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Long-term outcome of children treated with neonatal extracorporeal membrane oxygenation: Increasing problems with increasing age

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ABSTRACT

As more and more critically ill neonates survive, it becomes important to evaluate long-term morbidity. This review aims to provide an up-to-date overview of medical and neurodevelopmental outcomes in children who as neonates received treatment with extracorporeal membrane oxygenation (ECMO). Most patients—except those with congenital diaphragmatic hernia—have normal lung function and normal growth at older age. Maximal exercise capacity is below normal and seems to deteriorate over time in the CDH population. Gross motor function problems have been reported until school age. Although mental development is usually favorable within the first years and cognition is normal at school age, many children experience problems with working speed, spatial ability tasks, and memory. In conclusion, children who survived neonatal treatment with ECMO often encounter neurodevelopmental problems at school age. Long-term follow-up is needed to recognize problems early and to offer appropriate intervention.

Introduction

Since the Extracorporeal Life Support (ECLS) registry was initiated in 1989, data of more than 30,000 children undergoing neonatal extracorporeal membrane oxygenation (ECMO) have been registered. More than 80% of them needed ECMO for severe respiratory failure and overall survival to transfer or home discharge in this group was 75%.[1] Thus, seeing that an increasing number of critically ill neonates survive, attention should be directed to possibly persisting morbidity. Most follow-up studies in neonatal ECMO survivors have been cross-sectional and in small study populations. In the past few years, there has seen a shift towards long-term multidisciplinary evaluations.

This article addresses both medical and neurodevelopmental outcomes in children and adolescents who as neonates were treated with ECMO. Based on current knowledge, recommendations will be made for follow-up of these children beyond infancy and childhood.

Medical outcomes

Lung function

Overall, 80% of neonates who need ECMO treatment suffer from severe respiratory failure[1] and may be expected to show persisting respiratory morbidity. Several studies have

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reported lung function after neonatal ECMO treatment, i.e., during or shortly after the intervention,[2–4] in infancy,[5–9] and in childhood.[10–13]

Reduced forced expiratory flows have been reported in infants, without signs of improvement within the first year of life,[7,8] whereas lung volumes were generally normal.[8] Beardsmore et al. concluded that lung function within the first year of life in survivors of the UK ECMO trial, recruited between 1993 and 1995. In this study, they showed a slightly better lung function in ECMO-treated children than in children receiving conventional treatment.[7] Lung function results of these UK ECMO trial survivors did not significantly differ from those of a cohort of ECMO-treated infants born between 1997 and 2003, despite changes in the population who are referred for ECMO.[5] Results were poorest in neonates who needed ECMO for respiratory distress syndrome and those who underwent ECMO at >2 weeks of age.[5] Children with congenital diaphragmatic hernia (CDH) were underrepresented in the cohorts studied by Beardsmore et al. Others have reported on infants with CDH undergoing ECMO treatment. One study showed that they had higher lung volumes within the first year of life than infants who underwent ECMO for meconium aspiration syndrome (MAS).[8] The authors of a second study assumed that the lung volumes above the normal range found in ECMO-treated CDH patients who were oxygen dependent after 28 days of life reflect hyperinflation rather than normal growth of the hypoplastic lungs.[9]

At 8 years of age, an entire cohort of 8-year-old survivors of severe neonatal respiratory failure showed airflow obstruction, and lung function was poorest in those treated with ECMO and children with CDH.[12] Normal lung volumes with mild airflow obstruction were reported in 48 ECMO survivors at mean age of 11 years.[11] A cross-sectional study in 10–15-year olds who underwent ECMO after MAS, revealed persistent airflow obstruction and air trapping.[10] Air trapping was also frequently found in the only longitudinal study on lung function in neonatal ECMO survivors.[13] In that study, Spoel et al. showed that mid-expiratory flows were slightly but significantly below normal in all participants studied at 5, 8, and 12 years. Children with CDH, however, had poorest lung function with deterioration over time. Determinants of persistent airflow obstruction are shown in Table 1. Diffusion capacity was normal for the entire cohorts at 8 and 12 years.[13]

Exercise capacity

Only few studies have reported on long-term exercise capacity in neonatal ECMO survivors. Two of these studies concerned cohorts born in the late 1980s: Boykin et al.[10] found similar maximal VO_2 levels and similar maximal endurance times in 17 ECMO-treated MAS patients and age-matched controls, whereas Hamutcu et al.[11] reported lower maximal VO_2 levels and lower oxygen saturation in 48 ECMO survivors compared with controls. The latter study included not only MAS patients but also children who needed ECMO for other diagnoses, including CDH and congenital heart disease. Van der Cammen et al.[14] longitudinally studied a cohort of 120 ECMO survivors, born between 1992 and 2004, at ages 5, 8, and 12 years. At all ages, the maximal endurance time was significantly below that of the normal population, with significant deterioration over time irrespective of the underlying diagnosis. Duration of ECMO, duration of ventilation, or oxygen dependency at 28 days were not of influence.[14] Findings from this study formed the basis for a randomized trial currently being performed in our department: the trial aims to assess the efficacy of an intervention, standardized exercise training, and/or coaching and to achieve an active lifestyle for the child and his/her family (personal communication).

Physical growth

In general, children treated with neonatal ECMO have normal physical growth with the exception of CDH patients.[12] Normal height and normal to slightly decreased body weights have been reported in infancy,[5,7,8] and normal to slightly decreased height, weight, and body mass index in childhood

Table 1 – Potential determinants of impaired outcome following neonatal ECMO.

Outcome parameter	Risk factor
Lung function/airflow obstruction	Diagnosis of RDS,[5] diagnosis of CDH,[8] prolonged duration ECMO,[5,13] and chronic lung disease[9,13]
Exercise capacity	No significant determinants reported[14]
Physical growth	Diagnosis of CDH[12]
Sensorineural hearing loss	Diagnosis of CDH,[18] prolonged duration ventilation,[a25,26] prolonged duration ECMO,[18,27] sepsis/bacterial meningitis,[a25,28] administration of aminoglycosides,[a18] severe birth asphyxia,[a26,28] intracranial abnormalities,[a28] and clinical seizures prior to ECMO[27]
Chronic kidney disease	?[31]
Motor function development	Low parental socio-economic status,[36] intracranial abnormalities,[33,38] and duration of hospitalization[37]
Cognition	Intracranial abnormalities,[38] low parental socio-economic status,[36,42] diagnosis of CDH,[42,43] and duration of hospitalization[37]
Neuropsychological outcome	Intracranial abnormalities[38] and highest mean airway pressure prior to ECMO[43]
Behavior	Need for extra help at school[43]

RDS = respiratory distress syndrome; CDH = congenital diaphragmatic hernia.
[a] Not specific for ECMO treatment but for neonatal intensive care treatment.