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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,

Division of Cardiothoracic Surgery, Department of Surgery, University of Utah Health, Salt Lake City, Utah, USA

Division of Emergency Medicine, Department of Surgery, University of Utah Health, Salt Lake City, Utah, USA

Darryl Abrams, MD,

Division of Pulmonary, Allergy and Critical Care Medicine, Department of Medicine, Columbia College of Physicians & Surgeons/New York-Presbyterian Hospital, New York, New York, USA

Daniel Brodie, MD,

Division of Pulmonary, Allergy and Critical Care Medicine, Department of Medicine, Columbia College of Physicians & Surgeons/New York-Presbyterian Hospital, New York, New York, USA

John C Greenwood, MD,

Department of Anesthesiology & Critical Care, Department of Emergency Medicine, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, Pennsylvania, USA

Jose Alfonso Rubio Mateo-Sidron, MD,

Intensivist, Cardiothoracic Critical Care, Hospital 12 de Octubre, Madrid, Spain

Asad Usman, MD, MPH,

Corresponding Author: Joseph E Tonna, MD, MS, *Division of Cardiothoracic Surgery, Department of Surgery, University of Utah Health, Salt Lake City, Utah, USA* and *Division of Emergency Medicine, Department of Surgery, University of Utah Health, Salt Lake City, Utah, USA*, joseph.tonna@hsc.utah.edu, @JoeTonnaMD.

Reviewers:

Nicholas Barrett, MBBS St. Thomas Hospital, London, England

Matthieu Schmidt, MD University of Paris, Paris, France

Thomas Mueller, MD St. Joseph Hospital, Berlin, Germany

Alain Combes, MD, PhD University of Paris, Paris, France

Kiran Shekar, MBBS, PhD Adult Intensive Care Services, The Prince Charles Hospital, Brisbane, Queensland, Australia

Author Contributions

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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.

Prior Version:

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

Department of Anesthesiology and Critical Care, University of Pennsylvania, Philadelphia, Pennsylvania, USA

Eddy Fan, MD, PhD
Interdepartmental Division of Critical Care Medicine, University of Toronto, University Health Network and Sinai Health System, Toronto, Canada

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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. VV ECMO is a therapy in the management of respiratory failure in multiple guidelines. ELSO 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 the Supplemental Content.

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 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

VV ECMO 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: a) increasing systemic oxygenation and CO_2 removal (ventilation); and b)

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 ARDS and refractory hypoxemia (PaO_2/FiO_2 < 80 millimeters of mercury [mmHg]), or severe hypercapnic respiratory failure (pH <7.25 with a $PaCO_2$≥60 mmHg), 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 non-recovery without a plan for viable decannulation (Table 1). This situation could be due to the disease process itself or to multi-organ 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 ECMO—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_2 = [hemoglobin (*in grams/liter*)] × 1.39 × [SaO_2] + (0.0034 × [PaO_2 (*in mmHg)*]). 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^2/minute.

Systemic oxygen delivery is the arterial O2 content times flow. The normal systemic oxygen delivery is 600 mL/m^2/minute. Systemic oxygen delivery as low as 300 mL/m^2/minute is sufficient to maintain metabolism at rest. In VV ECMO, the circuit should be designed to provide at least 240 mL/m^2/minute of oxygen supply and 300 mL/m^2/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 grams/dL would require an ECMO flow of about 4 L/min to reach

those goals. 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 right ventricle 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.[3] 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_2<90% in the context of ARDS.[4] A comprehensive discussion of oxygenation is presented in Chapter 4 ("The Physiology of Extracorporeal Life Support") in the 5th Edition of the ELSO Red Book.

Recirculation: Recirculation refers to post oxygenator blood returning to the pre-pump 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 internal jugular 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, while 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_2), 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).[5]

Incorporating recirculation, the body's saturation (which results from the ratio of ECMO flow to total body cardiac output) is calculated as ([total ECMO flow] – [recirculation flow]) / 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_2/VO_2). 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

DO2/VO2 ratio of 5:1, but certainly above the critical threshold of supply dependence which occurs near a ratio of 2:1.

CO_2 Removal: Gas exchange via the oxygenator accomplishes CO_2 removal from the blood and is controlled by the "sweep gas" inflow rate to the oxygenator, for a given oxygenator membrane size; CO_2 removal increases with increasing sweep gas flow. Sweep gas typically ranges from 1–9+ LPM, and for VV is typically 100% O_2. Sweep gas very effectively lowers P_aCO_2. 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_aCO_2 and pH. A rapid decrease in CO_2 is associated with neurologic injury.

Cannulation

General Principles—VV ECMO flows are typically limited by cannula size to 5–6 liters per minute (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 due to insufficient uptake of venous blood into the ECMO circuit, this may improve with the use of multistage (multi-hole) drainage cannula or with placement of additional venous drainage cannula.[6]

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 to 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.

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

Cannula Size—In order to select the correct cannula size, first priority should be given to titrating to estimated patient cardiac output needs. For example, in a 180cm tall male, a 25F drainage cannula will often be sufficient, though 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, though 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 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 as well as flow curves are provided in the manufacturer's instructions for use (IFU). 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.

Until the advent of the DLSC for venovenous ECMO support, traditional cannulation involved placement of two single lumen cannulas, typically in the femoral (drainage) and internal jugular (return) positions. While 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. [8–11] Mobility with femoral cannulation has been described, though is not yet widely adopted.[12] While 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.[13–15] As cannulas as placed with modified Seldinger technique, they can be placed by appropriately trained surgeon and non-surgeon 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 to blind placement. Depth of cannula placement can be estimated prior to 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.[16,17]

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 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: Transthoracic and transesophageal echocardiography has most commonly been described for use in combination with fluoroscopic guidance for cannula positioning,[18,19] though has also been described alone.[17,20] While 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 towards the

tricuspid valve, and has been described.[16] 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, prior to 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. While not providing direct support, the extracorporeal circuit will provide indirect hemodynamic support through optimization of pH, P_aCO_2 and P_aO_2. This often improves pulmonary arterial pressures and therefore RV dysfunction as well as coronary oxygenation and left ventricular function.[21]

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, though 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 [MAP] ≥ 65 mmHg, cardiac index [CI] > 2.2 L/min/m^2, normal lactate).

The initiation of VV ECMO can lead to a number of abrupt hemodynamic changes. 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 due to a systemic inflammatory response after exposure to the extracorporeal circuit or hypovolemia related to unrecognized hemorrhage due to 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, while others recommend a 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 (VILI). However, the optimal ventilatory strategy in patients with severe ARDS undergoing ECMO is not well defined.[22] Historically, typical ventilator settings during VV ECMO are pressure controlled ventilation (PCV) mode, with an FiO_2 0.3, plateau pressure of 20 cmH_2O, positive end expiratory pressure (PEEP) of 10 cmH_2O, respiratory rate (RR) of 10 breaths per minute, and an inspiratory to expiratory ratio of 1 to 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 cmH_2O, with a PEEP of 10 cmH_2O, a RR of 10 breaths per minute, and an FiO_2 0.3.[2] In the recent and largest ECMO trial to date (EOLIA), settings were similar with plateau pressure of ≤24 cmH_2O, PEEP of ≥10 cmH_2O, RR of 10–30 breaths per minute, and an FiO_2 0.3–0.5.[1]

Ventilator settings are adjusted as conditions change (decreasing rate as CO2 is cleared by the circuit, for example), but should not exceed the rest settings you have chosen. At a minimum, rest ventilator settings should target values established in these two trials[1,2] (i.e., plateau pressure ≤ 25 cmH_2O) or inspiratory pressure ≤15 cm, with a PEEP of ≥10 cmH_2O. [23] 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, while some experts endorse a higher PEEP strategy (>10 cmH_2O) to keep the lung open and prevent atelectasis,[28] some endorse a strategy that includes no external PEEP (i.e., patient extubated).[29–31] Regardless of choice of specific rest settings, during VV ECMO when oxygenation and CO2 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 respiratory rate and ventilatory pressures are recommended.[32–34] In general, any mode (e.g., volume/assist-control, pressure/assist-control, airway pressure release ventilation [APRV]) that can achieve this lung-protective ventilation during VV ECMO would represent a reasonable ventilatory strategy. Chapter 40, “Medical Management of the Adult with respiratory Failure on ECLS” in the 5th Edition of the ELSO Red Book, provides additional detailed discussion of choice of rest ventilator settings, extubation during VV ECMO, as well as 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 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.[24,35]

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. While 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 1–2LPM from baseline. This can result in flows of <1LPM 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 auto-diuresis. A conservative fluid management strategy has shown benefit in patients with ARDS without ECMO;[36,37] 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 Content). Thus, the best available data at this time suggests 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 above. Even small operations like chest tube placement are done with 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, though 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 prior to considering weaning from VV ECMO and subsequent steps to prepare for decannulation are discussed below. 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 5th 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 non-

intubated patients on VV ECMO who can undergo a weaning trial, including radiographic criteria. To initially assess oxygenation ability, ECMO flow can be decreased to 1–1.5 LPM to ensure the patient maintains adequate oxygenation. Alternatively, ECMO flow can be maintained and fraction of delivered O_2 can be weaned. To assess ventilatory reserve, the patient should tolerate a low sweep gas flow (<2 LPM) with an acceptable P_aCO_2 and work of breathing/respiratory rate. As a last step, patients can be placed on 100% FiO_2 for 15 minutes and check an ABG 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/min per cannula to avoid thrombosis.

LIMITATIONS

VV ECMO 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 prior to 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 US centers underwent prone positioning at any point during their course.[38] 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 prior to 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 VV ECMO 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).

While 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 VV ECMO 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 ultra-low 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 VA ECMO when VV ECMO will suffice.—While 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 VV ECMO to VA ECMO for low saturations.—ECMO provides a variable content of oxygen to the blood that is directly related to the hemoglobin x 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.[39] 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.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviation List:

ELSO	Extracorporeal Life Support Organization
VV ECMO	Venovenous extracorporeal membrane oxygenation
CaO_2	oxygen content of arterial blood
SaO_2	Saturation of arterial oxygen
CO	cardiac output
O_2	oxygen
DO_2	oxygen delivery
VO_2	oxygen utilization
CO_2	carbon dioxide
LPM	liters per minute
VA ECMO	Venoarterial extracorporeal membrane oxygenation
DLSC	dual-lumen single cannula
TEE	transesophageal echocardiography
TTE	transthoracic echocardiography
IVC	inferior vena cava
IJ	internal jugular
RV	right ventricle
P_aCO_2	partial pressure of arterial blood carbon dioxide
P_aO_2	partial pressure of arterial blood oxygen
MAP	mean arterial pressure
CI	cardiac index
PCV	pressure-controlled ventilation
PEEP	positive end-expiratory pressure
RR	respiratory rate

F_iO_2	fraction of inspired oxygen
PBW	predicted body weight
ARDS	acute respiratory distress syndrome
ABG	arterial blood gas
P_{PLAT}	plateau pressure
cmH_2O	centimeters of water
VILI	ventilatory induced lung injury
V-AC	volume-assist control ventilation
APRV	airway pressure release ventilation

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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 mmHg)*, 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 cmH_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, aspiration)
• Acute eosinophilic pneumonia
• Diffuse alveolar hemorrhage or pulmonary hemorrhage
• Severe asthma
• Thoracic trauma (*e.g.* traumatic lung injury, severe pulmonary contusion)
• Severe inhalational injury
• Large bronchopleural fistula
• Peri-lung transplant (*e.g.* primary lung graft dysfunction, bridge to transplant)
Relative contraindications for venovenous extracorporeal membrane oxygenation (VV ECMO)
• 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 cmH_2O and FiO_2 > 90%

*Clinical trials have utilized several cut-off points for the indication of the start of VV ECMO: PaO_2/FiO_2 <80 mmHg [EOLIA Trial[1]], Murray Score >3 [CESAR Trial[2]], without strong data indicating the superiority of any one.

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 via internal jugular vein	Inferior vena cava via femoral vein		Limited patient mobility
Bicaval dual-lumen single cannula (DLSC)	Tricuspid valve via 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,[7] may be more difficult to achieve higher flows
Bifemoral venous cannulation	Right atrium via femoral vein	Inferior vena cava via femoral vein		Limited patient mobility

Abbreviations: ICH-intracranial hemorrhage

Table 3:

Recommended Mechanical Ventilation Settings During Adult VV ECMO

Parameter	Acceptable Range	Recommendation	Comments
Inspiratory plateau pressure (P_{plat})	≤ 30 cmH_2O	< 25 cmH_2O	Further reductions in P_{plat} below 20 cmH_2O may be associated with less VILI and improved patient outcomes[24–26]
PEEP	10–24 cmH_2O	≥ 10 cmH_2O	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-FiO_2 table or Express trial strategy) while maintaining the P_{plat} limit[27]
Respiratory rate (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)
FiO_2	30–50%	As low as possible to maintain saturations	Oxygenation is being provided primarily by VV ECMO, reducing the need for high FiO_2 from the ventilator unless required to maintain adequate oxygenation

Table 4:

Ventilatory Strategies From Recent Clinical Trials for Adult VV ECMO

	CESAR[2]	**EOLIA[1]**	
Ventilatory Mode	PCV	V-AC	APRV
Set Parameter	10 cmH_2O above PEEP	V_T for $P_{plat} \leq 24$ cmH_2O	$P_{high} \leq 24$ cmH_2O
PEEP (cmH_2O)	10	≥ 10	≥ 10
Respiratory Rate (breaths/min)	10	10–30	Spontaneous
FiO_2	0.30	0.30–0.50	0.30–0.50

Abbreviations: APRV, airway pressure release ventilation; FiO_2, fraction of inspired oxygen; PCV, pressure controlled ventilation; PEEP, positive end-expiratory pressure; V_T, tidal volume; V-AC, volume-assist control ventilation

Table 5:

Oxygenation, ventilation and radiographic conditions sufficient for initiating a weaning trial

	Intubated Patients	Non-Intubated Patients
Oxygenation*	■ FiO_2 consistently ≤ 60% ■ PEEP ≤ 10 cmH_2O ■ P_aO_2 ≥ 70 mmHg	■ P_aO_2 ≥ 70 mmHg on no more than a moderate amount of supplemental O_2 (example: ≤6 LPM NC or facemask, or ≤40LPM with F_iO_2 ≤0.3 on high flow nasal cannula)
Ventilation	■ Tidal volume ≤ 6mL/kg PBW ■ Plateau pressure ≤ 28 cmH_2O ■ Respiratory rate ≤ 28 bpm ■ ABG demonstrates acceptable pH and P_aCO_2 based on the patient's clinical condition without excessive work of breathing	■ ABG demonstrates acceptable pH based on the patient's clinical condition without excessive work of breathing
Imaging	Chest radiograph demonstrates improvement in appearance	

Table 6:

Weaning Ventilator Challenge in Intubated Patients on VV ECMO

	Volume-regulated modes of ventilation	Pressure-regulated modes of ventilation
Respiratory Compliance	■ Liberalize tidal volume by 1 mL/kg increments up to 6 mL/kg ■ Plateau pressure at each increment remains ≤ 28 cm H_2O	■ Liberalize total pressure to no more than 28 cm H_2O ■ Ensure that tidal volumes increase to 6 mL/kg
Clinical Parameters	■ Monitor respiratory rate and minute ventilation ■ Avoid excessive work of breathing based on patient's physiologic status and underlying co-morbidities.	

Table 7:

Suggested approach to weaning from VV ECMO via reduction of gas flow with preserved higher blood flows

Step	Purpose	Process
1	Reduce fraction of delivered oxygen (FDO_2)	■ Stepwise reduction in FDO_2 from 1.0 to 0.21 in decrements of approximately 20%. ■ Maintain acceptable SpO_2 > 92% or P_aO_2 of at least ≥ 70 mmHg ■ ABG as clinically indicated
2	Reduce sweep gas	■ Stepwise reduction in sweep gas flow rate by 0.5 – 1 L/min to goal of 1 L/min ■ Check ABG with each decrement in sweep gas flow rate ■ Maintain acceptable pH based on the patient's clinical condition without excessive work of breathing
3	Off-sweep gas challenge	■ If patient able to tolerate discontinuation of ECMO, trial off sweep gas for 2–3 hours or longer. ■ Monitor SpO2 ■ Check ABG off sweep gas after allotted time
4	Prepare for decannulation	■ Notify surgeon or whomever decannulates. ■ Confirm off-sweep gas ABG demonstrates PaO_2 ≥ 70 mmHg and acceptable pH based on the patient's clinical condition without excessive work of breathing ■ *Nil per os/nothing by mouth* status ■ Active blood type (ABO) & antibody screen in case of significant blood loss ■ Prepare to give sedation depending on patients' pre-decannulation sedation status. ■ Hold heparin for at least 1 hour prior to decannulation. ■ Trendelenburg position if jugular vein cannula ■ Close cannulation site with a suture, apply slight compression dressing and observe carefully ■ Check for deep vein thrombosis after 24 hours

Table 8

Additional Guidance for Essential Topics

Topic	ELSO Guidelines	5th Edition Red Book Chapter
Anticoagulation	ELSO Anticoagulation Guideline 2014	7 – “Anticoagulation and Disorders of Hemostasis”
Bridge to lung transplantation		58 – “ECMO as a Bridge to Lung Transplanation”
Cannulation Strategies	ELSO Guidelines General v1.4 – Section III, Ultrasound Guidance for VV ECMO	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		Chapters 40, 41, 43
ECMO team design	ELSO Guidelines for ECMO Centers v1.8, ELSO Guidelines for Training and Continuing Education of ECMO Specialists	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	ELSO Guidelines for Adult Respiratory Failure v1.4 – Section VI	61 – “Procedures during ECLS”
Sedation	ELSO Guidelines for Adult Respiratory Failure v1.4 – Section IV	40 – “Medical Management of the Adult with Respiratory Failure on ECLS”
Selective CO2 removal ($ECCO_2R$)	ELSO Guidelines for Adult Respiratory Failure v1.4 – Section VI	63 – “Extracorporeal Carbon Dioxide Removal”
Transfusion management	ELSO Guidelines for Adult Respiratory Failure v1.4 – Section IV	8 – “Transfusion Management during Extracorporeal Support”
Unusual patient populations (pregnancy, immunosuppressed, etc.)	ELSO Guidelines for Adult Respiratory Failure v1.4 – Section I	Section 7 – Extracorporeal Life Support : Special Indications – Chapters 53, 54, 56, 58, 60.