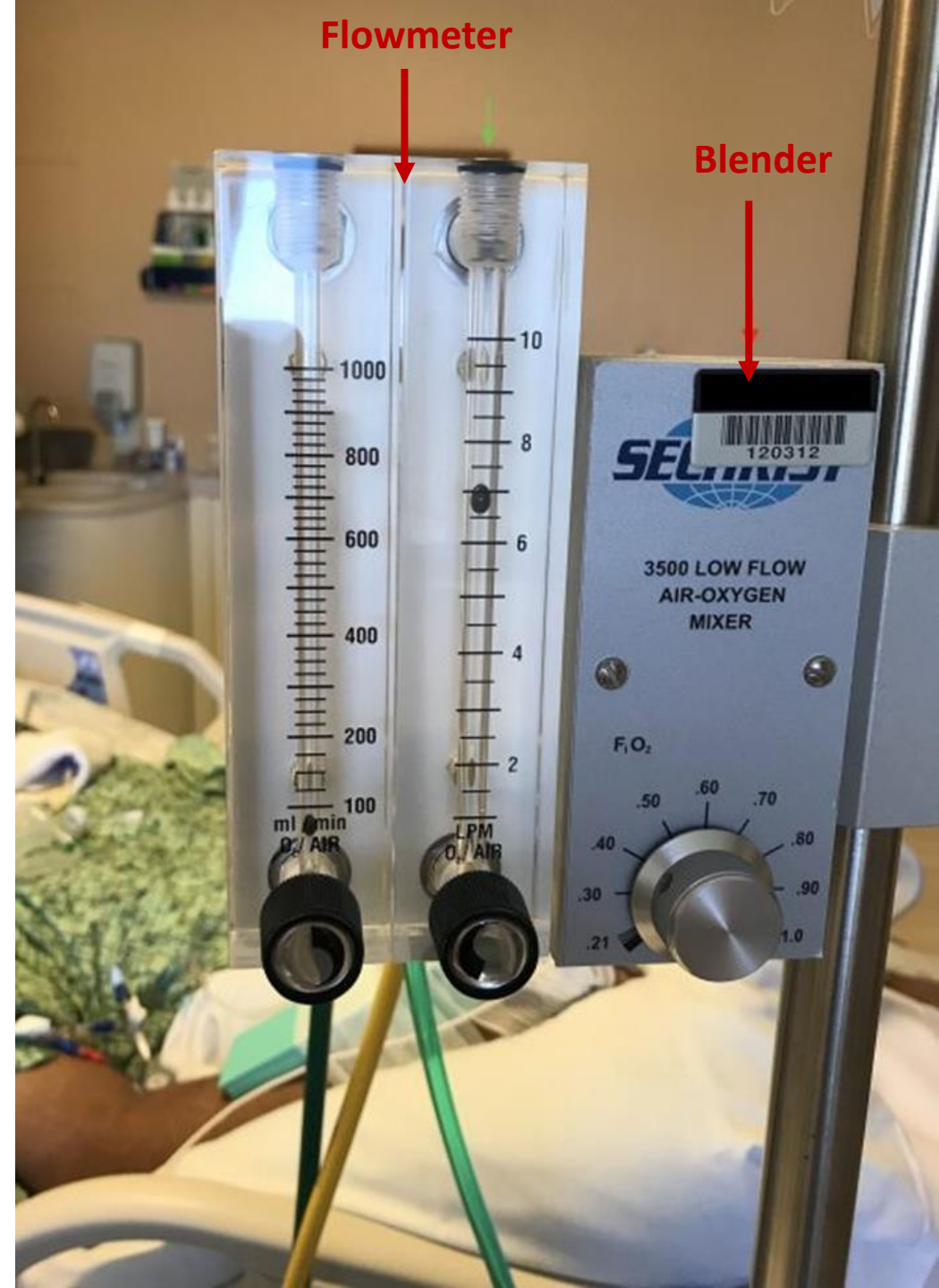
Cannulae

- Drainage
 - Multi-stage
 - 19 Fr – 27 Fr
- Return
 - 15 Fr – 21 Fr



Gas Blender / Flowmeter

- O₂ source
- Usually start at 100%, can change the fraction of O₂ 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

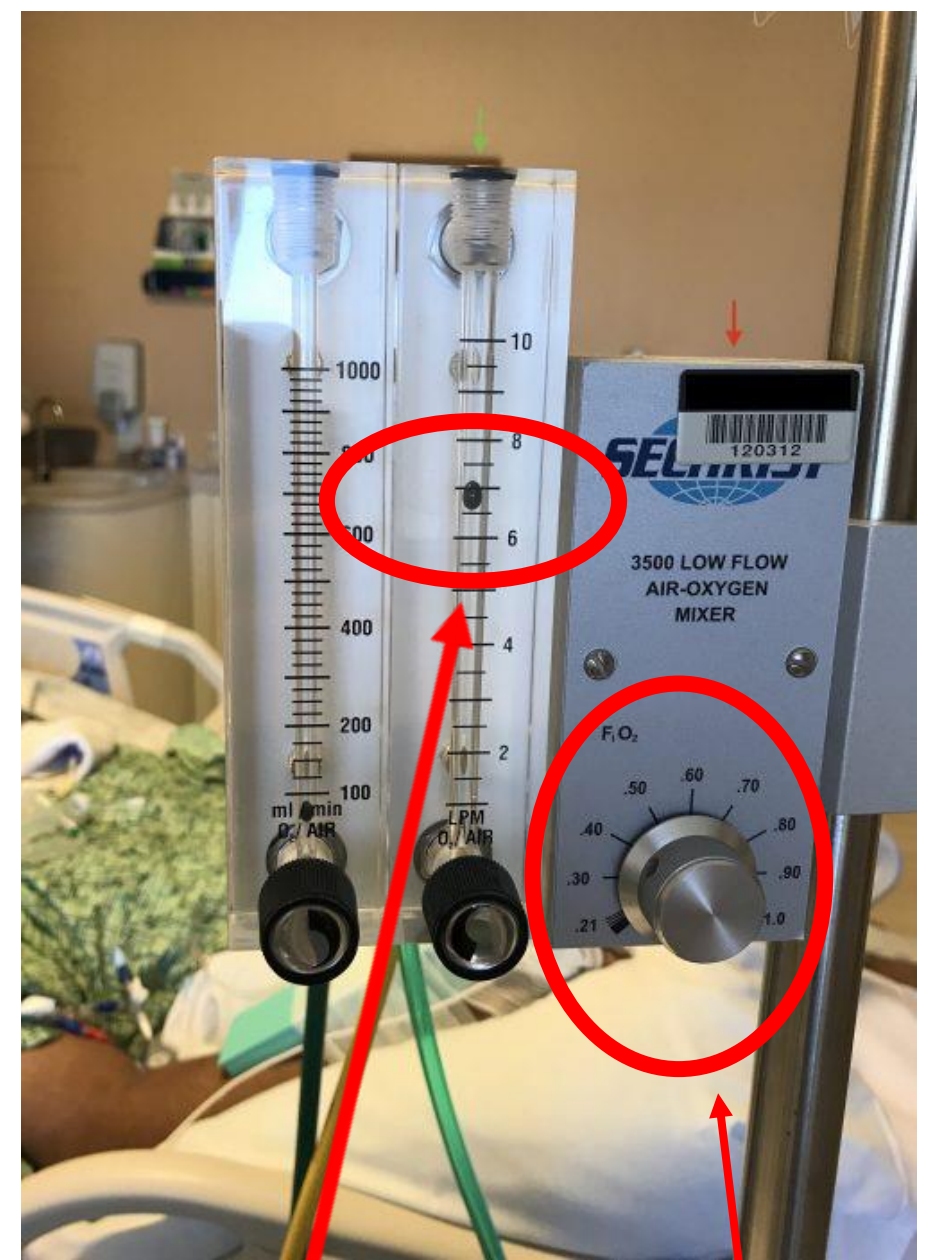
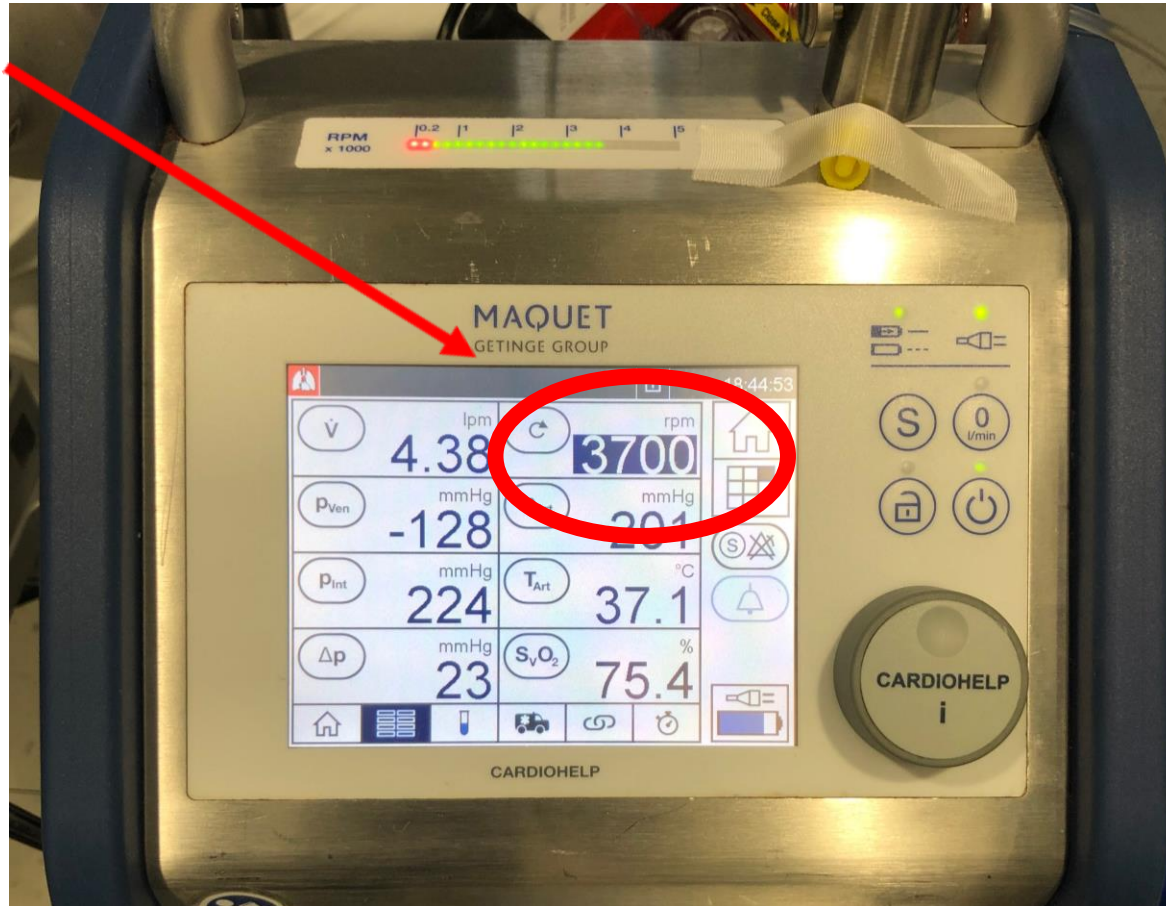


Console



Parameters that can be set

RPM

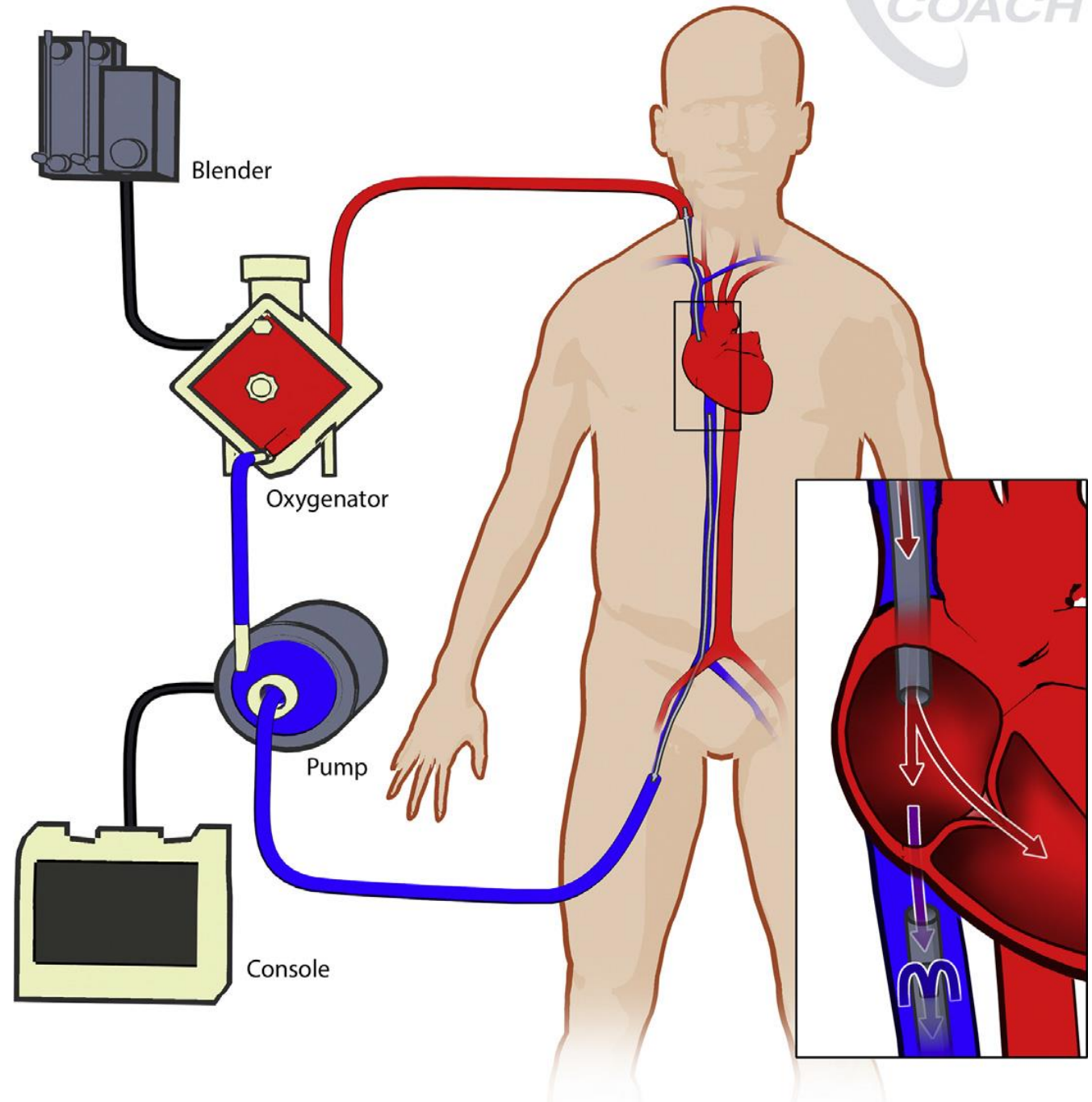


Sweep

FDO₂

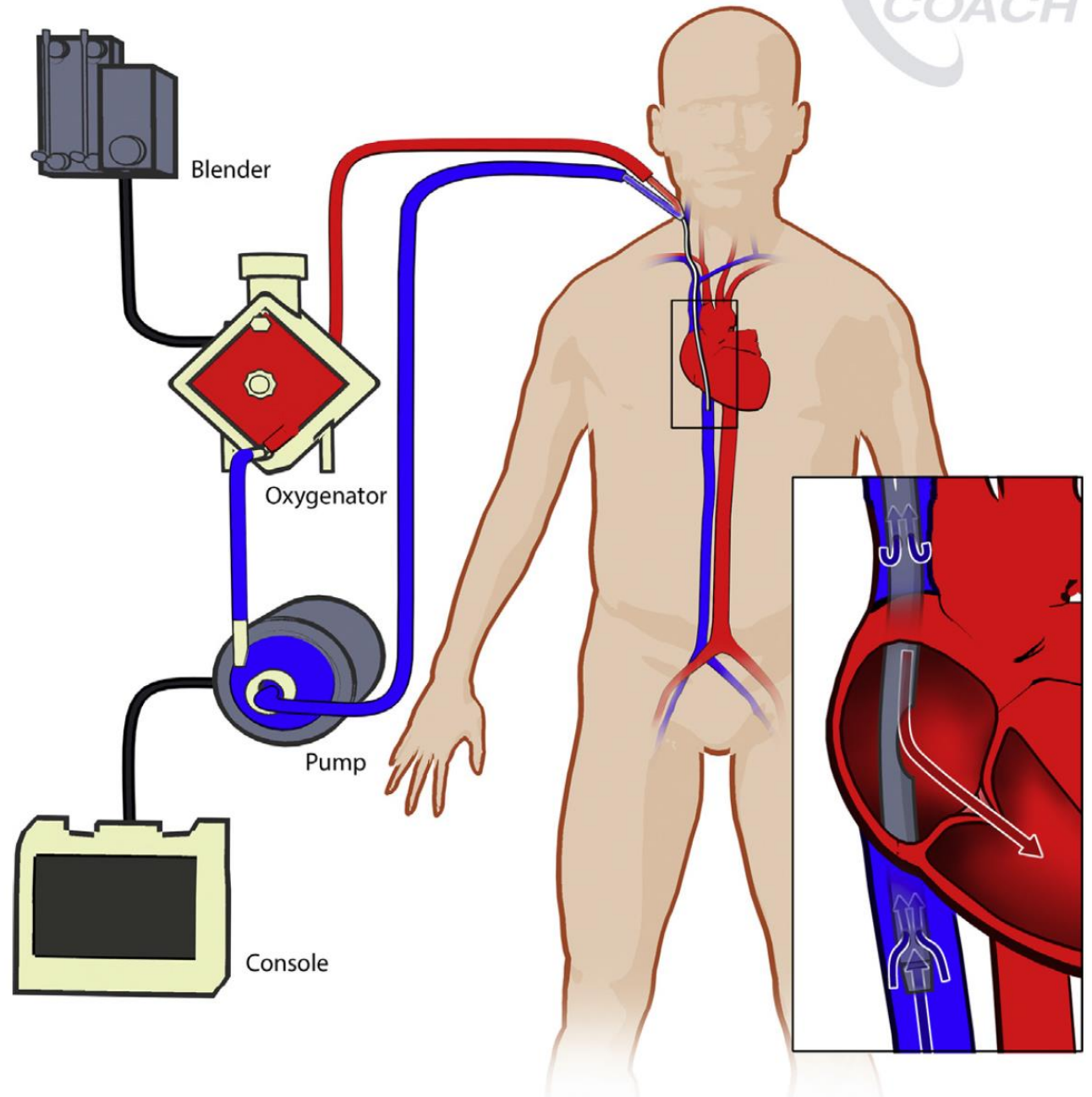
VV ECMO

- Only lung support



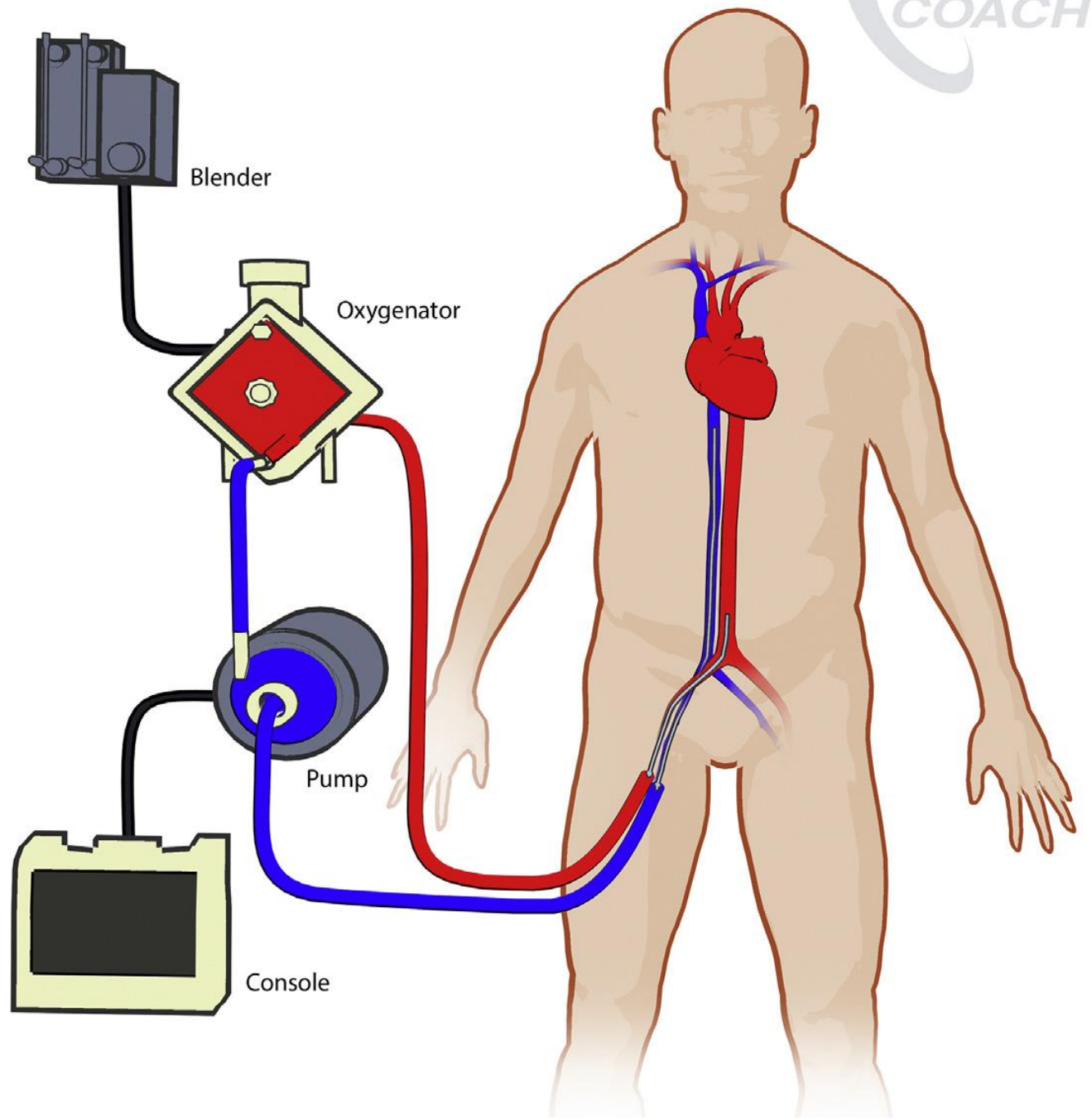
VV ECMO

- **Only lung support**

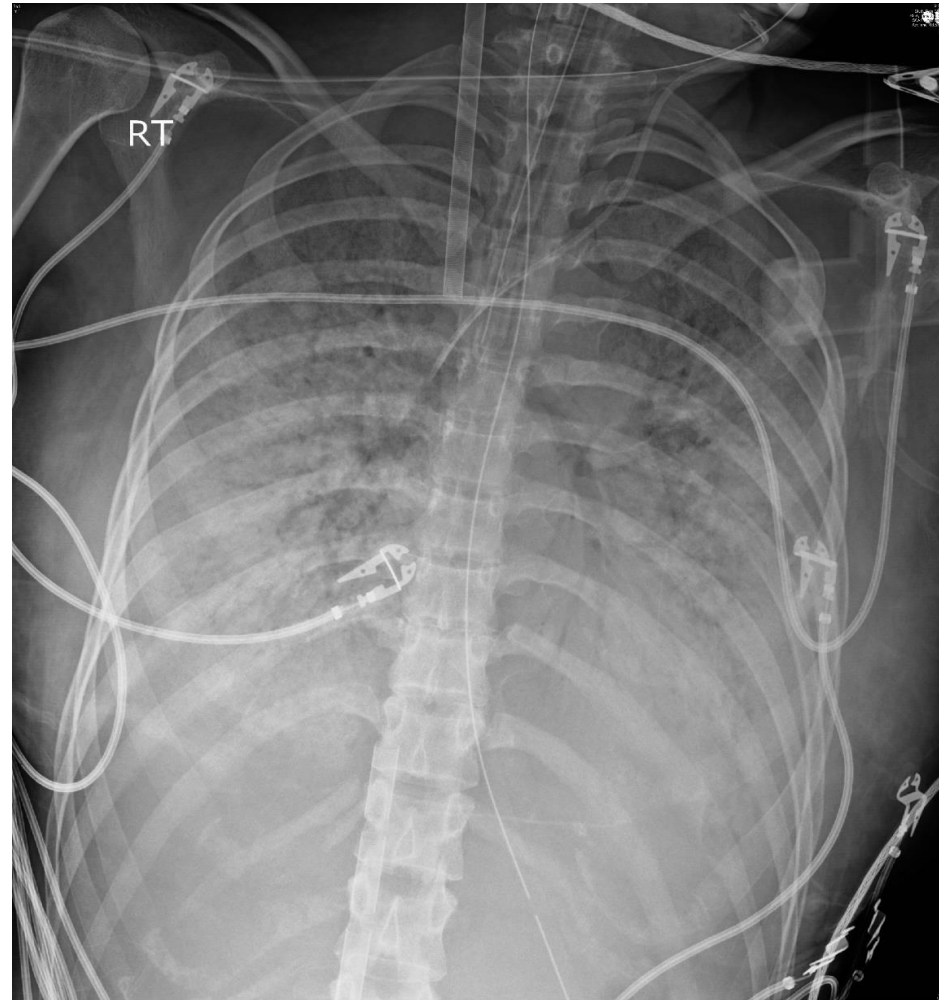


VA ECMO

- Heart AND lung support



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



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

JOSEPH E. TONNA¹, MD, MS,*† DARRYL ABRAMS, MD,‡ DANIEL BRODIE¹, MD‡ JOHN C. GREENWOOD¹, MD,§ JOSE ALFONSO RUBIO MATEO-SIDRON, MD,¶ ASAD USMAN¹, 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 ($\text{PaO}_2/\text{FiO}_2 < 80 \text{ mm Hg}$)*, after optimal medical management, including, in the absence of contraindications, a trial of prone positioning.
- 2) Hypercapnic respiratory failure ($\text{pH} < 7.25$), despite optimal conventional mechanical ventilation (respiratory rate 35 bpm and plateau pressure [P_{plat}] $\leq 30 \text{ cm H}_2\text{O}$).
- 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)



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 $P_{plat} > 30 \text{ cm H}_2\text{O}$ and $F_{iO_2} > 90\%$
-

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 ₂ O PEEP < 10 cm H ₂ O 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 _{IO₂} 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 Paco 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



Indications for VV-ECMO:

1. Severe hypoxemic respiratory failure
 - a. $\text{PaO}_2:\text{FiO}_2$ 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. $\text{pH} < 7.2$ and $\text{PaCO}_2 > 80$ mm Hg for more than 3 hours
3. Inability to maintain lung protective ventilation for ARDS patients
 - a. P_{plat} > 30 cm H_2O 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 H₂O)
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?



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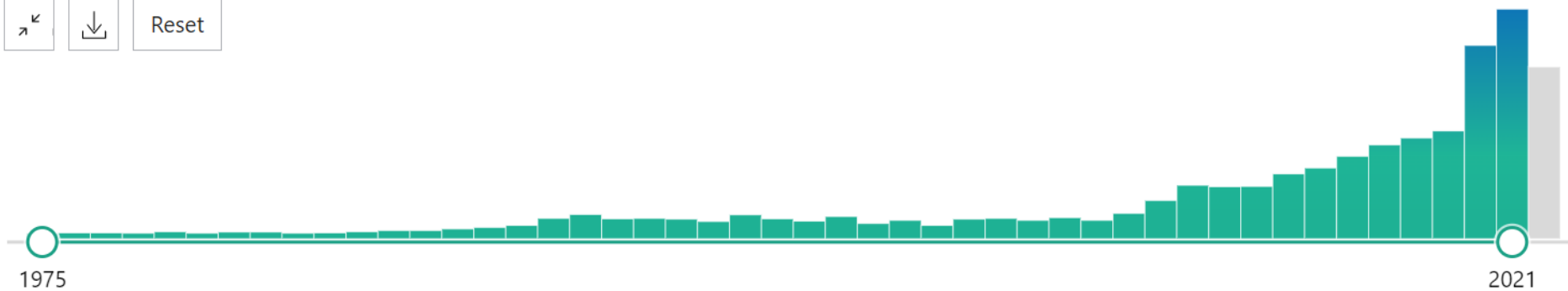
RESULTS BY YEAR

3,298 results

Page 1 of 330



Reset



2009
Influenza A
(H1N1)

2020
COVID-19

ECLS Registry Report

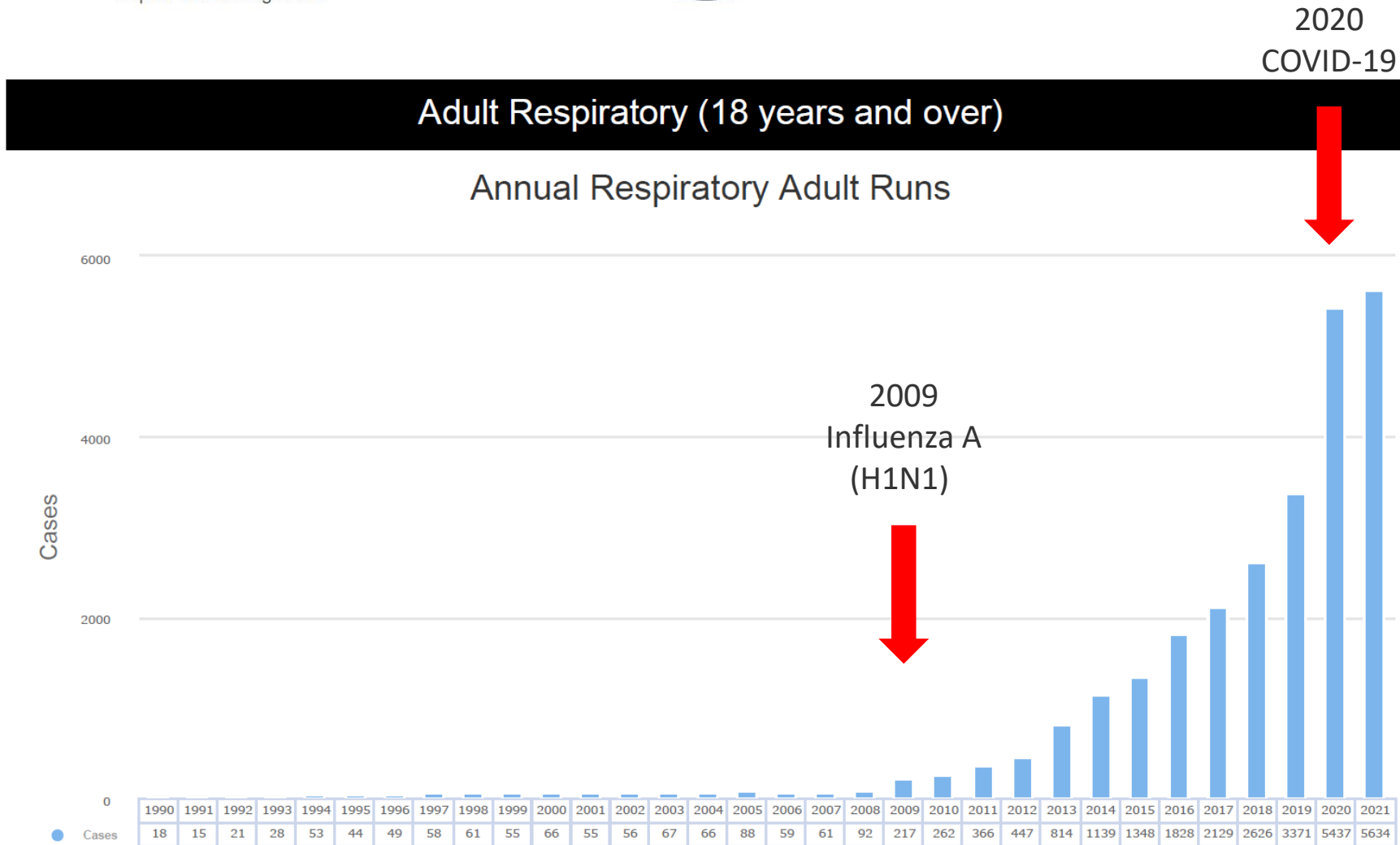
United States Summary

April, 2022

Report data through 2021



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



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 H₂O or FIO₂ $> 80\%$ for 7 days
- Signs of intracranial bleeding
- Any other contraindication to limited heparinisation
- Any contraindication to continuation of active treatment

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

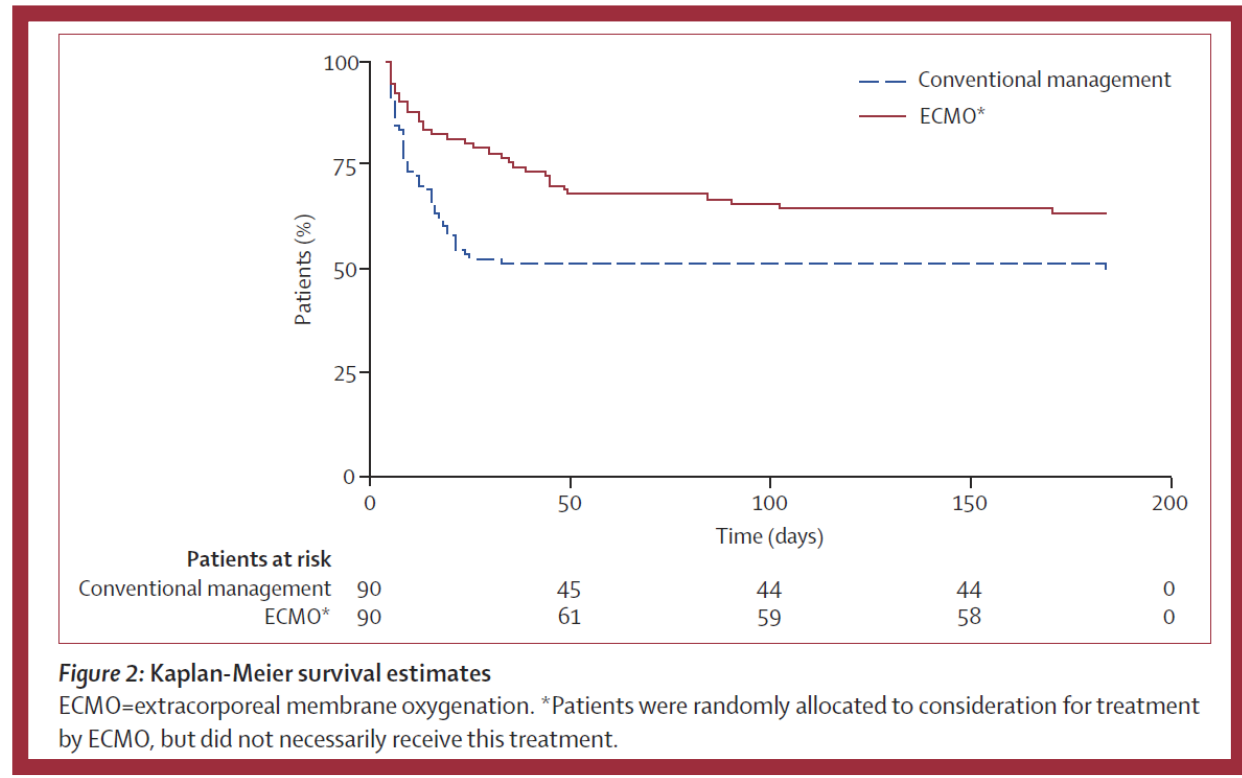


Figure 2: Kaplan-Meier survival estimates
ECMO=extracorporeal membrane oxygenation. *Patients were randomly allocated to consideration for treatment by ECMO, but did not necessarily receive this treatment.

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ESTABLISHED IN 1812

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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 HIT
- 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

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

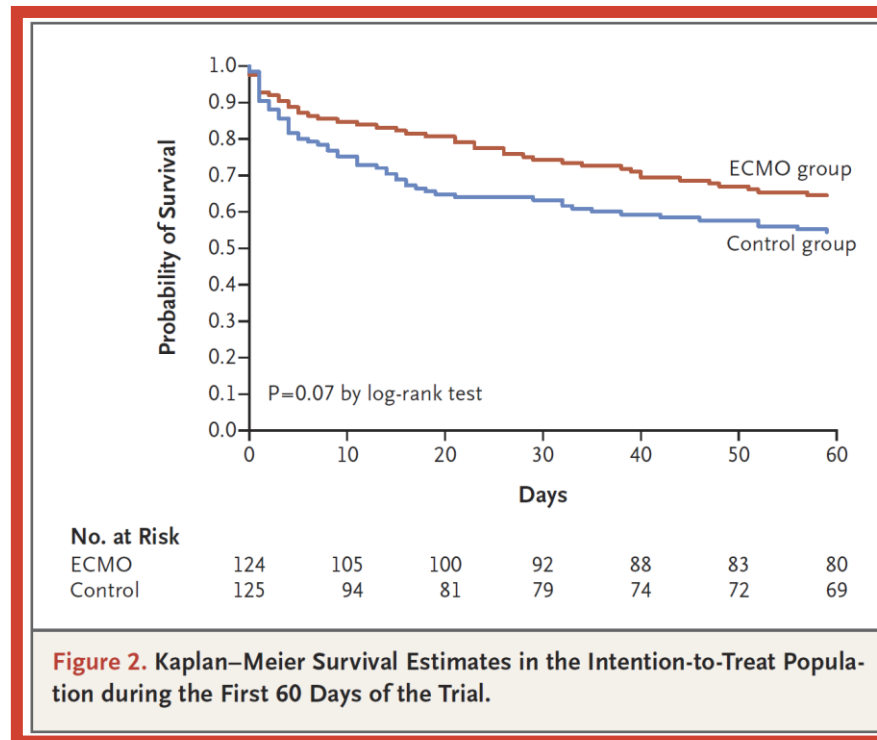


Figure 2. Kaplan–Meier Survival Estimates in the Intention-to-Treat Population during the First 60 Days of the Trial.

ORIGINAL

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



Alain Combes^{1,2*} , Giles J. Peek³, David Hajage⁴, Pollyanna Hardy⁵, Darryl Abrams^{6,7}, Matthieu Schmidt^{1,2}, Agnès Dechartres⁴ and Diana Elbourne⁸

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

Meta-analysis - Results

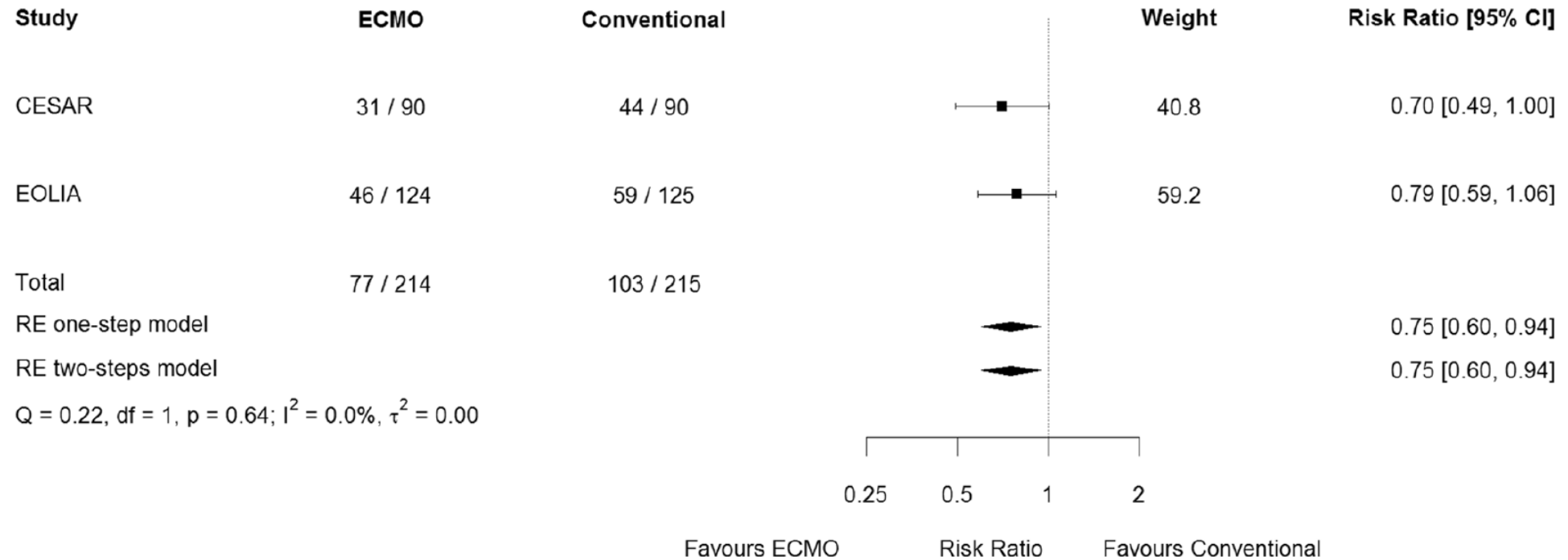
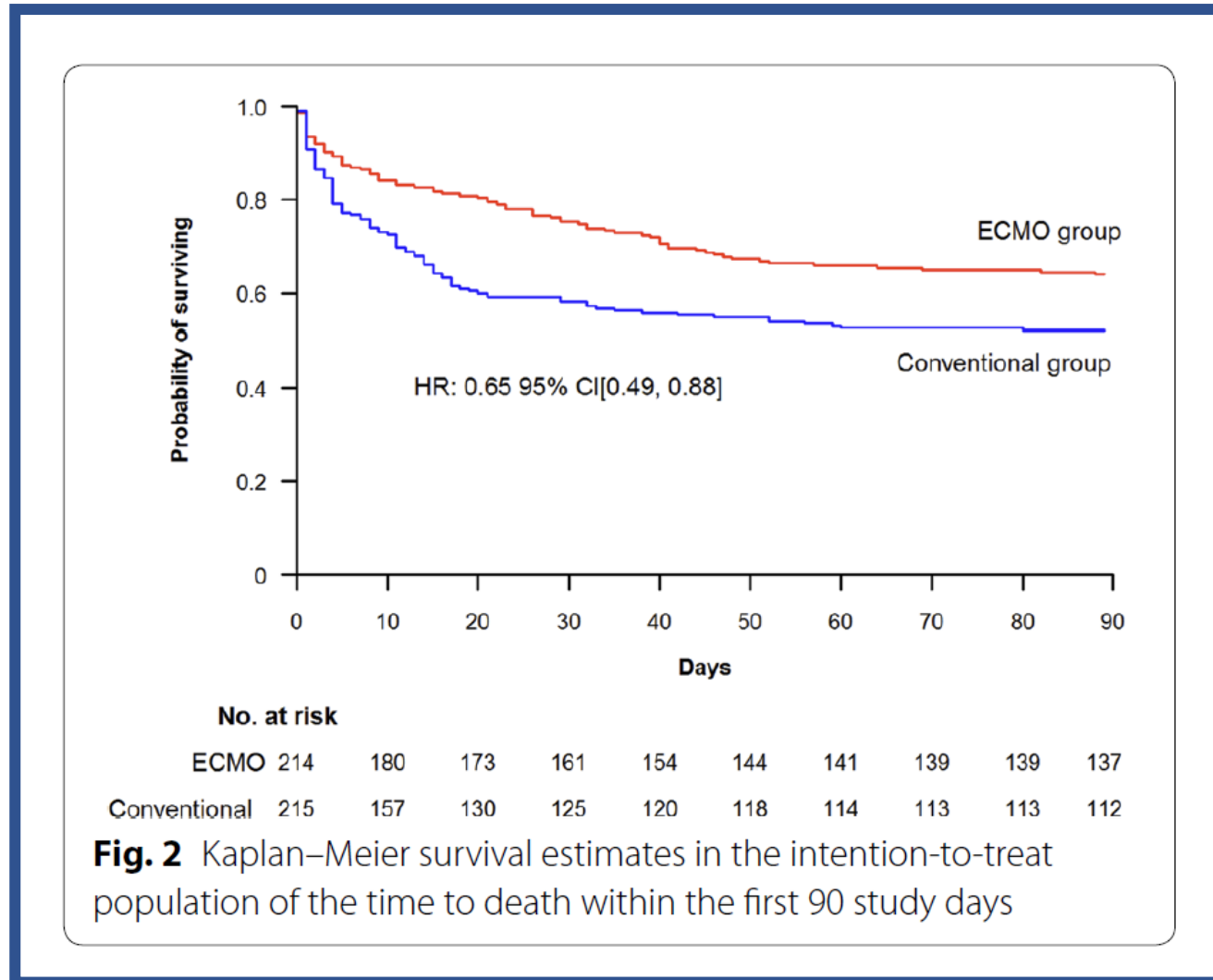


Fig. 1 Forest plot of 90-day mortality in the intention-to-treat population

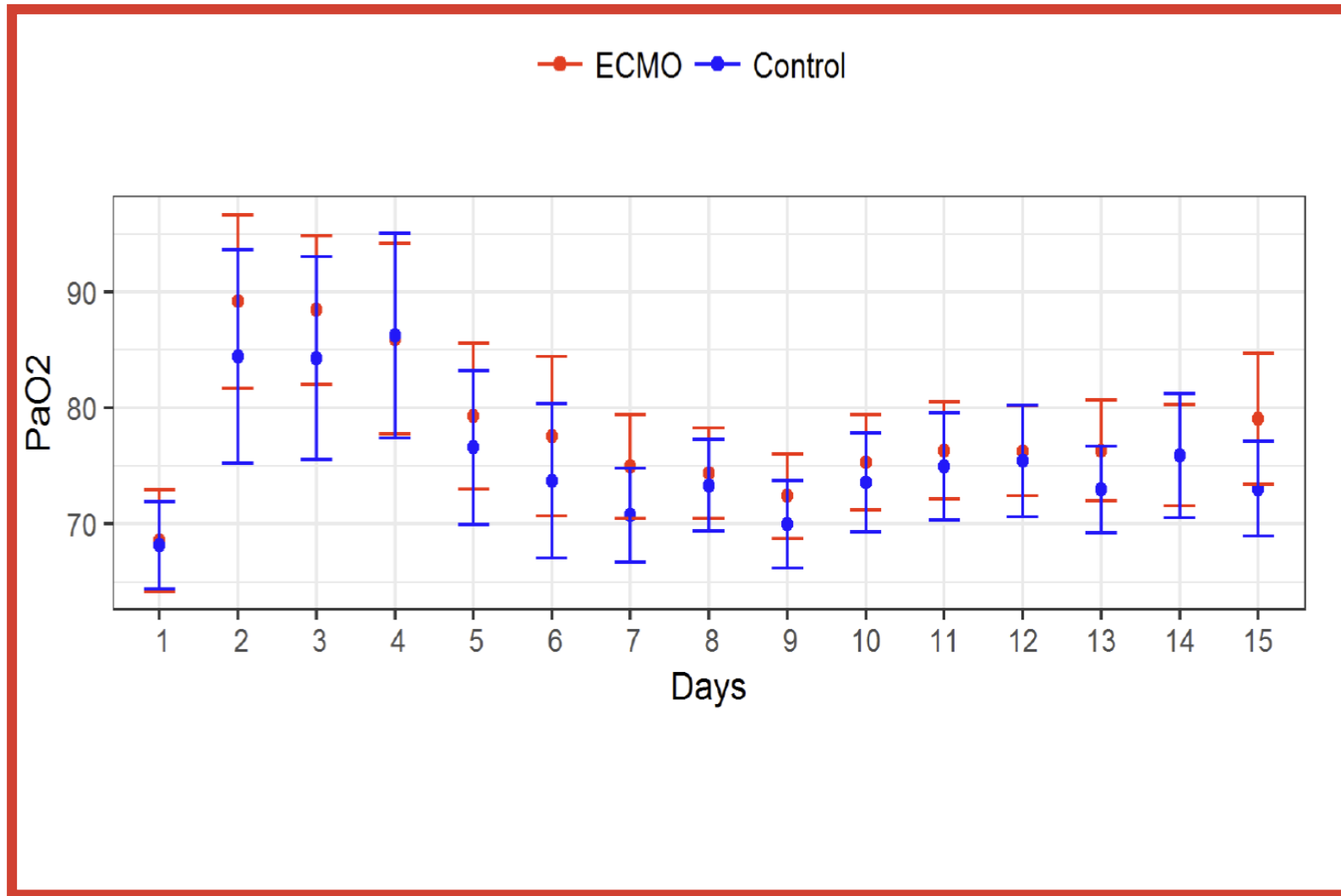
Meta-analysis - Results



How does VV-ECMO help in ARDS??

- Maintain oxygen delivery
- Remove CO₂
- **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

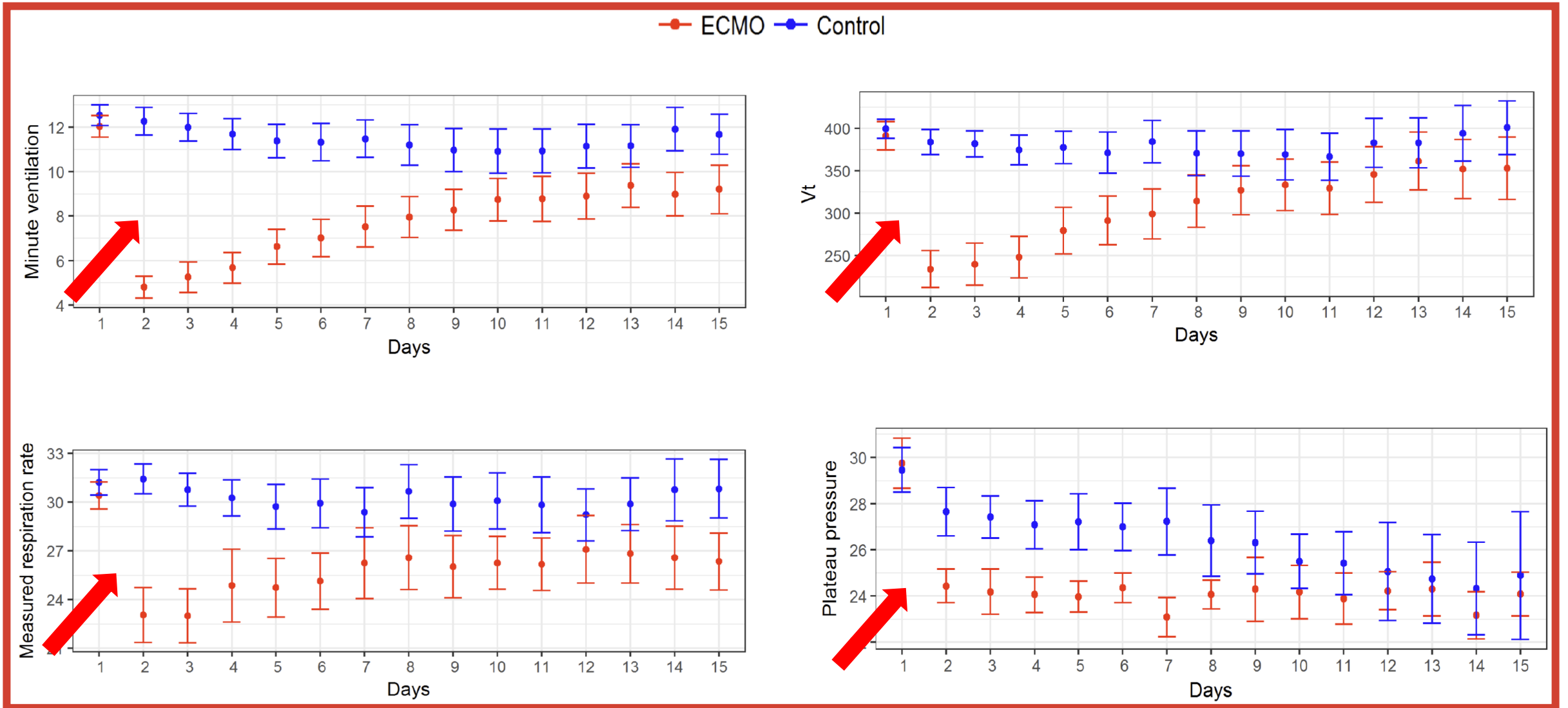


Table 1. Ventilatory Parameters before and after Extracorporeal Life Support Initiation in Studies of ECLS for Acute Respiratory Distress Syndrome

	Retrospective Studies						Prospective Studies							
	Schmidt <i>et al.</i> (54)		Marhong <i>et al.</i> (55)		Serpa Neto <i>et al.</i> (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
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 ₂ O	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 ₂ O	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 ₂ O	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 ₂ O	23.2	19.9	22.7	19.4	26.8	23.2	34.4	32.2	25.0	20.1	—	—	24	19
F _I O 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 _I O ₂ , mm Hg	67.0	—	61.0	—	72.6	152.5	152	154.5	73	—	168	168	71	—
Q _E , L/min	—	4.5	—	3.0	—	4.3	—	1.3	—	5.0	—	0.4	—	4.2

Recommendations from International ECMO Network

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

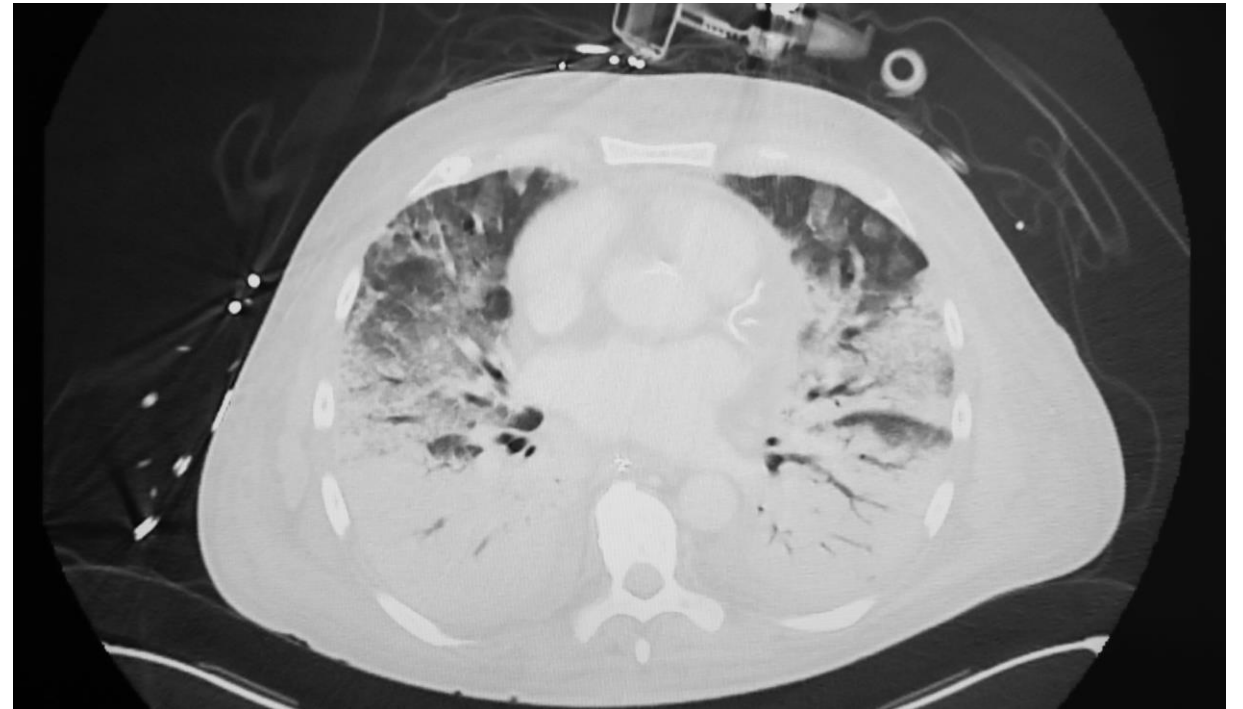
Parameter	Target	Notes
Pplat*	≤24 cm H ₂ O; may choose to go lower if feasible	
Driving pressure*	≤14 cm H ₂ O	
V _T	Adjust for goal Pplat	Typically ≤4 ml/kg PBW, often much lower
Respiratory rate [†]	≤10 breaths/min	Typically only achieved when sedation, with or without NMBA, is being used. Consider increased sweep flow to achieve, when appropriate
PEEP*	≥10 cm H ₂ O	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 SaO ₂

Table 3. Recommended Mechanical Ventilation Settings During Adult VV ECMO

Parameter	Acceptable Range	Recommendation	Comments
Inspiratory plateau pressure (P_{plat})	≤ 30 cm H ₂ O	< 25 cm H ₂ O	Further reductions in P_{plat} below 20 cm H ₂ O may be associated with less VILI and improved patient outcomes ²⁴⁻²⁶
PEEP	10–24 cm H ₂ O	≥ 10 cm H ₂ O	Reductions in P_{plat} and tidal volume may lead to atelectasis without sufficient PEEP; PEEP can be set according to various evidence-based methods (e.g., ARDSNet PEEP- F_iO_2 table or Express trial strategy) while maintaining the P_{plat} limit ²⁷
RR	4–30 breaths/min	4–15 breaths/min (set RR) or spontaneous breathing	CO ₂ elimination is being provided primarily by VV ECMO, reducing the need for high minute ventilation (which may be associated with more VILI)
F_iO_2	30–50%	As low as possible to maintain saturations	Oxygenation is being provided primarily by VV ECMO, reducing the need for high F_iO_2 from the ventilator unless required to maintain adequate oxygenation

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
- Close monitoring for ECMO complications



Sedation/Analgesia

- **The guiding principle during VV-ECMO management is minimizing iatrogenic lung injury.**
- First 24 hours patient usually heavily sedated and paralyzed as a remnant of prior strategy pre-ECMO cannulation
- Next 24 – 48 hours discontinue paralytics, and allow patient to awaken
- Goal is to have patient on minimal sedation that allows patient to tolerate ECMO and rest ventilator settings, until recovery
- If patient is uncomfortable and having significant ventilator dyssynchrony then need to heavily sedate and or even paralyze
 - Harmful breathing pattern will further injure the lung
 - Can also interfere with ECMO flow, chugging, etc.



Volume management

- Minimize volume
- “Dry lungs are happy lungs”
- Despite external appearance patients can have excessive intravascular lung water
- Fluid creep is real ...
 - Leads to delayed recovery -> non-recovery
 - Leads to RV failure



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Comparison of Two Fluid-Management Strategies in Acute Lung Injury

The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network*

Sit back and relax

- Monitor for complications
- Await lung recovery



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

In the era of COVID

- Our BWH experience:
- Median duration 24 (11 – 39) days
- Longest run 90+ days

ECLS Registry Report

International Summary

April, 2021

Report data through 2020

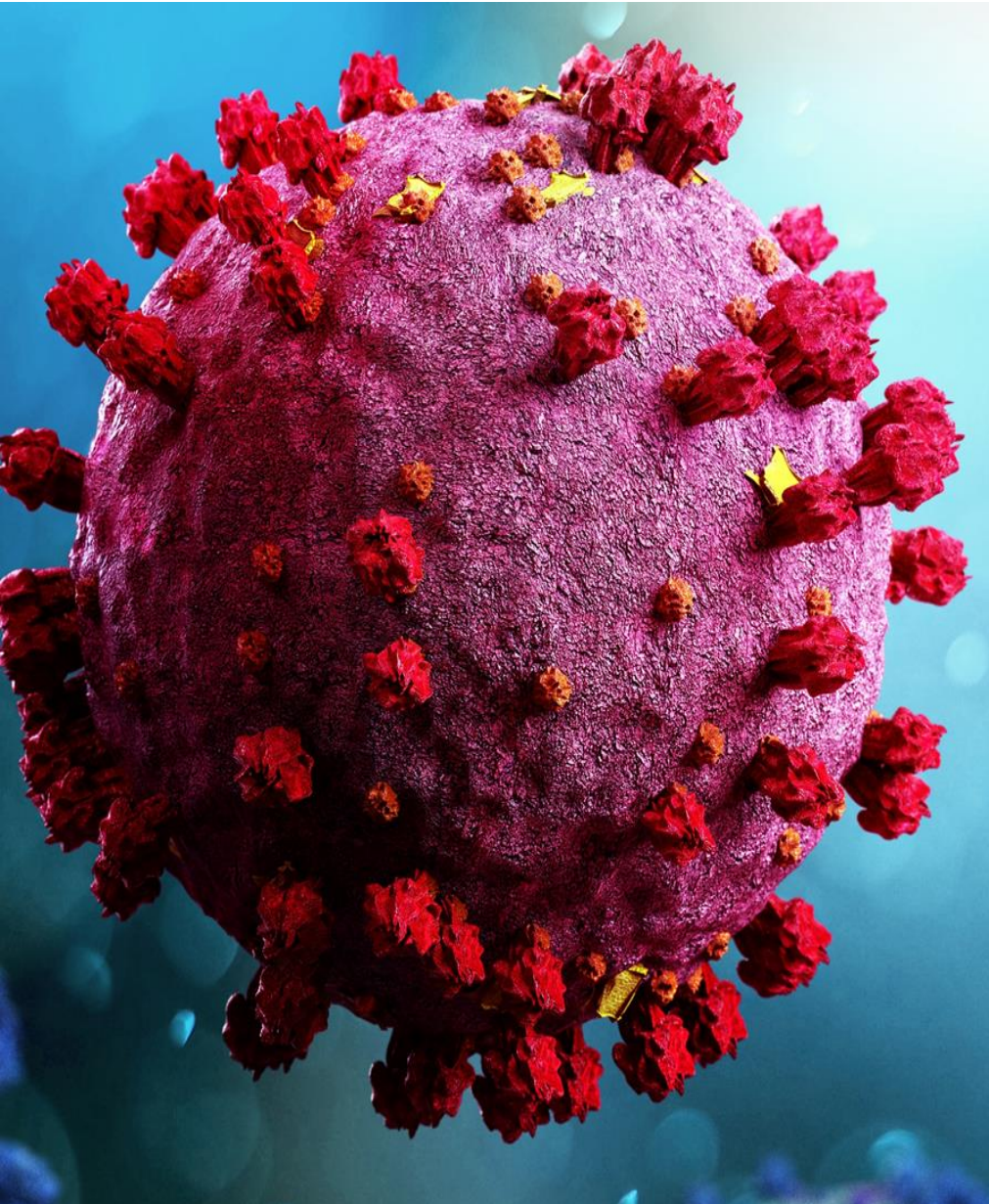


Extracorporeal Life Support Organization
3001 Miller Rd
Ann Arbor, MI 48103 USA

Adult Respiratory Complications from 2016 to 2020

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%

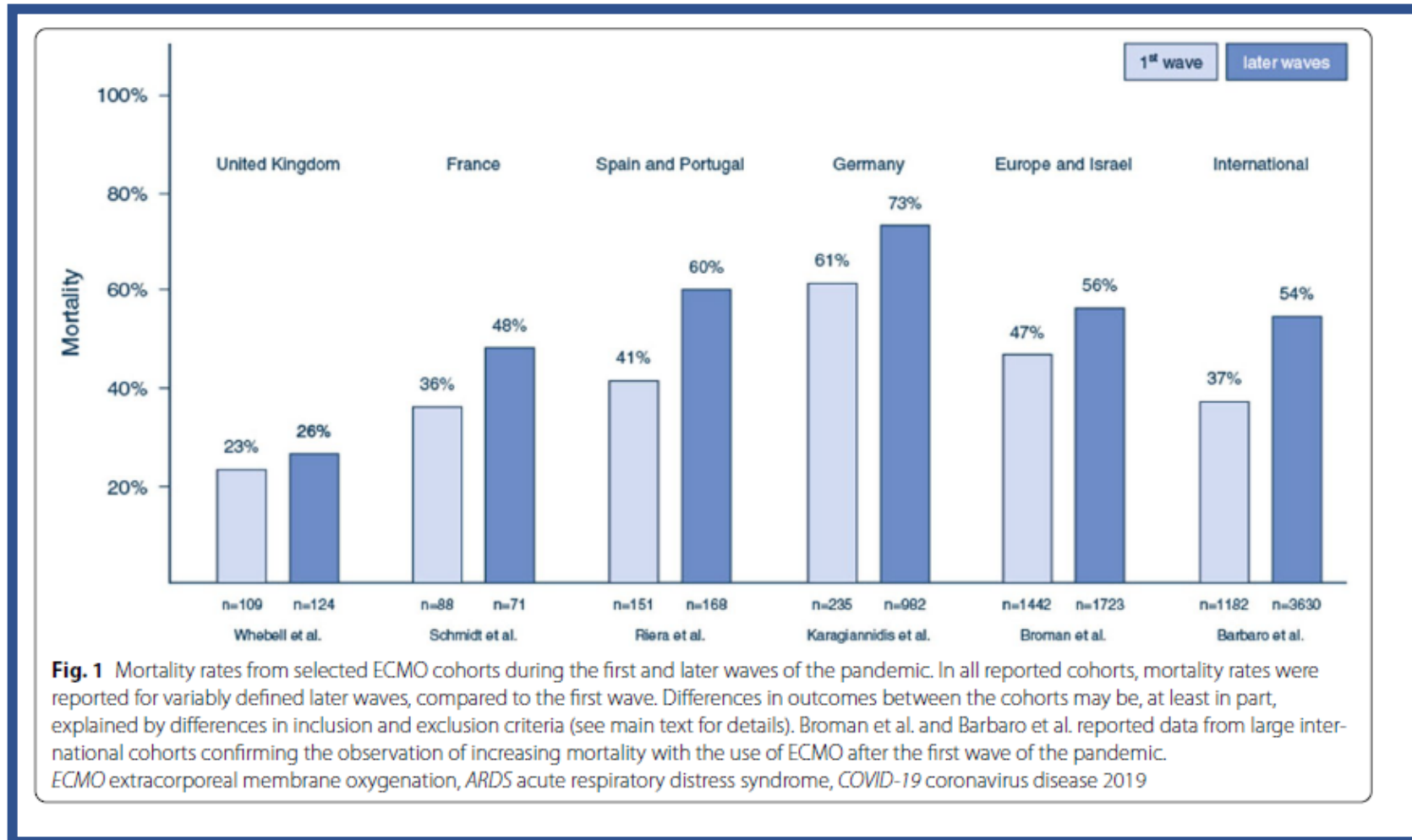
Renal: Renal Replacement Therapy Required	26.9%
Cardiovascular: Inotropes on ECLS	6.9%
Cardiovascular: CPR required	4.7%
Cardiovascular: Cardiac arrhythmia	8.5%
Cardiovascular: Tamponade (blood) 218 1% 98 45%	1%
Pulmonary: Pneumothorax requiring treatment	7%
Pulmonary: Pulmonary hemorrhage	3.4%
Infectious: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



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]

Mortality rate differences between first and later waves of COVID-19





- 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 pCO_2
 - 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 velettri, and proning.

Pre-cannulation ventilator settings: ACVC: Vt: 340 (6 cc/kg/IBW), RR: 28 PEEP 18 cm H₂O, FIO₂ 100%. Pplat: 30 cm H₂O

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 H₂O, FIO₂ 30%. Pplat: 24 cm H₂O
- c) CPAP: 15 cm H₂O, 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

Answer

- E is correct. The goal after initiating VV-ECMO for ARDS is to rest the lungs. There are no randomized control trials demonstrating the best post-ECMO ventilator settings. Expert opinion and guidelines recommend “ultra-lung protection.” These are ventilator settings that are thought to be more protective than standard lung protective settings for ARDS. The mode can vary, but basic goals are to achieve the following: low tidal volumes - V_t (target 4 cc/kg/IBW), low plateau pressures - P_{plat} (target < 25 cm H₂O), low FIO₂ – lowest possible possible (ideally < 60%), low respiratory rate < 10, low driving pressure < 15 cm H₂O. All of the above answers achieve these goals.