Extracorporeal Life Support Organization (ELSO) guidelines for pediatric cardiac failure

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Extracorporeal Life Support Organization (ELSO): Guidelines for Pediatric Cardiac Failure

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These guidelines are applicable to neonates and children with cardiac failure as indication for extracorporeal life support. These guidelines address patient selection, management during extracorporeal membrane oxygenation, and pathways for weaning support or bridging to other therapies. Equally important issues, such as personnel, training, credentialing, resources, follow-up, reporting, and quality assurance, are addressed in other Extracorporeal Life Support Organization documents or are center-specific.

Key Words: pediatrics, heart failure, extracorporeal membrane oxygenation

This guideline is informed by available evidence and based on expert opinion, with targeted clinical recommendations for emerging centers and small volume programs as institutional standards are developed. The guideline may also be of benefit to experienced providers and centers in the process of reviewing local protocols. Circuit configuration, equipment specifications, anticoagulation recommendations, extracorporeal cardiopulmonary resuscitation (ECPR), and some specific patient populations are presented in other Extracorporeal Life Support (ELSO) guidelines.

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Extracorporeal membrane oxygenation (ECMO) is the most commonly utilized mechanical circulatory support in neonates and children with refractory cardiac failure (Figure 1).[1,2] Veno-arterial ECMO (VA ECMO) augments systemic cardiac output and respiratory gas exchange to facilitate adequate tissue oxygen delivery (DO_2). Survival for children with heart disease supported with VA ECMO has improved over the past decade, despite expanding indications and increasing patient complexity.[2] Increased utilization and experience of pediatric cardiac ECMO is reflected in a number of publications, but large evidence gaps remain. High-quality VA ECMO support for pediatric cardiac indications necessitates systems, protocols, interdisciplinary teams, and training.

Patient Selection, Modes of Support, and Technical Considerations

Patient Selection

The indication for the use of VA ECMO for cardiac indications in children is cardiogenic shock unresponsive to standard medical therapies. Persistent systemic systolic pressure less than 50 mm Hg, urine output <1 ml/kg/h, lactic acidosis, central venous oxygen saturation (SVO_2) <60% or arteriovenous oxygen saturation difference (AVO_2) >30% in cyanotic congenital heart disease, an altered mental status due to low cardiac output may all be indicators of cardiogenic shock in children. Examples of pathologies causing shock are listed in Table 1. Consideration for early initiation of ECMO is important as delayed initiation (beyond 6 hours of cardiogenic shock state) is associated with worse outcomes.[1,3–25] Local resources should be taken into account when determining ECMO candidacy (Figure 2).

Veno-arterial ECMO should be considered with four primary strategies for ECMO support:

1. Bridge to recovery: In patients with reversible underlying disease processes where cardiac function recovery can occur with time, medical interventions, or surgical correction;
2. Bridge to bridge: In patients with acute single organ disease who can be supported to a ventricular assist device (VAD);
3. Bridge to organ transplantation: In patients who may require cardiopulmonary support until heart transplantation;
4. Bridge to decision: In patients who may recover end-organ function, facilitate diagnosis, or determine candidacy for alternative support/transplantation.

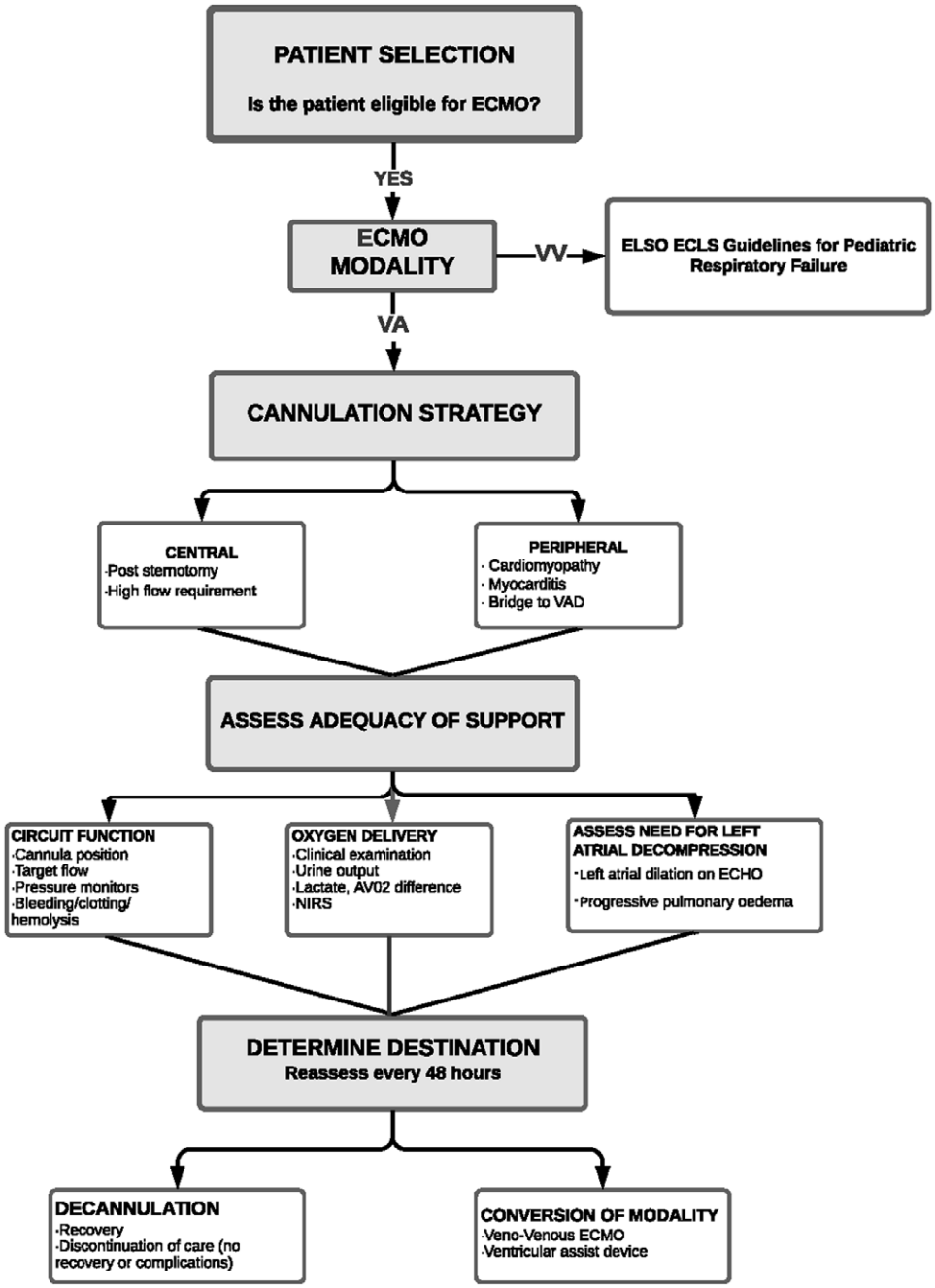

Figure 1. Decision-making flowsheet for VA ECMO for pediatric cardiac indications. VA ECMO, veno-arterial extracorporeal membrane oxygenation.

Patient Selection Practice Points

1. Institute ECMO before evidence of severe oxygen deficiency and end-organ damage. Early initiation is important for developing and low-volume ECMO centers without capacity for rapid initiation of ECPR.
2. Individual institutions should consider their center experiences and resources when evaluating indications and contraindications for ECMO.
3. Extracorporeal membrane oxygenation following pediatric cardiac surgery should prompt early investigation and management of possible residual lesions.

Mode of Support

In children with cardiac dysfunction not responding to maximal medical therapy, VA ECMO support facilitates respiratory gas exchange and augments cardiac output for DO_2 while allowing time for myocardial recovery or diagnosis and repair of anatomical lesions. Effective VA ECMO support should be assessed by surrogates of tissue oxygen delivery including blood lactate, SVO_2 or AVO_2, near-infrared spectroscopy (NIRS), measures of end-organ function, for example, urine output, creatinine, liver function tests, and adequacy of cardiac decompression assessed by echocardiography, chest radiography, and ultimately by cardiac catheterization.

Table 1. Indications, Contraindications, and Special Considerations for Cardiac Indications for Extracorporeal Membrane Oxygenation

INDICATIONS	
Periprocedural Cardiac Surgery and Catheterization	
Preprocedural stabilization for inadequate systemic cardiac output—in cases where physiologic stability is likely to be achieved over time or early operative repair is likely to have a successful outcome	Preoperative neonates with obstructed total anomalous pulmonary venous return or transposition of the great arteries with inadequate mixing or persistent pulmonary hypertension Circular shunt with Ebstein's anomaly or pulmonary regurgitation following balloon dilation Anomalous left coronary artery from the pulmonary artery Restrictive pulmonary blood flow in tetralogy of Fallot or obstructed Blalock-Taussig shunt Tetralogy absent pulmonary valve with airway or lung parenchymal compromise and inadequate pulmonary blood flow Undifferentiated congenital heart disease with cardiopulmonary compromise
Failure to wean from cardiopulmonary bypass or low cardiac output in the postoperative period	Ischemic reperfusion injury following cardiopulmonary bypass or inadequate cardioplegia Myocardial edema related to the inflammatory bypass process or ventriculotomy
Postoperative arrhythmia	Junctional ectopic tachycardia with Tetralogy of Fallot with hemodynamic compromise refractory to antiarrhythmic measures
Circulatory Failure Due To Other Etiologies	
Cardiogenic	Myocarditis Cardiomyopathy Postcardiac arrest ventricular dysfunction Intractable tachyarrhythmia or bradycardia
Obstructive	Pulmonary hypertension Pulmonary embolus
Distributive*	Sepsis Anaphylaxis
Cardiopulmonary Arrest—see Extracorporeal Cardiopulmonary Resuscitation (ECPR) Guideline.	
CONTRAINDICATIONS	
Patient-level factors—ECMO support would be unlikely to facilitate survival without likelihood of major morbidity	Prolonged state of cardiogenic shock (over 6 hours) unlikely to benefit from initiation of ECMO Relative prematurity or low birth weight in neonates (<34 weeks of gestational age or <2.0 kg) with significant morbidity and mortality Extremes of prematurity or low birth weight (<32 weeks of gestational age or <1.5 kg) Severe chromosomal abnormalities (*e.g.*, Trisomy 13 or 18) Irreversible brain damage or Intracranial hemorrhage (grade III or IV IVH) Uncontrollable hemorrhage should be considered a contraindication for ECMO unless cannulation to ECMO would assist in source control
Procedural factors	Inability to achieve vascular or central access for cannulation
SPECIAL CONSIDERATIONS	
Aortic regurgitation	VA ECMO flow results in increased afterload on the left ventricle, and even mild aortic regurgitation progress to become clinically significant Attention to left heart decompression or early transition to cardiopulmonary bypass may be required
Interrupted aortic arch	Careful attention to the anatomy of head and neck vessels (*i.e.,* location of interruption of arch) is required before ECMO cannulation to ensure brain perfusion with oxygenated ECMO flow
Stage 1 palliative surgery (S1P)	ECMO support after S1P for hypoplastic left heart syndrome is the most frequent postoperative ECMO indication in neonates In S1P with systemic to pulmonary shunt, higher ECMO flow may be required (150–200 ml/kg/min) Temporary shunt restriction to limit pulmonary blood flow and promote systemic blood flow may be necessary In patients with RV-PA conduit, maintaining cardiac ejection (and thus flow across the conduit) may prevent shunt thrombosis
Stage 2 and 3 palliative surgery	Infants and children after surgical palliation with cavopulmonary anastomoses (Glenn and Fontan circulations) represent a complex physiologic group in whom stable support with ECMO can be difficult to establish given the separation of systemic venous return (Table 2)

**Note: May be challenging to achieve adequate ECMO flow for delivery of oxygen to tissues in the setting of vasoplegia.*
ECMO, extracorporeal life support; RV-PA, right ventricle to pulmonary artery; VA ECMO, veno-arterial extracorporeal membrane oxygenation.

Cannulation

In children supported with ECMO for cardiac indications, cannulation site, and strategy are determined by the patient's size, underlying cardiac anatomy, the anatomy and surgical palliation of congenital heart disease, and any recent surgical intervention (Table 2). Central cannulation is commonly used

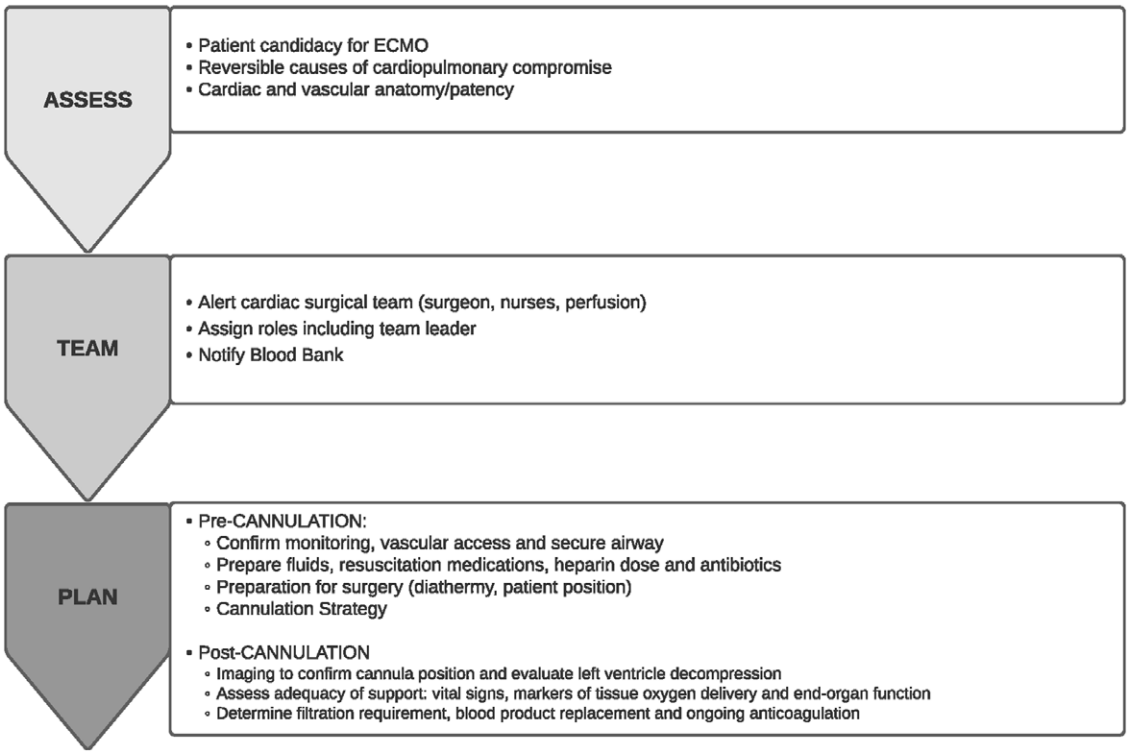

Figure 2. ICU ECMO cannulation preparation. ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit.

in the postcardiopulmonary bypass period or in the presence of a recent sternotomy (*i.e.*, less than 10–14 days), with right atrial access for venous drainage and cannulation of the aorta for arterial return.[19,20,26] Neck access *via* the internal jugular vein and common carotid artery is the favored peripheral cannulation sites in many smaller children (<5–6 years or <30 kg), balancing optimized ECMO flow through the larger upper body vessels against possible increased risk of neurologic adverse events.[27,28] For older children, the femoral vein and femoral artery approach may be utilized.[26] Neck vessel cannulation in younger children typically necessitates open surgical access, while femoral vessels may be cannulated using either open or Seldinger technique. When femoral vessels are used, limb ischemia is avoided by using the smallest arterial cannula for desired flow rate, distal reperfusion cannula insertion, and opposing femoral arterial and venous vessel site cannulation strategies.[29,30]

Table 2. Cannulation Strategy in Children With Cardiac Disease

	Central Cannulation		Peripheral Cannulation		
Anatomy or Surgical Palliation	Venous Access	Arterial Access	Venous Access	Arterial Access	Additional Strategies
TWO VENTRICLES					
Biventricular circulation or structurally normal heart	Right atrium	Aorta	Internal jugular or femoral	Common carotid or femoral	Left atrial decompression may need to be considered
SINGLE VENTRICLE					
Shunted or RV-PA conduit physiology (stage 1)	Common atrium	Aorta	Internal jugular	Common carotid	*Peripheral = neck access due to patient size. Care re: cannula position with respect to shunt—may result in overcirculation to lungs or shunt occlusion
Superior cavopulmonary anastomosis (stage 2)	SVC or common atrium	Aorta	Internal jugular or femoral	Common carotid	*If femoral approach only used, passive venous return must flow through lungs—ventilation must be optimized. Additional venous cannula may be required
Total cavopulmonary anastamosis (Fontan, stage 3)	Fontan baffle or common atrium	Aorta	Internal jugular or femoral	Common carotid or femoral	Additional venous cannula often required

RV-PA, right ventricle to pulmonary artery; SVC, superior vena cava; VA ECMO, veno-arterial extracorporeal membrane oxygenation.

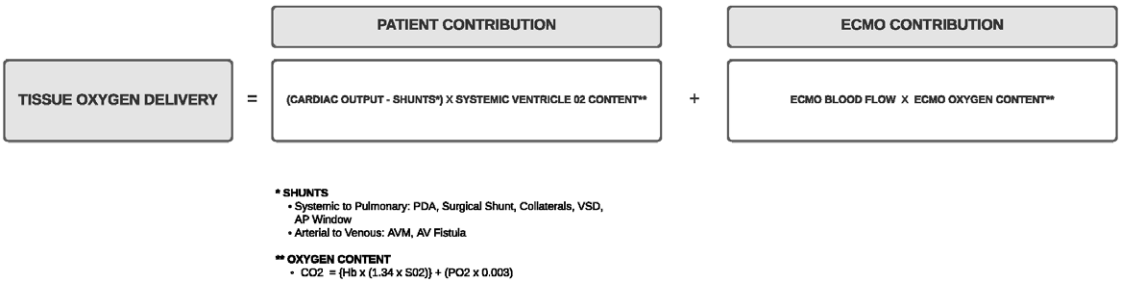

Figure 3. Determinants of tissue oxygen delivery on veno-arterial ECMO. ECMO, extracorporeal membrane oxygenation.

Children with congenital heart disease are at risk of peripheral vessel occlusion due to cardiac catheterization access, and knowledge of vessel patency is important before attempted cannulation.[10] This is particularly relevant for children with single-ventricle physiology palliated to cavopulmonary circulations who often require multisite cannulation to maximize venous drainage (Table 2).

If ventricular function is inadequate to open the aortic valve during systole, left ventricular diastolic pressure and left atrial pressure increase resulting in inadequate myocardial decompression, subendocardial ischemia, and pulmonary venous congestion. Decompressing the hypertensive left atrium can be achieved by atrial septostomy, left atrial cannulation (directly or *via* catheter crossing the atrial septum), left ventricular venting *via* an open approach,[31–34] or an axial transaortic valve pump (Impella Abiomed, Danvers, MA) device.[35] Left atrial decompression performed early (<18 hours postcannulation) minimizes the duration of ECMO and mechanical ventilation.[34]

In children with congenital heart disease, predominant right ventricular failure can be observed in patients in the post-operative period (*e.g.,* patients with Tetralogy of Fallot or Ebstein's anomaly). Here, a special case can be made for VA ECMO for right-sided support. This can be achieved *via* standard cannulation or with targeted support by cannulation of the right atrium (venous cannula) and the pulmonary artery (arterial cannula), facilitating oxygenation and supplementing subpulmonary ventricle function. Isolated right ventricular support, therefore, warrants central cannulation.[36,37]

Mode of Support Practice Points

1. Central cannulation is used following recent sternotomy.
2. Peripheral cannulation in infants is *via* the neck and, for older children, the femoral vessels.
3. Consider preplanning a cannulation strategy in patients with congenital heart disease and difficult vascular access.
4. Early evaluation for the need for cardiac decompression in the setting of severe myocardial dysfunction without native ejection.

Management During Extracorporeal Life Support

Tissue oxygen delivery is determined by the sum of patient and ECMO output which independently contribute to oxygen delivery (Figure 3).

Systemic Blood Flow

Normal homeostatic mechanisms maintain DO_2 to oxygen consumption (VO_2) at a ratio of 5:1 (20% extraction). During shock states, a DO_2:VO_2 ratio of less than 2:1 (50% extraction) leads to anaerobic metabolism and metabolic acidosis. The goal during VA ECMO support is to maintain DO_2 as close to normal as possible—at least three times VO_2 (ratio of >3:1). During VA ECMO, the systemic oxygen extraction is continuously monitored *via* the drainage cannula (SVO_2), and as the arterial oxygen concentration and hemoglobin are known, a DO_2:VO_2 ratio can be monitored. If the arterial saturation is 100% and the SVO_2 is 80% the ratio is 5:1. So adjusting flow and hemoglobin to maintain SVO_2 >66% assures that the goal of DO_2:VO_2 >3 is met. Typically, this is achieved with a cardiac index of 2.5–3 L/min/m^2 or 100–150 ml/kg/min in infants, 70–100 mL/kg/min in larger child. Further details available in the ELSO Red Book.[38]

To commence VA ECMO support after cannulation, pump flow is gradually increased until adequate flow (as above) is achieved. Blood flow is subsequently decreased to the lowest level that will provide adequate support to meet cellular metabolic demands (typically a cardiac index of 2.5–3 L/min/m^2 or 100–150 ml/kg/min in infant, 70–100 mL/kg/min in larger child). Ideally, arterial pulse pressure will be at least 10 mm Hg, indicating systemic ventricular ejection, which reduces the risk of systemic ventricular thrombosis. This may not be achieved if ventricular function is poor, despite inotropic support, and should prompt consideration of left atrial decompression or alternate support strategies. Inability to achieve desired blood flow or ongoing evidence of inadequate cardiac output necessitates urgent consideration of adjustment or additional drainage cannulae. Because the pulse pressure is low, the mean systemic arterial pressure will be somewhat lower than normal. In addition, patients placed on ECMO for cardiac support are often managed with inotropes before ECMO initiation. As these drugs are titrated down, systemic vascular resistance (SVR) decreases, and systemic pressure falls proportionately. If the perfusion pressure is inadequate (low urine output and poor perfusion), systemic arterial pressure can be increased by increasing pump flow, transfusing blood products, or titrating vasopressor infusions.

Oxygenation

The rated flow is the blood flow rate at which venous blood with a saturation of 75% and hemoglobin of 12 g/dl exits the gas exchange device with a saturation of 95%. The

rated flow is a standard to compare the maximum oxygenation capacity of gas exchange devices and is determined by surface area and blood path mixing. As long as the blood flow is below recommended rated flow for that gas exchange device (and the inlet saturation is 70% or higher), the oxyhemoglobin saturation at the outlet should be greater than 95%. Usually, the outlet saturation will be 100%, and the pO_2 will be over 300 mm Hg. If the fraction of oxygen on the sweep gas (FdO_2) is 100%, at or below the device rated flow, and the outlet saturation is less than 95%, the gas exchange device is not working at full efficiency (due to irregular flow, clotting). It may be necessary to replace it. Oxygen delivery from the circuit should be adequate for full support (systemic saturation greater than 95% at low ventilator settings and FiO_2). AVO_2 difference should be less than 20–30%. In states of high oxygen demand or poor oxygen delivery (low cardiac output, impaired lung gas exchange), maintaining the hematocrit over 40% (hemoglobin ~12 g/dl) can optimize oxygen delivery. Patients with already impaired oxygen delivery, such as those with palliated single-ventricle physiology, should be maintained with a hematocrit above 40%, particularly during partial VA ECMO support and in preparation for weaning. Target paO_2 should be maintained within normal limits, as hyperoxia during VA ECMO support has been associated with mortality.[39]

Carbon Dioxide Clearance

CO_2 transfer across the membrane lung is more efficient than that of oxygen, and CO_2 removal will exceed oxygen uptake. CO_2 clearance is controlled by the sweep gas flow rate. Increasing sweep gas flow rate increases CO_2 clearance but does not affect oxygenation. Initial gas flow to blood flow ratio varies across institutions. As a guide, gas flow rate less than blood flow rate can be used to begin support, with early arterial blood gas monitoring to avoid hypocarbia, aiming for a gradual reduction (over 4–8 hours) in $PaCO_2$ to minimize rapid shifts in cerebral perfusion in patients who are hypercapnic at the time of cannulation. If the initial $PaCO_2$ is greater than 70 mm Hg, the $PaCO_2$ should be normalized over several hours to avoid rapid changes of cerebral perfusion related to CO_2 and pH, which are associated with neurologic injury and mortality.[40,41] If CO_2 clearance is decreased, but oxygenation is adequate, the cause is usually water accumulation within the gas compartment of the membrane lung. This may be cleared by intermittently increasing sweep gas flow to a higher rate.

Goals Following Cannulation Practice Points

1. Following ECMO initiation, inability to achieve desired blood flow or ongoing evidence of inadequate tissue oxygen delivery requires an urgent reassessment of ECMO strategy/cannulation.
2. With myocardial recovery, the patient's contribution to systemic oxygen content and oxygen delivery increases and may require adjustments to ventilation/FiO_2.
3. Increasing the sweep flow will increase CO_2 clearance but will not improve oxygenation.

Anticoagulation; See Extracorporeal Life Support Anticoagulation Guideline and Extracorporeal Life Support Red Book, Ch 7

Unfractionated heparin (UFH) remains the most commonly utilized anticoagulant for pediatric ECMO.[38,42] A bolus dose of UFH (50–100 units/kg) is given at cannulation and subsequently administered as a continuous infusion (Figure 2). The goal is to maintain circuit flow without thrombosis despite artificial circuit exposure. Anticoagulation therapy and monitoring strategies vary between institutions and according to patient diagnosis and thrombotic *versus* bleeding considerations.[43] Neonates and infants pose particular challenges due to physiologic differences in hemostasis.[44,45] Extracorporeal membrane oxygenation programs must develop an institutional approach to monitoring and managing anticoagulation for patients.[46]

In recent years, some programs have evolved protocols incorporating direct thrombin inhibitors (DTIs) such as bivalirudin and argatroban, citing some practical and theoretical benefits.[47,48] While initially limited to specific instances in which UFH was specifically contraindicated (*e.g.*, heparin-induced thrombocytopenia, heparin-induced thrombocytopenia [HIT], and heparin resistance) the relative predictability of response and stability in patients on long-term support have led to increased adoption and preferential use in some programs. Advantages of the use of DTIs include the ability to treat or prevent HIT, the lack of dependence on antithrombin, and reduced time to achieving steady-state concentrations due to their short half-life (25 minutes for bivalirudin and 45 minutes for argatroban).[47,49] Relative disadvantages of DTIs include higher cost (10–70× that of UFH in some institutional comparisons) and the lack of reversal agents (mitigated by short half-life). Due to the lack of reversal agents, DTIs are less commonly utilized for cardiopulmonary bypass, and transition from heparin as used in the operating room must be managed carefully, especially for patients with recent cardiotomy and central cannulation.

Viscoelastic tests, including thromboelastography or rotational thromboelastometry are whole-blood assays measuring the rapidity and strength of thrombus formation. These tests provide additional data to standard coagulation panels on clotting time, clot formation time, the firmness of clot formation, and clot lysis. They are particularly beneficial in diagnosing specific aspects of coagulopathy in bleeding patients, such as those supported for failure to wean from cardiopulmonary bypass after complex reconstruction. These tests can identify states of fibrinolysis and help guide targeted treatment of specific factor or component deficiencies.

Indications for blood product administration relate to patient and circuit factors, specifically bleeding, evidence of thrombus formation, and flow rates. Centers should refer to the ELSO anticoagulation guideline for detail.

Blood Product Administration

Patients often receive blood products to maintain hemoglobin and product targets on ECMO.[50–52] In the recent Pediatric Critical Care Transfusion and Anemia Expertise Initiative consensus statements regarding red blood cell transfusion in

Table 3. Indications for vasoactive infusion during VA ECMO support for cardiac indications

Vasoactive support	Indication and Benefits and Specific Risks	Medication	Starting Dose Range
Inotrope	Enhancement of contractility in a patient with severe cardiac dysfunction to facilitate aortic valve opening and prevent stasis of blood in the systemic ventricle and aortic root	Epinephrine Dobutamine	0.02–0.05 μg/kg/min 5 μg/kg/min
	To optimize blood pressure and end-organ perfusion Does not facilitate myocardial rest		
Vasopressor	Peripheral vasoconstriction is indicated in a patient on VA ECMO for distributive shock, on maximal circuit blood flow with inadequate cardiac output to optimize blood pressure and end-organ perfusion.	Norepinephrine Vasopressin	0.02–0.05 μg/kg/min 0.01–0.06 IU/kg/hr
Vasodilator	Peripheral vasodilation will reduce systemic afterload improving circuit blood flow and systemic perfusion as well as decreasing left ventricle afterload, promoting ejection	Sodium nitroprusside Milrinone	0.5–3 μg/kg/min 0.25–1.0 μg/kg/min

VA ECMO, veno-arterial extracorporeal membrane oxygenation.

critical illness, there was insufficient evidence for a specific red blood cell transfusion threshold for children on ECMO,[53] instead recommending transfusion decision-making to take into account evidence of inadequate systemic or regional oxygen delivery, adoption of blood conservation procedures and minimization of donor exposure.[54] Many center protocols maintain hemoglobin between 10–12 g/dl. There is some evidence that children on ECMO are more likely to have bleeding complications with a platelet count below 80,000; however, this may depend on the age of the patient and other factors such as recent cardiac surgery and cannulation strategy.[50,55] Centers should refer to the ELSO anticoagulation guideline for suggested transfusion targets and thresholds.

Patient Management During Extracorporeal Life Support

Cardiovascular

Heart rate and rhythm. Veno-arterial ECMO is capable of providing full cardiac output during cardiac arrythmias. However, arrhythmia can increase myocardial oxygen demands, delay ventricular recovery, and if associated with a lack of cardiac ejection, can lead to ventricular distension and inadequate myocardial decompression. Restoration of sinus rhythm and atrioventricular synchrony with antiarrhythmic therapy, overdrive pacing, direct current cardioversion, and electrophysiological ablation should be considered.

Blood pressure and vasoactive medications. Patient blood pressure is determined by two modifiable factors: blood flow (pump flow plus native cardiac output, Figure 3), and SVR. The pulse pressure is narrow when the native cardiac output is minimal on full VA ECMO support. Ideally, the arterial pulse pressure is at least 10 mm Hg, with left ventricle ejection reducing intracardiac thrombosis risk. Severely reduced left ventricular systolic function may prevent ejection against the VA ECMO flow, even with inotropic support. This should prompt early consideration of left atrial decompression or alternate support strategies. Adequacy of systemic cardiac output is determined by an assessment of clinical parameters of tissue oxygen delivery: warmth and color of extremities, urine output, lactate, premembrane oxygen saturation or AVO_2 difference, and NIRS.[56] In the setting of inadequate cardiac output with hypotension, after addressing hypovolaemia, VA ECMO flow can be increased or inotropes or vasopressors commenced (Table 3). Signs of low cardiac output with hypertension on ECMO may necessitate optimization of sedation and use of vasodilator infusions. To maintain some intracardiac and pulmonary blood flow, target VA ECMO flow can be around 80% of venous return, reflected by pulse pressure of approximately 10 mm Hg monitored with an invasive arterial line. Changes in arterial waveform may reflect myocardial recovery or an acute complication (circuit dysfunction, reduced preload, increased afterload).

Ventilator Management

Ventilation management on ECMO should minimize lung injury and optimize lung function to facilitate ECMO separation with cardiac recovery. Of note, for patients cannulated *via* femoral vessels with poor lung function, as cardiac function recovers, it is native lung function that determines oxygen content of antegrade flow from the heart into coronary arteries and head and neck vessels. These patients may consequently require higher FiO_2 ± positive end-expiratory pressure (PEEP) than the "lung rest" settings used when patients are supported on ECMO for pulmonary indications.

Suggested protective lung strategy: Pressure-limited ventilation, PEEP (8–10 cm H_2O), tidal volume <6–8 ml/kg ideal body weight, peak inspiratory pressures <18–20 cm H_2O, with a low rate (10 bpm).[57–60]

No single ventilation strategy is universally practiced, and the suggested strategy may need modification in patients with an open sternum or pulmonary/intrathoracic pathology.[61,62] Adjuncts to mechanical ventilation may include suctioning, use of ventilator, bronchoscopy, and prone positioning.[63,64] It may be appropriate in carefully selected patients to allow spontaneous breathing or extubate in the absence of lung pathology.

Fluid Management, Blood Volume, and Fluid Balance

After stability has been achieved following cannulation, resuscitation, and blood product replacement, diuresis should be instituted to target euvolemia. If pharmacologic diuresis is ineffective, continuous ultrafiltration or renal replacement therapies can be used, often incorporated into the ECMO circuit.

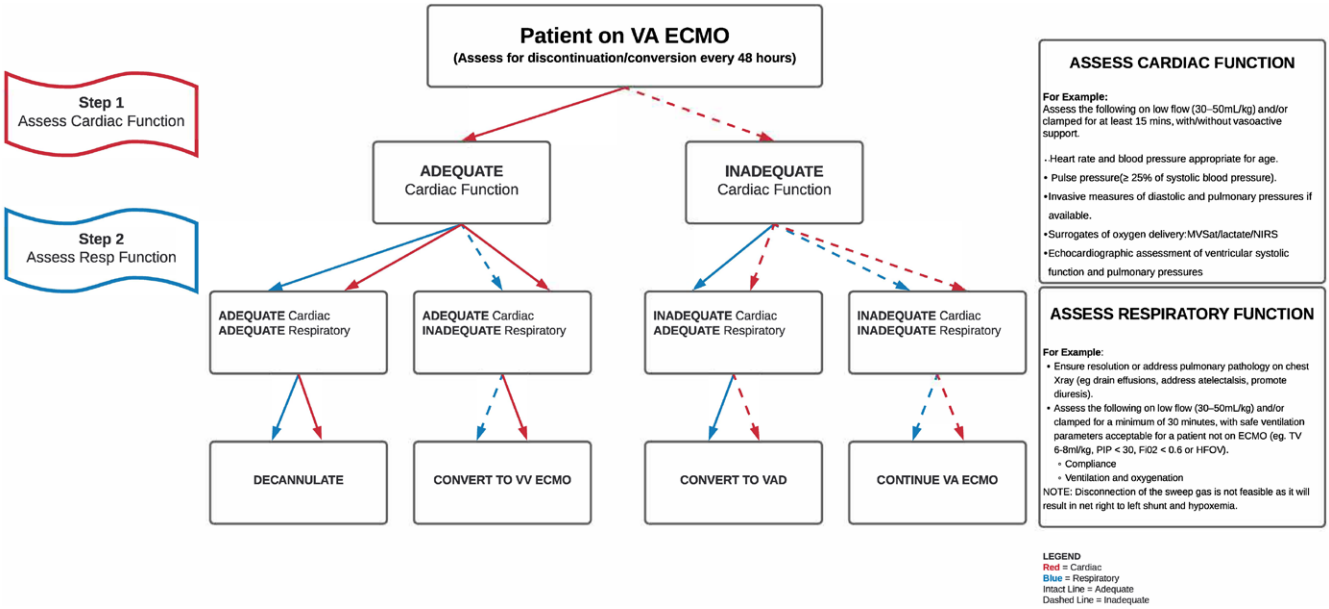

Figure 4. ECMO weaning flowsheet. ECMO, extracorporeal membrane oxygenation. full color online

Neurology and Sedation (Also See Extracorporeal Life Support Sedation Guideline)

Neurologic complications (hemorrhage, thrombosis, and seizures) are relatively common and adversely affect morbidity and survival outcomes of children on ECMO for cardiac indications.[21,65–67] Risk factors include weight <3 kg, gestational age less than 34 weeks, CPR, degree of precannulation vasoactive support, and acidosis.[21,68] Surveillance for neurologic events includes daily clinical examination if feasible, screening cranial ultrasounds, and EEG with more definitive neuroimaging (CT brain) recommended to detect intracranial hemorrhage or embolic events if heightened concern. Intermittent or continuous EEG monitoring is recommended as seizures may only be detected electrographically, but this is not universally available.[67]

Analgesia and sedation strategies for patients supported on ECMO reflect strategies for critically ill children, trending towards minimizing sedation, permitting spontaneous movement, and facilitating neurologic assessment. While permitting awake ECMO is not practically possible in neonates on VA ECMO, it may be carefully considered in a select group of older children who have secure peripherally placed ECMO cannulae, good circuit function, closed-chest, and a level of understanding that will permit wakefulness without discomfort and anxiety, along with full engagement of wider multidisciplinary team and caregivers including parents/guardians. A multidisciplinary approach with protocolized management of sedation as per institutional preferences is recommended. Opioids have been the mainstay of sedation management, but increasingly dexmedetomidine is being used over benzodiazepines. Dosing requirements may be elevated, as drugs are adsorbed into the circuit, tolerance can develop, and hemofiltration may remove administered drugs.[69,70] For example, midazolam, lorazepam, and fentanyl can show reductions greater than 50% in levels due to adsorption to the ECMO circuit.[71] A practice of daily interruption of sedation medications on ECMO in neonates and infants, particularly if impaired renal and liver function, may be considered to prevent the accumulation of sedative agents and reduce tolerance and later effects of sedation withdrawal. Assessment and management of delirium and overlap with signs of sedation withdrawal is an important consideration and should not be missed in children supported on ECMO.

Nutrition

Enteral nutrition in patients receiving VA ECMO is well tolerated, provides adequate nutrition, is cost-effective, and has minimal risk.[72,73]

Infection

Infectious complications are frequent and are associated with mortality.[3,19,24] The most important risk factor is support duration.[74] Vigilance is essential, as standard markers (temperature, white cell count, inflammatory markers) may not adequately reflect the presence (or absence) of infection. There is little evidence to support routine surveillance cultures or the use of prophylactic antibiotics outside of that for administration within 30 minutes of emergent surgical procedures.[75]

Endocrine

Normoglycemic targets are effective for pediatric cardiac patients on ECMO.[76,77]

Patient Management Practice Points

1. Arrhythmias should be addressed to promote myocardial recovery and cardiac ejection.
2. Vasoactive medications can be useful to manipulate SVR, complement VA ECMO flow and optimize tissue oxygen delivery (Table 3).
3. Inotropes may promote cardiac ejection and decompression but do not facilitate myocardial rest.
4. Attention should be given to oxygenating blood traversing the pulmonary vasculature in the setting of femoral VA ECMO to avoid differential oxygenation.

Weaning Off Extracorporeal Life Support and Decannulation

Successful VA ECMO wean is defined as discontinuation of mechanical circulatory support because the patient improved and is expected to recover.[78] Assessment of readiness to wean should occur at regular intervals of 24–48 hours from the time of ECMO cannulation (Figure 1). Factors for consideration before weaning VA ECMO (shown in Figure 4) include the patient phenotype being compatible with recovery, preserved lung function, end-organ function recovering, and improved myocardial function with vasopressors and inotropes at low levels (*e.g.* epinephrine/norepinephrine ≤0.02–0.05 μg/kg/min or dopamine/dobutamine <5 μg/kg/min).[79,80]

Timing of Myocardial Recovery

The clinical course of myocardial improvement may be rapid, for example, 24 hours to 5 days, postcardiotomy or cardiopulmonary bypass, or more prolonged in the case of primary myocardial dysfunction or prolonged ischemia before correction of the cardiac lesion.[81–85] While the former may be well supported with ECMO, those with prolonged myocardial dysfunction (>7–10 days) should be considered for other forms of mechanical circulatory support as end-organs recover (Figure 4).[81,86]

Signs of Myocardial Recovery

While supported on VA ECMO, evidence of myocardial recovery includes increasing pulse pressure, increasing systolic pressure, rising end-tidal CO_2, and improving ventricular systolic function on echocardiography.[80,87–89] Loading conditions impact assessment of ventricular systolic function on ECMO, but other parameters (aortic velocity time integral ≥10 cm, left ventricular ejection fraction >20–25%, and lateral mitral annulus peak systolic velocity ≥6 cm/s) under low flow conditions have been predictive of successful ECMO decannulation in adult patients with cardiogenic shock.[80,89]

Special Considerations

Left atrial decompression. In patients whose support includes a left atrial vent or atrial septostomy, lower vent flows, and a drop in circuit, mixed venous oxygenation coincide with left ventricular recovery. Tolerating left atrial or left ventricular vent clamping and subsequent removal are initial steps towards weaning.

Systemic to pulmonary artery shunts. Some patients require partial occlusion of their systemic to pulmonary artery shunt or right ventricle to pulmonary artery (RV-PA) conduit to achieve sufficient systemic perfusion on ECMO. In these patients, the surgeon may need to adjust or remove the partial occlusion to balance pulmonary and systemic blood flow during weaning and trialing off ECMO. RV-PA conduits, valved or otherwise, usually do not require any restriction to balance systemic and pulmonary blood flows on ECMO.

Weaning With LA Decompression Practice Points

1. If myocardial recovery has occurred, clamping of the LA/LV line should improve native cardiac output (increase pulse pressure).
2. Clamping and removal of the LA/LV line and confirmation of sustained LV decompression can be the first component of a staged ECMO wean.

Weaning and Trailing Off Extracorporeal Membrane Oxygenation

Weaning is the term applied to the reduction of ECMO flow, which accompanies myocardial recovery. It may be conducted over several days. The purpose of weaning ECMO is to determine if the patient is ready to trial-off ECMO. The weaning process varies according to institutional and patient factors but would commonly occur over 4–8 hours with a gradual decrease in ECMO flows while optimizing lung ventilation strategy, intravascular volume status, and vasoactive medications. The purpose of the trial-off (15 minutes to 2 hours) is to determine if the patient is ready for decannulation. Clinical examination, targeted echocardiography, and serial laboratory parameters should be used to assess the adequacy of cardiac output and ventricular function during ECMO weaning. Once the patient has demonstrated satisfactory hemodynamics on minimum ECMO support, typically around 50 ml/kg/min, it is reasonable to trial the patient off ECMO. The main risk during ECMO Trial-Off is circuit thrombus. Extracorporeal membrane oxygenation should not be reduced below the lowest compatible with the oxygenator in the circuit. The risk of clot formation depends on anticoagulation, circuit size, existing clot burden, and circuit complexity. Adequate anticoagulation during ECMO trial-off must be maintained (using either infusions or intermittent boluses). It is usual to carry out a trial-off ECMO for 1–2 hours before decannulation.

There are two broad trial-off strategies:

1. Clamp trial. This is the classic approach. Clamping the cannula proximal to the patient (clamp trial) allows complete separation of the patient from the circuit; circuit flow is maintained around the bridge. Adequate anticoagulation should be established in the ECMO circuit to slow thrombosis of the cannulae and lines during the no-flow state. Every 10–15 minutes, the cannulae are intermittently flushed by releasing the clamps and clamping the bridge for 15–30 seconds.
2. Pump-controlled retrograde trial-off is a more recently described technique that has been shown to be a safe, simple, and reproducible approach. This relies on the retrograde flow generated by the patient's native cardiac output to maintain circuit integrity, provides a 'stress test' to evaluate cardiorespiratory reserve during the trial period off ECMO by creating an obligatory left to right shunt.[90,91] This method avoids manipulation of the ECMO circuit without insertion of an arteriovenous bridge and circuit clamping.
3. Some centers omit the trial-off completely and just discontinue ECMO after weaning but leave the cannula in place, fill them with heparinized saline and run a heparin flush through the cannula to maintain patency. Decannulation is then carried out after several hours if the patient remains stable.

Preparation for Extracorporeal Membrane Oxygenation Wean, Trial-Off, and Decannulation

Physiologic conditions during the wean should closely approximate those after decannulation, including optimized volume status and consideration of inotropy commencing several hours before weaning. Preparing for ECMO trial-off and decannulation should include:

1. Confirm endotracheal tube position. Optimize ventilation and lung recruitment for adequate oxygenation and ventilation. Consider transition to VV-ECMO if ventilation is contributing to the failure to wean (Figure 4);
2. Correct hematological and metabolic abnormalities;
3. If temporary pacing wires are available, connect and test pacemaker;
4. Consider the use of inhaled nitric oxide or pulmonary vasodilator therapy in lesions that may predispose to pulmonary hypertension;
5. Optimize preload (central venous pressure [CVP] > 5mm Hg) and determine inotropic medication plan (often epinephrine 0.02–0.05 μg/kg/min or dopamine/dobutamine 3–5 μg/kg/min);
6. ECMO flows are reduced (by 20 ml/kg/min increments). Clinical hemodynamic assessment of HR, BP, and CVP should determine the timing of further decrements inflow. If hemodynamic parameters remain within acceptable limits with minimal change post wean, flows can continue to be further reduced;
7. Assessment of clinical status, lactate, AVO_2 difference, and respiratory gas exchange (arterial blood gas) should be made at low ECMO flow (50 ml/kg/min);
8. Echocardiography may be used for assessment of systolic ventricular function, estimation of RV pressures, adequacy of volume status, and additional evaluation for valvular regurgitation/stenosis;
9. During weaning, the adequacy of cardiac output and respiratory gas exchange should be assessed, and ongoing requirement for support should be determined (Figure 4).

VA ECMO decannulation can be performed in the operating room or the intensive care unit according to local protocols. Potential complications should be considered, including low cardiac output, pulmonary hypertension, bleeding, arrhythmias, and the need to rapidly reinitiate VA ECMO support. Candidacy for recannulation should be discussed before attempting weaning and decannulation since survival declines with subsequent ECMO runs.[82,92,93]

Decannulation is a surgical operation that should be supervised by a suitably qualified surgeon and undertaken with formal general anesthesia and aseptic technique. The circuit tubing proximal to the cannula should be prepared and placed in the operative field. When removing a venous cannula, venous air embolism may occur through the cannula side holes if the patient is breathing spontaneously. This is prevented by either a Valsalva maneuver on the ventilator or by the use of short-term pharmacological paralysis. For peripheral cannulation, vascular reconstruction may be required depending on the cannulation technique. For central cannulation, chest closure can be considered if the ventricular function has improved significantly and indices of end-organ oxygen delivery are reassuring.

Failure to Wean

Failure to progress according to expected timing for etiology of cardiovascular failure should be investigated early to assess for residual lesions, inadequacy of hemodynamic or pulmonary support, or alternate diagnoses.[20,31] Cardiac catheterization may reveal residual lesions amenable to surgical or interventional correction not apparent on echocardiography.[94,95] With each attempt at weaning, the underlying cause of failure to wean (pulmonary, cardiovascular, or cardiopulmonary) should be determined to target optimal mechanical support strategies (Figure 4).

Risk Factors for Death

The mortality associated with pediatric cardiac ECMO is between 45% and 50% depending on the indication.[1,19,20] Risk factors for mortality in children on ECMO for cardiac indications include acute renal failure, bleeding, and pre-ECMO lactatemia and acidosis with delayed resolution post-ECMO initiation and ECMO duration.[19,96–101] Primary cardiac diagnosis has a significant bearing on mortality, in particular patients with single-ventricle physiology.[6] If myocardial function remains poor despite optimization of ECMO support and identification and management of residual lesions, consideration may be given to transition to longer-term device support (Figure 4). Such transition to longer-term VAD should occur along with assessment for cardiac transplantation. Transparent discussions with patient families and decision-makers must occur regarding the risk of mortality increasing over the course of longer duration VA ECMO. Setting expectations and goals of care in the event of failure of organ recovery should be built over the ECMO course, with shared values informing end-of-life care.

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