

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

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**Disclaimer:** The use of venovenous extracorporeal membrane oxygenation (VV ECMO) in adults has rapidly increased worldwide. This ELSO guideline is intended to be a practical guide to patient selection, initiation, cannulation, management, and weaning of VV ECMO for adult respiratory failure. This is a consensus document which has been updated from the previous version to provide guidance to the clinician.

**Key Words:** venovenous ECMO, extracorporeal life support, ventilatory management, mechanical ventilation, circuit management, fluid management, cannulation/decannulation

## INTRODUCTION

The use of venovenous extracorporeal membrane oxygenation (VV ECMO) among adults is rapidly increasing worldwide. By 2020, the Extracorporeal Life Support Organization (ELSO) Registry had recorded >24,000 cases of adult respiratory ECMO use among 282 centers internationally. Venovenous extracorporeal membrane oxygenation is a therapy in the management of respiratory failure in multiple guidelines. Extracorporeal Life

Support Organization provides guidelines to inform and guide the initiation, use, management, and weaning of VV ECMO for adult patients with respiratory failure.

In this statement, we provide recommendations for the clinical management of adult patients supported with VV ECMO. Although these recommendations were not developed using a formal, reproducible methodology, we have reviewed English-language publications in PubMed, where available, in developing the guidance provided herein. As this is the fifth revision of these adult respiratory VV ECMO guidelines, we expect that it will be revised at regular intervals as new information, devices, treatments, and techniques become available. As with all guidelines, this statement should not replace the medical judgment and the multidisciplinary decision to establish and manage a patient's ECMO support strategy. A number of important management principles and recommendations are made in other ELSO guidelines, including: circuit components, patient selection, patient and circuit management, patient sedation, and nutrition. This document contains numerous additional literature references, organized by topic, found in Supplemental Digital Content 1, <http://links.lww.com/ASAIO/A626>.

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Submitted for consideration January 2021; accepted for publication in revised form January 2021.

Disclosure: Dr. Tonna: Chair, Scientific Oversight Committee, ELSO Registry. Dr. Abrams: At-large member, ELSO Steering Committee. Dr. Brodie: President-elect, Extracorporeal Life Support Organization. Dr. Fan: Chair, Research Committee, ELSO. The other authors have no conflicts of interest to report.

Dr. Tonna was supported by a career development award (K23HL141596) from the National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health (NIH), and reports consulting for Philips Healthcare and LivaNova, outside of the submitted work. This study was also supported, in part, by the University of Utah Study Design and Biostatistics Center, with funding in part from the National Center for Research Resources and the National Center for Advancing Translational Sciences, NIH, through Grant 5UL1TR001067-02 (formerly

8UL1TR000105 and UL1RR025764). Dr. Greenwood was supported by The Abramson Family Emergency Medicine Clinical and Research Fund for Resuscitation & Critical Care. Dr. Fan is supported by a New Investigator Award from the Canadian Institutes of Health Research, reports personal fees from Abbott, ALung Technologies, and MC3 Cardiopulmonary outside of the submitted work. Dr. Brodie received research support from ALung Technologies, he was previously on their medical advisory board. Dr. Brodie has been on the medical advisory boards for Baxter, Abiomed, Xenios and Hemovent. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH. None of the funding sources were involved in the design or conduct of the study, collection, management, analysis or interpretation of the data, or preparation, review or approval of the manuscript.

J.E.T. had full access to all the sections in the guideline and takes responsibility for the integrity of the submission as a whole, from inception to published article. J.E.T., D.A., and E.F. conceived guideline design; all authors drafted the work; all authors revised the article for important intellectual content, had final approval of the work to be published, and agree to be accountable for all aspects of the work.

This version replaces ELSO Guidelines for Adult Respiratory Failure Version 1.4 from August 2017.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text, and links to the digital files are provided in the HTML and PDF versions of this article on the journal's Web site ([www.asaiojournal.com](http://www.asaiojournal.com)).

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DOI: 10.1097/MAT.0000000000001432

## PATIENT SELECTION

When assessing adults with acute severe respiratory failure for ECMO, it is important to establish that the cause of respiratory failure is potentially reversible, refractory to conventional treatments, and without formal contraindications for the initiation of this support. In the case of irreversible disease (e.g., end-stage pulmonary disease), the patients may be suitable candidates for ECMO, if it is as a bridge to lung transplant.

## INDICATIONS AND CONTRAINDICATIONS

Venovenous extracorporeal membrane oxygenation should be considered in patients with severe, acute, reversible respiratory failure that are refractory to optimal medical management. The physiologic rationale for use of VV ECMO includes: 1) increasing systemic oxygenation and CO<sub>2</sub> removal (ventilation) and 2) avoiding the need for injurious mechanical ventilation. In response to the most recent data and ECMO trials, at minimum, we now recommend patients with severe acute respiratory distress syndrome (ARDS) and refractory hypoxemia (PaO<sub>2</sub>/FiO<sub>2</sub> < 80 mm of mercury [mm Hg]), or severe hypercapnic respiratory failure (pH < 7.25 with a PaCO<sub>2</sub> ≥ 60 mm Hg), should be considered for ECMO after optimal conventional management (including, in the absence of contraindications, a trial of prone positioning); a more complete list of indications is found in **Table 1**. As it is also known that increasing duration of mechanical ventilation before extracorporeal life support (ECMO) is associated with worsening mortality after ECMO, optimal medical management should be rapidly and maximally implemented, not delaying ECMO when indicated.

Currently, the only absolute contraindication for the start of ECMO is anticipated nonrecovery without a plan for viable decannulation (**Table 1**). This situation could be due to the disease process itself or to multiorgan failure, within the context of no options for organ transplantation. Sometimes it is

unknown whether the patient is a transplant candidate at the point when a decision to initiate ECMO needs to be made; in these situations, ECMO can be initiated under the indication of “bridge to decision.” Importantly, we advise that this *only* occur in the context of an ongoing multidisciplinary discussion regarding “ECMO decannulation” options, and with a clear discussion regarding the duration of ECMO support being offered.

### *Transfer for Extracorporeal Membrane Oxygenation*

At centers not capable of initiating ECMO, intentional planning for early transfer should occur in patients in whom the provider feels ECMO may be of benefit. In this assessment, the RESP and Murray Scores are useful. The RESP score provides predicted survival once on ECMO. The Murray Score provides estimated mortality without. If ECMO is to be a consideration, and transfer would be necessary, it should be done early.

## MODE OF SUPPORT

### *Indications/Rationale*

**Oxygen Delivery.** It is fundamental to understand that ECMO provides a variable quantity of oxygen delivery to the body. This quantity of oxygen is equal to the product of ECMO circuit flow (in liters per minute [LPM]) and outlet minus inlet oxygen content of the blood (CaO<sub>2</sub> = [hemoglobin (in g/L)] × 1.39 × [SaO<sub>2</sub>] + (0.0034 × [PaO<sub>2</sub> (in mm Hg)]). After cannulation for ECMO, this quantity of oxygen is added to total body circulation as oxygen supplied from the circuit. The amount required for total support at rest is 120 ml/m<sup>2</sup>/minute.

Systemic oxygen delivery is the arterial O<sub>2</sub> content times flow. The normal systemic oxygen delivery is 600 ml/m<sup>2</sup>/minute. Systemic oxygen delivery as low as 300 ml/m<sup>2</sup>/minute is sufficient to maintain metabolism at rest. In VV ECMO, the circuit should be designed to provide at least 240 ml/m<sup>2</sup>/

**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<sub>2</sub>/FiO<sub>2</sub> < 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<sub>plat</sub>] ≤ 30 cm H<sub>2</sub>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)

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<sub>plat</sub> > 30 cm H<sub>2</sub>O and F<sub>I</sub>O<sub>2</sub> > 90%

\*Clinical trials have utilized several cutoff points for the indication of the start of VV ECMO: PaO<sub>2</sub>/FiO<sub>2</sub> < 80 mm Hg [EOLIA Trial<sup>1</sup>], Murray Score >3 [CESAR Trial<sup>2</sup>], without strong data indicating the superiority of any one.

minute of oxygen supply and 300 ml/m<sup>2</sup>/minute of systemic oxygen delivery. Based on these equations, blood flow rates and hemoglobin should be managed to achieve these oxygen delivery goals. As an example, an 80 kg adult with a hemoglobin level of 12 g/dl would require an ECMO flow of about 4 L/minute to reach those goals. The ECMO flow is adjusted down when the native lung is recovering, and increased when the metabolic rate increases in the absence of native lung function.

In VV ECMO, only a portion of the venous return is directed to the circuit, oxygenated to a saturation of 100% and returned to the right atrium. The remainder of the venous return, with a typical saturation of 60–80%, continues through the RV without further oxygenation. These flows mix in the right atrium and ventricle and proceed through the lungs into the systemic circulation. The resultant saturation of the patient's arterial blood is the result of mixing these flows and oxygen contents.<sup>3</sup> Given this setting, the arterial saturation will always be less than 100%, and is typically 80–90%. This physiologic principle becomes relevant during VV ECMO because the ECMO flow must be adjusted relative to the total venous return (the cardiac output) to achieve the desired arterial content and, therefore, the systemic oxygen delivery. In clinical practice, an ECMO flow that is less than 60% of total CO is frequently associated with a SaO<sub>2</sub> <90% in the context of ARDS.<sup>4</sup> A comprehensive discussion of oxygenation is presented in Chapter 4 (“The Physiology of Extracorporeal Life Support”) in the fifth Edition of the *ELSO Red Book*.

**Recirculation.** Recirculation refers to post oxygenator blood returning to the prepump drainage cannula. Recirculation decreases the amount of oxygenated blood being delivered to the patient and is more common with single lumen dual cannulation in the femoral and IJ positions. It is identified by increased venous saturation or brightening of the color of the drainage cannula blood, indicating oxygenation. Recirculation should be treated if this is noticed and should be ruled out in cases of insufficient systemic oxygen delivery. Recirculation should also be suspected with a paradoxical decrease in systemic saturation with increasing VV ECMO flow. In this case, although the total flow may have increased, the recirculation fraction has also increased, leading to a net decrease the amount of oxygenated blood returning to the body from the ECMO circuit.

**Hypoxemia.** Hypoxemia on ECMO can have many causes. Increased metabolic demand will increase oxygen utilization and decrease systemic saturation. Common causes of elevated oxygen utilization (VO<sub>2</sub>), including sepsis, fever, agitation, movement, and shivering should be considered. Hypoxemia can also be caused by recirculation (see *Recirculation*). After all other causes of hypoxemia and their therapies have been tried, mild hypothermia can be employed to decrease oxygen utilization; finally, beta-blockade has been used to decrease the amount of blood flow bypassing the ECMO circuit through the native circulation, but also decreases oxygen delivery with the overall effect being difficult to predict for an individual patient (see *Fluid Management*).<sup>5</sup>

Incorporating recirculation, the body's saturation (which results from the ratio of ECMO flow to total body cardiac output) is calculated as  $([\text{total ECMO flow}] - [\text{recirculation flow}]) / \text{CO}$ . The ratio of ECMO flow to patient cardiac output will impact the overall systemic saturation. Other relevant factors in the estimation of adequate oxygenation are the ratio of oxygen delivery to oxygen utilization (DO<sub>2</sub>/VO<sub>2</sub>). As the oxygen

delivered by VV ECMO is directly proportional to circuit flow returning to the body, in cases of inadequate tissue oxygen delivery, VV ECMO flows can be increased in an attempt to achieve a normal DO<sub>2</sub>/VO<sub>2</sub> ratio of 5:1, but certainly above the critical threshold of supply dependence which occurs near a ratio of 2:1.

**CO<sub>2</sub> Removal.** Gas exchange via the oxygenator accomplishes CO<sub>2</sub> removal from the blood and is controlled by the “sweep gas” inflow rate to the oxygenator, for a given oxygenator membrane size; CO<sub>2</sub> removal increases with increasing sweep gas flow. Sweep gas typically ranges from 1 to 9+ LPM, and for VV is typically 100% O<sub>2</sub>. Sweep gas very effectively lowers P<sub>a</sub>CO<sub>2</sub>. Upon initiation of ECMO, it is reasonable to start sweep at 2 LPM, and blood flow at 2 LPM, and titrate frequently to ensure a controlled slow modulation of P<sub>a</sub>CO<sub>2</sub> and pH. A rapid decrease in CO<sub>2</sub> is associated with neurologic injury.

### Cannulation

**General Principles.** Venovenous extracorporeal membrane oxygenation flows are typically limited by cannula size to 5–6 LPM. In patients with concomitant high cardiac output, ECMO drainage will not be able to keep up with the native cardiac output. As flow limitation is often because of insufficient uptake of venous blood into the ECMO circuit, this may improve with the use of multistage (multihole) drainage cannula or with placement of additional venous drainage cannula.<sup>6</sup>

**Basic Configuration.** Cannulation for VV ECMO involves removal of blood from the venous system of the patient (termed a *drainage cannula*), passing that blood through a centrifugal pump then through a membrane oxygenator for gas exchange, followed by return of the blood to the venous system (termed a *return cannula*). This *in series* cannulation strategy (as opposed to the *in parallel* strategy of VA ECMO) underlies some fundamental characteristics of VV ECMO compared with VA ECMO that should be understood. For VV ECMO:

- 1) Gas flow to the oxygenator can be completely turned off without creating a venous to arterial shunt in the patient.
- 2) Increasing circuit flow will *not* improve patient blood pressure.
- 3) Increasing circuit flow will increase the ratio of [blood entering the circuit: total cardiac output], and therefore total oxygen content in the patient, assuming no recirculation.

Although uncommon, VV ECMO can additionally be accomplished through hybrid configurations, such as VVA, which are discussed elsewhere.

**Cannula Size.** To select the correct cannula size, first priority should be given to titrating to estimated patient cardiac output needs. For example, in a 180 cm tall male, a 25F drainage cannula will often be sufficient, although in cases of severe respiratory failure, a larger (~29F) cannula will provide better flow and therefore oxygenation. Within a given cannula, increasing pump speed results in increasing flow, although at higher pressure. Assuming adequate filling, larger cannulas have greater flow at lower pump speed. An appropriately sized cannula will allow sufficient ECMO flow at a below-maximum speed for the given pump. The venous drainage cannula (or bicaval dual lumen cannula) should be maximized according to the



**Table 2. Three Major Cannulation Strategies Which Dictate Cannula Selection for Venovenous Extracorporeal Membrane Oxygenation**

Type	Return Location	Drainage Location(s)	Advantages	Disadvantages
Single-lumen dual cannula	Right atrium <i>via</i> internal jugular vein	Inferior vena cava <i>via</i> femoral vein		Limited patient mobility
Bicaval dual-lumen single cannula	Tricuspid valve <i>via</i> the right internal jugular vein.	superior vena cava; cannula extends across the right atrium and drains from within the inferior vena cava	Potentially facilitates patient mobility	Insertion more difficult, cannula movement, cerebral venous congestion, air embolism upon removal, possibly higher ICH with larger diameter catheters, <sup>7</sup> may be more difficult to achieve higher flows
Bifemoral venous cannulation	Right atrium <i>via</i> femoral vein	Inferior vena cava <i>via</i> femoral vein		Limited patient mobility

ICH, intracranial hemorrhage.

potential physiologic needs of the patient due to the fact that future patient physiology will change throughout the ECMO run. Importantly, oversized cannulas can result in venous congestion, vessel injury and deep vein thrombosis, the latter occurring even with appropriately sized cannula. Cannula peak flow and flow curves are provided in the manufacturer's instructions for use. Standardized cannula sizes within an institution/program allow rapid deployment in urgent clinical scenarios.

**Cannulation Approach.** For VV ECMO, there are three major cannulation strategies which dictate cannula selection (Table 2).

Until the advent of the dual-lumen single cannula (DLSC) for venovenous ECMO support, traditional cannulation involved placement of two single-lumen cannulas, typically in the femoral (drainage) and IJ (return) positions. Although the DLSC has clear advantages discussed below, single-lumen double cannulation retains the advantage of being able to be placed with surface vascular ultrasound.

The benefit of a DLSC strategy for VV ECMO is the potential for easier patient mobilization, which is feasible in this population.<sup>8-11</sup> Mobility with femoral cannulation has been described, although is not yet widely adopted.<sup>12</sup> Although there is limited outcome data, in non-ECMO patients, mobility during critical illness has been inconsistently associated with a variety of patient relevant improved outcomes.<sup>13-15</sup> As cannulas placed with modified Seldinger technique, they can be placed by appropriately trained surgeon and nonsurgeon operators.

**Imaging.** Imaging for cannula placement typically involves either fluoroscopic or echocardiographic (TEE) guidance, or both, depending on the cannula. Each has advantages and disadvantages. For single-lumen cannula placement, surface ultrasound for vascular access is preferred and has been demonstrated to be safest compared with blind placement. Depth of cannula placement can be estimated before placement, and then confirmed with radiography or echocardiography. For dual-lumen cannula placement, the DLSC traverses the right atrium into the inferior vena cava (IVC). Accordingly, live fluoroscopic or echocardiographic imaging is *required* to avoid misplacement, which can be fatal.<sup>16,17</sup>

**Fluoroscopic Guidance.** Fluoroscopic guidance enables visualization of the wire traversing the right atrium and into the IVC. This is important, as blind advancement of a wire from the internal jugular (IJ) often travels into the tricuspid valve and right ventricle (RV). Unrecognized ventricular wire position and advancement of the dilators and cannula into the RV can easily result in perforation, which is often fatal. Disadvantages of fluoroscopic guidance include the need for transport to a fluoroscopy

laboratory, which may not be feasible in some patients, or the need for portable fluoroscopy and a trained operator.

**Echocardiographic guidance.** TTE and TEE have most commonly been described for use in combination with fluoroscopic guidance for cannula positioning,<sup>18,19</sup> although has also been described alone.<sup>17,20</sup> Although the outflow port of the DLSC can often be visualized at the level of the right atrium using fluoroscopy alone, echocardiographic guidance allows for visualization of the outflow jet directed toward the tricuspid valve, and has been described.<sup>16</sup> Echocardiographic guidance alone has the benefit that, with skilled operators, patients do not need to be transported.

## PATIENT MANAGEMENT DURING VV ECMO

### Hemodynamics

The consequences of hypoxemia and hypercarbia, before VV ECMO support, are significant. They can each lead to increases in pulmonary vascular resistance, elevated pulmonary arterial pressures, right heart strain or failure. The consequences of this situation are two-fold:

- 1) The VV ECMO circuit provides no direct hemodynamic support; the clinician must be prepared to medically manage significant hemodynamic changes that can arise during the initiation and maintenance phase of a patient on VV ECMO.
- 2) Although not providing direct support, the extracorporeal circuit will provide indirect hemodynamic support through optimization of pH,  $P_a\text{CO}_2$  and  $P_a\text{O}_2$ . This often improves pulmonary arterial pressures and therefore RV dysfunction as well as coronary oxygenation and left ventricular function.<sup>21</sup>

With initiation of VV ECMO, an accompanying decrease in ventilatory settings will decrease intrathoracic pressure, which may increase cardiac filling and output.

Central venous access and invasive arterial blood pressure monitoring are recommended. Echocardiography continues to be an excellent tool to assess hemodynamic function and guide management during VV ECMO. Pulmonary artery catheterization may be considered in patients with complex hemodynamic compromise or right ventricular failure, although thermodilution cardiac output measurements are not reliable during ECMO. Inotropic and vasopressor support are often required to achieve standard circulatory goals (e.g., mean arterial pressure  $\geq$  65 mm Hg, cardiac index  $>$  2.2 L/minute/m<sup>2</sup>, normal lactate).

**Table 3. Recommended Mechanical Ventilation Settings During Adult VV ECMO**

Parameter	Acceptable Range	Recommendation	Comments
Inspiratory plateau pressure ( $P_{plat}$ )	$\leq 30$ cm H <sub>2</sub> O	$< 25$ cm H <sub>2</sub> O	Further reductions in $P_{plat}$ below 20 cm H <sub>2</sub> O may be associated with less VILI and improved patient outcomes <sup>24-26</sup>
PEEP	10–24 cm H <sub>2</sub> O	$\geq 10$ cm H <sub>2</sub> 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 <sup>27</sup>
RR	4–30 breaths/min	4–15 breaths/min (set RR) or spontaneous breathing	CO <sub>2</sub> elimination is being provided primarily by VV ECMO, reducing the need for high minute ventilation (which may be associated with more VILI)
FiO <sub>2</sub>	30–50%	As low as possible to maintain saturations	Oxygenation is being provided primarily by VV ECMO, reducing the need for high FiO <sub>2</sub> from the ventilator unless required to maintain adequate oxygenation

ARDS, acute respiratory distress syndrome; PEEP, positive end-expiratory pressure; RR, respiratory rate; VILI, ventilator-induced lung injury.

The initiation of VV ECMO can lead to a number of abrupt hemodynamic changes. A gradual increase in ECMO flow during initiation can help reduce the risk of this complication. Hypotension and impaired circuit flow can occur as a result of significant vasoplegia because of a systemic inflammatory response after exposure to the extracorporeal circuit or hypovolemia related to unrecognized hemorrhage caused by complications during cannulation. Decisions regarding volume resuscitation with intravenous crystalloid, colloid, or blood transfusion should be patient-specific.

After stabilization on VV ECMO, vasoactive support can often be titrated down significantly. Hemodynamic goals should be reviewed daily and adjusted if necessary. In general, a fluid restrictive approach to volume resuscitation is promoted after the acute phase of critical illness to avoid excessive capillary leak and improve pulmonary function. A restrictive transfusion practice may also be considered. Some practitioners target a hemoglobin threshold  $> 7$  g/dl, whereas others recommend hemoglobin of 12 g/dl to optimize oxygen delivery.

*Ventilator Management*

A key principle of lung protection during VV ECMO is that gas exchange is primarily supported by the extracorporeal circuit, not the native lungs, and thus ventilator settings should be chosen to limit ventilator-induced lung injury. However, the optimal ventilatory strategy in patients with severe ARDS undergoing ECMO is not well defined.<sup>22</sup> Historically, typical ventilator settings during VV ECMO are the pressure controlled ventilation (PCV) mode, with an FiO<sub>2</sub> 0.3, plateau pressure of 20 cm H<sub>2</sub>O, positive end expiratory pressure (PEEP) of 10 cm H<sub>2</sub>O, respiratory rate (RR) of 10 breaths per minute, and an inspiratory to expiratory ratio of 1:1. In the CESAR trial, ventilator settings were gradually reduced to allow so-called lung

rest, using PCV to limit the inspiratory pressure to 20–25 cm H<sub>2</sub>O, with a PEEP of 10 cm H<sub>2</sub>O, an RR of 10 breaths/minute, and an FiO<sub>2</sub> 0.3.<sup>2</sup> In the recent and largest ECMO trial to date (EOLIA), settings were similar with plateau pressure of  $\leq 24$  cm H<sub>2</sub>O, PEEP of  $\geq 10$  cm H<sub>2</sub>O, RR of 10–30 breaths/minute, and an FiO<sub>2</sub> 0.3–0.5.<sup>1</sup>

Ventilator settings are adjusted as conditions change (decreasing rate as CO<sub>2</sub> is cleared by the circuit, e.g.), but should not exceed the rest settings you have chosen. At a minimum, rest ventilator settings should target values established in these two trials<sup>1,2</sup> (i.e., plateau pressure  $\leq 25$  cm H<sub>2</sub>O) or inspiratory pressure  $\leq 15$  cm, with a PEEP of  $\geq 10$  cm H<sub>2</sub>O.<sup>23</sup> Ventilatory settings for patients supported with VV ECMO may fall into the following ranges (Table 3). The ventilatory strategy employed in recent clinical trials provides some examples (Table 4). Finally, although some experts endorse a higher PEEP strategy ( $> 10$  cm H<sub>2</sub>O) to keep the lung open and prevent atelectasis,<sup>28</sup> some endorse a strategy that includes no external PEEP (i.e., patient extubated).<sup>29-31</sup> Regardless of choice of specific rest settings, during VV ECMO when oxygenation and CO<sub>2</sub> goals are not being met, return to our key principle—the management should be *via* adjustments in the ECMO circuit and not by increasing ventilator settings.

Some well-selected patients may tolerate extubation, but others may have profound tachypnea, which itself may be injurious. The balance between injury prevent from reduced ventilator pressures and injury caused from tachypnea in patients with ARDS on ECMO is not known, and the effect of spontaneous breathing on transpulmonary forces during lung injury is an area of ongoing research. Based on published studies to date, ventilator settings that minimize RR and ventilatory pressures are recommended.<sup>32-34</sup> In general, any mode (e.g., volume/assist-control, pressure/assist-control, airway pressure release ventilation) that can achieve this lung-protective ventilation during

**Table 4. Ventilatory Strategies From Recent Clinical Trials for Adult VV ECMO**

	CESAR <sup>2</sup>	EOLIA <sup>1</sup>	
Ventilatory mode	PCV	V-AC	APRV
Set parameter	10 cm H <sub>2</sub> O above PEEP	$V_T$ for $P_{plat} \leq 24$ cm H <sub>2</sub> O	$P_{high} \leq 24$ cm H <sub>2</sub> O
PEEP (cm H <sub>2</sub> O)	10	$\geq 10$	$\geq 10$
Respiratory rate (breaths/min)	10	10–30	Spontaneous
FiO <sub>2</sub>	0.30	0.30–0.50	0.30–0.50

APRV, airway pressure release ventilation; FiO<sub>2</sub>, fraction of inspired oxygen; PCV, pressure controlled ventilation; PEEP, positive end-expiratory pressure;  $V_T$ , tidal volume; V-AC, volume-assist control ventilation.

VV ECMO would represent a reasonable ventilatory strategy. Chapter 40, "Medical Management of the Adult with respiratory Failure on extracorporeal life support (ECLS)" in the fifth Edition of the *ELSO Red Book*, provides additional detailed discussion of choice of rest ventilator settings, extubation during VV ECMO, as well as the management of ventilatory support during ECMO.

**Initial Fluid Management.** The ability of the ECMO circuit to provide gas exchange is dependent on sufficient blood flow through the oxygenator. Ignoring recirculation for a moment, increasing blood flow during VV ECMO to achieve rated flow of the oxygenator predictably increases systemic oxygen delivery. It follows that the goal of fluid management during ECMO therapy is initially to ensure adequate vascular volume to enable ECMO flow commensurate with desired gas exchange. Practically, this means that many patients need fluid resuscitation after the initiation of VV ECMO.

**Effect of Fluid Administration on Tidal Volumes.** It is important to recognize that this initial need for fluid administration, plus any decreases in mean airway pressure that accompany ventilatory rest settings, may together result in an increase in pulmonary edema. During this resuscitative phase, lung compliance decreases; at stable inspiratory pressures, tidal volumes rapidly and predictably fall. The evidence to date suggests that changes should not be made to increase tidal volume, assuming adequate systemic oxygen delivery.<sup>24,35</sup>

**Chatter and Suck-Down.** Over the course of an ECMO run, the patient's condition and treatment will affect intravascular volume. Additionally, it is important to remember that the IVC will often exhibit rhythmic collapse during respiration, periods of coughing or valsalva. Unless there is venous engorgement such that the cannula does not contact the venous walls, there will be some element of *partial* dynamic cannula occlusion in many patients along the lateral fenestrations of the cannula. Although chattering should be prevented by careful administration of fluid or reduction of flow, if possible, excessive fluid administration must be avoided. Inadequate intravascular volume, or cannula misplacement, can result in suck-down, in which the ECMO flows acutely drop by more than 1–2 LPM from baseline. This can result in flows of <1 LPM at full pump speed and is dangerous, as it can result in hemolysis, and, at worse, cavitation of air within the pump and air embolization. Suck-down should be treated by rapidly decreasing motor speed, adjusting the ventilator as necessary for oxygenation, and then slowly ramping back up while changing patient position to increase venous filling, and by giving fluid as needed.

**Subsequent Fluid Management and Diuresis.** After initiation of ECMO, increases in blood flow and oxygen delivery often lead to improvement in organ function, and in cases of preserved renal function, an autodiuresis. A conservative fluid management strategy has shown benefit in patients with ARDS without ECMO<sup>36,37</sup>; in the absence of other data, we assume the same holds true for critically ill patients managed with ECMO after initial fluid resuscitation. Multiple studies now indicate that a negative fluid balance is associated with improved outcomes (Supplemental Digital Content 1, <http://links.lww.com/ASAIO/A626>). Thus, the best available data at this time suggest that after the initial resuscitative phase of VV ECMO, patients should achieve a negative fluid balance whenever hemodynamically possible, until achieving their dry weight.

**Procedures on ECMO.** Procedures from venipuncture to liver transplantation can be done with success during ECMO. When an operation is necessary, coagulation should be optimized (anticoagulation minimized) as described earlier. Even small operations like chest tube placement are done with an extensive use of electrocautery.

Tracheostomy is often done in ECMO patients, but the technique is different than standard tracheostomy. The trachea is exposed through a small incision, all with extensive electrocautery. The smallest opening in the trachea is made between rings, preferably with a needle, wire, and dilation technique. Do not incise a ring or create a flap. Because the patient is on ECMO support there is no urgency about gaining access or conversion from endotracheal tube to trach tube. The operative site (and trachea) should be bloodless after operation. Subsequent bleeding (common after a few days) should be managed by complete reexploration until bleeding stops.

**Anticoagulation.** Anticoagulation for ECMO is covered in a separate guideline.

**Duration of Support.** The expected duration of VV ECMO support is dependent on multiple factors, but among published studies, most patients are on ECMO for 9–14 days, although some may require 4 weeks or more.

**Futility.** Consideration should be given to discontinue ECMO if there is no reasonable hope for meaningful survival or bridge to organ replacement (e.g., transplant, durable left ventricular assist device, etc.) through shared decision-making with the patient's surrogate/family, in accordance with local laws and practice. The possibility of stopping for futility should be explained to the family before ECMO is begun. The definition of irreversible heart or lung damage depends on the patient, the resources of the institution, and the region/country. In general, it is important to clearly set expectations early on during an ECMO course.

## WEANING OFF VV ECMO

Assessing adequate gas exchange reserve before considering weaning from VV ECMO and subsequent steps to prepare for decannulation are discussed in the following. It is important to note that weaning may occur over several hours to days, based on clinical condition of the patient. Arterial blood gases should be obtained throughout the process when significant adjustments are made, as clinically indicated. A detailed discussion of this topic is included in Chapter 42, "Weaning and Decannulation of Adults with Respiratory Failure on ECLS" in the fifth Edition of the *ELSO Red Book*.

### Recommendations

1. Assess readiness to be weaned from VV ECMO. This includes assessing for both ventilatory and oxygenation reserve. **Table 5** lists criteria for intubated and nonintubated patients on VV ECMO who can undergo a weaning trial, including radiographic criteria. To initially assess oxygenation ability, the ECMO flow can be decreased to 1–1.5 LPM to ensure the patient maintains adequate oxygenation. Alternatively, the ECMO flow can be maintained and fraction of delivered O<sub>2</sub> can be weaned. To assess ventilatory reserve, the patient should tolerate a low sweep gas flow (<2 LPM) with an acceptable P<sub>a</sub>CO<sub>2</sub> and work of breathing/RR. As a last step, patients can be placed on 100% FiO<sub>2</sub> for 15 minutes and check an ABG

**Table 5. Oxygenation, Ventilation, and Radiographic Conditions Sufficient for Initiating a Weaning Trial**

	Intubated Patients	Nonintubated Patients
Oxygenation*	<ul style="list-style-type: none"> <li>■ <math>F_{iO_2}</math> consistently <math>\leq 60\%</math></li> <li>■ PEEP <math>\leq 10</math> cm <math>H_2O</math></li> <li>■ <math>P_{aO_2} \geq 70</math> mm Hg</li> </ul>	<ul style="list-style-type: none"> <li>■ <math>P_{aO_2} \geq 70</math> mm Hg on no more than a moderate amount of supplemental <math>O_2</math> (example: <math>\leq 6</math> LPM NC or facemask, or <math>\leq 40</math> LPM with <math>F_{iO_2} \leq 0.3</math> on high-flow nasal cannula)</li> </ul>
Ventilation	<ul style="list-style-type: none"> <li>■ Tidal volume <math>\leq 6</math> mL/kg PBW</li> <li>■ Plateau pressure <math>\leq 28</math> cm <math>H_2O</math></li> <li>■ Respiratory rate <math>\leq 28</math> bpm</li> <li>■ ABG demonstrates acceptable pH and <math>P_{aCO_2}</math> based on the patient's clinical condition without excessive work of breathing</li> </ul>	<ul style="list-style-type: none"> <li>■ ABG demonstrates acceptable pH based on the patient's clinical condition without excessive work of breathing</li> </ul>
Imaging	Chest radiograph demonstrates improvement in appearance	

ABG, arterial blood gas; LPM, liters per minute; PBW, predicted body weight; PEEP, positive end-expiratory pressure.

to assess  $P_{aO_2}$  buffer. Finally, perform ventilator challenge in intubated patients (Table 6).

2. Table 7 lists the steps and criteria for a trial off of VV ECMO. Weaning may occur over several hours to days based on clinical condition of the patient. Ensure oxygenator is cleared of condensation and blood flow is maintained at  $>1$  L/minute per cannula to avoid thrombosis.

**LIMITATIONS**

Venovenous extracorporeal membrane oxygenation use in adults has rapidly increased worldwide. This document is intended to be a practical, consensus based guide to patient selection, initiation, cannulation, management, and weaning of VV ECMO for adult respiratory failure. This document is not comprehensive and cannot stand alone as a sole management guide for all of adult respiratory ECMO. As examples, additional

guidance for essential topics not covered in this document are provided in Table 8. Additionally, these recommendations will be updated as new information becomes available, and the latest version of this document will be available at <https://elso.org/Resources/Guidelines.aspx>.

**PRACTICE POINTS TO REMEMBER**

Utilize evidence-based ARDS therapies before ECMO, including low tidal volume ventilation (4–6 mL/kg PBW) and, in the absence of contraindications, prone positioning. As recently as 2017, it was demonstrated that only 11% of ECMO patients at the US centers underwent prone positioning at any point during their course.<sup>38</sup> Available evidence at this time demonstrates a clear and strong mortality benefit from prone positioning for ARDS; ECMO should *not* be an alternative to proning; proning is a complement that should be performed

**Table 6. Weaning Ventilator Challenge in Intubated Patients on VV ECMO**

	Volume-Regulated Modes of Ventilation	Pressure-Regulated Modes of Ventilation
Respiratory Compliance	<ul style="list-style-type: none"> <li>■ Liberalize tidal volume by 1 mL/kg increments up to 6 mL/kg</li> <li>■ Plateau pressure at each increment remains <math>\leq 28</math> cm <math>H_2O</math></li> </ul>	<ul style="list-style-type: none"> <li>■ Liberalize total pressure to no more than 28 cm <math>H_2O</math></li> <li>■ Ensure that tidal volumes increase to 6 mL/kg</li> </ul>
Clinical Parameters	<ul style="list-style-type: none"> <li>■ Monitor respiratory rate and minute ventilation</li> <li>■ Avoid excessive work of breathing based on patient's physiologic status and underlying comorbidities</li> </ul>	

**Table 7. Suggested Approach to Weaning From Venovenous Extracorporeal Membrane Oxygenation via Reduction of Gas Flow with Preserved Higher Blood Flows**

Step	Purpose	Process
1	Reduce $FDO_2$	<ul style="list-style-type: none"> <li>■ Stepwise reduction in <math>FDO_2</math> from 1.0 to 0.21 in decrements of approximately 20%.</li> <li>■ Maintain acceptable <math>SpO_2 &gt; 92\%</math> or <math>P_{aO_2}</math> of at least <math>\geq 70</math> mm Hg</li> <li>■ ABG as clinically indicated</li> </ul>
2	Reduce sweep gas	<ul style="list-style-type: none"> <li>■ Stepwise reduction in sweep gas flow rate by 0.5–1 L/min to goal of 1 L/min</li> <li>■ Check ABG with each decrement in sweep gas flow rate</li> </ul>
3	Off-sweep gas challenge	<ul style="list-style-type: none"> <li>■ Maintain acceptable pH based on the patient's clinical condition without excessive work of breathing</li> <li>■ If patient able to tolerate discontinuation of ECMO, trial off sweep gas for 2–3 hours or longer.</li> <li>■ Monitor <math>SpO_2</math></li> </ul>
4	Prepare for decannulation	<ul style="list-style-type: none"> <li>■ Check ABG off sweep gas after allotted time</li> <li>■ Notify surgeon or whomever decannulates.</li> <li>■ Confirm off-sweep gas ABG demonstrates <math>P_{aO_2} \geq 70</math> mm Hg and acceptable pH based on the patient's clinical condition without excessive work of breathing</li> <li>■ <i>Nil per os/nothing by mouth</i> status</li> <li>■ Active blood type (ABO) and antibody screen in the case of significant blood loss</li> <li>■ Prepare to give sedation depending on patients' predecannulation sedation status.</li> <li>■ Hold heparin for at least 1 hour before decannulation.</li> <li>■ Trendelenburg position if jugular vein cannula</li> <li>■ Close cannulation site with a suture, apply slight compression dressing and observe carefully</li> <li>■ Check for deep vein thrombosis after 24 hours</li> </ul>

ABG, arterial blood gas;  $FDO_2$ , fraction of delivered oxygen.



Table 8. Additional Guidance for Essential Topics

Topic	ELSO Guidelines	Fifth Edition Red Book Chapter
Anticoagulation Bridge to lung transplantation Cannulation Strategies	ELSO Anticoagulation Guideline 2014 ELSO Guidelines General v1.4—Section III, Ultrasound Guidance for VV ECMO	7—“Anticoagulation and Disorders of Hemostasis” 58—“ECMO as a Bridge to Lung Transplantation” 38—“ECLS Cannulation for Adults with Respiratory Failure”
Circuit design	ELSO Guidelines General v1.4—Section II, ELSO Guidelines for Adult Respiratory Failure v1.4—Section II	5—“The circuit”
Complication management ECMO team design	ELSO Guidelines for ECMO Centers v1.8, ELSO Guidelines for Training and Continuing Education of ECMO Specialists	Chapters 40, 41, 43 65—“Implementing an ECLS program”
Extubation during ECMO	Endotracheal Extubation in patients with respiratory failure receiving VV ECMO	Chapters 40, 41
Management of fluid balance/renal failure/ nutrition	ELSO Guidelines for Adult Respiratory Failure v1.4—Section IV	40—“Medical Management of the Adult with Respiratory Failure on ECLS”
Procedures during ECMO Sedation	ELSO Guidelines for Adult Respiratory Failure v1.4—Section VI ELSO Guidelines for Adult Respiratory Failure v1.4—Section IV	61—“Procedures during ECLS” 40—“Medical Management of the Adult with Respiratory Failure on ECLS”
Selective CO <sub>2</sub> removal (ECCO <sub>2</sub> R) Transfusion management Unusual patient populations (pregnancy, immunosuppressed, etc.)	ELSO Guidelines for Adult Respiratory Failure v1.4—Section VI ELSO Guidelines for Adult Respiratory Failure v1.4—Section IV ELSO Guidelines for Adult Respiratory Failure v1.4—Section I	63—“Extracorporeal Carbon Dioxide Removal” 8—“Transfusion Management during Extracorporeal Support” Section 7—Extracorporeal Life Support: Special Indications—Chapters 53, 54, 56, 58, 60

ECLS, extracorporeal life support; ELSO, extracorporeal life support organization; VV ECMO, venovenous extracorporeal membrane oxygenation.

before ECMO. On ECMO, continue to adhere to the principles of lung protection: reduce the intensity of mechanical ventilation and avoid high airway/driving pressure (Table 3).

#### *Plan Ahead for Potential Venovenous Extracorporeal Membrane Oxygenation Cases*

Determine who has the skill and experience to cannulate, who the team will be, and what resources are needed, such as echocardiography or fluoroscopy. If patients are to be transferred for VV ECMO, make the referral call early enough to allow for worsening without extremis.

#### *Ground Assessments of Adequate Oxygenation on Objective Measures of Tissue Perfusion, Rather Than on Percent Saturations of Arterial Blood*

It is important to pay attention to hemoglobin, systemic vascular resistance, and cardiac output (in short, oxygen delivery). Although it is possible to have inadequate saturations and oxygen delivery on VV ECMO, it is critical to not confuse the two as often they are distinct.

### PITFALLS TO AVOID

#### *Overreacting to Low Saturations on Venovenous Extracorporeal Membrane Oxygenation and Increasing the Ventilator Settings to Compensate*

The rationale to initiate VV ECMO includes augmentation of oxygenation and ventilation, but increasingly, also the implementation of ultralow settings and lung rest. Failing to decrease ventilatory settings once on VV ECMO obviates a major potential benefit of VV ECMO.

#### *Waiting too Long for Cannulation*

Cannulation for VV ECMO may involve transport to a fluoroscopically enabled area or to a center that can cannulate, or if the patient is already prone, supination of the patient. Any of these movements often result in temporary desaturation as consolidations redistribute and lung recruits. We advocate a combined use of the Murray Score (Lung Injury Score) and the RESP score to guide decisions regarding initiation of VV ECMO, utilizing initiation threshold criteria discussed earlier from the EOLIA trial. If ECMO is to be a consideration, and transfer would be necessary, it should be done early.

#### *Initiation of Venoarterial Extracorporeal Membrane Oxygenation When Venovenous Extracorporeal Membrane Oxygenation Will Suffice*

Although it is common to see elevated pulmonary pressures and right ventricular dysfunction in the setting of acute respiratory failure due to hypoxemia and hypercarbia, this is not to be confused with pre-existing heart failure. The former typically improves with oxygenation and ventilation and initiation of VA ECMO for a process that will improve with VV ECMO results in additional unnecessary and significant risk. Some patients with hypoxemia in the setting of sepsis can develop a concomitant severe cardiomyopathy that may benefit from VA ECMO.



*Conversion of Venovenous Extracorporeal Membrane Oxygenation to Venoarterial Extracorporeal Membrane Oxygenation for Low Saturations*

Extracorporeal membrane oxygenation provides a variable content of oxygen to the blood that is directly related to the hemoglobin  $\times$  blood flow rate. Delivery of that oxygen content to the arterial system achieves little or no increase in systemic oxygen delivery over VV, with an increase in meaningful complications.<sup>39</sup> In the case of severe ARDS treated with VA ECMO, as the heart recovers, patients can have upper body (and cerebral) hypoxemia; this is known as Harlequin or North/South syndrome.

### ACKNOWLEDGEMENTS

We thank Elaine Cooley, MSN RN, Peter Rycus, MPH, and the ELSO Board Members for help in the overall process.

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