CHAPTER 195

Extracorporeal Membrane Oxygenation for Cardiac Support

Gianluca Villa, Stefano Romagnoli, Zaccaria Ricci, and Nevin Katz

OBJECTIVES

This chapter will:

1. Describe the general configuration and operating principles of a venous-arterial extracorporeal membrane oxygenation (ECMO) system.
2. Review the main indications for starting and stopping ECMO.
3. Detail specific pathophysiologic conditions of ECMO patients.
4. Discuss the possible side and negative effects of an ECMO treatment.

Extracorporeal membrane oxygenation (ECMO) is an artificial extracorporeal therapy that consists of a specific heart-lung machine aimed at providing temporary respiratory and/or circulatory support.[1,2] Extracorporeal life support (ECLS) specifically for cardiocirculatory assistance (commonly named venous-arterial extracorporeal membrane oxygenation, VA-ECMO) allows circulatory support and blood gas exchange in patients with reversible cardiac failure.[3] On the other hand, venovenous extracorporeal membrane oxygenation (VV-ECMO) allows extracorporeal oxygenation, and it is used for lung support during acute respiratory failure.

Studies on ECMO began many years ago, and its use for cardiac support has increased steadily over the past decade.[4] Feasibility and efficacy of ECMO for pediatric patients have been well established in literature since the 1990s,[5] whereas adult routine applications are more recent. Depending on the indications for treatment initiation, several studies have reported the positive outcome of ECMO in children requiring cardiac support.[6] On the other hand, benefits in adult patients have been more difficult to demonstrate,[7,8] and ECMO was reported to be less successful in adult patients requiring cardiovascular support. Recent data have shown improvement in safety, clinical efficacy, and cost effectiveness of VA-ECMO for adult patients requiring cardiocirculatory support.[6,9,10]

Since the 1990s, the Extracorporeal Life Support Organization (ELSO) collects data on ECMO utilization, compares outcomes, and worldwide shares different experiences and expertise on ECMO use in pediatric and adult patients.[3]

Currently, the results of recent positive trials, improvements in technology (improving successful ECMO applications), and the development of specialized centers, capable of transporting patients requiring ECMO from outside facilities to their intensive care units (ICUs), contributed to a growing interest in ECMO assistance for adults with cardiogenic shock.[3] Over the last 10 years, the use of ECMO, regardless of indication, has been progressively increasing; in particular, the volume of patients undergoing ECMO in the United States increased fourfold from 2006 to 2011.[3] According to the last ELSO Registry Report/International Summary update to Jan 2016, data from 30,000 patients undergoing ECMO for cardiac support have been collected (7500 neonatal, 10,800 pediatric and 10,200 adult patients) with a mean survival rate of 60% (http://www.elsonet.org/).

TECHNICAL ASPECTS

The main purpose of VA-ECMO application is to guarantee an adequate oxygen delivery (DO_2) through the improvement of tissue perfusion. ECMO involves the use of mechanical devices including a pump, a circuit, and an artificial lung (see Fig. 195.1).

Specifically, for cardiac support, venous blood is drained from a cannula usually inserted via the femoral vein into the right atrium. Venous blood is pushed through an artificial lung for CO_2 removal and oxygenation and then back into the systemic circulation via an artery (usually the femoral). The native and artificial lungs are in parallel in this configuration and the function of the native lung can be replaced, totally or partially. The different circuit components are selected to support a blood flow rate above 3.0 L/min/m^2. According to ELSO indications, target flow rates should be at least 100 mL/kg/min for neonates, 80 mL/kg/min for pediatric patients, and 60 mL/kg/min for adults. A mixed venous saturation greater than 70% is considered a satisfactory indication of adequate systemic perfusion.[11]

In VA configuration, if venous blood is not totally drained (partial VA bypass), circulating blood results from a combination of (1) blood ejected by the left ventricle into the aorta, after the native lung circulation (potentially poorly oxygenated in case of lung associated damage/dysfunction); (2) artificially highly oxygenated and normohypocapnic blood pumped into the aorta (usually via a femoral artery with a retrograde flow toward the heart, Fig. 195.1) by a mechanical pump. The highly oxygenated blood pumped through the femoral artery mixes with the poorly oxygenated blood coming from the aorta (variable in flow) potentially leading to proximal circulatory hypoxemia including the coronary circulation and the brain (mainly from the right carotid artery) in the so-called Harlequin syndrome.[11] To partially address this issue, additional inflow cannulation into the right internal jugular vein thus has been proposed, creating a venous-arterial-venous ECMO (VA-V-ECMO).[11] Alternatively, a better drainage of the right heart could be attempted, by increasing the pump flow and/or improving the ventilation and oxygenation of the native lung. Gas analysis from the right radial artery and peripheral oxygen saturation of the right hand should be monitored carefully during VA-ECMO to verify the adequate oxygenation in the proximal vascular branches.

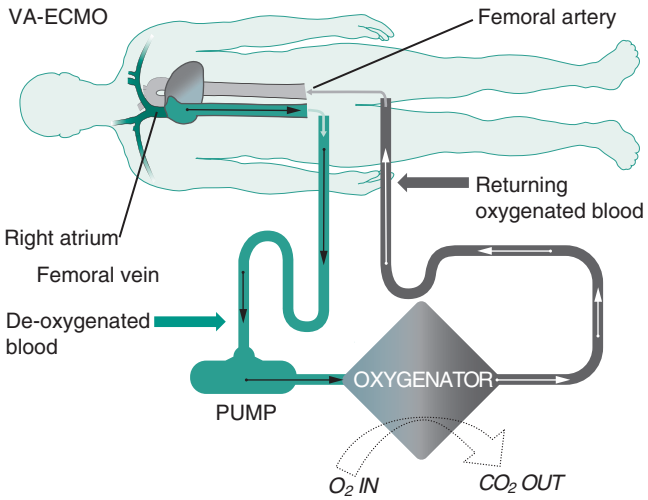

FIGURE 195.1 Components of the ECMO circuit in VA configuration. The venous blood is drained from a cannula inserted via the femoral vein into the right atrium; it is pushed through an artificial lung for CO_2 removal and oxygenation and then back into the systemic circulation via femoral artery.

Circuit Components

Technology of ECMO circuits (heparin-coated), pumps, and oxygenators have been improved considerably during recent years. The ECMO system consists of four main components: (1) tubing and cannulas; (2) pump; (3) gas exchanger (artificial lung); (4) heat exchanger. This main system commonly is completed by pressure monitoring sensors, accesses for therapy infusion, hemofiltration circuit, user interface displaying the main treatment parameters. Circuit setup is tailored to the patient depending on body weight, clinical purposes, and institutional protocols.

The venous cannula (drainage side) and blood tubing are the major flow-limiting components through the circuit. In line with the Poiseuille's equation, the shorter and larger (internal diameter) is the cannula placed in the right atrium, the higher is the blood flow into the circuit. In the adult setting, vascular cannulation usually is accomplished percutaneously using the Seldinger technique and ultrasound guidance, whereas the surgical vessel exposure is more common in the pediatric population. However, cannulation techniques vary depending on the type of support needed, patient's age and size, and clinical situation. In VA-ECMO for adults, the femoral vessels are usually the first choice; only in particular conditions (e.g., burns or significant peripheral vascular disease) could the axillary artery be used alternatively as an inlet line. Small shunting catheters generally are placed distally to the arterial femoral cannula to avoid limb ischemia (a not-uncommon complication before shunting technique application); alternatively, the femoral artery can be approached by anastomosing a PTFE vascular graft (end-to-side) to create a bidirectional flow.[12] Additional inflow cannulation into the right internal jugular vein has been proposed to guarantee the adequate oxygenation of the upper body.[11]

Roller or centrifugal pumps are the main systems currently used for ECMO circuits. The roller pumps have been replaced almost totally by the centrifugal ones for routine ECMO assistance because of the application of nonocclusive propeller that reduces the trauma on the tubing system and of smaller priming volumes. Centrifugal pumps consist of an impeller arranged with either vanes or a nest of smooth plastic cones inside a plastic holder. The impeller couples magnetically with a small and light motor. The impeller spins at 2000 to 5000 revolutions per minute (RPM), creating a constrained vortex that draws blood into the pumphead and drives it out toward the gas-exchanger. The magnet inside the disposable pump head creates a centrifugal force that contributes to blood circulation (i.e., a negative pressure at the inlet port of the pump pulling blood into the pump holder and a positive pressure at the outlet port). Blood stagnation and heating in the pump, thrombus formation, cavitation (i.e., air bubbles in the blood), and hemolysis are rare but potential complications that should be considered during the treatment with centrifugal pumps. Because centrifugal pumps are preload and afterload dependent, the generated blood flow decreases if blood volume coming from the draining vein is reduced and/or post-pump pressure increases. Pulsatile flow is recently available for VA assistance, potentially allowing a better perfusion than with continuous nonpulsatile flow. For similar reasons, the intraaortic balloon pump has been tested while VA-ECMO is applied.[13]

Modern oxygenators are manufactured as hollow fiber microporous membrane lungs, significantly more efficient, easier to prime than the older silicon rubber membranes. Plasma leakage may be associated with the use of this oxygenator, and it has been addressed by coating the fibers with a very thin skin of gas permeable membrane. Less platelet and plasma protein consumption, more effective gas exchange, lower resistance to blood flow (facilitating the use of centrifugal pumps), and minimal priming volumes are advantages associated with hollow-fiber oxygenator. An air–oxygen mixture flow, delivered to the oxygenator, maintains the diffusion gradients for O_2 supplementation and CO_2 removal across the membrane. The gas flow rate must be set to obtain the desired pCO_2 of the postoxygenator blood while the FIO_2 determines its pO_2.

Patient's body temperature is maintained by hot water circulating in the heat exchanger of the ECMO circuit that puts the circuit and the water bath in contact. Thanks to the heat exchanger, therapeutic hypothermia and/or controlled temperature and rewarming are possible during VA-ECMO treatment.[11]

During VA-ECMO, if left atrial pressure is elevated (e.g., in case of failing left ventricle), a transseptal catheter (vent) can be placed to drain the left atrium, or the left ventricle can be directly drained from the apex, via a left minithoracotomy.

During VA-ECMO, the patient's arterial O_2 content depends on the blood coming from the oxygenator (highly oxygenated and well decarboxylated), the blood coming from the native lung (potentially badly oxygenated and decarboxylated), and the site of sampling. Oxygenation obtained by means of ECMO oxygenator mainly depends on (1) technical characteristics of the membrane (geometry, thickness of the blood film, materials, red blood cells transit time and FiO_2), (2) oxygen saturation in the ECMO drainage cannula (coming from the patients), and (3) hemoglobin concentration and blood flow in the ECMO circuit.[11] Depending on the organ's dysfunction, the ventilator usually is set in protective modality (low pressure, low volume, low FiO_2) while sweep gas and oxygen supply to the ECMO oxygenator are targeted to the desired arterial CO_2 and O_2.[11]

An adequate anticoagulation is necessary during ECMO because the different biomaterials and plastics can induce thrombosis. However, as current generation circuits and oxygenators are heparin coated, or coated with a biocompatible materials, bleeding complications are more frequent and serious than thrombosis.[11] Heparin should be titrated to obtain 40 to 55 seconds for activated partial thromboplastin

or 1.2 to 1.8 times normal; alternatively 1.5 times normal activated clotting time can be considered.[14]

The ECMO circuit should be monitored several times daily by the medical and nursing team and at least once a day by a perfusion technician or other ECMO specialists for fibrin deposits and clots. Moreover, the circuit should be evaluated periodically for appropriate functioning and cannulation site for signs of inflammation and infection. Similarly, particular attention should be paid for patients monitoring during ECMO. In particular, perfusion pressure, arterial pulsatility, lactate levels, urine output, and creatinine levels should be checked carefully. Oxygen saturation of the superior vena cava, together with common indicators of tissue perfusion and oxygenation (e.g., lactates, urine output), are indicators of oxygen delivery/oxygen consumption ratio adequacy during VA-ECMO.[11]

INDICATIONS FOR STARTING AND STOPPING VA-ECMO

VA-ECMO indications in adult and pediatric patients with cardiac failure are determined mainly by (1) the presence of cardiogenic shock resulting from potentially reversible causes (with the exception of cases for bridge to long-term therapies); (2) inadequate tissue perfusion despite adequate intravascular volume and inotropes-vasoconstrictors administration; and (3) lack of ECMO contraindications.[15]

According to ELSO, there are no absolute contraindications to ECMO support. Nevertheless, some conditions are known to be associated with a poor outcome despite ECMO and always should be considered before initiating ECMO assistance: major pharmacologic immunosuppression (absolute neutrophil count < 400/mL^3) and recent or expanding central nervous system hemorrhage. Furthermore, specific patient conditions also should be considered. Although no specific age is considered as a contraindication, extreme ages are considered to increase risk for ECMO complication; weight over 125 kg can be associated with technical difficulties and risk of inadequate perfusion based on patient size; comorbidities also should be taken into consideration.[11]

Extracorporeal Membrane Oxygenation for Cardiogenic Shock

ECMO offers several advantages over conventional medical therapy for cardiogenic shock. Vasoactive drugs (including inotropes and vasopressors), which improve cardiac output by increasing myocardial oxygen consumption (with the exception of levosimendan), can be reduced significantly, leading to a lowered risk for myocardial ischemia and/or arrhythmias. Furthermore, ECMO increases cardiac output without placing additional demands on myocardial tissue. One of the main aspects to be considered in VA-EMO is left ventricular unloading: the possibility of leaving myocardial tissue at rest (possibly accepting a small quote of blood volume flowing through the left ventricle) has a key role for allowing the damaged organ to restore.[16]

Furthermore, ECMO is helpful for lung rest from aggressive mechanical ventilation in cases of concomitant pulmonary failure.[3]

In two historical cohort studies[17,18] on patients with cardiogenic shock secondary to acute myocardial infarction, ECMO was associated to an improved short-term survival. In particular, the availability of ECMO before or during percutaneous coronary intervention was associated to 70% of patients' survival to 30 days. Similar results have been observed in studies in which ECMO has been applied to rescue patients with cardiogenic shock of a nonischemic cause, such as fulminant myocarditis.[19] Indeed, patients with fulminant myocarditis (defined as those patients without sufficient response to maximum medical therapy for acute myocarditis) achieved a successful weaning rate of 71%, and all weaned patients survived long term.

Although ECMO also has been used increasingly to support patients suffering postcardiotomy shock (PCS), only case series are currently available to assess the effectiveness of ECMO in this condition in the adult population.[9,20–22] A relatively scarce survival has been reported in this condition (25%–42%); nevertheless, VA-ECMO clearly offers an advantage to patients and surgeons who have virtually no other alternative in the rare instances of PCS, and an excellent long-term survival is reported for patients surviving the acute perioperative period.[22]

Extracorporeal Membrane Oxygenation and Cardiac Transplantation

ECMO has been applied successfully to bridge patients to orthotopic heart transplantation and to support patients with primary graft dysfunction (PGD) posttransplantation. Several studies have investigated optimal bridging pathways for patients requiring cardiac transplantation and/or left ventricular assist devices (LVAD) support.[23,24] Most of these concluded that ECMO resuscitation is an effective, resource-sensitive strategy to salvage patients in extreme conditions, rather than the immediate implantation of a LVAD, which instead can be offered after a period of ECMO support, organs function rescue and, in successful cases, with no impact on subsequent survival.

In this condition, the appropriate role for ECMO as a bridge to cardiac transplantation appears to be in the initial resuscitation of patients before implantation of LVAD in eligible candidates.

Although patients requiring ECMO support for PGD have decreased 30-day survival compared with patients without PGD and not requiring support, patients with PGD supported by ECMO who survive beyond the acute posttransplantation period have equivalent survival to non-ECMO patients. Furthermore, survival analyses performed at 30 days postoperatively demonstrates survival equivalence in the ECMO salvage groups, suggesting that early ECMO support may not have long-term consequences on cardiac graft function if the supported patient survives salvage therapy.[25–27]

EXTRACORPOREAL MEMBRANE OXYGENATION FOR CARDIOPULMONARY RESUSCITATION

Finally, the use of ECMO for cardiopulmonary resuscitation (E-CPR) after cardiac arrest has been increasing in recent years. Superior short- and long-term outcomes[28] in patients treated with E-CPR compared with conventional CPR (C-CPR) have been reported in inpatient[28–30] and out-of-hospital settings.[31,32] Furthermore, an improved long-term neurologic status has been demonstrated in successfully resuscitated E-CPR patients. Younger age, C-CPR duration less than 35 minutes before initiation of E-CPR, pupil size on arrival

to the hospital, and subsequent coronary intervention may identify patients who are likely to benefit from E-CPR.[31]

Weaning

Signs of cardiac recovery include appearance or increase in peripheral arterial pulsatility and improving echocardiographic signs of ventricular contraction. The improvement of heart function is the *conditio sine qua non* for starting a progressive weaning protocol from VA-ECMO. Although weaning strategies are usually center dependent and monitored through different systems, the most frequent procedure in clinical practice include progressive reduction of ECMO flows under close hemodynamic and echocardiographic monitoring together with the titration of inotropes-vasoactive drugs. In particular, echocardiographic signs of cardiac recovery, as improved ventricular contractility and consistent opening of the aortic valve, may predict successfully weaning despite ECMO flows are not interrupted completely yet.[33] Once cardiorespiratory functions are considered adequately restored, the pump can be stopped totally and cannulas clamped and removed before clotting complications occur.

Side Effects

The exact complication rate associated with the use of VA-ECMO for cardiac support is not defined in literature, and it widely ranges among different case series.[34,35] Cheng et al. recently have analyzed 20 studies encompassing more than 1800 patients treated with VA-ECMO to ascertain complication rates.[36] Vascular and neurologic complications, as well as acute kidney injury, bleeding, and infective events, have been described as frequent complications associated with VA-ECMO.[36]

In particular, the pooled estimate rate of lower extremity ischemia was 16.9%; 10.3% of patients underwent fasciotomy or compartment syndrome and up to 4.7% to lower extremity amputation. Interestingly, although the use of distal leg perfusion shunts was not uniformly reported in these studies, one study on 517 patients reported a decrease in leg ischemia and leg fasciotomy with the use of distal cannulation.[36]

Three studies including 630 patients have analyzed the pooled estimate rate for hemorrhage and ischemic stroke (5.9%). Nine studies on 1019 patients have analyzed the pooled estimate rate for neurologic complications (13.3%), such as coma, diffuse anoxic brain injury, and brain death.[36]

Alterations in kidney function in a patient supported with VA-ECMO may be related to several conditions, derived or associated with the extracorporeal therapy. The pooled estimate rate reported by Cheng et al. for acute kidney injury was 55.6%. Furthermore, 46% of analyzed patients required renal replacement therapy for renal support.[36] Several studies in the literature outline the rapid progression of the acute kidney insult toward chronic kidney disease in patients who have undergone ECMO.[37] The rate of renal replacement therapy dependence in patients treated with ECMO ranges between 2% and 65%.[9,38,39] Although limited information is available for adult patients, experiences in the pediatric population suggest that primary renal disease at presentation is the main risk factor for chronic kidney disease in these patients.[37]

Finally, major bleeding and significant infection have been reported in 40.8% and 30.4% of analyzed patients, respectively.[36]

CONCLUSION

VA-ECMO currently can be considered a feasible and effective modality for refractory cardiogenic shock management in a broad range of ages and heart diseases. Indication to start a VA-ECMO should be balanced carefully by the actual possibility of heart and multiple-organ dysfunction recovery, and by patients' comorbidities, because of the cost and to the risk of adverse effects. In the hands of expert operators and with the correct timing, VA-ECMO is now considered a lifesaving procedure with very good long-term outcomes in successfully treated patients.

Key Points

1. VA-ECMO application guarantees an adequate oxygen delivery (DO_2) through the improvement of tissue perfusion. ECMO involves the use of mechanical devices, including a pump, a circuit, and an artificial lung.
2. Target blood flow rates should be at least 100 mL/kg/min for neonates, 80 mL/kg/min for pediatric patients, and 60 mL/kg/min for adults. A mixed venous saturation greater than 70% is considered a satisfactory indication of adequate systemic perfusion.
3. VA-ECMO indications in adult and pediatric patients with cardiac failure are determined primarily by (1) the presence of cardiogenic shock resulting from potentially reversible causes (with the exception of cases for bridge to long-term therapies); (2) inadequate tissue perfusion despite adequate intravascular volume and inotropes-vasoconstrictors administration; and (3) lack of ECMO contraindications.
4. ECMO should be weaned when cardiac function has been restored to a premorbid condition. Different weaning protocols may be present in different centers.
5. Thrombotic and hemorrhagic complications are the most frequent during ECMO (up to 15% of cases), together with acute kidney injury (up to 50%).

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A complete reference list can be found online at ExpertConsult.com.

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