Management of Extracorporeal Membrane Oxygenation for Cardiogenic Shock

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KEYWORDS

• VA-ECMO • Cardiogenic shock • Mechanical circulatory support • Left ventricular unloading • Myocardial recovery • Harlequin syndrome • Bridging strategy • Multidisciplinary management

KEY POINTS

- Venoarterial-extracorporeal membrane oxygenation is a bridge therapy for refractory cardiogenic shock (recovery, transplant, durable ventricular assist device, or palliation) guided by a multidisciplinary shock team.
- Cannulation: peripheral (often femoral) or central, with hybrids (veno-arteriovenous, veno-venous venoarterial, and veno-venous arterial) to manage left ventricular (LV) distension and differential hypoxemia.
- Critical-care management: optimize oxygen delivery/oxygen consumption, monitor lactate and mixed venous oxygen saturation, LV unloading, anticoagulation, ventilatory and renal support, infection prevention, and early mobilization when feasible.
- Weaning and outcomes: use flow-reduction trials and imaging to assess native recovery; define exit strategy early; outcomes depend on etiology and center expertise.

INTRODUCTION

Cardiogenic shock (CS) is a critical state of inadequate tissue perfusion caused by diminished ventricular function, ultimately overwhelming cellular and physiologic compensatory mechanisms, leading to metabolic and inflammatory changes. Despite significant advances, CS remains a life-threatening syndrome with persistently high mortality rates. Various etiologies can lead to CS, including myocardial infarction (MI), acute myocarditis, severe arrhythmias, and other structural or ischemic cardiac injuries.[1–3]

Early intervention with mechanical circulatory support (MCS) in patients with acute heart failure is crucial for optimal outcomes. MCS strategies can include devices that provide either univentricular or biventricular support platforms. Univentricular support can include platforms such femoral Impella CP (Abiomed, Massachusetts, United

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Abbreviations

ACT	activated clotting time
ALI	acute limb ischemia
AMI	acute myocardial infarction
aPTT	activated partial thromboplastin time
CARDShock	General cardiogenic shock risk score
CI	cardiac index
CPR	cardiopulmonary resuscitation
CRRT	continuous renal replacement therapy
CS	cardiogenic shock
DO_2	oxygen delivery
DPC	distal perfusion catheter
ECMO	extracorporeal membrane oxygenation
ECPR	extracorporeal cardiopulmonary resuscitation
F_iO_2	fraction of inspired oxygen
HIT	heparin-induced thrombocytopenia
LV	left ventricle/left ventricular
LVAD	left ventricular assist device
LVEF	left ventricular ejection fraction
MAP	mean arterial pressure
MCS	mechanical circulatory support
MI	myocardial infarction
MOF	multiorgan failure
PCWP	pulmonary capillary wedge pressure
PEEP	positive end-expiratory pressure
PfHb	plasma free hemoglobin
RA	right atrium
RPM	revolutions per minute
RRT	renal replacement therapy
RV	right ventricle/right ventricular
RVEF	right ventricular ejection fraction
SAVE	Survival after veno-arterial ECMO
$ScvO_2$	central venous oxygen saturation
SV	stroke volume
SvO_2	mixed venous oxygen saturation
TTE	transthoracic echocardiography
VAD	ventricular assist device
VA-ECMO	venoarterial-extracorporeal membrane oxygenation
V-AV	veno-arterio-venous
VO_2	oxygen consumption
VV	veno-venous
V-VA ECMO	veno-venous–arterial extracorporeal membrane oxygenation

States) or 2.5 or axillary Impella 5.5 that provide left ventricular support. Other devices include Impella RP or the Protek Duo or Spectrum percutaneous right ventricular assist devices, which support the right heart. Despite improved survival with these univentricular platforms, veno-arterial extracorporeal membrane oxygenation (VA-ECMO) allows for comprehensive biventricular support to restore circulation. A delay in initiating VA-ECMO for CS is directly related to worsening outcomes and a higher mortality rate. Every 12-hour delay in initiating VA-ECMO has been shown to increase mortality,[4] while initiating VA-ECMO within 6 hours has been shown to decrease morbidity and mortality among patients with CS.[5] This article will focus on the role and management of VA-ECMO in CS.

INDICATIONS FOR VENO-ARTERIAL EXTRACORPOREAL MEMBRANE OXYGENATION IN CARDIOGENIC SHOCK

Clinical Criteria and Assessment (Hypotension, Hypoperfusion, Rising Lactate, and Escalating Vasopressors)

Profound hypotension, ongoing CS despite optimal medical treatment, escalating vasopressor requirements, rapidly deteriorating cardiac function, worsening lactic acidosis, and signs of end-organ hypoperfusion are the main clinical clues that MCS is required in CS. The ECMO-CS trial characterized rapidly deteriorating cardiogenic shock as a progressive hemodynamic instability necessitating repeated vasopressor boluses to maintain a mean arterial pressure greater than 50 mm Hg, together with impaired LV systolic function left ventricular ejection fraction (LVEF <35% or LVEF 35%–55% when accompanied by severe mitral regurgitation or aortic stenosis). Severe CS has been defined by a cardiac index (CI) less than 2.2 L/min/m^2 while receiving norepinephrine greater than 0.1 μg/kg/min and dobutamine greater than 5 μg/kg/min or by a systolic blood pressure less than 100 mm Hg while receiving norepinephrine greater than 0.2 μg/kg/min and dobutamine greater than 5 μg/kg/min with LVEF less than 35% or LVEF 35% to 55% in the presence of severe valvular pathologies.[6] Two consecutive lactate measurements ≥3 mmol/L or 2 consecutive mixed venous oxygen saturations (SvO_2) less than 50% (both ≥30 min apart) with a nondecreasing trend despite steady doses of inotropes or vasopressors can also reflect CS.[7] ELSO guidelines further highlight that CS appropriate for VA-ECMO can include a systemic systolic pressure less than 90, urine output less than 30 mL/hour, lactate greater than 2, SVO_2 less than 60%, and altered mental status for 6 hours unresponsive to optimal treatment. These studies stress that CS that is unresponsive to optimal medical management should prompt an early discussion regarding the use of VA-ECMO.

Common Etiologies

Common etiologies of CS requiring VA-ECMO support include acute MI (AMI), fulminant myocarditis, postcardiotomy shock, advanced chronic heart failure decompensation, cardiac arrest/refractory ventricular fibrillation (VF) or ventricular tachycardia (VT) (extracorporeal cardiopulmonary resuscitation [ECPR]), and drug-induced acute heart failure. The ELSO guidelines have included emerging etiologies for VA-ECMO support in recent years, such as massive pulmonary embolism, backup support for cardiological interventions (periprocedural support), arrhythmic storm, trauma (cardiac contusion), acute postpartum cardiomyopathy, sepsis, and drug intoxication[8] (**Fig. 1**).

Relative and Absolute Contraindications

Beyond the criteria and indications for VA-ECMO use in CS, being cognizant of exit strategy and recovery pathway for each patient is of great importance. One of the most common areas of discussion is whether the patient requiring VA-ECMO for CS is a candidate for transplant or a durable ventricular assist device (VAD) or whether the initial pathology is considered recoverable. VA-ECMO is generally not considered for patients who have unrecoverable disease and are not candidates for either transplant or VAD. However, there may be a role for VA-ECMO as a bridge to recovery alone. Another factor in decision-making is a reliable neurologic examination. This might be challenging during situations like ECPR, especially if CPR was on-going for more than 20 minutes before initiating VA-ECMO.

PATIENT SELECTION AND TIMING

Risk Stratification Tools (SAVE and ENCOURAGE Scores)

Risk stratification tools have been developed to predict survival following VA-ECMO and to assist with optimal patient selection. The Survival After Veno-Arterial ECMO (SAVE) score is a weighted prognostic model designed to estimate in-hospital survival in adults with refractory CS supported by VA-ECMO. The SAVE score integrates multiple pre-ECMO variables across several domains, including the etiology of cardiogenic shock, age, body weight, and acute pre-ECMO organ dysfunction involving the liver, kidneys, or central nervous system. Additional predictors include the duration of mechanical ventilation before ECMO initiation, peak inspiratory pressure, pre-ECMO cardiac arrest, diastolic blood pressure, pulse pressure, and serum bicarbonate concentration before ECMO initiation. An online calculator (www.save-score.com) enables clinicians to estimate survival probability before VA-ECMO initiation. Other risk models used to predict survival following VA-ECMO include the ENCOURAGE, REMEMBER, and CARDShock scores.[9]

Multidisciplinary Shock Team Approach

Although existing prognostic scoring systems, including SAVE, ENCOURAGE, CARDShock, and

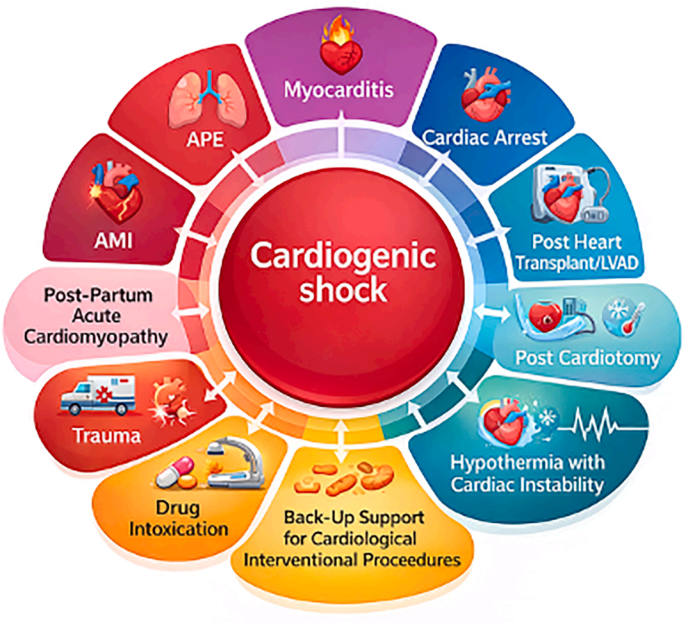


Fig. 1. Summary of the most common etiologies and clinical scenarios may lead to initiation of VA-ECMO. Conceptual schematic illustrating common clinical conditions associated with cardiogenic shock, including ischemic, inflammatory, arrhythmic, postprocedural, and systemic causes.

REMEMBER, aim to estimate survival in patients with CS, candidacy for VA-ECMO ultimately depends not only on predicted outcomes but also on the presence of a clearly defined exit strategy, such as myocardial recovery, bridge to heart transplantation, or bridge to durable ventricular assist device implantation. This concept is discussed later in this article.

Given the complexity of decision-making in this population, initiation of MCS should ideally involve a multidisciplinary team. At a minimum, this team should include a cardiothoracic surgeon, heart failure cardiologist, cardiac interventionalist, and intensivist working collaboratively as a dedicated cardiogenic shock team to optimize patient evaluation and management. In certain clinical scenarios, patients may require VA-ECMO support despite the absence of absolute contraindications to heart transplantation or transition to durable left ventricular assist device (LVAD), or heart transplant yet be unable to undergo comprehensive evaluation because of rapid clinical deterioration. This scenario, commonly referred to as a *bridge to decision*, necessitates expedited assessment.

EXTRACORPOREAL MEMBRANE OXYGENATION CONFIGURATIONS AND CANNULATION STRATEGIES

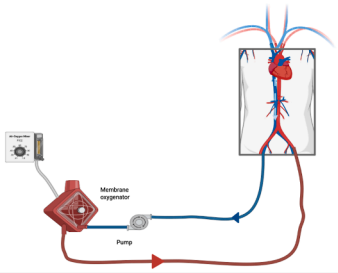
Veno-Arterial Extracorporeal Membrane Oxygenation

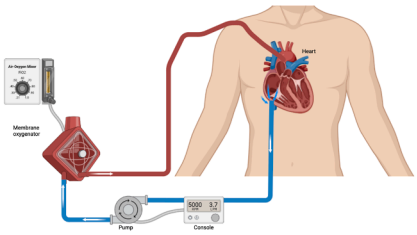
VA-ECMO delivers circulatory and respiratory support by diverting venous blood for oxygenation and removal of carbon dioxide and returning it to the arterial circulation. Cannulation can be performed using either peripheral or central approaches, each with distinct technical considerations, physiologic effects, risks, and clinical indications. Peripheral VA-ECMO is most commonly performed via the femoral vessels, with venous drainage through the femoral vein (advancing the cannula to the inferior vena cava [IVC] or right atrium[RA]) and arterial return through the common femoral artery.[10,11] Peripheral VA-ECMO offers rapid, percutaneous deployment and is therefore advantageous in arrest and quick onset shock. It is less invasive and compatible with some mobility. Its principal drawbacks include increased LV afterload from retrograde aortic flow, susceptibility to differential hypoxemia, risk of femoral access–related limb ischemia, and limited achievable flows in patients with small vessels or high cardiac output. On the other hand, central VA-ECMO is performed by draining venous blood from the RA and returning it to the ascending aorta via direct aortic or proximal branch-artery cannulation (subclavian, innominate, or axillary). Implementation commonly requires a sternotomy, open chest configuration, or axillary surgical exposure. However, it can deliver higher flow rates and is well suited for patients requiring maximal circulatory support. It also avoids limb ischemia and carries a lower risk of Harlequin syndrome.[12] While traditional central VA-ECMO may limit patient mobility, modified configurations—such as axillary or subclavian arterial return combined with percutaneous femoral or internal jugular venous drainage—can facilitate ambulation and rehabilitation.[13] Nonetheless, central VA-ECMO remains more invasive, cannot be deployed outside the operating room, and carries a higher risk of bleeding and mediastinal complications. **Fig. 2** highlights the key differences between the 2 cannulation methods.

Hybrid Configurations

These extend beyond traditional VA-ECMO configuration by integrating VV elements or by adding additional cannulas or circuits to address the physiologic limitations of VA-ECMO. They are most often implemented when CS patients experience differential hypoxemia (North-South Syndrome) or when higher hemodynamic support is needed beyond the capabilities of standard VA-ECMO flow. **Fig. 3** depicts the key pros and cons of different hybrid ECMO configurations.

- Among hybrid configurations, V-AV ECMO is most commonly used with coexisting severe pulmonary dysfunction to correct differential hypoxemia. It incorporates an additional venous return cannula, typically via the internal jugular vein, to augment oxygenated blood flow through the right heart and pulmonary vasculature, thereby improving coronary and upper-body oxygenation. This approach can be operationally complex due to the need for careful flow balancing, particularly in high-output states.[14,15]
- The dual VV-VA ECMO hybrid strategy involves 2 circuits—one supporting cardiac function, the other supporting pulmonary function. It allows for higher total ECMO flows and can correct differential hypoxemia. The technique is resource- and expertise-intensive, generally reserved for experienced, high-volume ECMO centers. It is not suitable for patients with small femoral veins or IVCs, and managing flow distribution across the 2 circuits can be technically challenging.[16,17]
- Single circuit VV-AV ECMO represents a hybrid approach that combines VV and AV support, offering both enhanced oxygenation and partial hemodynamic support when standard VV or VA-ECMO is inadequate.





Feature	Peripheral VA-ECMO	Central VA-ECMO
Cannulation	Femoral vessels	RA + ascending aorta
Flow direction	Retrograde	Antegrade
Placement speed	Fast, percutaneous	Slower, surgical
LV afterload	Higher	Lower
LV distention risk	Higher	Lower
Differential hypoxemia	Possible	Not typical, but possible
Invasiveness	Low–moderate	High
Ideal scenarios	UShock/ECPR, ICU/ED	Post-cardiotomy, OR

Fig. 2. Key differences between the peripheral and central cannulation methods.

Although conceptually similar to dual VV-VA ECMO, it employs only one ECMO circuit and oxygenator, with 2 venous drainage cannulas typically via the femoral veins.[18]

- Another notable hybrid configuration is VV-A ECMO. By adding an extravenous drainage cannula, it increases total venous return when conventional venous drainage is

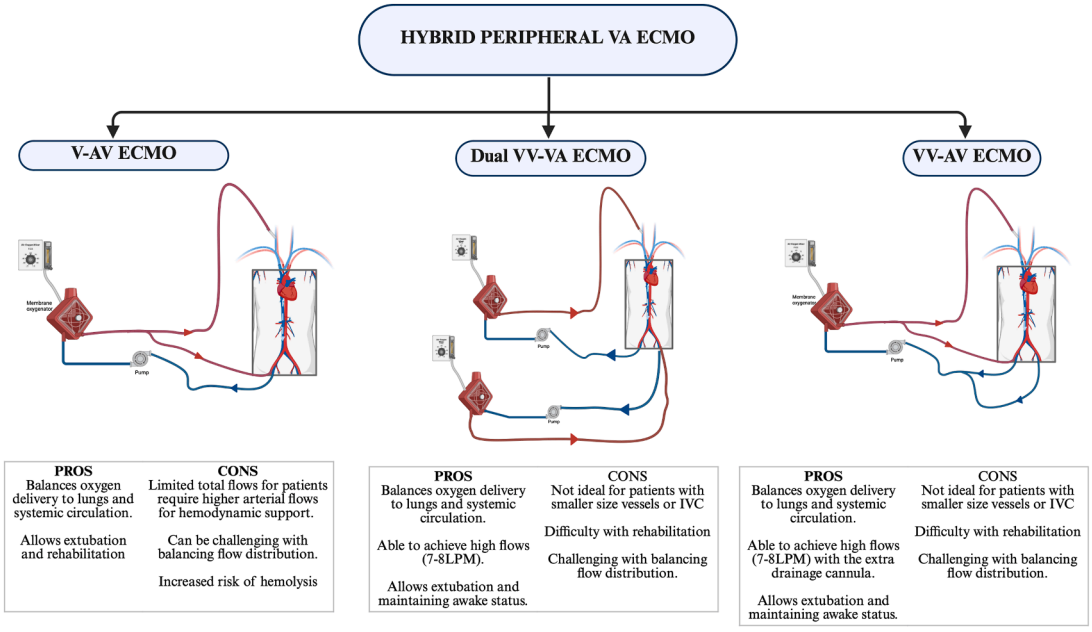


Fig. 3. Pros and cons of different hybrid ECMO configurations.

insufficient in VA-ECMO. This approach enables high-flow cardiac support, particularly in patients with large body size or severe right heart congestion. Unlike the other hybrid configurations, VV-A does not correct differential hypoxemia.[15]

Cannulation Techniques and Site Selection

The choice of ECMO cannulation strategy and site depends on the type of support required, the patient's anatomy and clinical status, as well as the risks and technical feasibility of the procedure. Fig. 4 depicts a flow chart process for cannulation strategy.

- *Physiologic support needed*: For patients in CS, the objective is to achieve adequate tissue perfusion, typically based on a CI 2.0 to 2.2 L/min/m^2 or higher (average adult male body surface area [BSA] ~1.9 m^2; female ~1.6 m^2). This translates to an average ECMO flow of approximately 3 to 5 L/min in most adults.[19] Furthermore, determining whether the support is intended primarily for cardiac or combined cardiopulmonary assistance guides the cannulation strategy, including consideration of appropriate hybrid ECMO configurations, and device management.
- *Anatomy, vascular access, and clinical condition*: Key factors in selecting a cannulation strategy include vessel size, presence of vascular disease, body habitus, hemodynamic stability, urgency of cannulation, and anticipated duration of ECMO support. The most used approach for VA-ECMO is peripheral cannulation via the femoral artery and vein. This technique can generally be performed rapidly and percutaneously under local anesthesia, making it suitable even for urgent scenarios such as saddle pulmonary embolism or emergency cannulation during cardiopulmonary resuscitation (CPR). In most adults, a 25 Fr venous cannula (suitable for veins >9 mm) and a 15 Fr arterial cannula (for arteries >5 mm) are adequate, providing ECMO flows of approximately 3 to 4 L/min. In rare circumstances, larger arterial cannulas such as a 17 or 19 Fr may be required. In patients with severe peripheral vascular disease, small peripheral vessels, significant lung injury, or high metabolic demand requiring flows that exceed the capacity of peripheral cannulas (typically >5 L/min), central or upper-body VA cannulation or hybrid ECMO configurations should be considered.[20]
- *Risk, complications, and technical feasibility*: Selection of the ECMO configuration, cannula type, and placement strategy should consider bleeding risk, limb ischemia, potential for left ventricular distension, goals for patient mobility and awake management, institutional expertise, and equipment availability. For

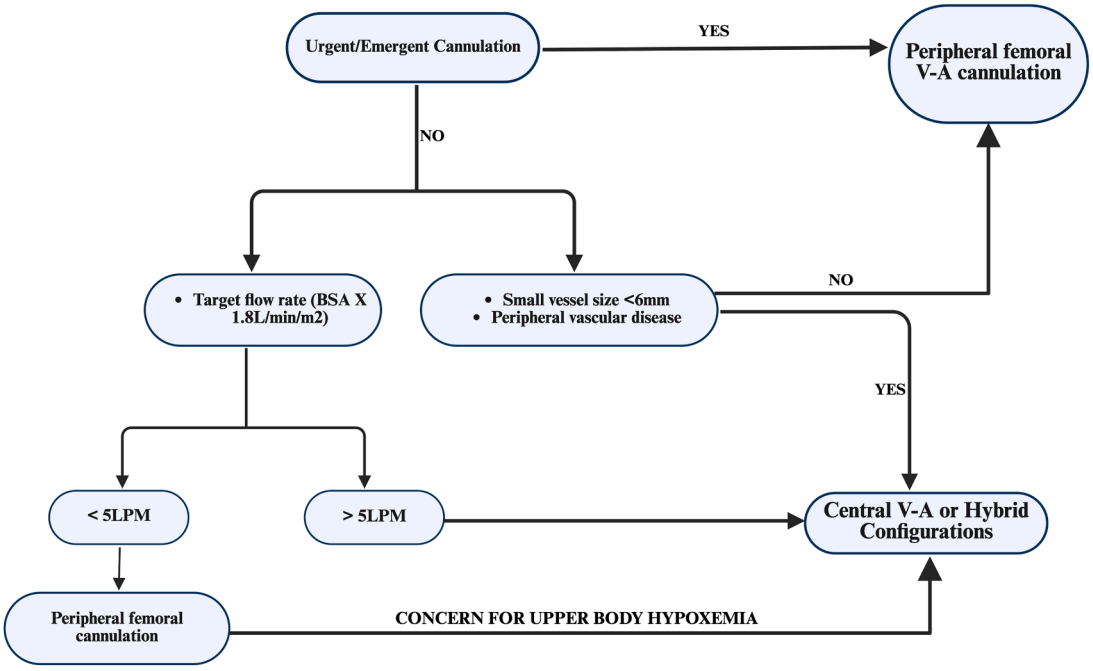


Fig. 4. Flow chart process for V-A ECMO cannulation strategies and configurations.

peripheral femoral VA-ECMO, the arterial cannula is typically positioned with its tip in the external iliac artery, delivering retrograde flow into the aorta. In this setting, blood from the left ventricle mixes with ECMO flow in the thoracic aorta, meaning the upper body is perfused primarily by native cardiac output. A key concern is limb ischemia in the cannulated limb, as large arterial cannulas can partially or completely obstruct flow in the common femoral artery, potentially leading to an under perfused or an ischemic limb. Routine use of an antegrade distal perfusion cannula is therefore recommended, typically via antegrade access of the superficial femoral artery using a 6 or 8 Fr cannula.[21] Femoral artery cannulation can be particularly challenging in patients with small or obese body habitus or preexisting peripheral vascular disease.[22,23] By contrast, central or upper-body VA cannulation is more invasive and generally requires general anesthesia. Central cannulation allows for higher ECMO flows through placement of large cannula and is associated with a lower risk of upper-body hypoxemia, making it especially advantageous in patients with severe pulmonary congestion or acute respiratory distress syndrome.

Impact of Cannulation Choice on Hemodynamics, Management, and Complications

Following is a summary of the different cannulation strategies, highlighting their hemodynamic effects, clinical management considerations, and principal complications (**Table 1**). Before initiating VA-ECMO in patients with CS, it is crucial to proactively evaluate the need for LV venting, with the aim of preventing or minimizing LV and aortic root stasis or thrombosis. The following flowchart illustrates a stepwise approach to assessing the requirement for LV venting (**Fig. 5**).

HEMODYNAMIC MANAGEMENT ON VENOARTERIAL-EXTRACORPOREAL MEMBRANE OXYGENATION

Physiology of Venoarterial-Extracorporeal Membrane Oxygenation Support

Normal tissue oxygen consumption (VO_2) and oxygen delivery to metabolizing tissues (DO_2) can be impacted by disease states, particularly those affecting oxygenation or cardiac output. The primary goal in managing critically ill patients is to maintain the DO_2:VO_2 ratio close to normal (~5:1) or, at a minimum, greater than the critical threshold of 2:1.[24] VA-ECMO restores a safe DO_2:VO_2 ratio and permits reduction of injurious ventilator settings and high-dose vasoactive medications. VA-ECMO preserves a near-normal DO_2:VO_2 ratio by diverting venous blood through a membrane oxygenator and returning it to the systemic circulation, thereby partially or completely substituting for the functions of the heart and lungs.[25] During partial VA-ECMO support, oxygenated blood from the circuit mixes in the aorta with blood ejected from the left ventricle after pulmonary passage. Consequently, arterial oxygen and carbon dioxide levels reflect the combined contribution of these 2 sources, and total systemic blood flow represents the sum of ECMO flow and native cardiac output. When VA-ECMO flow accounts for 100% of venous return, systemic pulsatility decreases due to minimal LV ejection.[26,27] Flow through the ECMO circuit is primarily limited by the size of the venous drainage cannula; therefore, the use of larger cannulas maximizes circuit blood flow potential. Physiologically adequate VA-ECMO flow enhances systemic oxygen delivery and blood pressure. However, high ECMO flow increases LV afterload due to elevated arterial pressure, which may impact myocardial recovery.[28] Despite this, the myocardium can generally recover, as preload is reduced, and coronary perfusion is maintained.

Monitoring Flow, Preload, Afterload, and Cardiac Recovery

Unlike other ICU patients, hemodynamic monitoring in CS patients supported with VA-ECMO differs significantly, requiring more invasive approaches. Monitoring typically includes, but is not limited to, arterial lines, Swan-Ganz catheters, and echocardiography. The 3 key elements of hemodynamic assessment in VA-ECMO patients are: systemic perfusion, circuit flow, and native cardiac function.[29]

- *Perfusion*: Clinical examination remains a cornerstone for assessing tissue perfusion in patients supported with VA-ECMO. Signs such as altered neurologic status, cold and clammy extremities, and oliguria may indicate impaired systemic or regional perfusion. Among laboratory indicators, serum lactate is a well-established marker of tissue hypoxia and inadequate oxygen delivery. Elevated lactate levels early after initiation of VA-ECMO are strongly associated with increased mortality, whereas lactate clearance has emerged as a marker of therapeutic response.[30,31] However, hyperlactatemia is not specific to hypoperfusion; adrenergic stimulation, hepatic

Table 1
Cannulation strategies, their hemodynamic effects, clinical management considerations, and principal complications

Cannulation Type	Hemodynamic Impact	Management Implications	Key Complications
Peripheral Femoral VA-ECMO	• Retrograde aortic flow ↑ LV after load • Risk of LV distention and pulmonary edema • Mixing point can cause differntial (Harlequin hypoxia)	• Monitor pulsatility closely for LV distention (may require IABP/Implella/vent) • Continuous right-arm arterial oxygen saturation (SaO_2) monitoring for Harlequin • Must place distal perfusion catheter to prevent limb ischemia • Limited mobility	• Limb ischemia (major risk) • Harlequin syndrome • Aortic root stasis/thrombosis from LV distension without adequate venting strategy • Stroke/embolism • Bleeding, vascular injury, pseudaneurysm
Central VA-ECMO	• Antegrade flow = more physiologic • Less increase in LV afterload • Excellent coronary	• Requires surgical sternotomy • Higher bleeding risk Allows high ECMO flows • Easy access for LV venting • Good for postcardiotomy support	• Major bleeding • Mediastinitis/infection • Tamponade or aortic injury • Surgical-site complications • Difficult maintaining awake state • Limited mobility
Hybrid VA-ECMO	• Lower risk of Harlequin syndrome	• Technically more complex • Monitor pulsatility closely for LV distension (may require IABP/Impella/vent) • Contiunous right-arm SaO_2 monitoring for Harlequin. • Must place distal perfusion catheter to prevent limb ischemia • Limited mobility	• Limb ischemia (major risk) • Harlequin syndrome • Aortic root stasis/thrombosis from LV distension without adequate venting strategy • Stroke/embolism • Bleeding, vascular injury, psudoaneurysm

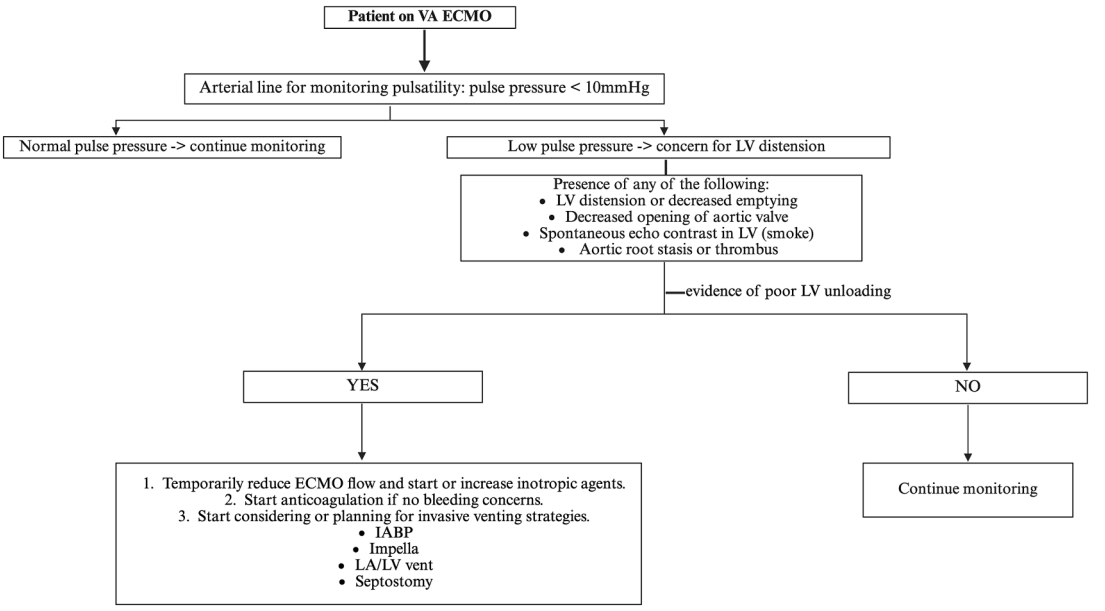


Fig. 5. Stepwise approach to assessing the requirement for LV venting.

dysfunction, and systemic stress can also contribute, and reduced lactate clearance often reflects underlying microvascular dysfunction.[32] Mixed venous oxygen saturation (SvO_2) and its surrogate, central venous oxygen saturation ($ScvO_2$), offer additional insight into the relationship between oxygen delivery and consumption.[33,34] Continuous monitoring of pre-membrane venous saturation within the ECMO circuit provides a practical real-time surrogate for $ScvO_2$, facilitating early detection of worsening perfusion.[35]

- *Flow:* The degree of ECMO support required depends largely on the patient's residual cardiac function. Individuals with severely depressed native cardiac output generally necessitate maximal support. ECMO support is primarily defined by circuit flow, with initial flow rates typically set at 50 to 70 mL/kg/min and targeted to maintain a mean arterial pressure greater than 60 mm Hg.[36] Flow is subsequently adjusted to optimize hepatic, renal, pulmonary, and neurologic perfusion. ECMO flow is determined by modifiable factors—including preload, afterload, and pump revolutions per minute (RPM)—and fixed factors such as cannula diameter and length. Increasing RPM generally augments flow, whereas reductions in flow at a constant RPM suggest decreased preload or increased afterload. Preload reductions may result from hypovolemia or bleeding, while afterload elevation commonly reflects increased systemic vascular resistance, cannula obstruction, or oxygenator thrombosis. From a physiologic standpoint, ECMO flow adequacy must be considered in relation to DO_2 and VO_2. DO_2 is a function of total cardiac output (native + extracorporeal), hemoglobin concentration, and arterial oxygen saturation.[37] In VA-ECMO patients, DO_2 should typically exceed 330 to 350 mL/min/m^2, with a DO_2/VO_2 ratio greater than 3 indicating adequate systemic oxygenation. Values lessser than this threshold may lead to tissue hypoxia despite apparently acceptable systemic hemodynamics.[38]
- *Cardiac function assessment:* Cardiac function during VA-ECMO is assessed through pulsatility, rhythm, and ventricular performance.
  - Low or absent pulsatility reflects reduced LV stroke volume and increased thrombotic risk, whereas improving pulsatility may indicate myocardial recovery.
  - Arrhythmias are frequent and may destabilize hemodynamics, necessitating continuous ECG monitoring. Life-threatening ventricular arrhythmias require immediate cardioversion or antiarrhythmic therapy, while severe bradyarrhythmia's may require temporary pacing, particularly during weaning of ECMO. Supraventricular tachyarrhythmias should be managed with rate control and correction of triggers. Early detection and treatment of rhythm disturbances are essential to support myocardial recovery.[30]
  - Ventricular performance: Echocardiography remains the standard modality for cardiac evaluation in VA-ECMO, enabling real-time characterization of loading conditions, ventricular function, and the interaction between the native circulation and the extracorporeal circuit.[39–41] It provides diagnostic and prognostic information throughout the course of support and is the preferred imaging modality. Comprehensive assessment includes chamber dimensions, global systolic function, and valvular performance, with particular attention to aortic valve opening as an indicator of left ventricular unloading. Persistent valve closure or progressive LV dilation denotes inadequate recovery with increased risk for intracardiac thrombosis, whereas the absence of biventricular dilation during flow reduction is consistent with improving cardiac function. Typically, ECMO flows are weaned to 1.5-2L of flow to get a reasonable assessment of cardiac function.

Ventricular Unloading Strategies

VA-ECMO elevates aortic afterload, and in the setting of severe LV dysfunction may result in a closed aortic valve, LV distention, and thromboembolic risk. Prompt identification of reduced pulsatility is essential. Low or absent pulsatility should prompt medical or noninvasive unloading measures before mechanical interventions are pursued.[42]

- Noninvasive LV unloading comprises ECMO optimization, pharmacologic support, and diuretics or renal replacement therapy. ECMO optimization entails avoiding excessive flow, maintaining preload, and improving oxygenation. Inotropes and vasodilators reduce afterload and promote LV ejection, while diuretics or renal replacement therapy lower preload and pulmonary congestion to facilitate LV recovery.
- Mechanical LV unloading is often required when the aortic valve remains closed, pulmonary edema is severe, PCWP is elevated, or echocardiography shows LV enlargement with *smoke* or blood stasis. **Table 2** summarizes

Table 2
Comparison of mechanical ventricular unloading strategies in veno-arterial extracorporeal membrane oxygenation

Strategy	Mechanism	Effectiveness	Advantages	Limitations/Risks	Best Clinical Situations
IABP	Counter pulsation reduces LV afterload and improves coronary perfusion	Moderate	Minimally invasive; widely available	Limited unloading in severe LV failure; vascular complications	Moderate LV distention; impaired coronary perfusion; preserved RV function
CP Impella (2.5/3.5)	Percutaneous axial flow device; LV→aorta	High	Rapid LV unloading; promotes myocardial recovery; percutaneous	Vascular injury; hemolysis; infection; cost; limited flow	Severe LV distention; closed aortic valve; pulmonary edema; high PCWP
Impella 5.5	Surgical or axillary placement; LV→ aorta	Very high	High flow; prolonged support; strong LV unloading	Invasive; vascular injury; bleeding; infection; cost	Severe LV distention; need for prolonged support; bridging to recovery or transplant
Atrial Septostomy	LA→ RA decompression	Moderate- high	Less invasive than surgical LV vent; continuous unloading	Technical complexity; risk of atrial injury; shunt-related hypoxemia	LV distention with high LA pressure; pulmonary edema; alternative to LV vent
LA Vent (via ECMO circuit or cannula)	Direct LA decompression	High	Continuous unloading; reduces pulmonary congestion	Invasive; risk of bleeding, infection	Severe pulmonary congestion; LV distention; closed aortic valve
PA vent	Drains blood from PA to ECMO circuit	Moderate	Reduces LV preload indirectly; decreases pulmonary congestion	Invasive; limited unloading; surgical risk	LV distention with pulmonary congestion; when other vents not feasible
LV Apical Vent	Direct LV apex cannula drains LV into ECCMO circuit	High	Direct, effective decompression	Highly invasive; surgical risk; bleeding, infection	Refractory LV distention; failure of percutaneous or IABP strategies

Abbreviations: CP, cardiac power; IABP, intra-aorta balloon pump; LA, left atrium; PA, pulmonary artery.

available strategies, highlighting their efficacy, benefits, and limitations.[43–48]

Management of Differential Hypoxemia (North-South Syndrome or Harlequin Syndrome)

With recovery of left ventricular function, antegrade ejection of blood from the pulmonary circulation may variably mix with retrograde, oxygenated flow from the ECMO circuit. If native lung function is impaired, this can result in preferential delivery of deoxygenated blood to the coronary arteries and aortic arch, leading to upper-body and cerebral hypoxia, known as Harlequin (North–South) syndrome. Monitoring includes right-sided upper-extremity or cranial oxygen saturation assessment, with arterial blood gas analysis obtained from the right radial arterial line. Key management principles are optimization of native lung oxygenation with mechanical ventilation, optimizing volume status, increasing ECMO flows if LV distension allows, and considering modifying to central VA or hybrid configurations. This may include an additional return cannula in the internal jugular vein providing additional oxygenated blood to the right heart (**Table 3**).[49,50]

CRITICAL CARE MANAGEMENT

Anticoagulation and Bleeding Management

Anticoagulation is essential in VA-ECMO to prevent circuit thrombosis and decrease risk of LV thrombosis, especially for CS patients with clinical evidence of LV distension or stasis. Unfractionated heparin is the most common choice of anticoagulation for VA-ECMO patients. However, bivalirudin is increasingly becoming favored in patients with heparin resistance, heparin-induced thrombocytopenia (HIT), or unpredictable heparin response. Bivalirudin is associated with more stable anticoagulation and possibly fewer bleeding and thrombotic events. Monitoring includes activated clotting time (ACT), activated partial thromboplastin time (aPTT), actived factor 10 (anti-Xa), or viscoelastic assays, with targets individualized to balance thrombosis and bleeding risk. Bleeding—often at cannulation, surgical, or gastrointestinal sites—may be managed by adjusting anticoagulation, correcting coagulopathy with platelets, plasma, or cryoprecipitate, and applying local hemostasis.[51] In patients at high risk for bleeding, low-dose or minimal anticoagulation strategies can be considered, emphasizing continuous monitoring and individualized management throughout VA-ECMO support.

Ventilator Strategies During Veno-Arterial Extracorporeal Membrane

Mechanical ventilation during VA-ECMO should prioritize lung protection while ensuring adequate gas exchange, as extracorporeal support partially or fully compensates for pulmonary function. Lung-protective strategies, including low tidal volumes (4–6 mL/kg predicted body weight), low

Table 3
Harlequin syndrome management on veno-arterial extracorporeal membrane oxygenation

Aspect	Key Points/Actions
Definition	Upper body hypoxemia due to mixing of poorly oxygenated native LV output with retrograde ECMO flow.
Causes/Risk Factors	Severe native LV ejection with poorly oxygenated lungs, peripheral femoral VA-ECMO, lung injury, low ECMO flow relative to native cardiac output.
Clinical Signs	Differential cyanosis (upper vs lower body), low right upper limb Spo2, low cerebral oxygenation, preserved lower limb saturation.
Monitoring	Right upper extremity ABG or Spo2, cerebral oximetry, arterial waveform, ECMO flow and LV function via echocardiography.
Stepwise Management	1. Optimize ventilator settings (Fio_2, PEEP) and treat underlying lung disease. 2. Increase ECMO flow if LV distention allows. 3. Modify ECMO cannulation (axillary/subclavian or central cannulation). 4. Adjust native cardiac output if safe (afterload reduction, inotropes). 5. Consider conversion to V-AV ECMO. 6. Continuous monitoring to ensure upper body oxygenation.
Key Points	Early recognition and prompt interventions are essential to prevent cerebral and myocardial hypoxia.

Abbreviations: ABG, arterial blood gas; Spo2, peripheral oxygen saturation.

plateau pressures (<25–28 cmH_2O), and adequate positive end expiratory pressure (PEEP) (8–15 cmH_2O), help minimize ventilator-induced lung injury.[52–54] Fraction of inspired oxygen (FiO_2) and respiratory rate can be reduced, leveraging ECMO flows and sweep gas for oxygenation and CO_2 clearance. In severe pulmonary compromise, hybrid ECMO configurations such as V-AV can be considered, ensuring ultraprotective or *lung rest* strategies to facilitate recovery. Ventilator settings should be continuously guided by blood gases, lung compliance, and hemodynamic interactions, particularly since VA-ECMO increases left ventricular afterload and may contribute to pulmonary congestion.

Fluid Balance, Renal Replacement Therapy

Fluid management is a critical aspect of VA-ECMO support, as both fluid overload and hypovolemia can adversely affect cardiac performance, ECMO flow, and end-organ perfusion. Positive fluid balance is associated with worsened pulmonary edema, impaired oxygenation, and increased morbidity and mortality. Therefore, careful titration of fluids guided by hemodynamics, echocardiography, and end-organ function is essential. Renal replacement therapy (RRT) is frequently required in VA-ECMO patients due to acute kidney injury, fluid overload, or electrolyte disturbances. Continuous RRT (CRRT) is preferred, allowing gradual fluid removal and solute control while minimizing hemodynamic instability. Early initiation of RRT may improve fluid balance and aid in myocardial recovery, particularly when combined with strategies to optimize left ventricular unloading.

Infection Prevention and Management

Infection is a frequent complication in VA-ECMO due to cannulation and extracorporeal circuits. Risk factors include urgency of ECMO cannulation (whether sterility was compromised), ECMO duration, mechanical ventilation time, and other factors (such as immunosuppression or CRRT). Prevention relies on decreasing ECMO and mechanical ventilation duration, strict aseptic technique, daily cannula assessment, and standard infection control practices. Early recognition through surveillance and prompt empiric antibiotics, with culture-guided deescalation, is essential to reduce morbidity and mortality. Multidisciplinary protocols integrating infection control with ECMO management to optimize patient outcomes.

Nutrition and Metabolic Support

Patients on VA-ECMO are often hypermetabolic, necessitating early nutritional support. Enteral nutrition is preferred to preserve gut integrity and immune function, with protein and caloric targets individualized. Parenteral supplementation is used if enteral feeding is insufficient. Close monitoring of glucose, electrolytes, and micronutrients is essential, with multidisciplinary coordination to optimize metabolic support and minimize complications.[55–57]

Mobilization and Rehabilitation on Venoarterial-Extracorporeal Membrane Oxygenation

Early mobilization and rehabilitation are feasible during VA-ECMO (especially on peripheral VA or modified central VA-ECMO with axillary or subclavian arterial return cannulas).[37,58,59] This helps prevent intensive care unite (ICU)-acquired weakness, preserve muscle mass, and improve functional outcomes. Activities range from passive exercises to sitting, standing, or ambulation, with progression guided by hemodynamics, ECMO flow, and patient tolerance. Multidisciplinary coordination and staff training are essential to ensure safety and optimize recovery.

WEANING AND DECANNULATION

The main goal for patients on VA-ECMO as a bridge-to-recovery is to determine the safe timing to liberate them from ECMO. In a systematic review conducted by Charbonneau and colleagues, they identified biomarkers, hemodynamic, and echocardiographic parameters that are associated with successful weaning from VA-ECMO in adult patients with cardiogenic shock. This review excluded ECPR and included 47 studies. In this study, the following indices predicted successful weaning from VA-ECMO[60]:

- Lower severity of initial shock (mean arterial pressure [MAP], lactates) and myocardial injury (troponins).
- Early recovery of systemic perfusion (lactate, liver enzymes, and microcirculation).
- LV recovery (LVEF > 20%–25%, left ventricular outflow tract velocity-time integral > 10 cm, Mitral TDSa > 10 cm/s).
- RV recovery (tricuspid annular plane systolic excursion $\geq$ 19 mm, RVEF $\geq$ 25%, Low RA/PCWP, High pulmonary artery pulsatility index).
- Stable MAP, CI, systolic blood pressure without significant increase in inotropic support and stable or improved LV/RV function during flow reduction trial and Pump-Controlled Retrograde Trial-Off.

Their designed algorithm to wean the patient from VA-ECMO can be seen in **Fig. 6**;

- Step 1: Assess baseline prognosis using severity of shock and myocardial injury markers.
- Step 2: Monitor for early recovery—systemic perfusion, lactate clearance, organ perfusion markers, and so on.
- Step 3: Evaluate native heart recovery—via transthoracic echocardiography (TTE)/transesophageal echocardiography (LV and RV function), hemodynamics—under *full support*.
- Step 4: Conduct a flow-reduction trial when stable, with close hemodynamic, perfusion, and inotropic/vasopressor monitoring.
- Step 5: If the patient remains stable during trial and shows adequate ventricular function, consider decannulation—that is, weaning success.

Overall, a trial of liberation from VA-ECMO should be undertaken only after the team has outlined specific weaning targets and ensured that no significant clinical variables are obscuring the true

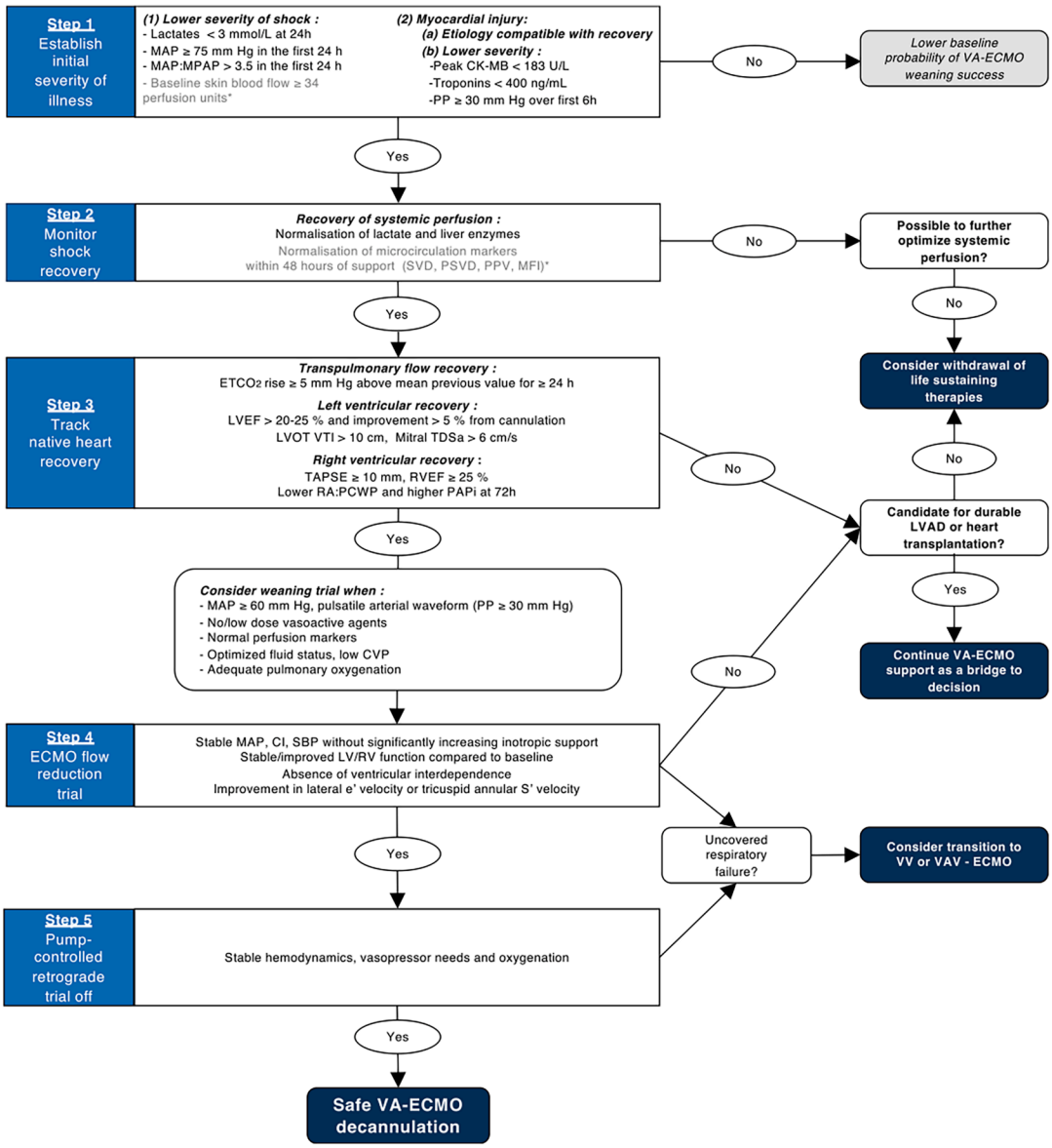


Fig. 6. VA-ECMO weaning protocol from Charbonneau and colleagues. *Investigational markers : this variable is considered an investigational marker. In practical terms, it means:It is not a standard, universally accepted bedside criterion for VA-ECMO severity or weaning readiness. (*Reproduced from* Charbonneau F, et al. Critical Care (2022) Dec 5;26(1):375. https://doi.org/10.1186/s13054-022-04249-w. Licensed under CC BY 4.0.)

hemodynamic status, considering that duration of VA-ECMO support beyond 4 days is also associated with higher mortality following liberation. The success rate can vary depending on the effectiveness of a center's liberation strategy and practice pattern. They recommended weaning VA-ECMO flows every 30 minutes to as low as possible (Toronto algorithm) to monitor hemodynamics and assess the patient's readiness for ECMO liberation.

In general, our group finds it extremely useful to perform daily bedside formal turn down trial with TTE on patients on VA-ECMO who do not exhibit signs of shock, their lactate is stable or down trending, they have greater than 10pts of systemic pulsatility and their inotrope and vasopressor requirements are decreasing. This approach provides insight into the trajectory of the patient and their chances of recovery. Critical TTE findings focus on RV and LV contractility, and dilation helps to optimize the patients before decannulation by starting a low dose of inotrope before decannulation.[60–63]

If patients are unable to be weaned or decannulated from VA-ECMO, it may indicate either they require additional time for recovery or that meaningful recovery is unlikely, in which case the care team should consider further evaluation and workup for candidacy for advanced therapies, durable mechanical circulatory support or palliative care.

COMPLICATIONS OF EXTRACORPOREAL MEMBRANE OXYGENATION IN CARDIOGENIC SHOCK

Bleeding and Thromboembolic Events

Bleeding and thromboembolic complications are frequent and have serious consequences with increased in hospital mortality of 40% to 50%.[64] Risk factors that increase bleeding complications on VA-ECMO include poor technical execution of cannulation resulting in vascular injury or retroperitoneal hematoma. Ultrasound or fluoroscopic guidance, and careful hemostasis are essential to minimize access-related bleeding complications. Thromboembolic events, including circuit thrombosis, limb ischemia, stroke, and systemic embolization, may occur despite anticoagulation. Prevention requires careful anticoagulation management, frequent monitoring of coagulation parameters (eg, ACT, aPTT, and anti-Xa), and prompt recognition of bleeding or thrombotic events. Strategies include adjustment of anticoagulation intensity, correction of coagulopathies, and use of mechanical interventions when necessary.

Limb Ischemia and Vascular Complications

Vascular complications are among the most frequent and clinically significant adverse events associated with VA-ECMO, particularly with peripheral arterial cannulation. Acute limb ischemia (ALI) is the most common vascular complication depending on patient factors, cannulation technique, and prophylactic measures such as distal perfusion catheter (DPC) use.[65] ALI may be precipitated by arterial obstruction, thromboembolism, loss of native pulsatility, venous compression, or systemic vasoconstriction from shock and vasoactive drugs.

Complications related to limb ischemia include compartment syndrome, fasciotomy, thrombectomy, and even limb amputation, with ALI associated with decreased in-hospital survival compared with patients without this complication. Acute vascular injury, pseudoaneurysm formation, hematoma, and groin wound infection are additional vascular complications observed during VA-ECMO support.[66] Early recognition with monitoring (eg, clinical examination, Doppler, near infrared spectroscopy) and prompt vascular surgical intervention when indicated are crucial to prevent permanent loss of limb and mitigate morbidity, although vascular complications remain a marker of higher overall morbidity in VA-ECMO populations.

Hemolysis

Hemolysis is a recognized complication of VA-ECMO caused by mechanical shear stress in the extracorporeal circuit, leading to rupture of red blood cells and release of plasma free hemoglobin (pfHb). It occurs at varying intensities, with severe hemolysis (eg, pfHb >500 mg/L) reported in up to ~4% of VAECMO patients, and broader ECMO associated hemolysis observed in ~5 to 18% of cases.[67] Elevated pfHb is associated with adverse sequelae including renal injury, increased transfusion requirements, and thrombotic events; even low-level hemolysis has been linked to complications such as nonhemorrhagic stroke during VAECMO.[68] Monitoring hemolysis with pfHb and lactate dehydrogenase is essential, and management focuses on identifying and correcting circuit or pump related sources of shear, optimizing cannula size and position, and addressing pump head thrombosis or high flow/pressure conditions that exacerbate red cell trauma.[69]

Neurologic Injury

Neurologic complications are relatively common and serious in patients supported with VA-ECMO. Pooled observational data demonstrate that overall neurologic injury is more frequent in VA-ECMO than in VV-ECMO, with neurologic complication rates of approximately 17% in VA-ECMO cohorts,

compared with ~10% in VV-ECMO patients.[70] Ischemic stroke is the most frequently reported event, while intracranial hemorrhage occurs less often and has been associated with factors such as central cannulation, low platelet count, and rapid changes in $PaCO_2$ at ECMO initiation.[71,72] Hypoxic-ischemic encephalopathy and seizures also contribute to the burden of neurologic injury. Spinal cord injury is rare but can be a devastating neurologic injury. Imaging and continuous neurologic monitoring are essential for early detection, as many events occur during the first week of support. Maintaining an awake patient aids in the rapid detection of neurologic injury and prompt intervention, which can mitigate the consequences of neurologic injury.

Multiorgan Failure Despite Support

Despite restoration of systemic perfusion with VA-ECMO, multiorgan failure (MOF) remains a leading cause of death in this population, reflecting both the severity of the underlying critical illness and persistent dysfunction of end organs from prior hypoperfusion, systemic inflammation, and complications of extracorporeal support. In large observational cohorts, MOF accounts for a substantial proportion of in-hospital mortality. Multiorgan failure can be compounded by organ-specific insults such as acute kidney injury requiring renal replacement therapy, systemic inflammatory responses, infection, and bleeding, which collectively contribute to a cycle of progressive organ dysfunction. Thus, early recognition of evolving organ dysfunction, optimization of perfusion and oxygen delivery, prevention and management of ECMO complications swiftly, and applying multidisciplinary care are crucial to mitigate progression of MOF and improve outcomes in patients supported with VA-ECMO.

OUTCOMES AND PROGNOSIS

Survival Rates and Functional Recovery

Survival outcomes for CS patients treated with VA-ECMO remain variable. Meta-analysis of large cohorts demonstrates differential mortality across etiologic groups, with myocarditis-related shock associated with lower mortality (~40%) and heart failure or massive pulmonary embolism showing intermediate mortality (~52%–53%), whereas causes such as AMI and postcardiotomy shock tend to have higher mortality (~59%–60%).[73] Observational studies report survival to hospital discharge ranging from approximately 29% to 63%, with many patients successfully weaned yet not surviving to discharge due to complications such as neurologic injury and MOF.[74] Long-term follow-up data suggest intermediate survival rates of about 35% to 37% at 1 to 5 years after VA-ECMO, indicating that a meaningful proportion of patients achieve durable survival beyond the acute hospitalization.[75] Among survivors, functional recovery is heterogeneous: some studies report that more than half of long-term- survivors regain independent activities and acceptable quality of life, although many may experience residual limitations in physical or psychosocial domains, highlighting the importance of structured rehabilitation and longitudinal follow-up.[76]

EXTRACORPOREAL MEMBRANE OXYGENATION AS A BRIDGE STRATEGY

ECMO is not a curative treatment, but rather temporary life support initiated to optimize care for critically ill patients expected to recover in weeks to months after receiving supportive or curative treatment.[77,78] It is also used as a bridge to decision as it allows for further evaluation for candidacy for advanced therapies (such as transplantation or durable mechanical circulatory support) for patients with no signs of cardiac recovery (**Fig. 7**). In certain cases, ECMO can play a role in palliative decision making for CS patients on ECMO with no chance of recovery and who are not candidates for advanced therapies.

Bridge to Recovery

By stabilizing hemodynamics and restoring end-organ perfusion, VA-ECMO allows time for myocardial recovery in reversible conditions or for comprehensive neurologic, end-organ, and psychosocial assessment in patients with uncertain prognosis. Recovery is most observed in potentially reversible conditions such as acute myocarditis, ischemia with timely revascularization, postcardiotomy shock, acute pulmonary emboli and stress-induced cardiomyopathy.[25]

Bridge to Advanced Therapies

In those without meaningful recovery, VA-ECMO serves as a bridge to advanced therapies, including heart transplantation or transition to durableLVAD support. Given its association with significant complications, careful patient selection, ongoing reassessment, and early planning for an exit strategy are essential to optimize outcomes.

Role in Palliative Decision-Making

When recovery or transition to durable support or transplantation is not feasible, VA-ECMO provides

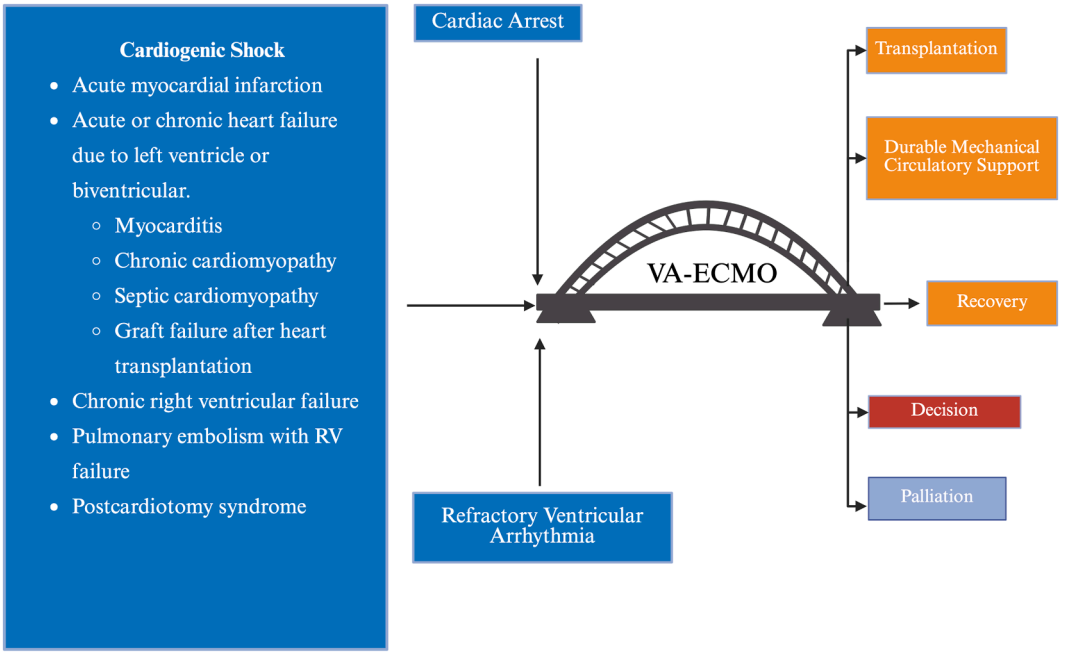


Fig. 7. VA-ECMO Bridging strategies.

a structured opportunity for shared decision making, including discussions about withdrawal of support and transition to comfort-focused care, emphasizing the importance of early goals-of-care conversations and multidisciplinary involvement.[79] In some cases, when consistent with patient preferences and institutional protocols, VA-ECMO can maintain hemodynamic stability during goals-of-care discussions and formal determination of death, facilitating donation after brain death or controlled donation after circulatory death.[80,81]

SUMMARY

VA-ECMO is an essential therapeutic modality for patients with refractory cardiogenic shock, offering immediate circulatory support and preservation of end-organ function. Clinical outcomes are closely linked to appropriate patient selection, early deployment, optimized cannulation strategies, effective left ventricular unloading, and vigilant management of ECMO-related complications within a multidisciplinary shock team framework. Ongoing advances in technology, cannulation techniques, and protocol-driven care are refining the role of VA-ECMO, strengthening its position as a structured bridge to decision, myocardial recovery, durable mechanical circulatory support, heart transplantation, or palliation.

CLINICS CARE POINTS

- Worsening shock despite optimized medical therapy should prompt early multidisciplinary evaluation for VA-ECMO before irreversible end-organ injury develops.
- VA-ECMO should be initiated with a defined exit strategy, including recovery, durable mechanical support, transplantation, bridge to decision, or palliation.
- Peripheral VA-ECMO can restore systemic perfusion but may increase LV afterload; pulsatility, aortic valve opening, pulmonary edema, and LV distension should be monitored closely.
- Narrowing pulse pressure on VA-ECMO should prompt urgent assessment for inadequate LV unloading and intracardiac or aortic root stasis.
- LV unloading strategies should be individualized according to anatomy, thrombus risk, severity of LV distension, institutional expertise, and anticipated duration of support.
- Patients supported with femoral VA-ECMO require monitoring for differential hypoxemia using right upper-extremity saturation or right radial arterial blood gas assessment.
- Cannulation strategy should account for urgency, vessel size, limb ischemia risk, mobility goals, oxygenation needs, and potential need for LV unloading.

DISCLOSURE

None.

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