Extracorporeal Membrane Oxygenation for Neonatal Respiratory Failure

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Abstract

Recent medical advances, such as permissive hypercapnia, inhaled nitric oxide, and the use of oscillatory ventilation, have spared numerous patients from ECMO, yet many children still benefit from this modality. Patients with reversible cardiopulmonary disease, who meet criteria, should be considered ECMO candidates. As of January 2015, 27,728 neonates (74% survival) and 6,569 pediatric patients (57% survival) have been treated with ECMO for respiratory failure and 13,124 neonatal and pediatric patients for cardiac failure. ECMO provides an excellent opportunity to provide “rest” to the cardiopulmonary systems thus avoiding the additional lung or cardiac injury which otherwise would be necessary to maintain life support. This chapter outlines the indications, contraindications, management
approach, and complications associated with ECMO as well as the various bypass configurations and cannulation strategies which may be employed.

**Keywords**
Extracorporeal membrane oxygenation · Extracorporeal support · Respiratory failure · Cardiac failure · ECMO · Cannulation

**Introduction**

Extracorporeal membrane oxygenation (ECMO) is a lifesaving technology that affords partial heart/lung bypass for extended periods. ECMO is a supportive rather than a therapeutic modality as it provides sufficient gas exchange and perfusion in patients with acute, reversible cardiac or respiratory failure. It provides a finite period to “rest” the cardiopulmonary systems at which time they are spared insults from traumatic mechanical ventilation and perfusion impairment. ECMO was first implemented in newborns in 1974. Most information on the use of ECMO comes from the Extracorporeal Life Support Organization (ELSO). International registering ELSO has recorded 50,903 neonatal and pediatric patients treated with ECMO for a wide range of cardiopulmonary disorders. Several randomized trials in the United States and the United Kingdom found that ECMO support improved survival outcomes when compared with conventional care and it has become accepted practice in neonatal care (Bartlett et al. 1985; Jenks et al. 2017). In the neonatal period the most common disorders treated with ECMO are meconium aspiration syndrome (MAS), congenital diaphragmatic hernia (CDH), persistent pulmonary hypertension of the neonate (PPHN), sepsis, respiratory distress syndrome (RDS), and cardiac support. For the pediatric population, viral and bacterial pneumonia, acute respiratory failure (non-ARDS), acute respiratory distress syndrome (ARDS), and cardiac disease are the most common pathophysiologic processes requiring ECMO intervention (Butler et al. 2017; Frenckner 2015; Campbell et al. 2003).

Candidates for ECMO are expected to have a reversible cardiopulmonary disease process, with a predictive mortality greater than 80–90%, and exhaustion of ventilatory and other therapies. Obviously, these criteria are subjective and vary between institutions. Criteria for mortality risk in neonatal respiratory failure have been suggested to identify infants with a >80% mortality (Bailly et al. 2017; Barbaro et al. 2016). These include (a) the oxygenation index (OI), calculated as FiO₂ * mean airway pressure * 100/PaO₂ (OI >25 is predictive of a 50% mortality rate and is a relative indication for ECMO while OI >40 equates with 80% mortality and mandates implementation of ECMO), and (b) an alveolar-arterial oxygen gradient (A-aDO₂) >625 mmHg for more than 4 h, or an A-aDO₂ >600 mmHg for more than 12 h. Older infants and children do not have as well-defined criteria for high mortality risk. The combination of a ventilation index (respiratory rate * PaCO₂ / peak inspiratory pressure/1,000) >40 and an OI >40 correlates with a 77% mortality, whereas a mortality of 81% is associated with an A-aDO₂ >580 mmHg and a peak inspiratory pressure of >40 cmH₂O. In general, ECMO is indicated in pediatric patients with respiratory failure when the A-aDO₂ is >600 mmHg on FiO₂ 1.0 despite optimal treatment. Indications for support in patients with cardiac pathology are based on clinical signs of cardiovascular failure such as hypotension despite the administration of inotropes or volume resuscitation, metabolic acidosis, oliguria (urine output <0.5 cc/kg per h), and decreased peripheral perfusion.

In addition, the gestational age should be at least 34–35 weeks due to the increased risk for intracranial hemorrhage (ICH) and the birth weight at least 2 kg secondary to cannula size limitations. The length of mechanical ventilation, and its associated toxicity from prolonged exposure to high concentrations of oxygen and elevated positive pressure ventilation prior to ECMO should be preferably no longer than 10–14 days due to the development of bronchopulmonary dysplasia. Babies with lethal
congenital anomalies should not be considered for ECMO support. Treatable conditions such as total anomalous pulmonary venous return and transposition of the great vessels, which may masquerade initially as pulmonary failure, can be corrected with surgery but may require ECMO resuscitation initially. Therefore, echocardiogram should be rapidly obtained to determine cardiac anatomy. There should be no evidence of significant neurologic injury such as seizures. Patients with suggestion of a small ICH (grades I–II) should be considered candidates for ECMO on an individual basis and monitored closely for worsening of the hemorrhage. In fact, all patients with gross active bleeding or major coagulopathy should be corrected prior to initiating ECMO.

Types of Extracorporeal Membrane Oxygenation

The goal of ECMO support is to provide gas exchange and oxygen delivery. Three different extracorporeal configurations: venoarterial (VA), venovenous (VV), and double-lumen single cannula venovenous (DLVV) bypass are available (Fig. 1a–c). VA bypass allows for support of both the pulmonary and cardiac systems. Venous blood is drained from the right atrium (RA) through the internal jugular vein (IJ), and oxygenated blood is returned via the carotid artery (CA) to the aorta. Potential disadvantages of this arrangement include the sacrifice of a major artery; risk of gaseous or particulate emboli into the systemic circulation; reduced pulmonary perfusion; increased afterload, which may reduce cardiac output; non-pulsatile flow; and perfusion of the coronaries by relatively hypoxic left ventricular blood. VV and DLVV avoid these disadvantages and provide pulmonary support but do not provide hemodynamic/cardiac support. VV bypass is accomplished with drainage from the RA via the IJ with reinfusion into the femoral vein or drainage from the IVC/femoral vein with reinfusion into the IJ/RA. DLVV is carried out by means of the IJ. A major disadvantage of VV and DLVV ECMO is that a fraction of freshly infused blood recirculates back into the circuit and requires approximately a 20% increase in flow rate. It is recommended that patients who require only respiratory support use VV or DLVV bypass and those that necessitate cardiac support use VA ECMO. If necessary, one can convert VV or DLVV to VA support.

Most reports have suggested that there is no overall advantage with either the VA or VV technique (McHoney and Hammond 2018). VA ECMO seem to be the more popular of the two modes according to the ECMO registries, presumably as the VA ECMO may give the additional benefit in the presence of severe cardiac dysfunction (McHoney and Hammond 2018). Size and vascular anatomy may sometimes dictate the mode use.

Technical Equipment

Blood is drained from the patient to a pump that advances blood to a membrane lung. The circuit is comprised of three main components: a roller pump, a membrane oxygenator, and a heat exchanger (Fig. 2). Right atrial blood is drained by gravity siphon into a venous servomechanism, which acts to ensure that venous return to the circuit is adequate for the current pump flow. To do so, the servo detects diminished venous return, slows or shuts off the pump, and sounds an alarm, hence stopping blood flow and relieving the risk of cavitation, introducing air into the circuit, and injury to the right atrium. Next, a roller pump, with continuous servoregulation and pressure monitoring, perfuses the blood through the membrane oxygenator. The oxygenator is a two-compartment chamber composed of a spiral wound silicone membrane and a polycarbonate core, with blood flow in one direction and oxygen flow in the opposite direction. The size of the oxygenator is chosen based on the patient’s size. The oxygenated blood flows through a heat exchanger and is then returned to the patient. A bridge is constructed to connect the venous line shortly after exiting the patient and the arterial line just prior to entering the patient so that during
weaning, the patient and the circuit can easily form two separate circuits. Technological improvements and the introduction of low-resistance oxygenators have resulted in the transition to centrifugal pump systems. Many centers now use circuits which incorporate centrifugal pumps and low resistance, blood on the outside/gas on the inside multiporous hollow fiber lungs. These systems are much simpler, cannot over pressurize, are at lower risk for negative pressure events which bring gas out of solution, and, therefore, are much safer and require less maintenance and supervision.

Fig. 1 Three different extracorporeal configurations; venoarterial (VA), venovenous (VV), and double-lumen single cannula venovenous (DLVV) bypass (Source: Puri P., Höllwarth M.E. (eds) Pediatric Surgery. Springer Surgery Atlas Series. Springer, Berlin, Heidelberg 2006)
Surgical Technique

Cannulation can be performed in the neonatal or pediatric intensive care units under adequate sedation, with proper monitoring. The patient is positioned with the head at the foot of the bed, supine, and the head and neck hyperextended over a shoulder roll and turned to the left (Fig. 3). Local anesthesia is administered over the proposed incision site. A transverse cervical incision is made over the sternomastoid muscle, one finger’s breadth above the right clavicle. The platysma muscle is divided with electrocautery. Self-retaining retractors are placed, and dissection is carried out with the sternomastoid muscle retracted to expose the carotid sheath. Using sharp dissection and meticulous hemostasis, the sheath is opened, and the internal jugular vein, common carotid artery, and vagus nerve are identified. All vessels must be handled with extreme care as to avoid spasm. The vein is dissected free first and mobilized over proximal and distal ligatures. Occasionally, it is necessary to ligate the inferior thyroid vein. The common carotid artery lies medial and posterior, contains no branches, and is mobilized in a similar fashion. The vagus nerve should be identified and protected from injury (Fig. 4).

The patient is then systemically heparinized with 50–100 U/kg heparin, which is allowed to circulate for 3 min. The arterial cannula (usually 10 F for newborns) is measured so that the tip will lie at the junction of the brachiocephalic artery and the aorta (2.5 cm neonates, one-third the distance between the sternal notch and the xiphoid). The venous cannula (12–14 F for neonates) is measured to have its tip in the distal RA (6 cm, one-half the distance between the suprasternal notch and the xiphoid process). For VA bypass, the carotid artery is ligated cranially. Proximal control is obtained with an angled clamp, and a transverse arteriotomy is made near the ligature (Fig. 5). Stay sutures, using 5/0 or 6/0 prolene, are placed through the full thickness of the medial and lateral proximal edges of the arteriotomy to help prevent subintimal dissection.
The sutures are gently retracted and the clamp slowly released as the arterial catheter is inserted into the carotid artery to its proper position. The cannula is then fastened into place with two silk ligatures (2/0), with a small piece of vessel loop, on the anterior aspect, inside the ligatures to protect the vessel from injury during decannulation.

In preparation for the venous cannulation, the patient is given succinylcholine to prevent spontaneous respiration. The vein is then ligated cranially. Gentle traction is placed on the lower ligature to help decrease back bleeding, and a venotomy is made close to the proximal ligation. The drainage catheter is passed to the level of the RA and secured in a manner similar to that used for the arterial catheter (Fig. 6). The cannulas are then debubbled with back bleeding and heparinized saline. Then they are connected to the ECMO circuit and bypass is initiated. Both cannulas are then secured to the mastoid process using 2–0 suture (Fig. 7). The wound is irrigated, meticulous hemostasis obtained, and the skin closed with a running nylon. The site is covered with a sterile dressing, and the circuit tubing is fixed securely to the bed.

For VV and DLVV bypass, the procedure is exactly as described above including dissection of the artery, which is marked with a vessel loop, so that a future switch from VV to VA ECMO can be accomplished, if necessary. The catheter tip should be in the mid-right atrium (6 cm in the neonate) with the arterial portion of the catheter pointed toward the ear. This directs the oxygenated blood flow toward the tricuspid valve.

Cannula position is confirmed by chest X-ray and by transthoracic echocardiogram when necessary. The venous catheter should be located in the inferior aspect of the right atrium and the
arterial catheter at the ostium of the innominate artery and the aorta. With a double-lumen venous catheter, the tip should be in the mid-right atrium with reinfusion of oxygenated blood flow toward the tricuspid valve (Hirschl and Bartlett 2012; Kim and Stolar 2003; Kim and Stolar 2000).

**Patient Management in ECMO**

Once the cannulas are connected to the circuit, bypass is initiated, and flow is slowly increased to 100–150 ml/kg per min so that the patient is stabilized. Continuous inline monitoring of the venous (pre-pump) SvO$_2$ and arterial (post-pump) PaO$_2$ as well as pulse oximetry is vital. The goal of VA ECMO is to maintain a mixed venous PO$_2$ (SvO$_2$) of 37–40-mmHg and saturation of 65–70%. VV ECMO is more difficult to monitor due to variation in the degree of recirculation, which may produce a falsely elevated SvO$_2$ assessment. Inadequate oxygenation and perfusion are indicated by metabolic acidosis, oliguria, and hypotension. Arterial blood gasses should be monitored hourly with PaO$_2$ and PaCO$_2$ maintained as close to normal level as possible. As soon as these parameters are met, all vasoactive drugs are weaned, and ventilator levels are adjusted to “rest” settings. Gastrointestinal prophylaxis is initiated, and mild sedation and analgesia is provided usually with fentanyl and midazolam, but the use of a paralyzing agent is avoided. A cephalosporin is often administered for prophylaxis. Routine blood, urine, and tracheal cultures should be taken.

Heparin is administered (typically 30–60 mg/kg per h) throughout the ECMO course in order to preserve a circuit free of thrombus. ACTs should be monitored hourly and maintained at 180–220 s. A complete blood count should be obtained every 6 h and coagulation profiles daily. In order to prevent hemorrhage, platelets are transfused to maintain a platelet count above 100,000/mm$^3$, and some authors sustain fibrinogen levels above 150 mg/dl. The hematocrit should remain above 40% using red blood cell transfusions so that oxygen delivery is optimized.

Volume management of patients on ECMO is extremely important. It is imperative that all inputs and outputs be diligently recorded and electrolytes monitored every 6 h. All fluid losses should be repleted and electrolyte abnormalities corrected. All patients should receive maintenance fluids as well as adequate nutrition using hyperalimentation. The first 48–72 h of ECMO typically involves fluid extravasation into the soft tissues. The patient becomes edematous and may require volume replacement (crystalloid, colloid, or blood products) in order to maintain adequate intravascular and bypass flows, hemodynamics,
and urine output greater than 1 cc/kg per h. By the third day of bypass, diuresis of the excess extracellular fluid begins and can be facilitated with the use of furosemide if necessary.

Surgical procedures, such as CDH repair, may be performed while the child remains on bypass. Hemorrhagic complications are a frequent morbidity associated with this situation and increases mortality. To avoid these complications, prior to the procedure, the platelet count should be greater than 100,000/mm³, a fibrinogen level above 150 mg/dl, an ACT reduced to 180–200 s, and ECMO flow increased to full support, and it is imperative that meticulous hemostasis be obtained throughout the surgery. Fibrinolysis inhibitor aminocaproic acid (100 mg/kg) just prior to incision followed by a continuous infusion (30 mg/kg per h) until all evidence of bleeding ceases is a useful adjunct.

As the patient improves, the flow of the circuit may be weaned at a rate of 10–20 ml/h as long as the patient maintains good oxygenation and perfusion. Flows should be decreased to 30–50 ml/kg per min, and the ACT should be at a higher level (200–220 s) to prevent thrombosis. Moderate conventional ventilator settings are used, but higher settings can be used if the patient needs to be weaned from ECMO urgently. If the child tolerates the low flow, all medications and fluids should be switched to vascular access on the patient, and the cannulas may be clamped with the circuit bypassing the patient via the bridge. The patient is then observed for 2–4 h, and if this is tolerated, decannulation should be performed. This should be executed under sterile conditions with muscle relaxant onboard to prevent air aspiration into the vein. The catheters are removed and the vessels are ligated. The wound should be irrigated and closed over a small drain, which is removed 24 h later.

Complications

Extracranial bleeding is a common complication of the heparinized ECMO patient either at the site of cannulation or at other sites and is noted in 21% of neonatal cases, 44% of pediatric respiratory cases, and 40% of all cardiac cases. Bleeding at the site of cannulation can often be treated with local pressure or the placement of topical hemostatic agents such as Gelfoam, Surgicel, or topical thrombin. For all sites of bleeding, the platelet count should be increased to >100,000 mm³ and the ACT lowered to 180–200 s. Sometimes the temporary discontinuation of heparin and normalization of the coagulation status is warranted to help stop the hemorrhage with availability of a second circuit should acute clotting of the circuit occur. Aggressive surgical intervention is warranted if bleeding persists.

Neurological sequelae are a serious morbidity of the ECMO population and include learning disorders, motor dysfunction, and cerebral palsy (Schiller et al. 2016; Madderom et al. 2013). These outcomes appear to be as much due to hypoxia and acidosis prior to the ECMO course as due to the time on ECMO itself. ICH is the most devastating complication, occurring in 7.4% of newborn patients with an associated 57% mortality among newborns who have ICH on ECMO. Frequent comprehensive neurologic exams should be performed, and cranial ultrasounds obtained daily for the first days of ECMO and then based on local protocols. Blood pressure should be carefully monitored and maintained within normal parameters to help decrease the risk of ICH. If necessary, electroencephalograms may be helpful in the neurologic evaluation.

Oliguria and increasing blood urea nitrogen and creatinine levels, may be seen in the ECMO patient during the initial 48 h, at which time renal function is expected to improve. If this does not occur, consideration must be toward poor tissue perfusion. This may be due to low cardiac output, insufficient intravascular volume, or inadequate pump flow, all of which should be corrected. In the event of continued renal failure, hemofiltration or hemodialysis can be performed to maintain proper fluid balance and electrolyte levels and are reported to be required in 14% of cases.
**Conclusion and Future Directions**

As of January 2015, 27,728 neonates (74% survival) and 6,569 pediatric patients (57% survival) have been treated with ECMO for respiratory failure and 13,124 neonatal and pediatric patients for cardiac failure. Tables 1, 2, and 3 demonstrate the common neonatal and pediatric respiratory and cardiac diagnoses along with survival with ECMO support (Extracorporeal Life Support Organization 2015). In the neonatal population, MAS is the most common indication for ECMO and carries with it a survival rate of 94%. Other frequent diagnoses (with survival rates in parentheses) include PPHN (77%), sepsis (73%), and CDH (51%). Viral pneumonia is the most common etiology amongst the pediatric population requiring ECMO and has a 65% survival. Aspiration carries the greatest survival at 68%, whereas non-ARDS respiratory failure has a 54% survival, ARDS 56%, and bacterial pneumonia 59% survival. Cardiac patients have an overall survival of

<table>
<thead>
<tr>
<th>Primary diagnosis</th>
<th>Number of patients</th>
<th>Survived</th>
<th>Percent survived to DC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital diaphragmatic hernia</td>
<td>7,228</td>
<td>3,691</td>
<td>51</td>
</tr>
<tr>
<td>Meconium aspiration syndrome</td>
<td>8,684</td>
<td>8,128</td>
<td>94</td>
</tr>
<tr>
<td>Persistent pulmonary hypertension of the newborn/persistent fetal circulation</td>
<td>4,800</td>
<td>3,696</td>
<td>77</td>
</tr>
<tr>
<td>Respiratory distress syndrome/hyaline membrane disease</td>
<td>1,546</td>
<td>1,300</td>
<td>84</td>
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<tr>
<td>Sepsis</td>
<td>2,856</td>
<td>2,084</td>
<td>73</td>
</tr>
<tr>
<td>Other</td>
<td>3,007</td>
<td>1,835</td>
<td>61</td>
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<tr>
<td>Total</td>
<td>28,121</td>
<td>20,734</td>
<td>74</td>
</tr>
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<table>
<thead>
<tr>
<th>Primary diagnosis</th>
<th>Number of patients</th>
<th>Survived</th>
<th>Percent survived</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral pneumonia</td>
<td>1,450</td>
<td>940</td>
<td>65</td>
</tr>
<tr>
<td>Bacterial pneumonia</td>
<td>686</td>
<td>402</td>
<td>59</td>
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<tr>
<td>Aspiration</td>
<td>304</td>
<td>208</td>
<td>68</td>
</tr>
<tr>
<td>Pneumocystis</td>
<td>35</td>
<td>18</td>
<td>51</td>
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<tr>
<td>Acute respiratory failure</td>
<td>1,186</td>
<td>641</td>
<td>54</td>
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<tr>
<td>ARDS</td>
<td>735</td>
<td>412</td>
<td>56</td>
</tr>
<tr>
<td>Other</td>
<td>2,306</td>
<td>1,195</td>
<td>52</td>
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<tr>
<td>Total</td>
<td>6,702</td>
<td>3,816</td>
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<table>
<thead>
<tr>
<th>Primary diagnosis</th>
<th>Number of ECLS runs</th>
<th>Number survived</th>
<th>Percent survived</th>
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</thead>
<tbody>
<tr>
<td>Congenital defect</td>
<td>9,807</td>
<td>4,757</td>
<td>49</td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>309</td>
<td>117</td>
<td>38</td>
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<td>Myocarditis</td>
<td>431</td>
<td>290</td>
<td>67</td>
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<tr>
<td>Cardiomyopathy</td>
<td>825</td>
<td>504</td>
<td>61</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>286</td>
<td>131</td>
<td>46</td>
</tr>
<tr>
<td>Other</td>
<td>2,056</td>
<td>1,035</td>
<td>50</td>
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<tr>
<td>Total</td>
<td>13,714</td>
<td>6,834</td>
<td>50</td>
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46%. Specifically, congenital defects have a 49% survival and cardiomyopathy 61%, and the highest survival rate is for myocarditis, 67%. While many centers have shown very good survival employing minimal or no ECMO in CDH, the highest overall survival rate in the sickest CDH patients are reported from centers that utilize ECMO (Kays 2017). Several centers have reported ECMO survival rates in CDH patients in excess of 70%, substantially different from the ELSO reported survival of 50% (Kays 2017). It is generally acknowledged that the ECMO improves survival in babies with severe cardiopulmonary disease over and above that currently available by non-ECMO techniques.

Recent medical advances, such as permissive hypercapnia, inhaled nitric oxide, and the use of oscillatory ventilation, have spared numerous babies from ECMO, yet many children still benefit from this modality.

In summary, any patient with reversible cardiopulmonary disease, who meets criteria, should be considered an ECMO candidate. ECMO provides an excellent opportunity to provide “rest” to the cardiopulmonary systems thus avoiding the additional lung or cardiac injury which otherwise would be necessary to maintain life support.

Cross-References

- ARDS
- Cardiovascular Physiology
- Congenital Diaphragmatic Hernia
- Respiratory Physiology
- Sepsis
- Vascular Access

References


