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Extracorporeal membrane oxygenation (ECMO) during pregnancy and postpartum

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ABSTRACT

Extracorporeal membrane oxygenation (ECMO) can provide respiratory support (VV-ECMO) or both respiratory and circulatory support (VA-ECMO). The use of ECMO has increased dramatically as a result of simpler technology. No level I evidence is yet available reflecting improved outcomes with ECMO. The use of this technology during pregnancy may be indicated in very select cases and should be delivered in centers with dedicated ECMO specialized units.

Introduction

The use of extracorporeal membrane oxygenation (ECMO) has increased dramatically in the last 2 decades. The availability of simpler, more efficient, and biocompatible equipment coupled with less invasive approaches account for the renewed interest in the use of this technology. Two main modalities of ECMO are currently used in clinical practice. Veno-venous ECMO (VV-ECMO) is a modality that provides only respiratory support by extracting deoxygenated blood from the venous system and returning oxygenated blood to the same venous system after oxygenation and carbon dioxide removal are accomplished within the extracorporeal circuit. In contrast, veno-arterial ECMO (VA-ECMO) provides both respiratory and hemodynamic support. In VA-ECMO, blood is extracted from the venous system of the patient, and after oxygenation and carbon dioxide removal are accomplished, blood is returned to the arterial system. The purpose of this article is to evaluate the available evidence regarding the use of these modalities and understand the basic components of each intervention and their potential applications in the obstetrical patient.

VV-ECMO

Conventional therapy for acute respiratory distress syndrome (ARDS) includes (among others) lung-protective mechanical ventilation, conservative fluid management, pharmacological paralysis with cisatracurium, and prone ventilation.[1–3] In refractory cases, VV-ECMO may be considered since it provides transient respiratory support while allowing the clinician to avoid injurious ventilator settings, providing a period of "lung rest" until the pulmonary insult resolves.[4]

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Table 1 – Potential indications for VV-ECMO support during pregnancy and postpartum.

- Severe (but potentially reversible) respiratory failure
- Hypercapnia with severe respiratory acidosis despite optimal conventional mechanical ventilation with respiratory rate increased up to 35 breaths/min
- PaO_2/FiO_2 ratio less than 100 with inspired fraction of oxygen ≥0.9 and PEEP ≥10 cm H_2O despite optimal ventilator support and use of usual adjunctive methods (e.g., cisatracurium, recruitment maneuvers, prone ventilation, and adequate PEEP)

Specifically, once the patient is on ECMO support, the clinician can lower both the tidal volume (to values as low as 100–300 mL to maintain plateau pressures well below 30 cm H_2O) and the inspired fraction of oxygen to avoid both ventilator-induced and oxygen-induced lung injury. Positive end-expiratory pressure (PEEP) is usually maintained between 8 and 15 cm H_2O to avoid lung collapse. Importantly, in ideal candidates, the underlying disease should be reversible (unless waiting for a lung transplant), and the patient should have a good chance of recovery after a few days of VV-ECMO support.[5]

Deciding when a patient becomes an ECMO candidate is complex. While VV-ECMO should not be used on every patient with ARDS, delaying "salvage therapies" until too late in the disease process may limit the benefit of the intervention. Table 1 provides criteria that may be used to identify appropriate candidates for VV-ECMO. Importantly, none of these criteria is an absolute indication for VV-ECMO; experienced clinicians must individualize patient selection.

For vascular access, most modern units utilize a double lumen cannula placed into the right jugular vein. A distal and a proximal lumen (both form the "draining lumen") will drain blood from the inferior and superior vena cava, respectively, into the extracorporeal circuit. Oxygenated blood is then returned through a second lumen (within the same cannula, located in the mid portion of the catheter) with its opening lying close to the right atrium (facing the tricuspid valve), from which blood flows into the right atrium and then into the right ventricle. Proper cannula position may be confirmed by echocardiography since cannula malposition may result in poor oxygenation if oxygenated blood returning from the circuit is returned above or below the desire target; optimally, the reinjection lumen should be facing the tricuspid valve. Within the circuit, blood passes through an oxygenator and a heat exchanger that warms the blood before it returns to the body. Oxygenation is determined by the rate of blood flow through the circuit (usually set between 3 and 4 L/min) and the fraction of delivered oxygen (FDO_2), which is usually set at 1.0 (100%). Fresh air (sweep gas) and oxygen are mixed (according to the FDO_2 set by the operator) in a blender, prior to exposure of the gas to the blood, through a semipermeable membrane. CO_2 removal depends on the amount of sweep gas flow set by the operator. CO_2 removal is independent of blood flow. Anticoagulation with unfractionated heparin is usually required to avoid circuit clotting since both the inflammatory and coagulation systems are activated upon contact with the ECMO circuit.[6] In patients with a very high risk of bleeding, minimal or no anticoagulation has been reported with good outcomes.[7] Alternative anticoagulants, such as bivalirudin and argatroban, may be used in cases where unfractionated heparin is contraindicated.[8] Fig. 1 depicts the main components of a VV-ECMO circuit. As stated before, while the patient is on VV-ECMO, the ventilator settings will be changed so that ventilator-induced lung injury is minimized. At the same time, other interventions to optimize lung function, such as aggressive diuresis and antibiotics (in cases of sepsis), must be provided. Table 2 summarizes some of the most common complications that may occur with ECMO. Once lung function is improving, a trial off of ECMO is easily accomplished by simply turning the sweep gas off. Once this happens, blood will simply flow through the circuit, but no gas exchange occurs. If oxygenation and ventilation are adequate after a few hours of observation, the patient may be decannulated.

The evidence behind the use of VV-ECMO for ARDS is extremely limited. One of the most quoted studies is the CESAR trial,[9] a large randomized clinical trial performed in the United Kingdom comparing conventional ventilatory support to VV-ECMO in patients with severe ARDS.[9] The

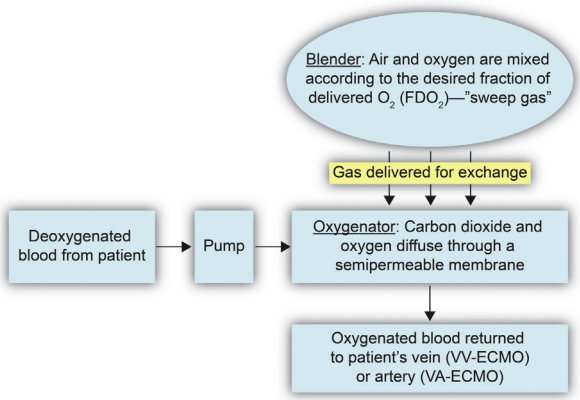

Fig. 1 – Main components of an ECMO circuit.

Table 2 – Common complications with VV-/VA-ECMO support.

Circuit thrombosis	Prevent with systemic anticoagulation (most commonly with unfractionated heparin).
Bleeding	Etiology is multifactorial, including anticoagulation, thrombocytopenia, and acquired Von Willebrand disease secondary to destruction of large multimers in the extracorporeal circuit. Threshold to transfuse varies among centers. Maintain hemoglobin above 7–8 g/dL.
Infection	Some centers advocate broad-spectrum antibiotics while on ECMO support despite limited evidence.
Hemolysis	Some degree of hemolysis may occur from the negative pressure generated by the pump. Excessive hemolysis may be due to cannula malposition or hypovolemia with less venous return to the circuit.
Thrombocytopenia	May require transfusion of platelets if active bleeding or less than 20,000/mm^3.

conclusion of the study was that transferring patients with severe ARDS and poor respiratory status despite "maximum conventional ventilatory support" to a center with ECMO experience resulted in improved outcomes. Important limitations of this trial must be discussed. First, the "conventional ventilatory support" in the control group was not standardized. It is unclear how these patients were actually managed. Specifically, it is not clear if these patients were ventilated with lung-protective mechanical ventilation with adequate levels of PEEP or if they received optimal adjuvant management for ARDS, including a restrictive fluid approach, cisatracurium, and prone ventilation, among others. A second limitation is that the benefit of VV-ECMO was only seen when comparing all patients who were transferred to the ECMO center with all patients who received conventional therapy and were not transferred to the center with ECMO capacity. However, only 75% of patients who were transferred to the ECMO center actually received ECMO; the rest were treated at the referral center with conventional state-of-the-art treatment modalities for ARDS. When limiting the analysis to those patients who actually received ECMO, the benefit was no longer evident.[10] As of now, there is no convincing evidence that VV-ECMO improves outcomes in severe ARDS. Ongoing trials will hopefully shed light on this area. As expected, the evidence in the obstetrical population is even more limited. Enthusiasm regarding the use of VV-ECMO to treat severe ARDS during pregnancy and postpartum emerged during the H1N1 epidemic in 2009. Observational data suggested a benefit of ECMO among obstetrical patients with ARDS secondary to H1N1 infection.[11] A recent meta-analysis concluded that the survival rate among obstetrical patients who received VV-ECMO for ARDS secondary to H1N1 was 75%.[12] Unfortunately, there is no data comparing ECMO with state-of-the-art lung-protective mechanical ventilation in pregnant women with ARDS. In summary, there is no conclusive data supporting the benefit of VV-ECMO for severe ARDS in any subpopulation. VV-ECMO may be considered in ARDS refractory to conventional treatment modalities in centers with extensive experience and a dedicated ECMO team. More data is needed to define the role of VV-ECMO in the treatment of ARDS.

VA-ECMO

VA-ECMO provides both respiratory support (in a manner similar to what was described for VV-ECMO) as well as hemodynamic support to patients with severe transient hemodynamic instability secondary to conditions, such as cardiac arrest from reversible causes (e.g., bupivacaine intoxication), refractory cardiogenic shock (e.g., peripartum cardiomyopathy and myocardial infarction), failure to wean from cardiopulmonary bypass, or obstructive shock (pulmonary embolism), among others.[13] Importantly, when deciding if a patient is a candidate for VA-ECMO, it is of paramount importance that the precipitating condition is expected to be reversible. Some of the potential indications for VA-ECMO are listed in Table 3. In the setting of cardiac arrest, there is insufficient evidence to use ECMO routinely; however, it may be considered in selected patients with potentially reversible causes of arrest after conventional cardiopulmonary resuscitation for at least 10 minutes.[14] In clinical practice, peripheral cannulation for VA-ECMO is more commonly used. Venous blood is usually drained through a cannula placed into the femoral vein, and flow is directed into the ECMO circuit. Similar to VV-ECMO, CO_2 clearance depends on the sweep gas flow set by the operator, and oxygenation depends on the pump flow and the FDO_2. Returning the oxygenated blood from the ECMO circuit into the arterial circulation, most commonly through a cannula placed into the femoral artery, provides hemodynamic support. Arterial blood flow is retrograde, advancing toward the central circulation. The point at which the retrograde flow of blood coming from the ECMO circuit meets the endogenous flow pumped by the patient's left ventricle is known as the "mixing point" (Fig. 2). In patients with acceptable cardiac output but poor lung function, the amount of poorly oxygenated blood (due to compromised native lung function) pumped by the left ventricle may predominantly perfuse the heart and the brain if the pump flow is too low and the mixing point is distal to the take-off of vessels that perfuse the heart and the brain. The ideal place to monitor arterial oxygenation while on VA-ECMO is the right radial artery.[15] If an arterial line is in the left arm, a normal partial pressure of oxygen does not guarantee adequate delivery of oxygenated blood into the coronaries and the brain because the take-off of the left subclavian artery is distal to the coronaries and the carotid arteries; the mixing point could be proximal to the left subclavian artery but distal to the brachiocephalic trunk and the left carotid artery, resulting in brain ischemia (Fig. 2). The latter situation can be suspected if oxygenation is satisfactory in the left radial artery but not in the right. To improve oxygenation, a clinician may attempt to "push the mixing point" proximally (toward the heart) by increasing the ECMO flow. Another option is to optimize ventilator management (increased PEEP, use recruitment maneuvers, and increase the FiO_2) to better oxygenate the blood that is pumped by the left ventricle.

Table 3 – Potential indications for VA-ECMO support during pregnancy and postpartum.

- Refractory left ventricular failure from peripartum cardiomyopathy, myocardial infarction, myocaditis
- Bupivacaine intoxication requiring prolonged cardiopulmonary resuscitation
- Refractory right or left ventricular failure in suspected cases of amniotic fluid embolism
- Inability to wean from cardiopulmonary bypass after heart surgery
- Massive pulmonary embolism with refractory right ventricular failure
- Need for prolonged cardiopulmonary resuscitation (at least 10 min) with a potentially reversible precipitating condition

While on VA-ECMO support, some degree of heart contractility is still desired since poor contractility of the left ventricle with minimal emptying will increase the risk of in situ thrombosis within the ventricle and embolic phenomena.[13] Moreover, severe left ventricular dilation due to inadequate contractility increases the left ventricular end diastolic pressure (intracavitary pressure), which will compromise coronary perfusion pressure, resulting in further ischemic insults to the myocardium. Poor contractility of

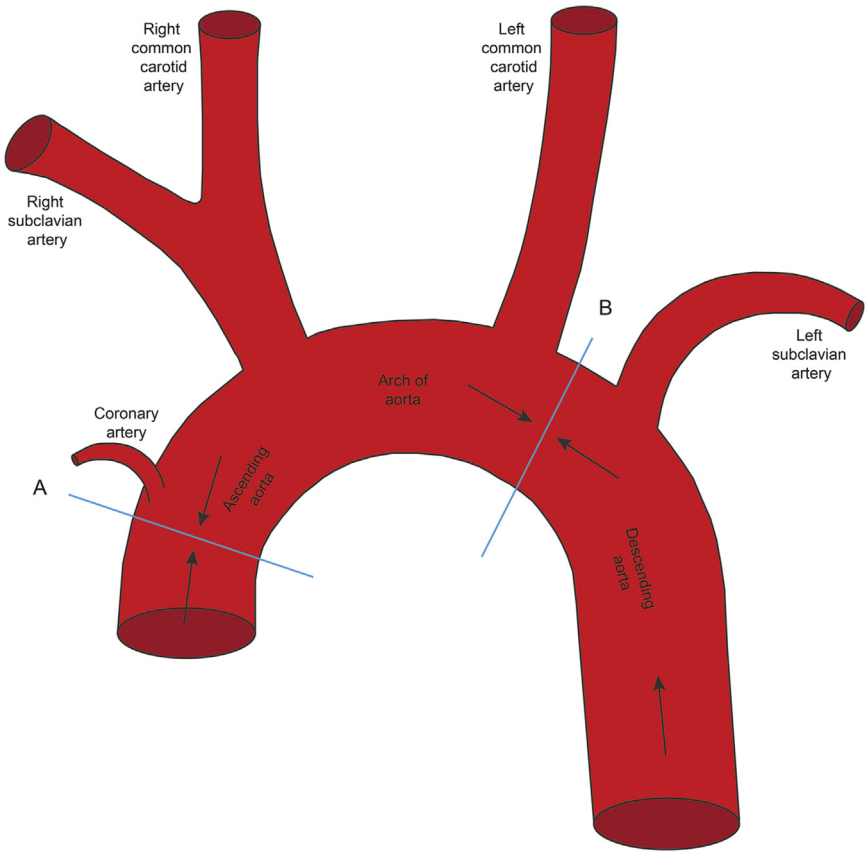

Fig. 2 – Mixing point concept in VA-ECMO. (A) is an ideal mixing point where oxygenated blood from the ECMO flow will preferentially perfuse the proximal branches of the aortic arch. If the patient's pulmonary function is compromised and the ECMO flow is set too low, the mixing point will be displaced distally (B), compromising brain oxygenation despite normal oxygenation in the left radial artery.

the left ventricle may be suspected when there is no (or minimal) pulsatility of the arterial line tracing since blood flow from the ECMO circuit is nonpulsatile. Evaluation of heart function with transthoracic echocardiography is mandatory. If poor contractility is present, the use of inotropes, such as dobutamine and milrinone, may be required. In some cases, the ECMO flow may need to be reduced because the retrograde nature of the flow will invariably increase the afterload on the left ventricle.

Cardiac recovery will result in better contractility as assessed by transthoracic echocardiography and more pulsatility in the arterial line tracing. At this time, the ECMO flow may be progressively weaned to a flow close to 1L/min. If hemodynamic stability is maintained at such low flows, the patient may be a candidate for decannulation.

ECMO support during pregnancy

The same basic principles described previously apply to the use of ECMO in obstetrical patients. The limited available evidence regarding ECMO in obstetrical patients refers mostly to VV-ECMO. Recently, Moore et al.[16] summarized the available evidence on ECMO support during pregnancy (excluding the postpartum period). A total of 45 cases were identified in the authors' search: 41 with VV-ECMO support and only 4 with VA support. Overall, maternal and fetal survival rates were 77.8% and 65%, respectively. These data mainly reflect outcomes from VV-ECMO since only a handful of cases on VA-ECMO have been reported so far. The effect of VA-ECMO on the uterine circulation is not known, and if this form of support is required in a viable pregnancy, continuous fetal monitoring is recommended. Patients should be in the lateral decubitus at all times (especially after 20 weeks of pregnancy) because uterine compression on the inferior vena cava and the aorta may interfere with blood flows in cases of VA-ECMO (not so much in VV-ECMO since most patients will have a single dual lumen cannula in the right jugular vein).

Conclusions

ECMO technology has changed dramatically, making its application significantly simpler and safer. The use of more biocompatible systems has decreased anticoagulation requirements, and new cannulas of smaller caliber have simplified vascular access. It is expected that ECMO will be used more commonly in the near future. Despite such enthusiasm, there is currently no definite evidence that either form of ECMO (VV or VA) improves outcomes significantly. If a patient is deemed

to be a candidate for ECMO, it should be delivered in a high-volume center with a dedicated ECMO team. Unlike VA-ECMO, the use of VV-ECMO during pregnancy is not expected to result in any significant hemodynamic changes that could negatively affect uterine perfusion.

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