RESEARCH REVIEW ARTICLE

Veno-Venous Extracorporeal Membrane Oxygenation in Pregnancy: A Literature Review

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ABSTRACT

Extracorporeal membrane oxygenation (ECMO) is a specialized technique providing temporary support for failed cardiac and respiratory functions. While commonly used in neonates and children, its application in obstetric patients is gaining traction. In hypoxemic and hypercapnic respiratory failure with intact cardiac function, Veno-Venous ECMO (VV-ECMO) offers artificial oxygenation and decarboxylation. This comprehensive article discusses VV-ECMO in obstetrics, covering prevalence, maternal and neonatal outcomes, mechanisms, protocols, access sites, indications, contraindications, anticoagulation, complications, and considerations.

The VV-ECMO procedure involves redirecting blood from the heart or major veins through an artificial lung and back to the heart, improving oxygenation, respiratory mechanics, and cardiac function while reducing lung injury risk. Cannulation methods range from double-lumen to bi-femoral. Prevalence of VV-ECMO in pregnancy is 8.9%. Outcomes vary based on factors like medical condition and gestational age. Survival rates range from 63% to 76% for pregnant patients and 70% to 86% for infants. Common indications encompass severe H1N1 influenza, pre-eclampsia, and viral infections.

Contraindications involve refusal, end-stage malignancy, and severe neurologic injury. Anticoagulation, crucial for preventing clotting in the ECMO circuit, primarily employs unfractionated heparin. Complications include bleeding, thrombosis, and infections. In pregnancy, similar indications exist, with VV-ECMO typically proving safe and effective for both maternal and fetal survival.

KEYWORDS - Veno-venous Extracorporeal Membrane Oxygenation; Pregnancy; Respiratory Failure; Peri-partum ¹MD, Pulmonary, Critical care and Sleep Medicine, University of Florida, Gainesville, Florida

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BACKGROUND

The utilization of extracorporeal membrane oxygenation (ECMO), a critical care intervention, has witnessed an increase in recent years owing to advancements in intensive care technology and the recent COVID-19 pandemic(1). ECMO represents a specialized technique of cardiopulmonary bypass, offering temporary support for failed respiratory and/or cardiac functions(2). While ECMO has been extensively and successfully employed in neonates and children, it's use in obstetrics is emerging(3-5). This trend is influenced by the growing number of women opting to delay childbirth until later stages of life, combined with the rising prevalence of chronic medical conditions like obesity and heart disease(6). Consequently, there is a notable rise in maternal morbidity and mortality rates, including cases of refractory acute respiratory syndrome that may require ECMO as salvage therapy(1, 5-9).

ECMO is categorized into Veno-Venous ECMO (VV-ECMO) and Veno-arterial ECMO (VA-ECMO). In cases of hypoxemic and/or hypercapnic respiratory failure with preserved cardiac function, VV-ECMO offers a solution for artificial oxygenation and decarboxylation (10). This specialist method aids in the healing of underlying respiratory conditions or offers interim assistance while awaiting a lung transplant, if necessary. (10). Despite its extensive usage, there is little information on the safety and effectiveness of ECMO when administered to patients who are pregnant or recently gave birth. This article will delve into a comprehensive discussion on VV-ECMO in obstetric patients, encompassing its prevalence, incidence, maternal and neonatal outcomes, long-term implications, mechanisms, protocols, target goals, access sites, indications, contraindications, anticoagulation strategies, complications, and special considerations.

VV-ECMO MECHANISM

Blood is collected from the right atrium (RA), superior vena cava, or inferior vena cava in the VV-ECMO technique, and then returned to the RA using a jet directed at the tricuspid valve. Contrary to cardiopulmonary bypass (CPB), this method sequentially connects the substitute lung to the body's lungs rather than excluding it as in the CPB. The ECMO circuit is composed of a draining and return cannula, a pump and an oxygenator membrane. The oxygenator membrane extracts carbon dioxide and oxygenates the blood. The arterial PaO2 and saturation represent a mixture of the oxygenated extracorporeal blood

and the deoxygenated venous blood traveling via the non-functional patient lungs after the oxygenated blood mixes with the unoxygenated venous blood that avoids the ECMO circuit. This mixed blood, in combination with a good cardiac output and a satisfactory hemoglobin, properly delivers systemic oxygen to meet metabolic demands, while respiratory control is optimized during periods of rest (2). Aside from oxygenation and carbon dioxide removal, VV-ECMO is associated with improved respiratory mechanics and decreased risk of ventilator induced lung injury. Furthermore, VV-ECMO initiation is associated with decrease in intrathoracic pressure and a decrease in pulmonary vascular resistance, improving cardiac mechanics.

USUAL SITES OF ACCESS

The choice of access site for VV ECMO depends on several factors, including the patient's anatomy, clinical condition, and physician preference. Each site has its own advantages and disadvantages, and the decision is made on a case-by-case basis. The cannulas used for VV ECMO are typically inserted percutaneously or through a small incision and are connected to the ECMO circuit to establish the extracorporeal support. The size of the drainage cannula directly determines blood flow. It is possible to drain and restore blood using a single, dual-lumen, or numerous cannulas. To increase the efficacy of ECMO, it is widely believed that the widest gauge cannula that can be safely introduced should be used (2,11).

The right femoral vein is typically used for one cannula, which is advanced to the junction of the inferior vena cava and the right atrium, and the right inferior jugular vein, which is used for the other cannula, is advanced through the superior vena cava into the right atrium. This configuration is known as the double VV ECMO cannulation which is the one classically used. An alternative arrangement involves inserting an Avalon cannula or a double-lumen single cannula into the right internal jugular vein while being guided by an echocardiogram or fluoroscopy.

Before the hepatic veins, the cannula will be advanced until its tip is in the mid-IVC. The IVC and SVC are the sources of drainage (2). The cannula has a side port that lies in the right atrium with a jet aimed towards the tricuspid valve. Other cannulation sites, such as the left IJV or the subclavian vein, aren't practical to use due to the rigidity and form of this type of cannula. Finally, bi-femoral cannulation is a different configuration for VV ECMO support that is employed when it is technically impossible to cannulate the IJV. The reinjection cannula's tip is positioned into the RA, while the drainage venous cannula's tip is positioned in the IVC (2,12).

PREVALENCE OF ECMO USE IN PREGNANCY

The exact prevalence of VV-ECMO in pregnant females is difficult to establish given the paucity of data available. While regularly monitoring ECMO recipients' results and problem rates, the ELSO does not keep track of a woman's pregnancy or postpartum condition (13). In the CESAR trial, the prevalence of VV-ECMO in pregnant women was 8.9% of all patients selected for the study (14). In addition, a 10-year case series research found that 20% of women in their reproductive years receiving ECMO were either pregnant or less than 6 weeks postpartum (15).

VV-ECMO OUTCOMES IN PREGNANCY

The outcomes related to the application of VV-ECMO during pregnancy can differ based on various factors, including the underlying medical condition and its severity, gestational age, the extent of maternal-fetal compromise, and the comprehensive management approach employed in each case.

Survival rates among obstetric patients receiving VV-ECMO for various etiologies ranged from 63% to 76% (5,16,17). 63% of patients receiving VV-ECMO survived without severe disability at 6 months compared with 47% survival of the patients receiving conventional management(14). Causes of death in patients receiving VV-ECMO included multiorgan failure (16%), respiratory failure (9%), neurological disorder (4%), cardiovascular disorder (1%), and complications related to VV-ECMO (1%) (14). Survival rates for infants of mothers placed on VV-ECMO ranged from 70% to 86% (16–18). Long term outcomes for infants were poorly documented.

VV-ECMO OUTCOMES IN COVID-19 PREGNANT WOMEN

In the recent years, COVID-19 pandemic affected all groups of people and that includes pregnant women. Hence it became important to consider this group for respiratory support by VV-ECMO if the patient deteriorated. Although not enough data is available, a multicenter study by Byrne et al demonstrated that the majority of expectant and recently delivered patients who needed ECMO due to COVID-19-related respiratory failure made it through, but they frequently suffered from miscarriages, severe maternal morbidity including thromboembolic events, and low neonatal birth wights requiring admission to the intensive care unit and intubation. These results imply that patients who are pregnant or recently gave birth should be carefully considered for ECMO for COVID-19-associated respiratory failure (19).

VV ECMO INDICATIONS

VV ECMO, is utilized for patients who have compromised ventilation or oxygenation that cannot be adequately treated with optimal mechanical ventilation and medical therapy (20). Normal cardiac function is essential for VV ECMO to ensure proper blood perfusion. Therefore, common VV ECMO indications include refractory hypoxemia, defined as the ratio between the partial pressure of oxygen and FiO2 (PaO2/FiO2) < 80 and/or hypercapnic respiratory failure (pH \leq 7.2) despite optimal conventional mechanical ventilation), ventilatory support as a bridge to lung transplantation in patients with advanced end-stage lung disease and primary graft dysfunction following lung transplant (11,12,21).

The most common indication for VV ECMO during pregnancy is severe H1N1 influenza complicated with ARDS (15). Additionally, VV ECMO might be considered for pregnant patients with pre-eclampsia or eclampsia as these can lead to pulmonary edema and acute respiratory distress. Another potential indication is amniotic fluid embolism (AFE), a rare but life-threatening condition where amniotic fluid or fetal debris enters the maternal bloodstream, causing an acute allergic-like reaction and profound respiratory compromise. Aspiration of gastric contents, status asthmaticus, severe sepsis, and severe viral infections such as influenza or COVID-19 are other factors that may lead to respiratory failure requiring VV ECMO support during pregnancy. The decision to use VV ECMO should be based on the severity of respiratory failure, gestational age, and individual patient considerations, with a multidisciplinary team of specialists collaborating to optimize outcomes for both the mother and the fetus (15,22).

CONTRAINDICATIONS FOR VV ECMO

ABSOLUTE CONTRAINDICATIONS TO THE INITIATION OF VV ECMO INCLUDE: (10,23-25) 1. The patient's refusal to use extracorporeal methods

2. End-stage malignancy with life expectancy less than 1 year or untreatable metastatic malignancy

3. Prolonged cardiac arrest

4 .A background of multiorgan failure that cannot escalate to transplantation (such as end stage liver disease or advanced cardiac failure).

5. Serious neurological damage with no chance of recovery, like a major stroke, fatal intracranial bleeding, brain herniation, or uncontrollable intracranial hypertension

RELATIVE CONTRAINDICATIONS TO THE INITIATION OF ECMO (10,26,27)

1. Extremes of age

2. Immunocompromised Patients

3. Invasive mechanical ventilation of 7 days or more

4. Contraindication to anticoagulation

5. Severe coagulopathy

6. Hematologic cancers, particularly those associated with bone marrow transplants and graft-versus-host disease

7. Unfavorable vasculature such as aortic dissection

8. Severe multi-organ failure

9. Simplified Acute Physiology Score (SAPS II) \geq 60 Points

10. Sepsis-Related/Sequential Organ Failure Assessment Score (SOFA) >12 points

11. A score of 5 points or less in PRE-SERVE (Predicting Death of Severe ARDS on VV-ECMO)

12. Respiratory Extracorporeal Membrane Oxygenation Survival Prediction (RESP) score Worse Than -2 Points

13. The PRESET (the Prediction of Survival on ECMO Therapy (PRESET)score ≥ 6points

14. "Do Not Attempt Resuscitation Order"

ANTICOAGULATION IN VV ECMO

Anticoagulation is a crucial aspect of VV ECMO, as it helps prevent clotting in both the circuit and the patient (28). However, anticoagulation also increases the risk of bleeding complications, which can be life-threatening in some cases. Therefore, anticoagulation must be carefully monitored and managed throughout the course of VV ECMO. The following tests should be used to assess hemostasis for individuals who are prospects for ECMO before the start of ECMO, according to the ELSO anti coagulation guidelines: Prothrombin time, fibrinogen, D-dimer, antithrombin, total blood count, and thromboelastography or thromboelastometry (12).

Due to its rapid onset and immediate reversal, unfractionated heparin (UFH) is the standard of care medication for patients receiving ECMO worldwide. An initial bolus at cannulation time and an ongoing intravenous infusion for the duration of the entire ECMO course are advised by the ELSO anti coagulation recommendations. After ECMO has started, anticoagulation monitoring should be considered in order to adapt the rate of infusion accordingly. Heparin administration should initially be regulated by the activated coagulation time (ATC). After collecting laboratory test results, heparin infusion ought to be influenced by the activated partial thromboplastin time (aPTT) or anti-Xa activity. (12,29).

VV ECMO Complications

VV ECMO is a complex and invasive procedure that carries significant risks, and complications can arise despite careful patient selection, management, and monitoring. These issues might be categorized as patient- or circuit-related. Numerous patient-related issues exist, and a system-based approach can further characterize them (10,12).

Hematological complications can be either hemorrhagic or thrombotic. Bleeding can range from minor to severe, necessitating transfusion. Bleeding can occur at the cannulation sites. inside the ECMO circuit, or in other regions of the body with intracranial hemorrhage (ICH) being the most worrisome one (26). Consideration should also be given to thrombotic problems since turbulent flow and blood exposure to non-physiologic surfaces result in a pro-thrombotic condition during VV ECMO. Seizures, strokes, and cerebral hemorrhages are the most prevalent neurological consequences, and they have the potential to be catastrophic. Other VV ECMO complications include infection, as the VV ECMO requires insertion of large cannulas into major veins, which can increase the risk of infection. Cannula mispositioning, circuit rupture, unintentional decannulation, air embolism, pump failure, oxygenator failure, circuit thrombosis, and venous insufficiency are only a few of the issues connected to the circuit. (29,30).

OPTIMAL TIME FOR DELIVERY

Optimal delivery time for fetuses in pregnant women data is lacking and there is not enough evidence to support any exact date of delivery. One interesting study though found that maintaining the pregnancy on ECMO support entails a higher risk of fetal death, less preterm birth-related morbidity, and no difference in the outcomes for mothers. It does not address though if there is an optimal time for delivery to reduce the risk of morbidity and mortality (31).

SPECIAL CONSIDERATIONS IN PREGNANCY

Pregnancy-related ECMO indications and contraindications are comparable to those for the general population. Acute respiratory distress syndrome (ARDS), which accounts for 49% of cases requiring VV ECMO in pregnant and postpartum patients, is the most frequent indication for the treatment. Severe viral lung infection is the main cause of these instances. Similar cannulation procedures apply to patients who are not pregnant. It is beneficial to include a cushion under the right hip to facilitate left uterine displacement during this procedure because aortocaval compression brought on by the gravid uterus may prevent femoral guidewire advancement (17).

Due to the rises in coagulation factors, pregnancy is regarded as a hypercoagulable. There isn't much proof that pregnancy makes ECMO circuit thrombosis more likely, though. Due to its accessibility, affordability, reversibility, difficulty to penetrate the placenta, and low association with congenital malformations, unfractionated heparin is the standard of care for systemic anticoagulation for ECMO during pregnancy (1,17). The use of ECMO during pregnancy is also governed by the fundamental ideas previously covered. Moore et al. recently examined the information that is currently available on ECMO support during pregnancy in their study. For instances requiring ECMO support, the rates of mother and fetal survival were 77.8% and 65%, respectively (1). It is not anticipated that using VV ECMO during gestation will cause major hemodynamic alterations that could harm uterine circulation (15).

CONCLUSION

In conclusion, VV ECMO has shown very good maternal and fetal survival rates in the short term

when used in select patients with normal cardiac function compared to patients who didn't use it or used other methods.

AUTHORS' CONTRIBUTIONS

Moustafa Younis was involved in conceptualization, overall supervision, and manuscript revision. All authors approved this version of the manuscript for submission. Waheed F. Hammad, Hala Almajali, Zaineh M. Alfreahat, and Yasmeen Jamal Alabdallat were involved in manuscript writing, editing and revision. Salem Alsalman was involved in overall supervision and manuscript revision.

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