Extracorporeal membrane oxygenation improved survival in mature newborn infants with severe respiratory failure

UK Collaborative ECMO Trial Group. **UK collaborative randomised trial of neonatal extracorporeal membrane oxygenation.** Lancet. 1996 Jul 13;348:75-82.

Objective
To compare the effectiveness of extracorporeal membrane oxygenation (ECMO) with conventional management in mature newborn infants with severe respiratory failure.

Design
Randomised controlled trial with 1-year follow-up.

Setting
Recruitment and conventional management took place in 55 hospitals in the United Kingdom. ECMO was provided in 5 specially equipped tertiary care centres.

Patients
185 mature (gestational age at birth ≥ 35 wk, birthweight ≥ 2 kg) newborn infants with severe respiratory failure (oxygenation index [OI] ≥ 40, arterial partial pressure of carbon dioxide [$PaCO_2$] > 12 kPa for ≥ 3 h). Exclusion criteria included > 10 days of high-pressure ventilation, age > 28 days, and contraindication for ECMO support.

Intervention
93 infants were allocated to be transported to an ECMO centre, and 92 to conventional management. ECMO support was withheld if the infant's condition was felt to render ECMO inappropriate. Otherwise, ECMO was provided according to a standardised protocol. Conventional management included liberal use of oxygen, correction of acidosis, maintenance of adequate blood pressure, paralysis, and use of any available pulmonary vasodilator, including nitric oxide.

Main outcome measures
Death before hospital discharge and to 1 year of age, and death or severe disability at 1 year of age.

Main results
The trial was stopped early. All infants were followed to hospital discharge, and 124 (67%) were followed until 1 year of age. 84% of infants allocated to ECMO actually received ECMO support. 28 of 93 infants (30%) allocated to ECMO died before hospital discharge compared with 54 infants (59%) who received conventional management ($P < 0.001$). {This absolute risk reduction of 29% means that 4 infants would need to be transported to an ECMO centre to prevent 1 additional death before hospital discharge, 95% CI 2 to 7; the relative risk reduction was 49%, CI 28% to 64%.}* 14 of 18 infants (78%) with congenital diaphragmatic hernia (CDH) who were allocated to ECMO died compared with all 17 (100%) in the conventional management group (absolute difference 22%, {CI 2% to 45%, $P = 0.04$}*). The benefit of ECMO availability was also seen at 1 year with 33% (21 of 63 infants) dead or severely disabled in the ECMO group compared with 62% (38 of 61 infants) of those allocated to conventional management ($P = 0.002$).

Conclusion
Referral to an ECMO centre improved survival in mature newborn infants with severe respiratory failure.

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For article reprint: Dr. D.J. Field, Department of Child Health, University of Leicester, Clinical Sciences Building, Leicester Royal Infirmary, Leicester LE1 5WW, England, UK. FAX 44-116-252-3282.

*Numbers calculated from data in article.

Commentary

This trial is an important milestone in the history of ECMO and confirms the results of the studies by Bartlett (1) and O'Rourke (2) and their colleagues. The U.K. ECMO trial was designed to reflect current clinical practice and was done early enough in the U.K. ECMO experience to ensure equipoise. The entry criteria are consistent with North American ECMO practice (apart from the requirement for prolonged and severe hypercarbia). This study confirms the benefit of ECMO referral and ensures that this therapy will become entrenched in British neonatal medicine. The attribution of deaths after randomisation, but before cannulation, to the ECMO group takes into account the risks inherent in the transport of these unstable infants.

In this trial, the outcome for infants with CDH is not consistent with current experience that suggests that approximately 60% of infants with similar illness survive with ECMO (3).

In the absence of CDH, the treatment approach for the near-term infant with severe hypoxic respiratory failure is clearer because inhaled nitric oxide and natural surfactant have been shown to reduce the need for ECMO (4, 5). Moreover, the acceptance of moderate permissive hypercarbia that reduces barotrauma, the judicious application of high-frequency ventilation techniques (used relatively infrequently in this trial), and the consideration of ECMO at an OI > 25 inclusive of the use of these therapies, should further increase intact survival rates. ECMO will continue to be utilised as the ultimate rescue therapy for infants who fail optimum conventional therapies and will also allow for the safe evaluation of newer therapies.

Neil Finer, MD
University of California, San Diego, Medical Center
San Diego, California, USA

References

1. **Bartlett RH, Roloff DW, Cornell RG, et al.** Pediatrics. 1985;76:479-87.
2. **O'Rourke PP, Crone RK, Vacanti JP, et al.** Pediatrics. 1989;84:957-63.
3. **Neonatal ECMO Registry of the Extracorporeal Life Support Organization (ELSO).** Ann Arbor, Michigan; July 1995.
4. **The Neonatal Inhaled Nitric Oxide Study Group (NINOS).** N Engl J Med. [In press].
5. **Lotze A, and the Survanta in Term Infants Study Group.** Pediatr Res. 1996; 39:226A.