Management of Extracorporeal Membrane Oxygenation for Postcardiotomy Cardiogenic Shock

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Postcardiotomy cardiogenic shock occurs in 3 to 5% of contemporary cardiac operations. Furthermore, refractory shock after cardiac surgery occurs in 0.5% of these procedures; the rate of patient survival to discharge is 25 to 44%.[1] Hence, early aggressive management with extracorporeal membrane oxygenation (ECMO) can offer a survival advantage. Overall criteria for using ECMO include failure to wean off cardiopulmonary bypass (CPB) in patients receiving maximum inotropic and vasopressor support with or without an intra-aortic balloon pump, postoperative cardiac arrest, and refractory cardiogenic shock (systolic blood pressure less than 80 mmHg, pulmonary capillary wedge pressure greater than 20 mmHg, and cardiac index less than 1.8 $l \cdot min^{-1} \cdot m^{-2}$).

ECMO initiated in the operating room or the perioperative period after cardiac surgery is referred to as postcardiotomy ECMO. Its most common indications are left ventricular, right ventricular, biventricular, and respiratory failure. ECMO provides cardiocirculatory assistance to support end-organ perfusion while allowing myocardial recovery. If recovery is not achievable, ECMO can bridge patients to durable mechanical circulatory support, heart transplantation, or palliation. The only absolute contraindication to ECMO is uncontrolled surgical bleeding. However, ECMO should not be considered if myocardial recovery is unlikely and if the patient is not a candidate for ventricular assist device implantation or heart transplant because of other considerations.

Postcardiotomy ECMO has become the most frequent ECMO application in the United States. Despite its use having rapidly increased with advances in technology, widespread availability, and increasing experience, this change has not been associated with improved outcomes.[1,2]

This review focuses on major clinical concerns that arise in the management of ECMO. Successful outcomes require close communication among the surgeon, anesthesiologist, and perfusionist in the operating room and with the critical care, nursing, and ECMO specialists in the intensive care unit (ICU). Daily multidisciplinary rounding focusing on all aspects of critical care and ECMO should be conducted by a protocol-based approach.

Cannulation Configuration

In ECMO, a centrifugal pump drives blood across an oxygenator for gas exchange. Approximately 40% of ECMO cannulation occurs in the operating room and 60% in the ICU.[3] Central aortic cannulation can be performed through the sternum with the cannulas already in place for CPB, or cannulation can be switched to a peripheral approach *via* the femoral, axillary, or subclavian artery to facilitate chest closure.

Central cannulation allows antegrade flow instead of retrograde peripheral flow, which can reduce the risk of differential hypoxemia (also known as Harlequin or north-south syndrome). Differential hypoxemia is a unique phenomenon that occurs during peripheral ECMO and is due to two blood circulation streams: antegrade from the left ventricle and retrograde from ECMO.[4] This creates a mixing zone that is located anywhere between the aortic root and the descending aorta, depending on the native cardiac output relative to ECMO flow. As the myocardium recovers, the mixing zone between the two circulations is pushed more distally along the aorta, from the root to the arch. As a result, with myocardial recovery in patients with severely reduced pulmonary gas exchange, upper parts of the body (heart, brain) receive poorly oxygenated blood, which can lead to hypoxia. In some patients, direct right atrial cannulation with a larger, multistage cannula can provide better drainage than femoral venous cannulation.

Peripheral cannulation can be performed percutaneously, directly by surgical cut-down, or with a short vascular graft. It allows chest closure, which can reduce mediastinal bleeding and facilitate early extubation with less sedation and earlier mobilization, and bedside decannulation in the ICU in selected patients. It is more readily performed outside the operating room than central cannulation and can also be done by nonsurgeons. In a systematic review and meta-analysis of ECMO studies (2,986 patients), peripheral

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ECMO was used in 79% of cases.[5] However, cannulation strategy varied widely, with the use of central ECMO ranging from 5 to 69% and peripheral ECMO from 25 to 94%, probably reflecting individual surgeon and institutional preference.[6] The short-term survival rate for ECMO patients is about 35% for either cannulation strategy.[7] The peripheral approach has been associated with less bleeding, transfusion, and renal replacement therapy, while the risk of limb complications, somewhat unexpectedly, is no higher than in central ECMO (see "Vascular Complications").[6,7] Finally, peripheral venoarterial ECMO may be associated with increased afterload, potentially resulting in more left ventricular distension than central cannulation. In addition, peripheral cannulation can result in suboptimal venous drainage, potentially resulting in less efficient ECMO than central cannulation. Randomized controlled trials directly comparing central to peripheral cannulation have not been conducted.

Coagulation Management

Anticoagulation management of ECMO requires thoughtful consideration because of the elevated risk of perioperative mediastinal hemorrhage and attendant coagulation system activation due to contact between blood and the synthetic surfaces of the ECMO circuit, resulting in thrombin generation and consumption of platelets. Thus, bleeding and thrombosis both remain common complications during ECMO.[8] Achieving the optimal coagulation balance is an art requiring continuous assessment of individual patient factors (eg, preoperative physical status, including antithrombotic exposure) and the effects of anticoagulation regimens deployed for ECMO. In the early transition from CPB to ECMO, the typically hemodiluted state after CPB presents a significant challenge for clinicians contemplating adding anticoagulant agents. Hemostatic changes can also be compounded in ECMO transition by clotting factor and platelet loss associated with intraoperative hemorrhage. Over time, the hemostatic system moves toward a more prothrombotic state as a feature of the acute phase response as the levels of affected hemostatic factors (eg, factor VIII, fibrinogen) increase, thereby increasing the need to introduce anticoagulant therapy.

The goal of anticoagulation in ECMO is to find the optimal degree of thrombin inhibition while avoiding excessive bleeding due to overanticoagulation. Intraoperatively, during the transition from CPB to ECMO support, it is common practice not to fully antagonize heparin unless there is excessive bleeding.

In managing bleeding, assessment for underlying coagulopathy is important, and any clinically relevant defects should be rapidly corrected. In the initial transition from CPB to ECMO, viscoelastic tests such as thromboelastography (TEG; Haemoscope Corporation, USA) or thromboelastometry (ROTEM; TEM International GmbH, Germany) in addition to partial thromboplastin time (PTT) can be used to supplement the traditional role of activated clotting time–directed assessment of heparin reversal. Among these additional tests for assessing heparin reversal, viscoelastic testing sometimes provides more rapid access to data (5 to 10 min) than PTT, which can take 30 to 60 min, depending on the laboratory system's design. The residual heparin effect is reversed with protamine if there is clinically significant bleeding.

The state of the residual heparin effect can be assessed by determining the prolongation of differential viscoelastic testing clot times between kaolin and heparinase reagent cups, with similar differential prolongation of clotting times in the ROTEM system. For routine laboratory assessment, the residual heparin effect manifests as elevated PTT that fails to correct with a test that mixes normal plasma with patient plasma showing the presence of an inhibitor—in this case, presumably heparin. The heparin effect can be confirmed with a thrombin time test. Given the multiple steps and lengthy interval required to assess heparin effect with traditional laboratory tests, they are generally not used for this purpose.

When addressing clinically significant bleeding, after the heparin effect is eliminated, additional parameters derived from either viscoelastic testing that examines clotting times and maximal clot strength or clot firmness, or conventional coagulation laboratory tests such as platelet count, PTT, international normalized ratio, and fibrinogen level, should be performed to guide transfusion therapy. Viscoelastic testing results can be displayed in real time in the operating room, helping to rapidly distinguish depletion of plasma coagulation factors and platelet effect from the heparin effect, thus allowing targeted blood product replacement. While not relevant during antifibrinolytic treatment already deployed during CPB, viscoelastic testing is the only clinically available means for assessing the fibrinolytic state, which may prove useful later in the postoperative period. Extracorporeal Life Support Organization (Ann Arbor, Michigan) guidelines suggest initial targets of a platelet count greater than 100,000/μl, international normalized ratio less than 1.5, activated PTT two to three times the upper limit of normal, and fibrinogen level greater than 100 to 150 mg/dl.[9] These targets should be adjusted if there is ongoing bleeding or thrombotic complications. There is a paucity of data regarding optimal platelet count, so we do not strictly adhere to a target platelet count greater than 100,000/μl in patients who are not bleeding. To avoid unneeded transfusions, we allow a platelet count as low as 50,000/μl if there is no evidence of bleeding. In severe cases of postcardiotomy bleeding, prothrombin concentrate complex and recombinant factor VIIa have been administered during ECMO, but we reserve these treatments for exceptional situations because of the risk of catastrophic circuit thrombosis. Given the unbalanced effect of factor VIIa on promoting thrombin generation, it should be used as a last resort and with modest dosing to avoid undesired circuit thrombosis.

Postoperatively, anticoagulation can be withheld for the first 12 to 24 h, as the risk of major bleeding is high during this period, provided that ECMO flows greater than 3 l/min are maintained to reduce the risk of circuit thrombosis. If there is major bleeding postoperatively, normalization of systemic coagulation status is preferred. A recent systematic review of six studies found satisfactory results of withholding anticoagulation for patients for ECMO in selected situations.[10,11] However, it is important to maintain native biventricular contractility to prevent thrombus formation in the left ventricular or aortic root. Multiple cases of thrombus formation have been reported in patients on ECMO despite coagulation test results indicating therapeutic anticoagulation.[12,13] Anticoagulation can be started once chest tube output has decreased to an acceptable rate (less than 50ml/h) and adequate hemostasis of the surgical sites is achieved. The intensity of anticoagulation and the time to achieve therapeutic levels depend on several considerations: open *versus* closed chest, the degree of coagulopathy, aortic valve opening, and the presence of a prosthetic valve or left ventricular vent.

Special precautions should be taken when using ECMO in patients with prosthetic valves; the low intracardiac flow associated with ECMO predisposes the prosthesis to thrombosis. Multiple cases of valvular thrombosis on ECMO have been reported in such patients despite adequate anticoagulation. Intuitively, the risk might be higher for patients with mechanical prostheses, but published reports comparing the incidence of thrombosis in bioprosthetic and mechanical valves are lacking.[14] The risks and benefits of initiating anticoagulation earlier or venting the left ventricle in patients with valvular prostheses should be considered.

We find value in performing several assays to assess the heparin effect in the early postoperative stages of ECMO anticoagulation management, since relying on PTT alone can result in higher doses of heparin due to assay-based heparin resistance, which is typically associated with high levels of factor VIII as part of an acute-phase postoperative response.[15] We sometimes observe excessively prolonged viscoelastic test–based clotting times, such as TEG clot time sometimes with no onset of clot formation, in patients with "therapeutic" PTT values. Some centers prefer to use more specific heparin assays based on measurable suppression of factor X cleavage of a chromophore since it is not affected by the elevated factor VIII levels seen in ECMO patients. This anti-Xa assay can at times be too specific, missing deficiencies in other clotting factors and thereby resulting in systemic overanticoagulation. Deficiencies of important coagulation factors like factor VII and fibrinogen are not detected by anti-Xa testing. This drawback underscores our rationale for using more than one probe of the coagulation system to monitor ECMO patient anticoagulation. We recommend close communication among the surgeon, the anesthesiologist, and intensivist teams in making these decisions. At our institution, coagulation management is also done in close consultation with transfusion medicine and perfusionists, and with nomograms for standardization.

Choice of Anticoagulation Agent

Unfractionated heparin (heparin) is most commonly used because of its quick onset, easy titration, low cost, and rapid neutralization with protamine. In patients with heparin-induced thrombocytopenia (HIT) or high clinical suspicion of HIT, direct thrombin inhibitors such as bivalirudin or argatroban are alternative anticoagulants. The HIT-risk scoring system most commonly used to assess pretest HIT probability is the 4-Ts score.[16] It has a lower predictive value in ECMO than in other clinical situations because of the thrombocytopenia frequently associated with ECMO—especially postcardiotomy ECMO—as well as the rapid decline in platelet count associated with ECMO circuit deployment.[17] In fact, circuit thrombosis is most commonly unrelated to HIT.[18] The incidence of HIT in ECMO patients ranges from 0.4 to 3.7% and is sometimes overestimated when immune assays available in most centers (*e.g.*, enzyme-linked immunosorbent assay–heparin–PF4 antibody testing) are used as the sole means to assess for HIT. Establishing an HIT diagnosis is difficult in this scenario, with many false-positive results noted on PF-4 enzyme-linked immunosorbent assay testing.[19,20] The strength of the heparin-PF-4 enzyme-linked immunosorbent assay test may help discern true HIT from false-positive cases. The laboratory should provide an optical density with heparin-PF4 results. In a commonly used heparin antibody test systems, an optical density greater than 0.400 is a positive result, but true cases tend to have optical density greater than 1.[19] Definitive diagnosis in ECMO-treated patients should be contingent on serotonin-release assay results that, while not immediately available, can be obtained in 1 to 2 days in operational systems that have established efficient specimen delivery and result reporting. Our typical reference laboratory throughput time for serotonin release assay results is 36 to 48 h.

For treating HIT, bivalirudin is preferred over argatroban because of its shorter half-life and its relatively independent organ-specific elimination. Bivalirudin is eliminated by proteolytic cleavage (80%) and renal excretion (20%), whereas argatroban is hepatically metabolized and cleared. Bivalirudin has been shown to be safe for use in ECMO patients, reportedly causing less bleeding than unfractionated heparin.[21,22]

Anticoagulation Monitoring

Anticoagulation monitoring and management remain significant challenges for patients on ECMO. Because high-quality evidence is lacking, anticoagulation practices vary among ECMO centers. Extracorporeal Life Support Organization guidelines[9] and a recent expert consensus statement[23] do not make specific recommendations. We

describe our anticoagulation practice here to help guide clinicians.

In our practice, anticoagulation monitoring begins with checking the coagulation status every 4 to 6 h during the initial postoperative period. This involves analyzing the activated PTT, antifactor Xa assay, and either thromboelastography (TEG) or thromboelastometry (ROTEM).[24] Viscoelastic testing can distinguish depletion of coagulation factors from the heparin effect. These targets should be adjusted if there is ongoing bleeding or thrombotic complications.

After we begin administering heparin, we first measure the activated PTT (goal, 50 to 70 s) and then assess the TEG (goal clot time [called R-time] prolongation of two to three times normal or 16 to 24 s) to determine concordance, which occurs about 35 to 40% of the time.[24] When these measures are discordant, we measure anti-Xa heparin activity (goal, 0.3 to 0.7 U/ml) to help resolve the discrepancy. We aim for at least two of the three monitoring laboratory values to be in the therapeutic range (table 1). Antithrombin and fibrinogen levels should be measured regularly, although the optimal antithrombin level for ECMO is unknown. Heparin resistance and the use of antithrombin III (antithrombin) supplementation are challenging aspects of management.[25] Antithrombin replacement can be considered in patients with heparin resistance and low antithrombin activity (less than 50%). We recognize that this is our algorithm in practice; other high-volume centers will differ, but the key is programmatic consistency to reduce variation. High-quality randomized trials of anticoagulation management are needed. Some centers prefer to use bivalirudin as the primary agent for anticoagulation since this eliminates any potential issue related to antithrombin levels.[26] Antithrombin supplementation is not frequently needed in our practice.

Left Ventricular Venting

In patients on venoarterial ECMO, increased afterload can lead to left ventricular distention, resulting in myocardial ischemia and pulmonary edema and reducing the likelihood of myocardial recovery. The actual prevalence of left ventricular distension is unknown.[27] The absence of left ventricular contraction alongside high ECMO flows results in the aortic valve not opening, the loss of pulsatility, and increased risk of thrombus formation in the cardiac chambers and aortic root.[28] The presence of left ventricular or aortic thrombus can result in catastrophic valvular thrombosis or systemic embolization in patients with improved myocardial contractility. Thus, preventing left ventricular distention can promote myocardial recovery, avoid pulmonary congestion, and prevent thrombus formation.

Table 1. Anticoagulation Assessment and Management

Time	Laboratory Test	Frequency	Goal
Intraoperative to 24 h	Platelets	Every 6 h	> 50–100 × 1,000/μl
	Fibrinogen		> 200 mg/dl
	PTT		< 40 s
	INR		< 1.5
After 24 h with hemostasis	Platelets	Daily	> 50–100 × 1,000/ μl
	Fibrinogen		> 200 mg/dl
	ATIII		> 50%
	PTT	Every 6–12 h	60–80 s
	Anti-Xa		0.3–0.7 U/ml
	TEG reaction time		2–3 times normal (16–24 s)

ATIII, antithrombin III; INR, international normalized ratio; PTT, prothrombin time; TEG, thromboelastogram.

Pulsatility in the arterial line and aortic valve opening on point-of-care echocardiography should be evaluated during daily ECMO rounds. Arterial pulsatility less than 15 mmHg, echocardiographic signs of aortic valve closure, left ventricular dilation, stasis, and elevated pulmonary capillary wedge pressure or pulmonary artery diastolic pressure may be manifestations of left ventricular distention (fig. 1). Noninvasive treatment strategies for left ventricular distention include decreasing ECMO flow, vasodilation, and increasing inotropic support; however, higher-dose inotropic support may increase myocardial work and the potential for arrhythmias. In patients with severe left ventricular distention, more invasive strategies, as listed below, may be considered.

In central ECMO, a catheter for direct left ventricular venting can be placed *via* a right superior pulmonary vein at the time of cannulation.[29] In a multicenter cohort study of 781 patients with a 36% overall survival, an left ventricular vent was used in only 8% of ECMO cases despite central cannulation being used in 31% of cases.[30] For peripheral ECMO, left ventricular unloading can be performed by percutaneous or minimally invasive procedures.[31,32] Percutaneous strategies include intra-aortic balloon pump support,[33] placement of percutaneous microaxial flow pumps such as the Impella (Abiomed; USA),[34] atrial septostomy,[35] pulmonary artery drainage,[11] and transseptal left atrial drainage.[13]

Intra-aortic balloon pump support is the most widely used unloading strategy, but it does not appear to offer a survival benefit.[36] In contrast, several studies have shown better survival with the combination of venoarterial ECMO and Impella support—a combination often referred to as "ECPELLA"—than with venoarterial ECMO alone.[34,37] This configuration is associated with increased cost, hemolysis,[37] and risk of vascular complications. The Impella is a microaxial flow pump that pumps blood antegrade from the left ventricular to the aortic root, thus reducing left ventricular end-diastolic pressure, myocardial wall stress, left ventricular stroke work, pulmonary capillary wedge pressure, and intracardiac and aortic root stasis.[37] Newer generations of Impella can continuously measure left ventricular end-diastolic pressure and cardiac power output to help assess left ventricular unloading. Moreover, in a systematic

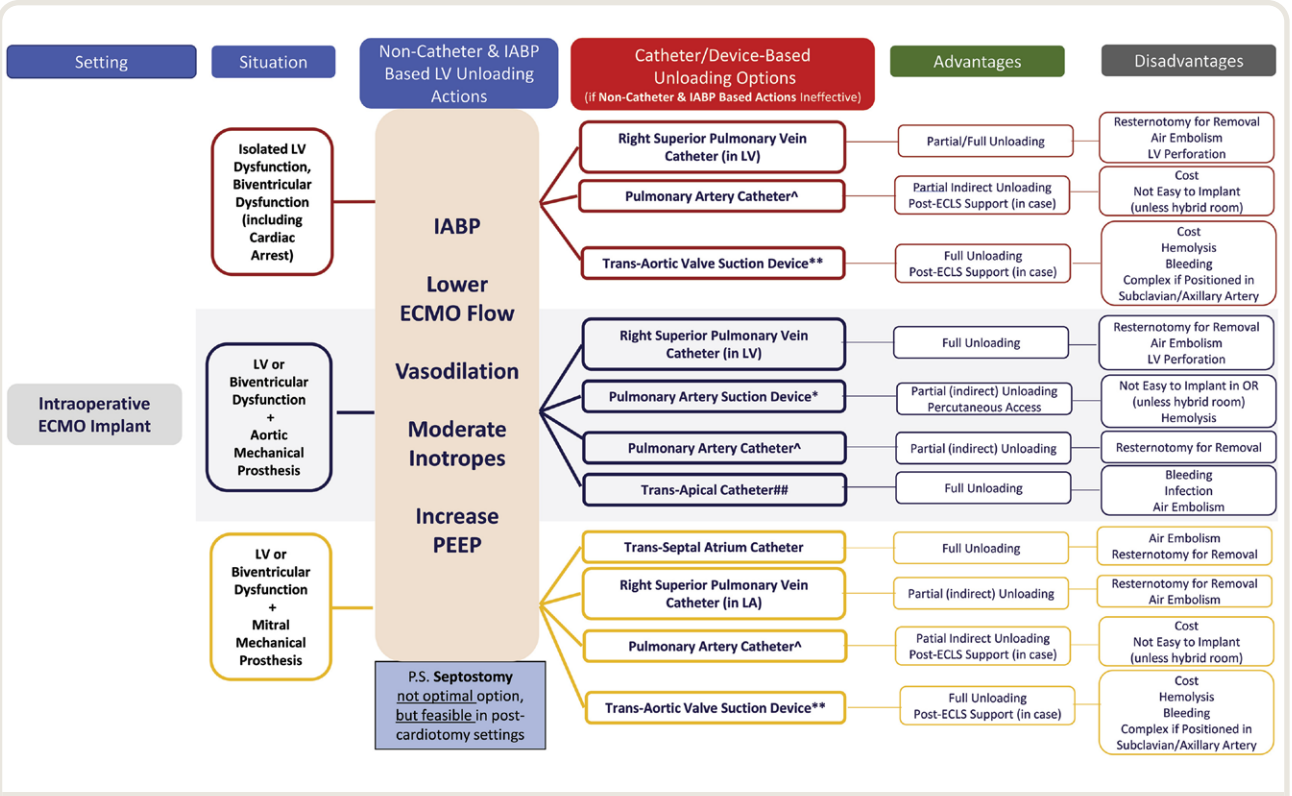

Fig. 1. Assessment of left ventricular distension and need for unloading by clinical monitoring. **Impella (Abiomed Inc., Danvers, Massachusetts); *Impella RP (Abiomed Inc.); ^single-lumen cannula; ##single- or double-lumen cannula. ECLS, extracorporeal life support; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; LA, left atrium; LV, left ventricle; OR, operating room; PEEP, positive end-expiratory pressure. (Reprinted from Lorusso R, Whitman G, Milojevic M, Raffa G, McMullan DM, Boeken U, Haft J, Bermudez C, Shah A, D'Alessandro DA: 2020 EACTS/ELSO/STS/AATS expert consensus on post-cardiotomy extracorporeal life support in adult patients. J Thorac Cardiovasc Surg 2021; 161:1287–331. Used with permission from Elsevier.)

review and meta-analysis of 7,995 patients and 62 observational studies, it appears that LV venting was better than no venting for early survival, and early venting (within 12 h of ECMO initiation) conferred a survival advantage over later venting.[38] A recent expert consensus statement declared that it was premature to recommend routine left ventricular venting for ECMO.[23] In our practice, when we use ECMO and the Impella concomitantly, we aim to provide adequate Impella venting as guided by echocardiography and pulmonary capillary wedge pressure to ensure left ventricular decompression while still maintaining arterial pulsatility. This often means a lower level of Impella support (P2 to P4) or some inotropic support than what is used in Impella-only management for cardiogenic shock without ECMO.

In treating cases of isolated or predominantly right ventricular failure, an alternative to conventional ECMO is using an isolated right heart support device with or without an oxygenator in the right ventricular assist device circuit called an "Oxy-RVAD" (oxygenator with right ventricular assist device) configuration.[23] Weaning of the oxygenator will facilitate a lower level of anticoagulation as well as reduce clot formation and hemolysis. However, the challenge is the limited durable mechanical circulatory support device options available when patients cannot be weaned from right ventricular support or ECMO. Palliative care may be necessary in these difficult cases.

Mechanical Ventilation

Most patients on ECMO have underlying pulmonary dysfunction and require mechanical ventilation in the immediate postoperative period. However, ventilator-induced lung injury can occur.[39] Lung-protective ventilation (tidal volume of 6 ml/kg of predicted body weight and a plateau pressure of less than or equal to 25 cm H_2O, with a positive end-expiratory pressure of 10 cm H_2O) is used to prevent barotrauma, volutrauma, atelectotrauma, and high driving pressure during ECMO for respiratory failure, although ECMO-specific criteria have not been established.[40] While positive end-expiratory pressure decreases left ventricular afterload, it increases right ventricular afterload and should be minimized in patients with right ventricular failure. The total carbon dioxide clearance is a result of alveolar ventilation and sweep flow. For a given alveolar ventilation, the sweep flow should be

titrated to maintain normocarbia, although data are still lacking on the optimal $Paco_2$ for the ECMO population.

Oxygenation Considerations

Total systemic oxygenation and ventilation result from the combination of native lung function and ECMO. Unlike central cannulation, peripheral cannulation involves retrograde arterial flow, which can lead to differential hypoxemia in patients with poor lung function after myocardial function recovers.[41] Therefore, oxygenation should be assessed in the right upper extremity to ensure adequate coronary and cerebral oxygenation and compared against a left radial or femoral arterial saturation if the right radial arterial line demonstrates hypoxemia. Differential hypoxemia can be mitigated by optimizing pulmonary function or increasing ECMO flows as tolerated. In cases of severe regional hypoxemia, switching from a venoarterial to a venoarterial venous configuration may be required, whereby another outflow cannula is placed in the right internal jugular vein and oxygenated blood is returned both retrograde *via* the femoral artery (about two thirds of ECMO flow) and anterograde *via* the jugular vein (about one third of ECMO flow). If cardiac function has recovered, the venous–arterial venous ECMO can then be converted to venovenous ECMO alone to provide only pulmonary support until the lungs recover.[4]

Weaning from ECMO

The decision to wean ECMO should be based on the indication for its use, individual patient characteristics, and patient readiness for weaning. Approximately 50% of patients are successfully weaned off ECMO.[23] Non–heart transplant patients should be given 72 to 96 h to allow stunned myocardium to recover[42]; the prospects of myocardial recovery begin to diminish after this period.[43] After the 72- to 96-hour recovery period, if neurologic function is preserved and refractory end-organ dysfunction is not present, conversion to a percutaneous microaxial pump (*e.g.*, the Impella 5.5) can be considered in patients who cannot be weaned because of left ventricular failure, which restores physiologic antegrade blood flow; alternatively, direct transition to durable ventricular assist device support may be considered in selected patients. For patients who are not potential candidates for a durable ventricular assist device or transplant, palliative withdrawal of ECMO should be considered if recovery is unlikely. Involvement of palliative care specialists is important in these challenging cases. ECMO can be continued for up to several days after transplantation to allow reversal of pulmonary hypertension or primary graft dysfunction.[43]

Weaning Trial

First, the patient should show hemodynamic and echocardiographic signs of myocardial recovery: pulsatile pulmonary and systemic arterial waveforms, adequate cardiac output, a stable mean arterial pressure (MAP), and requirement of only low to moderate doses of vasoactive medications. Second, the patient should show signs of improvement in metabolic disturbances such as lactic acidosis and ischemic hepatitis. Third, the patient should demonstrate improving pulmonary compliance and radiographic findings. In patients with myocardial recovery and severe residual pulmonary injury, bridging from venoarterial to venovenous ECMO should be considered.[44]

Weaning trials, alongside hemodynamic and echocardiographic variables, are critical to assessing underlying biventricular function and cardiopulmonary reserve. Before weaning is attempted, anticoagulation should be at therapeutic levels, or a small bolus of 2,000 to 4,000 U of heparin should be administered to decrease the risk of thromboembolic events during the low flow period. The flow rate should be reduced stepwise by 0.5-l/min increments to a minimum of 1 l/min under continuous hemodynamic and respiratory monitoring. Continuous echocardiographic biventricular assessment and pulmonary arterial pressure monitoring are advised. Pulse pressure appears to be the only clinical predictor of weaning success, but no universal predictive threshold value has been identified.[45] Echocardiographic parameters such as aortic velocity time integral greater than 10 cm, left ventricular ejection fraction greater than 20 to 25%, lateral mitral annulus peak systolic velocity greater than 6 cm/s, and more than 10% improvement in the tricuspid annular systolic velocity (right ventricular function assessment) are associated with successful weaning.[46,47] Furthermore, acceptable hemodynamic parameters include cardiac index greater than 2.2, central venous pressure less than 15 mmHg, MAP greater than 60 mmHg, and stable biventricular function with adequate gas exchange. In appropriate patients without left ventricular recovery but with preserved right ventricular function, ventricular assist device implantation can be considered.[48]

Major Complications

Bleeding

Bleeding is the most common complication with ECMO, with an incidence as high as 90% (fig. 2).[49,50] The most frequent sources of bleeding are the cannulation and surgical sites. The Extracorporeal Life Support Organization defines major bleeding as a hemoglobin decline greater than or equal to 2 g/dl or transfusion of greater than 10 ml/kg packed red blood cells in 24 h, as well as bleeding in the retroperitoneum, lungs, or central nervous system, or other bleeding requiring surgical intervention.[9] The ECMO circuit itself can exacerbate coagulopathy.[51] However, CPB-related coagulopathy, surgical bleeding, hypothermia, and residual heparin effect increase bleeding risk. Thrombocytopenia is common in patients on ECMO, secondary to platelet activation and functional impairment. The circuit induces

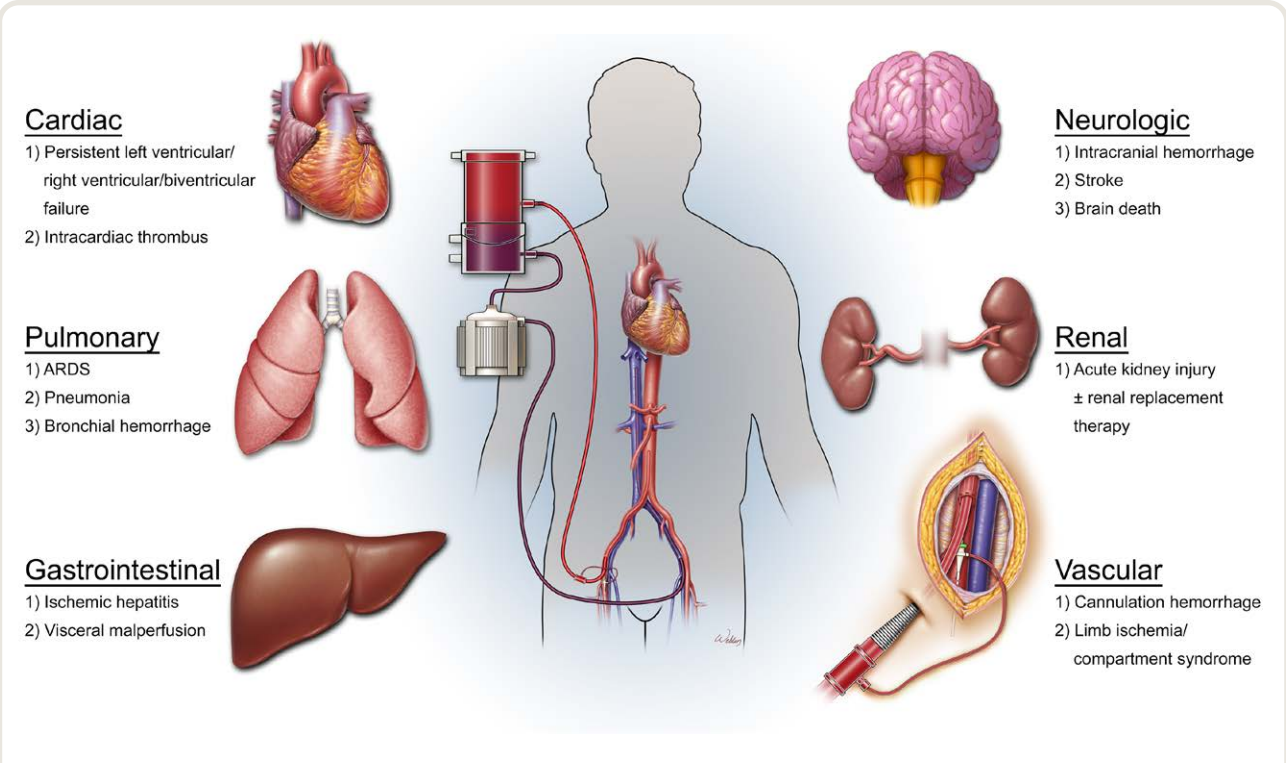

Fig. 2. Major complications during extracorporeal membrane oxygenation by organ system. Multiple organ systems are vulnerable to injury and dysfunction during a postcardiotomy extracorporeal membrane oxygenation run. Close attention and expectant management of complications are necessary to minimize the adverse consequences. ARDS, acute respiratory distress syndrome.

activation and aggregation, which can lead to thrombus formation. Concurrently, high shear stress leads to loss of platelet surface receptors, as well as loss of high-molecular-weight von Willebrand factor multimers, resulting in decreased binding to platelets and, thereby, an increased risk of bleeding. Coagulopathy should be managed as discussed in "Coagulation Management." Suspending anticoagulation during ECMO can be safe and reduce bleeding without increasing the risk of thromboembolic events, pump failure, or mortality.[11,52]

Central Nervous System Complications

Neurologic complications are more frequent in postcardiotomy ECMO than in other forms of ECMO, occurring in up to 30% of patients (fig. 2).[53] Major complications include embolic and hemorrhagic stroke, with embolic stroke more common in postcardiotomy ECMO.[54] Intracranial hemorrhage is the most devastating central nervous system bleeding complication and has been associated with long-term disability and mortality.[55] Ischemic stroke is usually embolic (air, thrombus).[56] Cerebral ischemia can result from unrecognized Harlequin syndrome or abrupt fluctuations in $Paco_2$, so consideration should be given to additional arterial line monitoring beyond a right radial line. Thrombocytopenia (platelet count less than 100,000/μl) and abrupt carbon dioxide fluctuation when ECMO starts have also been associated with intracranial bleeding and high mortality rates.[54] Diagnosis by neurosurveillance can be challenging because of sedation. Thus, a prompt diagnosis should be made with brain computed tomography imaging. Accurate neuroprognostication requires 72 to 96 h, and determining brain death requires careful deliberation with neurologists.

Vascular Complications

Major vascular complications during ECMO include limb ischemia, arterial dissection, and vascular injury leading to retroperitoneal hematoma; these have been shown to increase mortality risk (fig. 2).[57,58] The causes of limb ischemia are multifactorial and include large cannulas, preexisting peripheral artery disease, shock liver, and disseminated intravascular coagulopathy. The most devastating complication of severe ischemia is compartment syndrome requiring either fasciotomy or amputation. In our practice, if we suspect that patients are at elevated risk of vascular complications (because they have smaller femoral vessels), we favor initiating therapeutic anticoagulation earlier.

Distal perfusion cannulas, smaller arterial cannula size, and vascular graft placement are associated with a lower incidence of limb ischemia, and their combination is a routine

part of our clinical practice.[59,60] Also, open surgical cannulation through a graft as seen mainly in postcardiotomy-ECMO is associated with fewer vascular complications than percutaneous cannulation.[61] Any clinical suspicion of distal hypoperfusion should be followed up with a thorough physical examination, Doppler sonography, and angiography if needed. Treatment depends on various considerations and should be made by a multidisciplinary approach per one's own institution's practices.

Other major complications that clinicians may encounter during the course of ECMO are listed in figure 2.

Operating Room Considerations for Patients on ECMO

As the use of ECMO increases, the number of patients requiring urgent/emergency cardiac and noncardiac surgical procedures while on ECMO support will increase. Indications for emergency surgery for patients on ECMO include acute vascular complication and acute abdominal process. We briefly discuss some considerations for these patients' perioperative management.

Intraoperative Management

Monitoring. Continuous assessment of volume status, biventricular function, and the adequacy of global and regional perfusion is important. In addition to the standard American Society of Anesthesiology (Schaumburg, Illinois) monitors, several other monitoring modalities should be used intraoperatively for patients on ECMO (table 2).

Hemodynamic Goals. The intraoperative goal is to maintain euvolemia, biventricular contractility, and adequate MAP. Total body perfusion is determined by both ECMO flow and native cardiopulmonary function. At stable pump speeds, ECMO flow is preload-dependent and afterload-sensitive, so any abrupt changes affect the ECMO flow. Blood pressure should be maintained around MAP 60 to 80 mmHg. Low MAP during high ECMO flows in patients with a low systemic vascular resistance suggests sepsis, whereas low MAP in patients with decreased ECMO flows, no pulsatility, or both suggests hypovolemia or hemorrhage. Once hemorrhage is ruled out, volume administration and inotropes can be titrated to maintain adequate ECMO flows and native cardiac output.

ECMO Flows. Total systemic flow results from ECMO flow and native cardiac output. ECMO flows are dependent on adequate intravascular volume; as a result, intraoperative blood loss, changes in body position, increased intrathoracic or intra-abdominal pressure, and venodilation can decrease venous return, reducing ECMO flow. ECMO circuit vibration or "chatter" suggests hypovolemia in the circuit. Intraoperative acid–base status, lactate levels, and end-organ function should be assessed continually to determine adequacy of perfusion and required minimum ECMO flows. Higher ECMO flows should be maintained if anticoagulation is withheld during the procedure.

Pulsatility. Pulmonary and systemic pulsatility represent myocardial contraction and valvular opening. Decreased or no pulsatility could be due to low preload from high ECMO flows, minimal contractility, or high systemic vascular resistance. Pulsatility should be maintained with inotropes and ECMO flow titration if tolerated, especially when anticoagulation is withheld, to prevent stasis and thrombus formation.

Table 2. Monitoring Tools for the Patient on Venoarterial ECMO

Monitor	Assessment
Arterial line	MAP, left ventricular pulsatility
Pulmonary artery catheter	Right ventricular pulsatility, PCWP, Svo_2, CVP
TEE	Volume, right ventricular size/function, left ventricular distention, ventricular stasis/thrombus
Pulse oximetry	Right upper extremity during peripheral ECMO to assess for regional differential hypoxia
Near-infrared spectroscopy	Regional cerebral oxygen saturation (brain and lower extremities in peripheral ECMO)

CVP, central venous pressure; ECMO, extracorporeal membrane oxygenation; MAP, mean arterial pressure; PCWP, pulmonary capillary wedge pressure; Svo_2, mixed venous oxygen saturation; TEE, transesophageal echocardiography.

Conclusions

Patients requiring postcardiotomy ECMO after cardiac surgery are at risk of needing urgent surgical intervention. Contemporary anesthesiologists and critical care physicians should be familiar with the fundamentals of hemodynamic and anticoagulation management, as well as aiming for early recognition of potential complications, for optimal outcomes.

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Competing Interests

The authors declare no competing interests.

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