Advances in Neonatal Extracorporeal Support

The Role of Extracorporeal Membrane Oxygenation and the Artificial Placenta

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KEYWORDS

• Extracorporeal membrane oxygenation • ECMO • Extracorporeal life support • Neonatal • Respiratory failure • Cardiac failure • Artificial placenta • EXIT to ECMO • Prematurity

KEY POINTS

- Extracorporeal membrane oxygenation (ECMO) is currently indicated for neonates 34 weeks or more estimated gestational age weighing 2.0 kg or more; however, evidence suggests that smaller and more premature infants may benefit.
- Use of ECMO peaked in 1992 and has declined since that time, primarily because of improvements in other forms of critical care life support. To some extent, these improvements have been realized as a result of lessons learned from the early ECMO experience.
- Ex utero intrapartum therapy to ECMO may be used in late-term fetuses with anticipated respiratory and/or cardiac failure at birth, but the indications and efficacy remain unproven.
- The artificial placenta is theoretically an ideal extracorporeal support strategy for extremely premature infants because it recapitulates the intrauterine environment and maintains fetal circulation without mechanical ventilation.
- Animal studies using an umbilical arteriovenous artificial placenta have met with limited success in the past. Contemporary studies support a venovenous mode of support, which obviates many inherent problems with arteriovenous strategy.
- Many challenges remain in the development of the artificial placenta before clinical translation.

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PROGRESS IN PERINATAL/NEONATAL EXTRACORPOREAL MEMBRANE OXYGENATION

Neonatal Extracorporeal Membrane Oxygenation: Past, Present, and Future

Robert Bartlett and his group had been studying extracorporeal support in laboratory animals for 10 years before the first neonatal extracorporeal membrane oxygenation (ECMO) patient was supported in 1975; this clinical application signified a radical shift in the treatment paradigm for neonatal respiratory failure.[1] The neonate, Esperanza, was suffering from respiratory failure secondary to meconium aspiration that was recalcitrant to conventional ventilator support. She was successfully supported and now is 37 years old.[2]

The currently accepted treatment of perinatal/neonatal cardiopulmonary failure includes low-volume protective ventilation,[3] inhaled nitric oxide,[4,5] surfactant therapy,[6,7] and high-frequency oscillatory ventilation.[8] If the cardiac or pulmonary failure is refractory to maximal medical therapy then ECMO should be considered.[9,10] The standard application of ECMO is primarily limited to neonates 34 weeks or more estimated gestational age (EGA) and weighing 2 kg or more. Clinical experience and laboratory work suggest extracorporeal support may be effective at lower gestational ages by using Preemie ECMO or the artificial placenta (**Table 1**).

History of Extracorporeal Life Support

John Gibbon is credited with envisioning total cardiopulmonary support in 1939. He published the first successful heart surgery with assistance of the heart-lung machine in 1954.[11] Lillehei and his group in Minnesota were the first to perform extracorporeal support of pediatric patients. In 1955, they published a series of 8 pediatric cardiac patients using the parents as the support mechanism.[12] This opened the door for the first successful application of ECMO in the clinical setting by J. Donald Hill in 1971.[13] The application of ECMO for postoperative cardiopulmonary failure in children was described as early as 1972.[14] The first series of neonatal patients was published in 1982, and reported 45 cases with a survival rate of 50%.[15] The first prospective randomized trials of ECMO for neonatal respiratory failure were published in 1985 and 1989. These 2 studies demonstrated high rates of survival (100% and 94%, respectively) in neonatal patients with respiratory failure. The first trial was published by the group at Michigan, and was criticized for both exposing neonates to the risks of ECMO and for having too few patients in the control arm.[16] Ironically, 2 years later the Boston trial was criticized for denying ECMO to too many patients in the control limb of the study.[17] Despite early criticism and skepticism of this novel treatment, by 1986 there were 18 centers with successful neonatal ECMO teams.[18] The early ECMO community was a model of professional collaboration. The Extracorporeal Life Support Organization (ELSO) was founded in 1989 and maintained a registry of extracorporeal life support (ECLS) cases, developed standard guidelines and practices, and published the textbook on ECLS known as the

Table 1
ECLS modality by age group

Gestational age (wk)	24 25 26 27 28	29 30 31 32 33	34 35 36 37 38 39 40
ECLS treatment modality	Artificial placenta[a]	Preemie ECMO[b]	ECMO[c]

[a] Laboratory research.
[b] Clinically feasible.
[c] Standard of care.