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ECMO for Neonatal Respiratory Failure

K. Rais Bahrami, MD,* and Krisa P. Van Meurs, MD†

Extracorporeal membrane oxygenation (ECMO) has been offered as a life-saving technology to newborns with respiratory and cardiac failure refractory to maximal medical therapy. ECMO has been used in treatment of neonates with a variety of cardio-respiratory problems, including meconium aspiration syndrome (MAS), persistent pulmonary hypertension of the neonate (PPHN), congenital diaphragmatic hernia (CDH), sepsis/pneumonia, respiratory distress syndrome (RDS), air leak syndrome, and cardiac anomalies. For this group of high-risk neonates with an anticipated mortality rate of 80% to 85%, ECMO has an overall survival rate of 84%, with recent data showing nearly 100% survival in many diagnostic groups. This article reviews the current selection criteria for ECMO and the clinical management of neonates on ECMO, and discusses the long-term outcome of neonates treated with ECMO.

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Extracorporeal membrane oxygenation (ECMO) is defined as the use of a modified heart–lung machine combined with a membrane oxygenator to provide cardiopulmonary support for patients with reversible pulmonary and/or cardiac failure in whom maximal conventional therapies have failed. ECMO is now well accepted as a standard treatment for neonatal respiratory failure unresponsive to conventional therapies. Most causes of neonatal respiratory failure are self-limited and ECMO allows time for the lung to recover from the underlying disease process and for reversal of pulmonary hypertension, which frequently accompanies respiratory failure in the newborn.

The first successful use of ECMO in a full-term newborn was in 1976.[1] Accumulating data suggested that ECMO was successful when compared with historical controls.[2,3] Ultimately, several randomized trials were performed, the first at the University of Michigan by Dr. R.H. Bartlett, published in 1985.[4] This trial used a "randomized play-the-winner" statistical method where the chance of randomly assigning an infant to one treatment or the other is influenced by the treatment outcome of each patient in the study. The trial concluded with only 1 patient assigned to the conventional arm, who died, and 11 that received ECMO and survived. The second trial was performed by Dr. P.P. O'Rourke at Boston Children's Hospital and was published in 1989.[5] This trial again used a study design intended to limit the number of deaths in the group of infants receiving the inferior therapy. Randomization continued until 4 deaths occurred in either group. The trial concluded after 4 of 10 babies died in the conventional medical therapy arm. All 9 infants in the ECMO group survived. Neither of these trials was deemed to be conclusive as they were small and used adaptive designs known to introduce bias.

A single, large, randomized control trial was performed by the UK Collaborative ECMO Trial Group and was published in 1996.[6] This trial enrolled 185 infants and showed a significant decrease in mortality in the ECMO group (32% versus 59%, relative risk 0.55; confidence intervals 0.39-0.77) as well as of disability at 1 year (33% versus 62%, relative risk 0.54; confidence interval 0.36-0.80). The improved survival was seen in all diagnostic categories, even for infants with congenital diaphragmatic hernia. A Cochrane meta-analysis concluded that use of ECMO in infants with severe, but potentially reversible respiratory failure, results in improved survival.[7]

Research, as well as clinical care, has benefited by ongoing

*The George Washington University School of Medicine, Department of Neonatology, Children's National Medical Center, Washington, DC.

†Division of Neonatal and Developmental Medicine, Stanford University School of Medicine, Palo Alto, CA.

Address reprint requests to Dr. K. Rais Bahrami, The George Washington University School of Medicine, Department of Neonatology, Children's National Medical Center, 111 Michigan Ave., NW, Washington, DC 20010. E-mail: KRAISBAH@cnmc.org

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Table 1 Neonatal ECMO Criteria

General Inclusion and Exclusion Criteria	
Gestational age ≥34 weeks or birth weight ≥2000 g	
No significant coagulopathy or uncontrolled bleeding	
No major intracranial hemorrhage	
Reversible lung disease with length of mechanical ventilation <10–14 days	
No uncorrectable congenital heart disease	
No lethal congenital anomalies	
No evidence of irreversible brain damage	
Respiratory Entry Critera*	
A_aDO_2†	>605–620 mmHg‡ for 4–12 hrs
Oxygenation index (OI)§	>35–60 for 0.5–6 hrs
PaO_2	<35 to <60 mmHg for 2–12 hrs
Acidosis and shock	pH <7.25 for 2 hrs or with hypotension
Acute deterioration	PaO_2 <30 to <40 mmHg

*50% of ECMO centers use more than one respiratory entry criteria.
†At sea level.
‡$\frac{P_{atm} - 47 - PaCO_2 - PaO_2}{FiO_2}$
§ $\frac{MAP \times FiO_2 \times 100}{PaO_2}$

data collection performed by ECMO practitioners. The Extracorporeal Life Support Organization (ELSO), established in 1989, is a consortium of hospitals and their health care professionals caring for ECMO patients. One of the central activities of ELSO is the maintenance of the ELSO Registry which collects data from member hospitals on all ECMO patients. The Registry now contains information on over 28,000 patients with separate databases for neonatal, pediatric, cardiac, and adult patients. The ELSO Registry has had an important role in communicating ECMO results, providing data for manuscripts, and benchmarking outcomes and complications.

Indications

ECMO is used for term or near-term infants at high risk of dying from respiratory failure. Specific criteria vary from center to center, and there are no universally accepted ECMO criteria. Several important inclusion and exclusion criteria are listed in Table 1 and reviewed below. There are some absolute and some relative contraindications to ECMO. The specific clinical circumstance and the predicted risk of death or reversibility of the underlying disease process often are the deciding factors.

All infants considered for ECMO should receive a complete history and physical examination, chest and abdominal radiographs, complete blood count and differential, coagulation studies, serum electrolytes with BUN and creatinine, cranial ultrasound, and echocardiogram.

Gestational Age

The requirement for systemic anticoagulation places significant limitations on the population treated. Currently, most ECMO centers exclude infants <34 weeks. Gestational age has been found to be the most powerful predictor of intracranial hemorrhage.[8] Infants <34 weeks were found to have a near 50% incidence of intracranial hemorrhage, while infants 34 to <36 and 36 to <38 weeks gestation had an odds ratio of intracranial hemorrhage of 4.1 and 2.1, respectively. Hirschl and coworkers reported that infants ≤34 weeks compared with term infants had lower survival (63% versus 84%, $P < 0.001$) and a higher rate of intracranial hemorrhage (37% versus 14%, $P < 0.001$).[9] Review of ELSO Registry data (1995–2002) demonstrates that with advancing gestational age there is a progressive increase in survival (57% at 34 weeks to 79% at 40 weeks) and decreasing rate of intracranial hemorrhage (20% at 34 weeks to 5% at 40 weeks).[10] The survival for the infant at 33 weeks gestation drops to 39% with a 26% incidence of intracranial hemorrhage. In a recent analysis of ELSO Registry data, Hardart[11] concluded that postconceptual age was better than both gestational and postnatal age as a predictor of intracranial hemorrhage.

Birth Weight

Although 2 kg is generally considered to be the lower limit, infants small for gestation age but ≥34 weeks should not be excluded. A higher rate of intracranial hemorrhage and mortality has also been documented in this low birth weight group.[12] Revenis and coworkers examined survival and the rate of intracranial hemorrhage in infants 2.0 to 2.5 kg and found a higher mortality when compared with infants >2.5 kg (34% versus 11%, $P < 0.0005$). Major intracranial hemorrhage was highly correlated with death.

In infants with a birth weight <2 kg, catheter size may be a limiting factor. Newer, thin-walled catheters have improved flow characteristics making this less of an issue.

Reversible Lung Disease

More than 10 to 14 days of mechanical ventilation is considered to be a relative contraindication. Chronic lung injury induced by prolonged mechanical ventilation and exposure to high oxygen concentrations may not improve within the time period that ECMO can be used safely. Early ECMO consultation allows time to judge the disease progression and intervene before irreversible injury occurs.

Infants with irreversible lung disease due to conditions such as surfactant B deficiency, alveolar capillary dysplasia, or pulmonary hypoplasia may be placed on ECMO inadvertently. Placement on ECMO allows time for the diagnosis to be confirmed.

Uncontrolled Bleeding or Coagulopathy

The requirement for systemic heparinization places ECMO patients with preexisting coagulopathy or bleeding at high risk for continued, uncontrollable hemorrhage. Attempts should be made to correct coagulation abnormalities before placement on ECMO. Severe uncorrected coagulopathy or

bleeding such as pulmonary hemorrhage are relative contraindications. Arnold and coworkers documented the presence of coagulation abnormalities before ECMO as well as the reduction in coagulation factors and activation of the coagulation cascade on bypass.[13] The authors postulate that these abnormalities contribute to bleeding complications on ECMO and an aggressive approach to replacement may be prudent. Nevertheless, neonates with significant coagulopathy or pulmonary hemorrhage have been successfully managed on ECMO.[14]

Intracranial Hemorrhage

The need for heparinization also precludes the treatment of infants with significant intracranial hemorrhage. Most ECMO centers exclude infants with greater than a grade 1 hemorrhage. Some centers will consider ECMO in a patient with a grade 2 hemorrhage on a case-by-case basis.

Congenital Heart Disease

Congenital heart disease should be excluded with an echocardiogram before placement on ECMO. Some diagnoses such as total anomalous pulmonary venous return may be missed. ECMO may be needed in some cases to stabilize infants with congenital heart disease considered too ill for cardiac surgery or to allow for diagnostic procedures such as cardiac catheterization. ECMO has been used with increasing frequency to support neonates following heart surgery.

Decision to Not Provide Full Support

Newborns with lethal anomalies such as Trisomy 13 and 18 are not ECMO candidates. Infants with severe and irreversible brain injury should be excluded, but it is inherently difficult to make this diagnosis in a precise manner. Most physicians opt to err on the side of offering ECMO.

Respiratory Entry Criteria

Various criteria have been used to select a population with a predicted mortality of 80% or greater. The various criteria used by ECMO centers are listed in Table 1.[15,16] Each of these criteria is limited by institutional specificity, retrospective data collection, and changes in intensive care over time. The oxygenation index (OI) is the most commonly utilized criteria. The use of an OI >40 for 3 hours in the UK trial selected a control group with a 61% mortality, slightly lower than the 80% as originally suggested.[7] Some have advocated that ECMO be used in infants with a lower OI. Schumacher and coworkers documented that infants randomized to receive ECMO at an OI >25, but <40 had a shorter length of hospitalization and lower hospital charges than infants who received ECMO using an OI >40.[17] There was also a trend toward improved outcomes at 1 year of age.

Diseases Treated

The diagnoses treated with ECMO include meconium aspiration syndrome, congenital diaphragmatic hernia (CDH), idiopathic pulmonary hypertension, sepsis/pneumonia, respiratory distress syndrome, air leak syndrome, and others. Recently, novel uses of ECMO have been reported in the neonatal population, including bridge to transplantation, hydrops fetalis, viral pneumonia (HSV and adenovirus), and cardiomyopathy. It has also been used as support for other procedures such as complex tracheal reconstruction or as part of the ex utero intrapartum treatment (EXIT) to ECMO procedure.[18]

The ECMO Team

Neonatal ECMO requires a highly specialized multidisciplinary team.[19] The team is composed of surgical personnel to include: a senior surgeon (pediatric, cardiovascular, or thoracic), a surgical assistant, a surgical scrub nurse, and a circulating OR nurse; medical personnel consisting of a physician (neonatologist, pediatric intensivist, or pediatric surgeon) trained in management of ECMO patients and cannulation techniques, responsible for medical management of the infant during the procedure; a bedside intensive care (NICU or PICU) nurse who will monitor vital signs, record events, and administer the required medications; a respiratory therapist who will change ventilator management; a circuit specialist (cardiovascular perfusionist, RN, or RT) specially trained in this procedure who will prime the pump; and a bedside ECMO specialist (RN, RT, or CV perfusionist with special training in ECMO management) who will manage the ECMO system after the patient has been placed on ECMO. Ongoing involvement of other appropriate subspecialty representation such as cardiologists, pediatric and cardiovascular surgeons, pediatric radiologist, neurodevelopmental psychologist, and biomedical engineers are essential factors to ensure high quality tertiary care and state-of-the-art practice in the field.

Procedure

The ECMO circuit consists of vascular access catheters, polyvinyl chloride tubing for drainage and reinfusion, a servoregulated pump, an appropriate size spiral coil membrane lung, and a heat exchanger (Fig. 1). To date, more than 80% of neonatal ECMO patients have received treatment with venoarterial bypass (VA ECMO).[10] This involves surgical cannulation of the right common carotid artery and internal jugular vein with the tip of the venous catheter advanced into the right atrium and the arterial catheter positioned at the junction of the right common carotid artery and aortic arch. Venous drainage is established by gravity into a venous reservoir and propelled by a servoregulated roller pump to the membrane oxygenator where gas exchange occurs (CO_2 is removed and O_2 is added). The circulating blood is subsequently warmed to body temperature by a temperature-regulated heat exchanger and returned to the aortic arch via the arterial catheter.[20] This type of ECMO provides both cardiac and pulmonary support. It is the treatment of choice for patients with significant blood pressure instability and for cases of primary cardiac dysfunction.[21,22] In patients with respiratory failure, VA ECMO is gradually being replaced by a venovenous (VV ECMO) technique, which uses a single

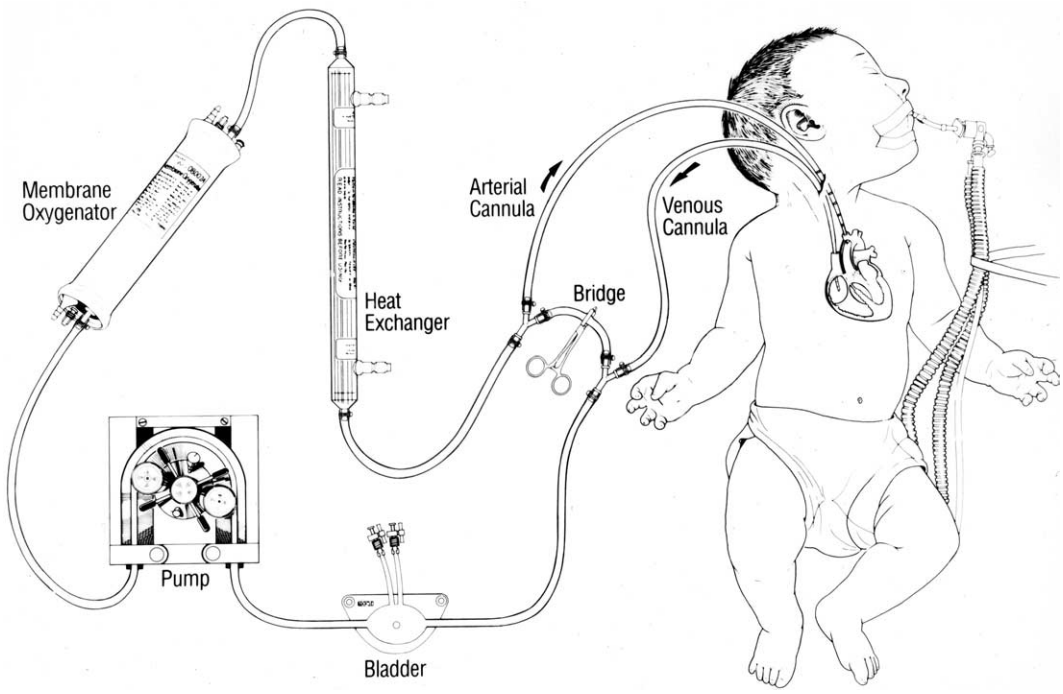


Figure 1 Schematic of the VA ECMO Circuit. Blood is drained from the right atrium by gravity into a reservoir bag, called "the bladder." The roller occlusion pump will then pump blood through the membrane lung where gas exchange occurs, through a heat exchanger to warm the blood to body temperature, and then return the blood through the arterial catheter into the arch of the aorta. (Reprinted with permission from CNMC ECMO Training Manual, Short, BL, Mikesell G, and Muir, R, (eds), 2004).

double-lumen catheter (Fig. 2). The catheter is placed in the right atrium, where blood is drained and reinfused into the same chamber, thus requiring cannulation of only the right jugular vein while sparing the carotid artery. Other advantages of VV ECMO include maintenance of normal pulsatile blood flow and the theoretical advantage that particles entering the ECMO circuit enter by way of the pulmonary rather than the systemic circulation. The design of the original VV catheter resulted in significant recirculation, limiting its use when ECMO flows >350 mL/min were required. Research by Rais Bahrami and coworkers resulted in development of a new catheter design which significantly lowers the degree of recirculation.[23] The double-lumen catheter should be placed within the right atrium, directing the oxygenated blood from the return lumen through the tricuspid valve to minimize recirculation. This catheter design in 12, 15, and 18 Fr. sizes allows the use of VV ECMO in a greater number of infants.

Patient Management

A decision is first made as to whether the infant would best be served with venovenous (VV) or venoarterial (VA) support. ECMO cannulation is done at the patient's bedside. Patients are given a neuromuscular blocking agent such as pancuronium bromide in addition to narcotics for the procedure. Before cannulation, infants are heparinized and infused with heparin continuously to maintain adequate anticoagulation. The preferred site for cannula placement is the vessels in the right side of the neck. The internal jugular vein and the carotid artery are accessed in the event of VA ECMO. For VV ECMO, a double-lumen catheter is placed within the right atrium via right internal jugular access carefully directed to return the oxygenated blood through the tricuspid valve to minimize recirculation.

A chest radiograph is obtained to confirm the position of the ECMO catheters. After initiation of ECMO, bypass flow is gradually increased to approximately 60% of the infant's calculated cardiac output (120 mL/kg/min) to maintain oxygenation adequate for the infant's metabolic requirements. Ventilator settings are adjusted to "rest setting" for lung support and the fraction of inspired oxygen is reduced to 0.21 to 0.30 depending on the mode of ECMO support (Table 2). The infant is allowed to awaken, with all pharmacological paralysis stopped. Sedation and pain medications are administered as needed.

Coagulation management is the most challenging component of managing the ECMO patient.[24] The patient must be systemically heparinized while on ECMO due to the activation of the clotting cascade by the contact of blood with the artificial surface of the ECMO circuit. A heparin bolus varying between 75 and 100 units/kg is given before or during the cannulation procedure. A continuous heparin drip ranging from 25 to 75 units/kg/min is maintained throughout ECMO to assure a specific level of anticoagulation. Commonly, activated clotting time (ACT) is measured to monitor anticoagulation. In noncomplicated patients, ACTs are kept between 180 and 200 seconds. This will vary in the patient with bleeding complications. Platelets, which are sequestered by the

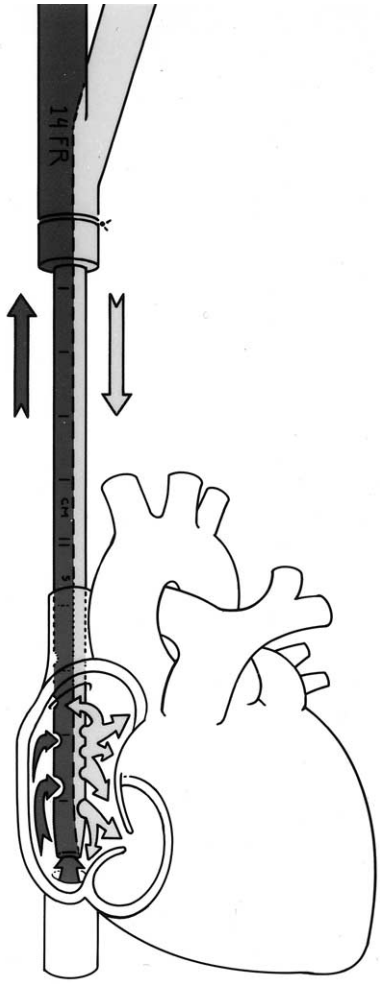


Figure 2 Schematic of the VV ECMO catheter placed in the mid right atrium. The venous drainage port on this catheter is inserted into the venous side of the ECMO circuit, while the arterial port is connected into the arterial side of the circuit. Limitation of VV ECMO are related to reperfusion that can occur in the right atrium and to poor cardiac function. (Reprinted with permission from CNMC ECMO Training Manual, Short BL, Mikesell G, and Muir R (eds), 2004).

membrane oxygenator, are administered when thrombocytopenia is observed. Fibrinogen levels are monitored daily and corrected when abnormal. The balance between clot formation and bleeding must be continually addressed. An experienced ECMO specialist is the most important component maintaining this balance.

Medications and total parenteral nutrition are delivered directly into the bypass circuit. Except for infants with CDH, the usual duration of ECMO for neonatal pulmonary support is approximately 5 days, during which the bypass flow is gradually decreased as pulmonary function improves, as assessed by arterial blood gas analysis and/or continuous venous saturation measurements from the circuit, serial chest radiographs, and lung compliance measurements.[25] After tolerating an "idling" flow of approximately 10% of calculated cardiac output (20 mL/kg/min) for 6 to 12 hours with blood gases within normal range, patients are decannulated from extracorporeal life support. Weaning off VV ECMO may be accomplished somewhat differently. The ECMO flow is usually weaned to 200 mL/min, then the FiO_2 to the membrane oxygenator is weaned to room air, and finally the airflow to the membrane is interrupted (referred to as "capping the membrane lung") which essentially removes the patient from ECMO. If the patient tolerates a trial of 1 to 2 hours off ECMO, surgical decannulation is performed. During the decannulation procedure, ventilator settings are adjusted after the infant is given a short-acting neuromuscular blocking agent and narcotics. With the exception of CDH, most neonatal ECMO patients wean from mechanical ventilatory support and are extubated within 48 hours following ECMO support.

Complications

The most common complications of ECMO are hemorrhagic and are caused by the necessity of systemic heparinization. Intracranial hemorrhage (ICH) is the most devastating complication of ECMO and is associated with high mortality and long-term morbidity. Severe ICH is the most common cause of death in the neonatal ECMO patient and is associated with poor outcome in survivors.[26-29] The incidence of major ICH diagnosed by cranial ultrasonography and/or cranial CT scan is 4.6% with an overall survival of 50%. There are an additional 10.7% of neonatal ECMO patients that demonstrate a nonhemorrhagic infarction of the central nervous system with an overall survival rate of 56%.[30] The incidence of ICH is increased in infants <35 weeks gestation and directly correlates with the poor outcome of the survivors.[9,12] Pre-ECMO factors which may contribute to increased risk for an intracranial insult include asphyxia and/or hypoxic insults, hyperventilation, and/or hypoventilation.[31] ECMO-associated risk factors for ICH include alteration in normal physiologic states such as nonpulsatile blood flow, ligation of major cerebral blood vessels, systemic heparinization, and thrombocytopenia. Studies by Short and coworkers have shown that VA ECMO alters pulsatile blood flow patterns and cerebral autoregulation in animal models of VA ECMO.[19] This alteration is thought to be due to effects of the altered blood flow patterns created by the nonpulsatile pumps used in ECMO on endothelial reactivity. They have shown an alteration of the nitric oxide pathway in cerebral vessels taken from animals exposed to VA ECMO.[32,33] These findings may indicate that the VA ECMO procedure may itself be a risk factor in the development of intracranial hemorrhage. These findings are

Table 2 "Rest" Ventilatory Settings during Venovenous vs Venoarterial ECMO Support

	Venoarterial	Venovenous
PIP (cmH_2O)	12–18	15–25
PEEP (cmH_2O)	5	5–10
IMV	15–20	20–30
FiO_2	0.21	0.30–0.50

PIP = peak inspiratory pressure; PEEP = peak end-expiratory pressure; IMV = intermittent mandatory ventilation; FiO_2 = fractional inspired oxygen.

Table 3 Changes in ECMO Survival by Diagnosis

Diagnoses	Cumulative Total (no. patients)	Cumulative Survival (%)	2003 Total (no. patients)	2003 Survival (%)
MAS	6560	94	179	89
CDH	4491	53	244	40
Sepsis/pneumonia	2650	73	43	72
PPHN	2914	78	156	81
RDS	1380	84	18	94
Other	1301	65	111	57
All	19,296	77	751	66

not noted in VV ECMO, where normal pulsatile flow patterns occur because the patient's heart is the pumping chamber for this form of ECMO.

Other than ICH, patients with congenital diaphragmatic hernia and other postoperative patients are at risk for hemorrhagic complications. The cannulation site always constitutes a potential hemorrhagic risk. Definitive treatment of severe, intractable hemorrhage on ECMO is termination of bypass, although conservative management such as higher platelet counts, lower activated clotting times, use of aminocaproic acid (Amicar®), and in extreme circumstances temporary cessation of heparinization has been recommended.[34]

Infants on ECMO may sustain acute tubular necrosis (ATN) marked by oliguria and increasing blood urea nitrogen (BUN) and creatinine levels. ATN may extend into the first 24 to 48 hours of ECMO before improvement is seen. If the renal condition does not improve, poor tissue perfusion should be considered. A combination of inadequate ECMO flow rate, low cardiac output, and intravascular volume depletion may lead to decreased renal function. If the infant remains in anuric renal failure, a hemofiltration system may be added in series to the ECMO circuit to remove excess fluid and stabilize electrolyte abnormalities.

Other known complications of ECMO are mechanical failure, infection, and failure to wean from bypass. Undiagnosed congenital heart disease must be excluded in patients unable to wean from bypass. Despite the pre-ECMO echocardiogram, certain diagnoses, especially total anomalous pulmonary venous return (TAPVR), could be missed. Cardiac catheterization may be necessary for definitive diagnosis. Other rare cases to consider include congenital surfactant protein B (SP-B) deficiency and alveolar capillary dysplasia.[35]

Survival and Outcome

To date 19,061 neonates with respiratory failure have been treated with ECMO; 86% were successfully decannulated and 77% survived to discharge.[10] The cumulative survival statistics are highest for MAS at 94% and lowest for CDH at 53% (Table 3). Changes in intensive care and the introduction of new therapies such as surfactant, selective antibiotic prophylaxis for mothers and babies, high frequency ventilation, and inhaled nitric oxide have reduced the numbers of infants who require ECMO. The current survival statistics for specific diagnoses have remained relatively stable except for CDH. The number of CDH infants treated with ECMO has remained unchanged, but survival rates have decreased from 60% in 1990 to 40% in 2003 (see Chapter 6).

Medical and neurodevelopmental outcome of the ECMO patient is encouraging considering the severity of illness in the newborn period. Analysis of outcome studies performed in PPHN survivors treated with conventional medical therapy, iNO, and ECMO yield grossly equivalent morbidities and outcomes.[36] This suggests that neurodevelopmental outcome is more related to the underlying illness than to the therapeutic intervention utilized.

Chronic lung disease (defined as oxygen use at 28 days) is seen in 15% of ECMO survivors, but long-term oxygen use is uncommon except in infants with CDH. Hospitalization for respiratory problems in the first year of life is needed in approximately 25%.[37] Normal somatic growth is seen in ECMO-treated children except those with CDH (see Chapter 6).

Progressive high frequency sensorineural hearing loss is seen in 3% to 21% of ECMO-treated infants.[38] An important aspect is the delayed onset, making diagnosis problematic. The position statement by the Joint Committee on Infant Hearing in 2000 added PPHN and ECMO as risk indicators for hearing loss and stated that they should receive audiologic evaluation every 6 months until 3 years of age.[39]

Numerous investigators have reported on the neurodevelopmental outcome of the ECMO patient and consistently report Bayley scores in the normal range in the first 2 years of life.[28,40,41] Fewer studies of ECMO survivors at older ages have been performed.[42,43] By 5 years of age, mean IQ scores remain in the normal range, but are lower than normal controls (96 versus 115, $P < 0.001$).[43] Glass and coworkers reported that approximately 15% of ECMO survivors at age 5 had a major handicap, most commonly mental retardation while less than 5% had severe or profound impairment. Nevertheless, 50% of ECMO survivors have an increased risk of learning and behavioral problems when compared with normal controls. As a result of these deficits, ECMO survivors are vulnerable to academic and psychosocial difficulties.

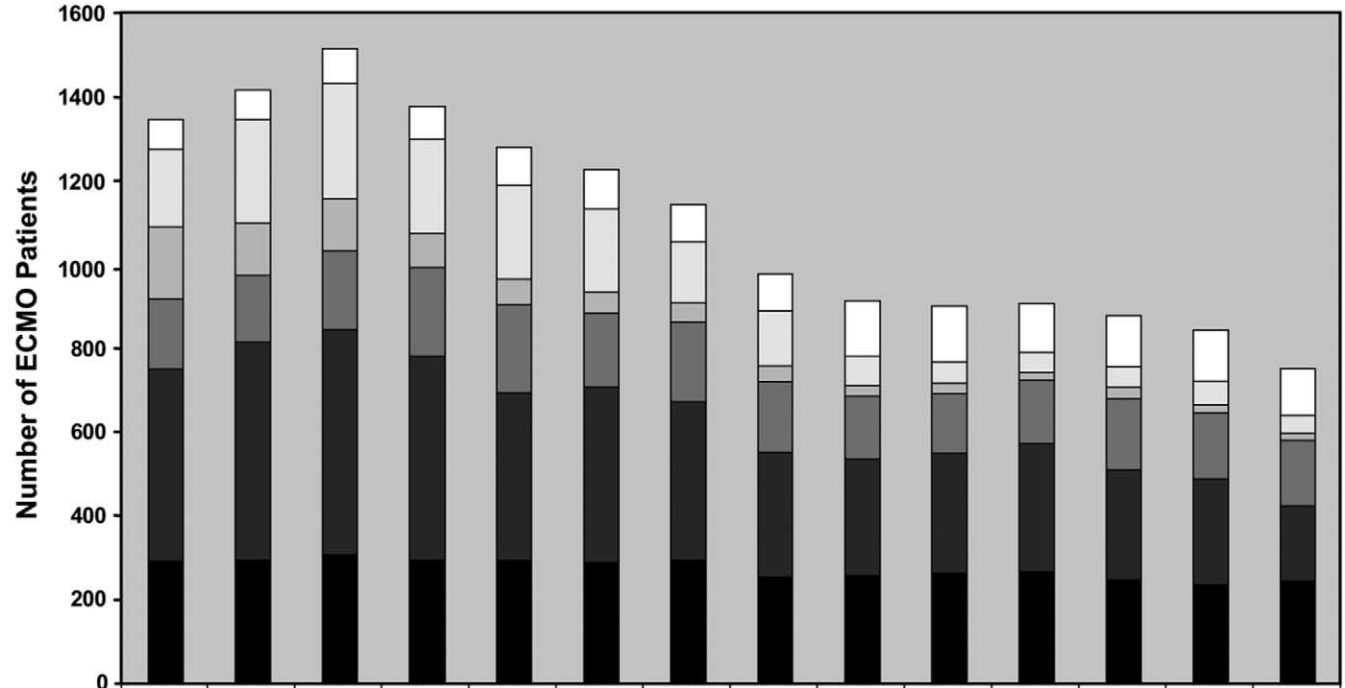
Changing Demographics of ECMO

Over the last decade a number of new treatments have been used for neonatal respiratory failure, including high fre-

quency ventilation, surfactant replacement, and iNO therapy (see Chapter 2).[44-51] The use of some of these pre-ECMO therapies has been observed to decrease the need for ECMO.[47-50]

Roy and coworkers used the ELSO Registry to understand changes in health care practices for infants with neonatal respiratory failure from 1988 to 1998.[44] Although there was no change in gestational age, gender, chronologic age, or pre-ECMO blood gases, there were significant differences in pre-ECMO therapies used, ventilator practices, and the diagnostic categories treated. The use of high frequency ventilation, surfactant, and inhaled nitric oxide increased dramatically over the study period. The pre-ECMO peak inspiratory pressure decreased from 47 ± 10 to 39 ± 12. The percent of ECMO patients with respiratory distress syndrome decreased from 15% to 4% while the percent with CDH increased from 18% to 26%. The number of infants treated with ECMO annually has steadily declined from 1500 patients in 1991 to approximately 1000 patients in 1997. The number of ECMO centers has been relatively stable since 1993, so the average number of patients treated at an ECMO center has decreased from 18 to 9 while the average length of an ECMO run for the non-CDH population increased from 124 ± 67 to 141 ± 104 hours. The use of VV ECMO has increased to 32%. The rate of intracranial hemorrhage has remained stable. Mortality for all neonatal respiratory failure increased from 18% to 22%, but this increase is due to both the relative increase in the percentage of ECMO patients with CDH and the downward trend for survival in these patients.

Review of the neonatal ELSO Registry data for July 2004 demonstrates ongoing demographic changes (Fig. 3). ECMO use continues to decline with 751 cases reported to the Registry for 2003.[10] Dramatic decreases in the use of ECMO for respiratory distress syndrome and sepsis/pneumonia are also noted with only 18 and 43 patients treated in 2003, respectively. There has also been a steady downward trend in the use of ECMO for meconium aspiration; it is no longer the most common indication for ECMO. The number of CDH infants placed on ECMO continues to be stable at approximately 250 per year, but the survival rates continue to decline.



	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003
Other	72	71	82	78	92	95	89	88	132	133	116	122	121	111
Sepsis	186	247	277	226	223	198	145	131	71	51	49	49	57	43
RDS	171	124	125	80	61	51	46	38	25	26	18	27	19	18
PPHN	169	161	187	212	211	176	191	170	152	142	152	171	159	156
MAS	459	522	540	489	402	421	379	299	278	288	306	263	253	179
CDH	291	293	305	293	292	287	293	252	256	261	266	246	234	244
Total	1348	1418	1516	1378	1281	1228	1143	978	914	901	907	878	843	751

Figure 3 Annual ECMO utilization. Significant changes in the proportion for each diagnosis have occurred over the time period 1990 to 2003. (Data from the Extracorporeal Life Support Organization Neonatal Registry, with permission).

Summary

Neonatal ECMO has resulted in a significant improvement in the survival of neonates with cardiopulmonary failure refractory to maximal medical therapy. Patients with an anticipated mortality rate of 80% to 85% have an overall survival rate of 84%, with recent data showing nearly 100% survival in many diagnostic groups. Long-term neurodevelopmental follow-up has been encouraging. Recently, less invasive medication and techniques have been developed which have kept many infants off ECMO. Over the years, much has been learned, indications have been expanded, and selection criteria honed. Currently, we are able to successfully treat a variety of neonatal respiratory diseases such as meconium aspiration syndrome, persistent pulmonary hypertension of the neonate, and severe pneumonia. ECMO may also be helpful in postoperative neonates with congenital cardiac lesions not successfully weaning from bypass. The biggest challenge over the next few years will be to determine whether ECMO should remain as a "rescue therapy" or should it be considered first line for some disease states. It may be time for a trial of early intervention with ECMO versus. present therapies trial to evaluate morbidity and cost of care, as the primary outcome variable instead of mortality. The cost of some new therapies such as iNO, which decrease the need for ECMO, but have not shown differences in long-term outcome when compared with the ECMO-treated infants, makes this question compelling.

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