ECMO for Adults with Severe Respiratory Failure

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Extracorporeal Membrane Oxygenation is being utilized with increasing frequency to treat adults with respiratory failure who have failed conventional therapy.

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Abstract

The technology to provide Extracorporeal Life Support (ELS) has existed for over four decades. Its use has increased markedly in the last decade, initially in response to severe Acute Respiratory Distress Syndrome (ARDS) in adults during the 2009 H1N1 influenza epidemic and continuing with the increasing acceptance of Extracorporeal Membrane Oxygenation (ECMO) for the treatment of severe respiratory failure in adults from other causes.[1] We highlight the use of ECMO, particularly at our institution.

Introduction

With the recent publication of the ECMO to Rescue Lung Injury in Severe ARDS (EOLIA) trial which compared early ECMO for severe ARDS with conventional ventilation, there now have been two randomized, controlled trials suggesting a benefit with the use of ECMO for severe ARDS, the first being the CAESAR trial published in 2009[2,3]. In the EOLIA trial, the early ECMO group's mortality benefit did not reach statistical significance, and the trial was stopped at the fourth interim analysis. Patients in the conventional ventilation group were allowed to crossover into the ECMO group at the discretion of the treating physicians, which made it difficult to draw definitive conclusions regarding the benefit of early ECMO. The trial investigators believed that not allowing crossover would be unethical, despite recognizing the potential difficulty it would cause in analyzing the data. There was a statistically significant benefit of ECMO in regards the secondary end-point of treatment failure, which was defined as death in the ECMO group and either death or crossover to ECMO in the conventional ventilation group.

Because placing an adult on ECMO is no longer considered to be experimental, it is likely that an increasing number of community-based physicians will either take care of patients who may benefit from ECMO or provide care to post-ECMO survivors. In this article, we will attempt to give a basic description of the mechanics of ECMO, the indications for ECMO, the decision making that goes into patient selection, and describe the clinical course and expected recovery for a patient that is placed on ECMO for respiratory failure.

Mechanical Considerations

Conceptually, an ECMO circuit is a simple device. It consists of a large drainage cannula that removes blood from a patient, a pump that moves blood forward, an oxygenator that adds oxygen to blood and removes carbon dioxide (CO_2), and a return cannula that returns

the oxygenated blood to the patient.[4] It is the location of the drainage and return cannulas that determines the type of support that ECMO provides.

If the drainage cannula is in a vein and the return cannula is in an artery, this is known as veno-arterial ECMO (VA ECMO). This type of support bypasses both the heart and lungs and provides both circulatory and respiratory support. It is VA-ECMO that was used on the first adult who survived ECMO in 1971; a patient who developed severe ARDS from traumatic lung injury due to a motor vehicle injury.[5] VA-ECMO continued to be the primary mode of ECMO for both cardio-pulmonary failure and isolated respiratory failure up until the early 2000s.

Figure 1. VA-ECMO Cannulation

Unfortunately, VA ECMO has significant drawbacks when used for isolated respiratory failure. The first and most obvious drawback is that VA ECMO requires a large bore catheter – often 14 French or larger – to be placed in an artery, typically the left common femoral artery (CFA). Concomitant with this, is the risk of bleeding from the arterial cannulation site and limb ischemia from impaired distal blood flow.[6] At our institution, we typically attach a Dacron graft in an end-to-side anastomosis to the CFA and place the return cannula in this graft with the tip of the cannula laying just inside the artery (Figure 1). We have found that distal blood flow is excellent and arterial bleeding can be directly controlled at the arterotomy site, which is not achievable with percutaneous cannulation.

Two less obvious drawbacks to VA-ECMO occur as a result of the ECMO circuit being in parallel to the cardiopulmonary circulation. The first is VA-ECMO causing left ventricular (LV) distension (Figure 2). As the arterial circulation is a high-pressure system, and VA ECMO returns blood under pressure to this system in a retrograde fashion, the LV faces increasingly high afterload (afterload is not synonymous with systemic vascular resistance, but rather reflects increased LV wall tension induced by the returned blood). This is particularly relevant in cases of impaired cardiac function as the heart may not eject blood with every beat. When blood does not eject from the LV, there are areas of stagnant blood flow within the heart that are prone to thrombus formation. Additionally, as LV cavity pressure increases, coronary perfusion pressure is reduced and coronary blood flow may become impaired.[6,7] Several strategies have been developed to combat LV distension including judicious use of inotropes, intra-aortic balloon pump counterpulsation, and percutaneous left ventricular assist devices such as the Impella.[7]

The second of these drawbacks is that of "red-blue mixing." The first vessels arising from the ascending aorta are the coronary arteries with the next major vessel being the brachiocephalic (innominate) artery. In contrast to LV distension, red-blue mixing is more likely to occur as cardiac function normalizes. If cardiac function is normal, the blood in the aorta will be a combination of antegrade flow from the patient's own cardio-pulmonary system and retrograde flow from the ECMO circuit. In a patient with severe lung injury, this antegrade flowing blood will be poorly oxygenated, despite blood from the ECMO circuit having a saturation of 100%. The poorly oxygenated blood will be most concentrated in the ascending aorta, with the coronary arteries and brachiocephalic artery being most affected and thus potentially delivering poorly oxygenated blood to the coronary and cerebral circulation.[5,6]

Veno-venous (VV-ECMO) avoids both of these issues. Unlike VA ECMO, both the drainage and return cannulas are in veins. At our institution, we typically implement an upper body single-site cannulation approach via the right internal jugular vein using a double lumen bicaval canula (Avalon Elite cannula [Maquet]). The drainage lumen has orifices that sit in both the superior and inferior vena cava, while the return lumen has a single opening in the right atrium directed towards the tricuspid valve. The distal end

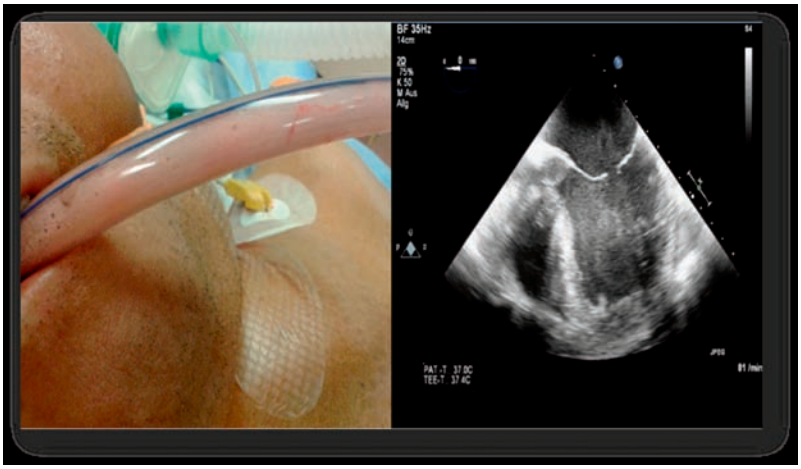

Figure 2. Pulmonary edema secondary to Left Ventricular distension on VA. ECMO and associated TEE image of the LV demonstrating stagnant blood in the LV cavity.

of the cannula, when properly placed, is located in the IVC caudal to the hepatic vein.

In addition to avoiding complications associated with arterial cannulation, VV ECMO also provides an advantage to VA ECMO in the treatment of respiratory failure because the circuit is in series with the patient's lungs. The practical effect of this is that blood is oxygenated by both the circuit and the lungs, not the circuit or lungs alone. As such, the ECMO circuit essentially pre-oxygenates blood and allows the lungs to further oxygenate and remove CO_2 from the blood. This avoids the "red-blue mixing" seen with VA ECMO and because the arterial system is not accessed, LV distension does not occur. Additional advantages of VV ECMO include lower anti-coagulation needs and the ability to decannulate at the bedside after lung recovery. The primary disadvantage of VV ECMO is that it cannot augment cardiac output, and so does not benefit a patient with combined cardio-pulmonary failure.

Indications and Patient Selection

The indications for VV ECMO for adults with respiratory failure are expanding. The three most common indications are severe ARDS, COPD exacerbations, and as a bridge to lung transplantation.[8] VV ECMO can provide complete pulmonary support allowing for adequate oxygenation and CO_2 removal without exposing the patient to potential ventilator associated lung injuries associated with conventional mechanical ventilation techniques.

In 2009, with the publication of the CAESAR trial in Lancet, the authors proposed several inclusion and exclusion criteria. The main inclusion criteria were severe respiratory failure with a Lung Injury Severity Score greater than 3.0 or uncompensated hypercapnia with a pH $<$ 7.20.[2] Exclusion criteria included contraindications for anti-coagulation, age $>$ 65, mechanical ventilation at high settings for greater than one week, and suspected non-reversibility of respiratory failure.[2] While the CAESAR trial's results were promising, not all of the patients in the ECMO group actually received ECMO therapy and lack of standardization of mechanically ventilated patients limited the trial.[3]

As institutions became more comfortable with ECMO, exclusion criteria have loosened. In 2014, Schmidt et al. performed a multi-factorial retrospective analysis for patients placed on ECMO looking for characteristics favorable or unfavorable for survival. Using logistic regression analysis, the RESP score was developed, and has been prospectively validated. Several poorly prognostic characteristics stand out as not favoring survival such as pre-existing neurological disability, advanced age, and prolonged periods on mechanical ventilation. Factors such as young age, asthma exacerbation, and others are favorable for survival.[9]

A patient undergoing ECMO is susceptible to a similar pro-inflammatory response syndrome to those patients undergoing cardiopulmonary bypass. This is mounted by the complement system leading to leukocyte activation, widespread endothelial cell injury, and upregulation of pro-inflammatory mediators.[10] Regardless of predictive scores, a patient who undergoes ECMO must be prepared for an extended recovery, often requiring weeks to months of rehab. Caution must therefore be used in placing patients with multiple severe, co-morbid medical conditions on ECMO.

ECMO in itself is strictly a life support device. It does not promote lung healing absent its ability to reduce the risk of ventilator associated lung injury. For this reason, ECMO should be used in patients with known or highly suspected etiologies of severe respiratory failure such as infection, trauma, or chemical irritation which are known to be reversible.[5] Patients whose respiratory failure is due to progression of chronic lung diseases such as COPD or interstitial lung disease should rarely be placed on ECMO as the potential for successful weaning is extremely low in these clinical scenarios.

Maintenance of the Patient on ECMO

Care for the patient on ECMO requires a multidisciplinary critical care team with additional training in management of ECMO patients. The circuit design of VV-ECMO is straightforward. Blood is pumped across a polymethylpentene (PMP) diffusion membrane countercurrent to a sweep gas containing a mixture of oxygen and air. In most critically-ill adult patients, blood will be fully oxygenated with as little as 3 ml/kg/min of oxygen flowing across the diffusion membrane. It is CO_2 removal that requires increased gas flow. Similar to minute ventilation on a ventilator, increasing the flow of gas across the diffusion membrane (sweep) reduces $PaCO_2$. For VV ECMO, we typically keep the gas blend between 90 and 100% O_2 with sweep adjusted to maintain normocapnia. Blood flow through the ECMO circuit should be maintained at greater than 60% cardiac output. If flow is significantly less than this, the ratio of oxygenated blood in the right atrium from the ECMO circuit and poorly oxygenated blood that entered the right atrium from the IVC or SVC and did not go through the drainage cannula becomes unfavorable to support adequate systemic oxygenation.

The time that a patient remains on ECMO is highly variable as ECMO does not provide lung healing, just prevention of further injury. The shortest successful ECMO run at our institution has been 48 hours, with our longest approaching 49 days. While on ECMO, the critical care provided to patients by our pharmacists, nutritionists, and physical therapists who are comfortable caring for ECMO patients becomes invaluable. Due to the membrane oxygenator, the pharmacokinetics of many drugs are altered when administered to an ECMO patient. Pharmacists with ECMO experience and knowledge are critical to optimizing outcomes.

ECMO patients are often kept sedated, however, some institutions are studying VV ECMO as first line therapy for certain pathologies while keeping the patient awake.[11, 12] More research is needed in this area, though. Cannulation strategy planning must take into account the patient's need for physical therapy and possible awake ambulation as early mobilization helps preserve functional status and optimization for transplant if being bridged.[13]

Bleeding is always a concern for patients on ECMO. This is due to both the need for anti-coagulation and alterations in blood composition from the ECMO circuit. Von Willebrand's factor is cleaved by the circuit, thrombocytopenia is common and a "circuit DIC" can develop. Heparin resistance occurs with relative frequency requiring increasing heparin doses or transfusion of anti-thrombin III. Occasionally, spontaneous bleeding occurs absent significant clotting abnormalities. The most serious of these is intracranial hemorrhage which is responsible for over ten percent of deaths on VV-ECMO. When needed, heparin-free ECMO can be performed, but there is an increased risk of circuit thrombosis.

Once a patient has demonstrated signs of lung recovery, the sweep can be turned off, and the patient can be supported solely on a ventilator. If the patient maintains acceptable oxygenation and normocapnia for approximately 24 hours, decannulation occurs. At our institution, this is performed at the bedside, negating the need for transport or operating room time.

Our center uses a single caregiver model to care for patients on ECMO. The nurses at St. Luke's care for both the patient and the circuit. This is in contrast with other institutions in which there is both a bedside nurse and a separate ECLS specialist. Our nurses go through an intensive training course complete with simulation and drills prior to being allowed to care for patients on ECMO. Since we do not have perfusionists in house at all times the nurses are trained to both troubleshoot the circuit and provide rescue maneuvers such as deairing a circuit, manually pumping a circuit, and stopping a leak. This training has been successfully used on several occasions.

Our critical care physicians manage both the critical care needs of the patient and the ECMO circuit. This includes both cannula insertion and decannulation of VV-ECMO. Cardiac surgeons and perfusionists are on call, but not in house, at all times to assist with the management of these patients if needed.

Conclusion

ECMO is being utilized with increasing frequency to treat adults with respiratory failure who have failed conventional therapy. The successful initiation, maintenance, and weaning of ECMO requires a multidisciplinary team of nurses, pharmacists, physical therapists, nutritionists, and physicians working in concert. As ECMO is no longer an experimental therapy, the number of patients who are candidates to be treated with ECMO and who are successfully weaned, will likely increase. Community-based physicians will serve an important role in the future directions of ECMO therapy as they will frequently be the first to recognize the need for ECMO, initiate consultations with ECMO centers, and prepare patients for a successful transport. Additionally, community-based physicians will be key players in the

recovery of ECMO patients, not only from a physical medicine perspective but also from a psychiatric standpoint as ECMO patients have a higher incidence of PTSD and development of new psychiatric pathology.[14] The future of ECMO will include continuing to optimize patients' physical status during cannulation and recovery, prevention and management of coagulopathy associated problems, improving cannulation strategies, and development of portable extracorporeal oxygenators. Despite the increased success in treating patients with ECMO, additional randomized trials must be performed to optimize its success and resolve controversy regarding ECMO's efficacy. In the recent EOLIA trial there was a non-statistically significant trend towards benefit of early ECMO with severe ARDS.[8] While the trial admittedly had several significant limitations that perhaps diluted ECMO's apparent benefits, it demonstrates the necessity of ECMO referral centers continuing to enroll their patients in the extracorporeal life support organization's (ELSO) databases for future studies. A list of registered ECMO referral centers in Missouri can be found at www.elso.org.[15]

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Disclosure

None reported. **MM**