

Extracorporeal Membrane Oxygenation for Cardiopulmonary Failure During Pregnancy and Postpartum

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Background. Extracorporeal membrane oxygenation (ECMO) has been used with increasing frequency to support pregnant and postpartum patients with severe cardiac or pulmonary failure, although patient management and clinical outcomes are underreported. This study represents patients who received ECMO during the peripartum period.

Methods. All pregnant or postpartum patients treated with ECMO in the medical intensive care unit between January 1, 2009, and June 30, 2015, were included in this study. Data were analyzed retrospectively. The primary objective was to characterize the circumstances and clinical characteristics of the patients who received ECMO, describe our management during pregnancy and at the time of delivery, evaluate maternal and fetal outcomes, and report bleeding and thrombotic complications.

Results. Eighteen peripartum patients were treated with ECMO during the study period; 4 were pregnant at

the time of cannulation. Median age was 32.6 years, and median gestational age in pregnant patients was 32 weeks. Sixteen patients (88.9%) survived to hospital discharge. Fetal survival was 14 (77.8%) in the entire cohort and 100% in patients cannulated after fetal viability. Two patients successfully delivered on ECMO. Bleeding complications developed in 6 patients (33.3%) and were associated with disseminated intravascular coagulation. No fetal complications were attributed to ECMO.

Conclusions. ECMO can be used during pregnancy and postpartum with favorable maternal and fetal outcomes, and it outweighs the risk of bleeding or thrombotic complications when managed by an experienced, multidisciplinary team.

(Ann Thorac Surg 2016;■:■-■)

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Extracorporeal membrane oxygenation (ECMO) has been used with increasing frequency in recent years to treat patients with severe cardiac or pulmonary failure [1, 2]. The development of safer, more durable devices, the widespread use of ECMO during the 2009 influenza A(H1N1) pandemic, and the publication of the CESAR (conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure) trial have contributed to its worldwide growth [2-5]. Although the overall use of ECMO has increased, the

outcomes of specific patient populations managed with ECMO remain underreported. One such area is the use of ECMO during pregnancy and postpartum.

The extent of published experiences with ECMO during and immediately after pregnancy is limited to case reports and small case series [6-10]. Much is unknown about the unique risks associated with ECMO in the peripartum period, although concerns have arisen about both hypercoagulability and hemorrhage. Likewise, the preferred method and timing of fetal monitoring and delivery are not well described. No current guidelines are available from the Extracorporeal Life Support Organization, the American College of Obstetricians and Gynecologists, or the Society for Maternal-Fetal Medicine on the use of ECMO during or after pregnancy. We report our institutional experience in the management of peripartum patients with ECMO. Our aim is to characterize the circumstances for which a patient received ECMO, describe our management practices during pregnancy

Accepted for publication March 2, 2016.

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Abbreviations and Acronyms

APACHE	= Acute Physiology and Chronic Health Evaluation
ARDS	= acute respiratory distress syndrome
ECMO	= extracorporeal membrane oxygenation
ECPR	= extracorporeal cardiopulmonary resuscitation
DIC	= disseminated intravascular coagulation
DVT	= deep vein thrombosis
FIO ₂	= fraction of inspired oxygen
ICU	= intensive care unit
IQR	= interquartile range
PaCO ₂	= partial pressure of arterial carbon dioxide
PaO ₂	= partial pressure of arterial oxygen

and at the time of delivery, and report maternal and fetal outcomes.

Material and Methods

All patients who were pregnant or up to 6 weeks postpartum and received ECMO in the medical intensive care unit (ICU) at New York-Presbyterian Hospital/Columbia University Medical Center from January 1, 2009, to June 30, 2015, were included in this study. Data were collected retrospectively from our institution's electronic medical record and are reported as median with interquartile range (IQR) or number with percentage unless otherwise specified. This study was approved by the Columbia University Institutional Review Board and performed in accordance with accepted ethical standards.

The decision to initiate ECMO was at the discretion of a multidisciplinary team that consisted of thoracic surgeons and medical intensivists. All patients with acute respiratory distress syndrome (ARDS) were classified as severe according to the Berlin definition [11]. At our institution, ECMO is considered in patients with ARDS when the ratio of partial pressure of oxygen in arterial blood (PaO₂) to fraction of inspired oxygen (FIO₂) is less than 80 mm Hg, pH is less than 7.15 in the setting of uncompensated hypercapnia, or the plateau airway pressure is greater than 35 to 45 cm of water, depending on body habitus and despite optimal ventilator management [12]. Our center has a robust ECMO transport program; hence, timing of ECMO and patient management before ECMO often reflect the clinical decisions and resources at referring institutions [13]. Patients who underwent extracorporeal cardiopulmonary resuscitation (ECPR) were either already admitted to our institution or experienced cardiac arrest at referring hospitals, after our mobile ECMO transport team was deployed for ARDS.

Patients who received venovenous ECMO were cannulated with a dual-site configuration with drainage from the right or left femoral vein and reinfusion to the right or left internal jugular vein, or with a bicaval dual-lumen

cannula positioned in the right internal jugular. Patients who received venoarterial or venoarterial-venous ECMO were cannulated with femoral venous drainage and femoral artery reinfusion, with the return blood flow split between the femoral artery and internal jugular vein in situations of venoarterial-venous ECMO. Our ECMO circuits were either a Rotaflow centrifugal pump (Maquet Inc, Rastatt, Germany) and Quadrox D oxygenator or a CARDIOHELP system (Maquet Inc). To minimize hemolysis and thrombus development, we do not use a bridge, and we minimize access ports within the circuit. In patients who received ECMO for ARDS, our center uses a blood conservation protocol that includes a transfusion threshold of hemoglobin less than 7.0 g/dL and titration of intravenous heparin infusion to an activated partial thromboplastin time between 40 and 60 seconds [14]. We screen for upper and lower extremity deep vein thrombosis (DVT) in all patients after decannulation.

Pregnant patients were closely followed by our institution's high-risk maternal-fetal medicine service. Fetal monitoring included twice daily fetal heart tones or nonstress tests and pelvic ultrasound scans. All patients with viable fetuses received steroids to support fetal lung development before delivery.

Results

Eighteen patients were treated with ECMO during the study period. Median age was 32.6 years (IQR, 26 to 39) and Acute Physiology and Chronic Health Evaluation II score was 27 (IQR, 23 to 30) (Table 1). Fourteen patients (77.8%) were postpartum and 4 (22.2%) were pregnant while receiving ECMO. Gestational age of pregnant patients was 29.1 weeks (range, 18.4 to 34.3 weeks). Postpartum patients delivered 3 days (IQR, 1 to 6 days) before cannulation. Other baseline demographic and clinical characteristics are detailed in Table 1. Indications for ECMO included pneumonia with ARDS (n = 17), ECPR (n = 3), pulmonary embolism (n = 2), amniotic fluid embolism (n = 2), and pulmonary hypertension (n = 1). Several patients had multiple indications for ECMO, including 2 with ARDS who underwent ECPR, 1 with an amniotic fluid embolism who underwent ECPR, and 1 with a massive pulmonary embolism that developed into an amniotic fluid embolism after emergent cesarean delivery (Table 1).

Before ECMO, patients were endotracheally intubated for a median of 1.5 days (IQR, 1 to 3 days). Pre-ECMO arterial blood gas data showed a median PaO₂ to FIO₂ ratio of 53 mm Hg (IQR, 38 to 62 mm Hg), pH of 7.2 (IQR, 7.1 to 7.3), and partial pressure of arterial carbon dioxide (PaCO₂) of 52 mm Hg (IQR, 40 to 60 mm Hg) with median positive end-expiratory pressure of 12 cm of water (IQR, 10 to 15 cm of water) and FIO₂ of 1.0. Additional rescue therapies used before ECMO included neuromuscular blocking agents and inhaled pulmonary vasodilators (Table 1). Twelve patients (66.7%) had a reduced left ventricular ejection fraction, with a median of 37.5% (IQR, 20% to 46%). Sixteen patients (88.9%) were in shock.

Table 1. Baseline Demographic and Clinical Characteristics (n = 18)

Characteristic	Value
Age, years	32.6 (26–39)
Body mass index, kg/m ²	33.6 (25.8–37.4)
Body surface area, m ²	1.8 (1.7–1.9)
APACHE II score	27 (23–30)
Postpartum	14 (77.8)
Pregnant	4 (22.2)
Comorbidities	
Asthma	2 (11.1)
Pulmonary hypertension/congenital heart disease	1 (5.6)
Pneumonectomy	1 (5.6)
Pregnancy-related comorbidities	
Hypertension/preeclampsia	4 (22.2)
HELLP	1 (5.6)
Abruptio placentae	1 (5.6)
Indication for ECMO ^a	
ARDS	17 (94.4)
Influenza	6 (33.3)
Culture negative pneumonia	2 (11.1)
Aspiration	3 (16.7)
TRALI	4 (22.2)
Nonpulmonary sepsis	2 (11.1)
ECPR	3 (16.7)
Pulmonary embolism	2 (11.1)
Amniotic fluid embolism	2 (11.1)
Pulmonary hypertension	1 (5.6)
Pre-ECMO ventilatory variables ^b	
Endotracheal intubation, days	1.5 (1–3)
PEEP, cm H ₂ O	12 (10–15)
FIO ₂	1.0
pH	7.2 (7.1–7.3)
PaCO ₂ , mm Hg	52 (40–65)
PaO ₂ , mm Hg	53 (38–61)
PaO ₂ /FIO ₂	53 (38–61)
Rescue therapies	
Neuromuscular blocking agents	9 (50.0)
Inhaled pulmonary vasodilators (nitric oxide or epoprostenol)	7 (38.9)
Pre-ECMO clinical course	
Shock	16 (88.9)
Renal failure/renal replacement therapy	6 (33.3)
Emergent operation	5 (27.8)
Cardiac arrest	4 (22.2)
Massive hemorrhage	4 (22.2)
Catheter-directed thrombolysis	1 (5.6)

^a Several patients had multiple indications for ECMO, including 2 with ARDS and ECPR, 1 with an amniotic fluid embolism and ECPR, and 1 with amniotic fluid embolism and pulmonary embolism. ^b n = 17; one patient was not intubated at ECMO initiation.

Data are median (interquartile range) or number (%).

APACHE II = Acute Physiology and Chronic Health Evaluation II; ARDS = acute respiratory distress syndrome; ECMO = extracorporeal membrane oxygenation; ECPR = extracorporeal cardiopulmonary resuscitation; FIO₂ = fraction of inspired oxygen; HELLP = hemolysis, elevated liver enzymes, low platelets; PaCO₂ = partial pressure of arterial carbon dioxide; PaO₂ = partial pressure of arterial oxygen; PEEP = positive end-expiratory pressure; TRALI = transfusion-related acute lung injury.

The median duration of ECMO was 6.6 days (IQR, 6 to 17.8 days). The initial ECMO configuration was venovenous in 14 patients (77.8%), venoarterial in 1 patient (5.6%), and venoarterial-venous in 3 patients (16.7%)

(Table 2). Four patients with a venovenous configuration received ECMO by a bicaval, dual-lumen cannula, whereas the remainder had dual-site cannulation. An initial venoarterial or venoarterial-venous configuration

Table 2. ECMO Variables (n = 18)

Variable	Value
Initial ECMO configuration	
Venovenous	14 (77.8)
Venoarterial	1 (5.6)
Venoarterial-venous	3 (16.7)
ECMO settings	
Blood flow, L/min	3.9 (3.2–4.8)
Sweep gas flow, L/min	3.8 (3.0–5.3)
FDO ₂	1.0
Preoxygenator saturation, %	75 (70–80)
ECMO blood flow/predicted cardiac output, %	91 (80–110)

Data are median (interquartile range) or number (%).

ECMO = extracorporeal membrane oxygenation; FDO₂ = fraction of delivered oxygen.

was used in patients who underwent ECPR or had a precannulation cardiac arrest. Time to ECMO cannulation in patients who received ECPR was 5 to 90 minutes. Median blood flow 24 hours after ECMO initiation was 3.9 L/min (IQR, 3.2 to 4.8 L/min). ECMO blood flow was 91% (IQR, 80% to 110%) of predicted cardiac output (Table 2).

Sixteen patients (88.9%) survived to hospital discharge (Table 3). The two patients who died both succumbed to severe shock and multisystem organ failure after 0.25 and 23 days on ECMO, the latter of whom had been placed on ECMO after 15 days of endotracheal intubation. Fetal survival in the entire cohort was 77.8% (n = 14) (Table 3). Of the 4 patients (22.2%) who were pregnant on ECMO, 2 delivered while receiving ECMO support. Deliveries were performed by cesarean delivery after extensive preoperative discussions between the ICU, ECMO, maternal-fetal medicine, and obstetric anesthesia teams. One patient also received extensive consultation by a pulmonary hypertension specialist.

Table 3. Clinical Outcomes (n = 18)

Outcome	Value
Maternal survival	16 (88.9)
Fetal survival	14 (77.8)
Details of pregnant patients	
Pregnant on ECMO with viable fetus	3 (75) ^a
Fetal survival if viable pregnancy	3 (100) ^b
Delivered on ECMO support	2 (66.7) ^b
ECMO duration, days	6.6 (6–17.8)
Extubated on ECMO	5 (27.8)
Active physical therapy on ECMO	7 (38.9)
Ambulated on ECMO	4 (22.2)
Hospital length of stay, days	22.5 (13–44.3)

^a Pregnant with viable fetus. ^b Patients pregnant at the time of ECMO cannulation.

Data are median (interquartile range) or number (%).

ECMO = extracorporeal membrane oxygenation.

The first patient to deliver while receiving ECMO had Eisenmenger syndrome with supra-systemic pulmonary arterial pressures from an unrepaired patent ductus arteriosus. She was admitted at gestational week 18 for observation and placed on venovenous ECMO by a dual-lumen cannula in the right internal jugular vein at 34.3 weeks to allow for fetal maturation in the setting of severe postductal hypoxemia. She underwent emergent cesarean delivery and bilateral tubal ligation 3 days after cannulation in the setting of decompensated pulmonary hypertension and hypoxemia despite optimized medical and mechanical support. The delivery itself was uncomplicated; however, disseminated intravascular coagulation (DIC) and intraabdominal hemorrhage with abdominal compartment syndrome developed several hours postpartum that required placement of an additional venous drainage cannula and exploratory laparotomy with clot evacuation, after which time she stabilized. She was decannulated 9 days after delivery, yet required recannulation with a venoarterial configuration 4 days later in the setting of severe septic shock. She was weaned from venoarterial ECMO after 12 days of support and stabilized to hospital discharge.

The second patient who delivered while receiving ECMO had influenza A(H1N1) pneumonia with severe ARDS, renal failure, and septic shock. She was cannulated with a venovenous configuration at 26.3 weeks and underwent cesarean delivery 16 days later, prompted by the development of preeclampsia and DIC with multisite bleeding. The operative course was uncomplicated, and there was resolution of the DIC and bleeding immediately after delivery after which time the patient stabilized. A third patient at 32 weeks' gestation was supported 6 days on venovenous ECMO for ARDS, secondary to urosepsis. She underwent Cesarean delivery 1 day after ECMO decannulation and several hours after extubation. Delivery followed an episode of fetal bradycardia not associated with an overt clinical change in the patient. Maternal and fetal survival to hospital discharge was 100% for these 3 cases.

One patient with severe pre-ECMO hypoxemia was cannulated before fetal viability at 18 weeks' gestation and miscarried several hours after transfer to our institution. Two additional patients were pregnant during their ICU admissions, but they miscarried before ECMO cannulation. No fetal complications were attributed to ECMO.

Fourteen patients (77.8%) received transfusions of packed red blood cells during their ECMO run, including 4 who had massive hemorrhage or DIC before ECMO initiation. The median number of transfusions was 2.5 units (IQR, 1 to 18.3 units), equivalent to 0.38 units/day. Bleeding complications developed in 6 patients (33.3%) while receiving ECMO, all of whom had concomitant DIC (Table 4). Of the 13 patients who underwent Cesarean delivery, 4 experienced intra-abdominal bleeding that resulted in abdominal compartment syndrome and required surgical exploration while receiving ECMO. All were associated with preexisting massive hemorrhage or DIC. One of these

Table 4. Complications

Complication	n (%)
Patients with hemorrhage, total	10 (55.6)
Hemorrhagic complications that developed on ECMO	6 (33.3)
Site of bleeding ^a	
Uterine/intra-abdominal	4 (22.2)
Epistaxis	2 (11.1)
Hematuria	2 (11.1)
Tracheostomy	2 (11.1)
Cannula	2 (11.1)
Chest tube	2 (11.1)
Pulmonary	2 (11.1)
Gastrointestinal	1 (5.6)
Retroperitoneal	1 (5.6)
Early decannulation	2 (11.1)
DIC	10 (55.6)
Thrombotic complications	
Nonocclusive DVT	4 (22.2)
Occlusive DVT	1 (5.6)

^a Several patients bled from multiple sites.

DIC = disseminated intravascular coagulation; DVT = deep vein thrombosis; ECMO = extracorporeal membrane oxygenation.

patients subsequently experienced limb ischemia from continued intraabdominal, surgical site bleeding near a femoral cannula site hematoma and ultimately required a below-the-knee amputation. A chest tube-related hemothorax that required decortication developed in another patient. Two patients were decannulated early because of bleeding, both of whom required recannulation. Four patients without overt bleeding required transfusions; the decreased hemoglobin was attributed to pre-ECMO blood loss, critical illness, and phlebotomy. No circuits required changing because of cannula or oxygenator thrombosis. Screening vascular ultrasound scans in survivors revealed cannula-associated DVTs in 5 patients (27.8%) (Table 4).

Comment

Our series reports on pregnant or postpartum patients supported with ECMO. Our high maternal and fetal survival rates suggest that ECMO may be used to support both of these populations and is consistent with other published reports of ECMO during the peripartum period [7].

Management of patients with ARDS was similar to that of our nonperipartum patients without ARDS treated with ECMO. Cannulation strategy was chosen on the basis of patient stability and underlying illness. We typically use dual-site venovenous cannulation because it obviates the need for fluoroscopy or echocardiography guidance that are preferred during placement of a bicaval, dual-lumen cannula, and which are often unavailable at referring facilities. Cannula size was selected to support a patient's predicted cardiac output at the

time of ECMO initiation. We did not experience difficulty with femoral cannulation from inferior vena cava compression in the setting of a gravid uterus. To ensure adequate fetal oxygen delivery during the ECMO run, we targeted a maternal PaO₂ greater than 80 mm Hg. To mimic the acid-base status of normal pregnancy, sweep was titrated to achieve a normal pH, while maintaining PaCO₂ greater than 30 mm Hg [15]. When chatter occurred, the patient was positioned with a slight left-tilted position to minimize venous compression. Transfusion thresholds and anticoagulation targets were not altered because of pregnancy or postpartum status. Although the optimal hemoglobin for patients with ARDS who receive ECMO is not known, our center's experience suggests that a transfusion threshold of hemoglobin of 7.0 g/dL is safe and associated with favorable outcomes [14]. We targeted a higher hemoglobin concentration in the patient with Eisenmenger syndrome and decompensated pulmonary hypertension. Patients who delivered while receiving ECMO had anticoagulation held for 1 hour before and after delivery.

Bleeding complications developed in one-third of this cohort during ECMO support, and several additional patients were placed on ECMO in the setting of preexisting, massive hemorrhage. Bleeding developed more frequently compared with our own institutional experience, although less often than in prior published reports of pregnant or postpartum women supported with ECMO, albeit any comparison is quite limited because of the relatively small number of patients in all series [7, 10, 14]. Bleeding in our cohort was consistently associated with DIC, which was attributed to pregnancy itself or pregnancy-related conditions (detailed in Table 1), with hemostatic balance possibly affected by interactions with the ECMO circuit. The interaction of normal, pregnancy-related hemostatic changes and ECMO circuitry is not known. However, DIC occurred far more commonly in this population than in our own institutional experience or than is reported in adults in the Extracorporeal Life Support Organization registry [16]. Notably, maternal and fetal survival was 100% in patients who experienced bleeding complications during ECMO support and in patients that had massive pre-ECMO hemorrhage or coagulopathy, suggesting that these characteristics need not be contraindications to the initiation of ECMO in this critically ill population.

A delivery plan should be prepared for all pregnant patients who receive ECMO which considers both patient and fetal condition. Oxygen delivery to the placenta is determined by oxygen content of uterine arterial blood and uterine artery blood flow, which is about 10% of maternal cardiac output (600 to 700 mL oxygen/min) at term [15]. Thus, timing of delivery should include assessment of the burden of the fetoplacental unit (ie, fetal oxygen consumption) on maternal oxygenation and fetal stability. We recommend early consultation with a high-risk maternal-fetal medicine specialist to ensure adequate fetal support, identify signs of physiologic stress, and optimize the fetus for potential premature or emergent delivery. Although ideally the pregnancy would be

supported to term or until the patient's cardiopulmonary recovery, planning for prompt delivery on ECMO is key to optimize both maternal and fetal outcomes.

There are few reports of deliveries occurring on ECMO support, which have occurred vaginally and by cesarean delivery [7, 10, 17]. In all patients, but particularly those with preexisting cardiomyopathy or pulmonary hypertension, when alterations in hemodynamic or intravascular volume status carry a high risk of death, careful consideration should be given to the risks and benefits of cesarean delivery versus vaginal delivery. ECMO can also be used in the delivery room on standby for extremely high-risk deliveries. In these cases, careful multidisciplinary planning with possible placement of micropuncture sheaths will enable the ECMO team to rapidly gain vascular access if the patient decompensates during delivery and may be an evolving application of extracorporeal support. We encourage early notification for high-risk patients who may need ECMO, thereby allowing our team to monitor them before cannulation becomes emergent. This study is limited by its relatively small size and retrospective design at a single center.

In conclusion, ECMO can be used successfully both during pregnancy and postpartum by an experienced, multidisciplinary team. Our high maternal and fetal survival rates suggest that the benefits of preventing maternal and fetal hypoxia outweigh the potential risks associated with ECMO. The expanded use of ECMO in high-risk obstetric populations, such as those with ARDS and pulmonary hypertension, may result in improved maternal and fetal outcomes and warrants further investigation.

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