

Neuropsychological Follow-up After Neonatal ECMO

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abstract

OBJECTIVE: To assess the longitudinal development of intelligence and its relation to school performance in a nationwide cohort of neonatal extracorporeal membrane oxygenation (ECMO) survivors and evaluate predictors of outcome at 8 years of age.

METHODS: Repeated measurements assessed intelligence of neonatal ECMO survivors at 2, 5, and 8 years ($n = 178$) with the use of validated, standardized instruments. Selective attention ($n = 148$) and type of education were evaluated in the 8-year-olds.

RESULTS: Intelligence remained stable and average across development (mean \pm SD IQ: at 2 years, 102 ± 18 ; at 5 years, 100 ± 17 ; and at 8 years, 99 ± 17 [$P = .15$]). Children attending regular education without the need for help ($n = 101$; mean z score: -1.50 ± 1.93) performed significantly better on the selective attention task compared with those children who needed extra help ($n = 65$; mean z score: -2.54 ± 3.18) or those attending special education ($n = 13$; mean z score: -4.14 ± 3.63) ($P = .03$). However, only children attending special education had below-average intelligence (mean IQ: 76 ± 15), compared with average intelligence for those attending regular education, both with help (mean IQ: 95 ± 15) and without help (mean IQ: 105 ± 16). Compared with children with other diagnoses, children with congenital diaphragmatic hernia (CDH) scored significantly lower on both IQ (CDH, mean IQ: 93 ± 20 ; meconium aspiration syndrome, mean IQ: 100 ± 15 ; other diagnoses, mean IQ: 100 ± 19 [$P = .04$]) and selective attention (CDH, mean z score: -3.48 ± 3.46 ; meconium aspiration syndrome, mean z score: -1.60 ± 2.13 ; other diagnoses, mean z score: -1.65 ± 2.39 [$P = .002$]).

CONCLUSIONS: For the majority of neonatal ECMO survivors, intelligence testing alone did not identify those at risk for academic problems. We propose internationally standardized follow-up protocols that focus on long-term, problem-oriented neuropsychological assessment.

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Ms Schiller and Dr Madderom conducted the analyses, drafted the initial manuscript, and reviewed and revised the manuscript; Drs Gischler, van Heijst, Tibboel, and IJsselstijn conceptualized and designed the study, and reviewed and revised the manuscript; Ms Reuser and Dr Steiner contributed to acquisition of the data, and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

DOI: 10.1542/peds.2016-1313

Accepted for publication Aug 4, 2016

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

WHAT'S KNOWN ON THIS SUBJECT: Neonatal extracorporeal membrane oxygenation (ECMO) survivors are at risk for long-term neuropsychological impairments and school problems, whereas cross-sectional studies have found generally average intelligence. Despite increased awareness of these problems, neonatal ECMO follow-up protocols are not equipped to detect these impairments.

WHAT THIS STUDY ADDS: Longitudinal evaluation of intelligence in neonatal ECMO survivors found stable and average IQ at 2, 5, and 8 years. School problems are related to worse selective attention, regardless of IQ. Patients with congenital diaphragmatic hernia are at highest risk.

To cite: Schiller RM, Madderom MJ, Reuser JJ, et al. Neuropsychological Follow-up After Neonatal ECMO. *Pediatrics*. 2016;138(5):e20161313

Extracorporeal membrane oxygenation (ECMO) has been used in >28 000 neonates with severe respiratory failure who are unresponsive to conventional medical management.¹ Survival rates have remained stable over the years, with 5% to 10% surviving with severe neurologic complications.¹ The remaining 90% of survivors are at risk for subtler long-term neurodevelopmental problems.²⁻⁴ Despite increasing awareness of these problems, the current standardized (international) follow-up protocols are inadequate for the detection of neuropsychological deficits in neonatal ECMO survivors.^{1,5} Because the Extracorporeal Life Support Organization recommendations have not been reviewed since 1997, an evidence-based update is mandatory.⁶

In many follow-up programs, intelligence remains the primary outcome measure in neonatal ECMO survivors.^{5,6} Previous studies have shown their intelligence to be comparable to that of healthy children at various stages of development.^{2,3,7-9} IQ testing can provide valuable insight into the overall cognitive functioning of an individual but is not suited to detect subtle neuropsychological impairments.¹⁰ Extensive neuropsychological testing in neonatal ECMO survivors has demonstrated deficits, especially in the attention and (working) memory domains in 8- and 17-year-olds,^{2,4} with an increased need for extra help in school.^{2,4,8} Because IQ is generally within the average range, their school problems are likely due to subtler neuropsychological impairments. However, this theory remains largely speculative, and IQ has not been studied longitudinally.

The goal of the present study was to investigate the relationship between school problems and cognitive outcome in neonatal ECMO

survivors. To do so, we first assessed the longitudinal development of intelligence at 2, 5, and 8 years of age in a nationwide cohort of neonatal ECMO survivors. We then evaluated type of education attendance in relation to intelligence and to selective attention at 8 years of age. Finally, we studied whether school performance and cognitive outcome at 8 years of age were influenced by clinical characteristics. We hypothesized that intelligence is normal across the 3 ages and unrelated to the school problems observed in neonatal ECMO survivors. Based on this hypothesis, we propose standardized, problem-oriented follow-up aimed at specific neuropsychological domains that can be internationally implemented.

METHODS

Population

Patients born between January 1996 and December 2006 treated with ECMO within the first 28 days of life and participating in the structured prospective post-ECMO follow-up program were eligible for the present study ($n = 278$). Children were either part of the follow-up program that was initiated in 2001 at the Erasmus MC–Sophia Children’s Hospital in Rotterdam ($n = 143$) or at the Radboud University Medical Center in Nijmegen initiated in 1998 ($n = 135$). ECMO support was given according to the criteria described by Stolar et al,¹¹ which did not change over time. Entry and exclusion criteria for follow-up have been described previously.^{2,7}

The post-ECMO follow-up program is the standard of care in the Netherlands,^{2,7,12} and institutional review board approval was therefore waived. The study included only those children for whom at least the mental developmental index at 2 years and IQ at 8 years of age were evaluated (Rotterdam, $n = 96$; Nijmegen, $n = 82$) (Fig 1).

Demographic and medical characteristics of the patients are reported in Table 1.

Neuropsychological Assessment

Intelligence

Intelligence was measured at 2, 5, and 8 years of age. For

2-year-olds, the Bayley Developmental Scales (BOS 2-30) ($n = 100$) or, from December 2003, the Dutch version of the Bayley Scales of Infant Development, Second Edition ($n = 78$), were used to assess mental outcome. These standardized instruments both assess verbal and nonverbal development of 2- to 30-month-old children and are substantially related to each other.¹³

The Revised Amsterdam Child Intelligence Test short-form was used at 5 years.¹⁴ For the 8-year-olds, this test ($n = 102$) or the Wechsler Intelligence Scale for Children ($n = 76$) was used.¹⁵ Both tests assess verbal and nonverbal intelligence, have been shown to have good reliability and validity,^{14,15} and have been used interchangeably by our group in previous research.¹⁶

For all 4 tests, a normalized population mean \pm SD IQ score of 100 ± 15 is used.¹³⁻¹⁵ The outcome on all 4 tests is referred to as intelligence or IQ.

Selective Attention

Selective attention was measured in the 8-year-old children ($n = 148$) by using the Dot Cancellation paper and pencil test. The main outcome measure was working speed, which was converted into z scores (ie, the individual score minus the population score divided by the population SD). Good validity, sensitivity, reliability, and Dutch normative data have been reported.¹⁷

Procedures and Study Design

Children underwent neuropsychological evaluation by a psychologist at 2, 5, and

8 years of age. Parents completed questionnaires on ethnicity (Dutch/ ≥ 1 nonnative Dutch parent) and maternal educational level (MEL). MEL refers to the highest type of education completed by the mother and was categorized as high, moderate, or low.¹⁸ Various medical characteristics were recorded prospectively; for example, birth weight, gestational age, diagnosis, age at the start of ECMO, ECMO duration/type (venoarterial/venovenous/venovenous conversion to venoarterial), duration of mechanical ventilation, extra oxygen supply postextubation, chronic lung disease (yes/no),¹⁹ and abnormal cranial ultrasound (yes [ie, parenchymal or intracranial bleeding]/no).

Data Analysis

Clinical characteristics of participants and nonparticipants were compared by using independent-sample *t* tests for the normally distributed data and Mann-Whitney *U* tests for the nonnormally distributed data.

The developmental trajectory of intelligence was evaluated by using repeated-measures analysis of variance. Normality tests were performed, and Mauchly's test was used to assess and correct for sphericity.

Type of education attendance at 8 years of age and its relations to intelligence at age 2, 5, and 8 years and selective attention at age 8 years were analyzed by using Kruskal-Wallis *H* tests. For post hoc analyses, the 3 education categories were transformed into 2 dummy variables: (1) regular education with help versus regular education and special education; and (2) special education versus regular education with and without help. Independent sample *t* tests were then conducted to evaluate which groups differed.

Next, the effect of diagnosis (ie, meconium aspiration syndrome, congenital diaphragmatic hernia

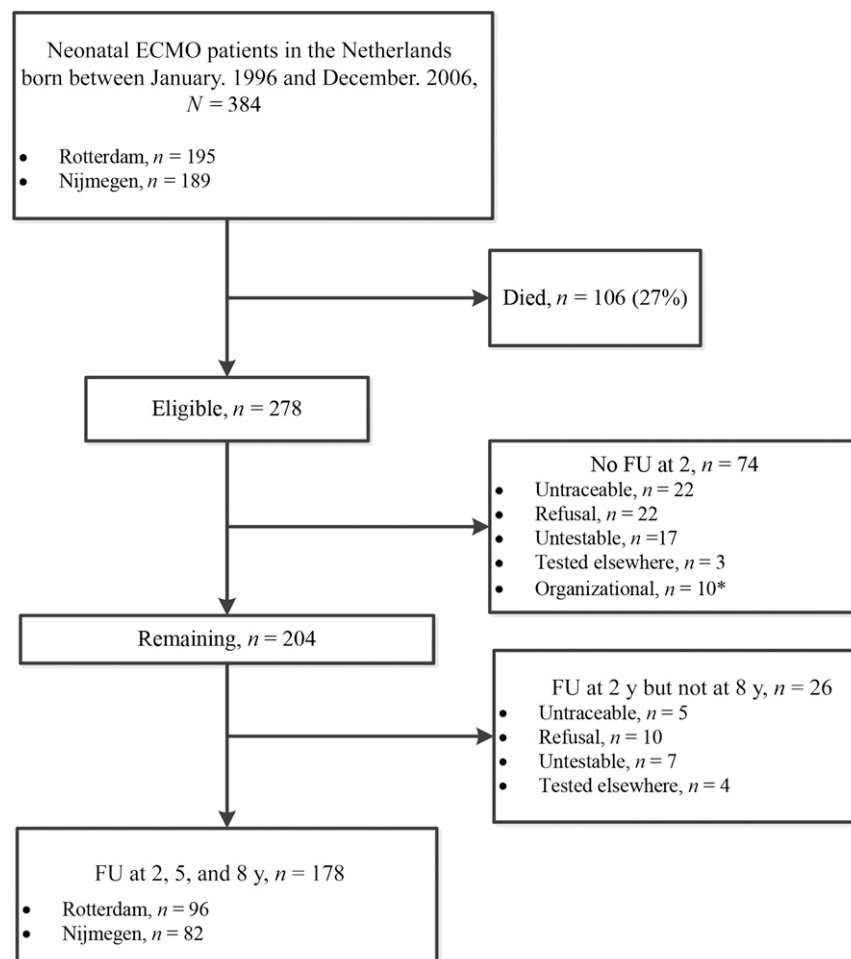


FIGURE 1 Inclusion flowchart of the neonatal ECMO survivors. FU, follow-up.

[CDH], other diagnoses) on intelligence at all ages and selective attention at 8 years were evaluated by using Kruskal-Wallis *H* tests, as previous research has shown that patients with CDH perform worse compared with children with other diagnoses.²

Finally, associations between IQ at 2 years, IQ at 5 years, and outcome at 8 years of age were evaluated by using multivariate linear regression analyses, adjusted for MEL and parents' ethnicity.²⁰⁻²² Parents' ethnicity was used because a child's verbal skills and thus neurodevelopmental outcome may be affected by a parent who was born outside of the Netherlands and does not have Dutch as their first language.²¹ The influence

of medical characteristics on IQ and selective attention at 8 years of age was tested in 2 separate models. Diagnosis, type of ECMO, duration of mechanical ventilation, and chronic lung disease were added into the multivariate linear regression analyses. The assumptions for multivariate linear regression analysis were checked with normal probability plots of the residuals and the Durbin-Watson test. Multicollinearity was evaluated by using the criterion that variance inflation factors could not exceed 2.5.²³

Analyses were performed by using SPSS version 22.0 (IBM SPSS Statistics, IBM Corporation, Armonk, NY). For all analyses, a *P* value

TABLE 1 Patient Characteristics

Characteristic	All (<i>n</i> = 178)	MAS (<i>n</i> = 97)	CDH (<i>n</i> = 36)	Other ^a (<i>n</i> = 45)
Demographic, <i>n</i> (%)				
Sex				
Male	96 (54)	46 (47)	24 (67)	26 (58)
Female	82 (46)	51 (53)	12 (33)	19 (42)
Ethnicity				
Dutch	143 (81)	75 (78)	31 (86)	37 (82)
Non-Dutch ^b	34 (19)	21 (22)	5 (14)	8 (18)
Unknown	1	1	0	0
MEL				
Low	45 (27)	21 (23)	11 (34)	13 (30)
Moderate	65 (39)	38 (42)	10 (30)	17 (40)
High	56 (34)	31 (35)	12 (36)	13 (30)
Unknown	12	7	3	2
Type of education at 8 y				
Regular	100 (56)	58 (60)	18 (51)	24 (53)
Regular with help	65 (37)	36 (37)	15 (43)	14 (31)
Special education	12 (7)	3 (3)	2 (6)	7 (16)
Unknown	1	0	1	0
Clinical				
Birth weight, mean ± SD, g	3461 (552)	3512 (551)	3316 (436)	3465 (624)
Gestational age, mean ± SD, wk	40 (2)	41 (2)	39 (1)	39 (2)
Type of ECMO, <i>n</i> (%)				
VA	155 (87)	77 (79)	36 (100)	42 (93)
VV	21 (12)	18 (19)	0 (0)	3 (7)
VV conversion to VA	2 (1)	2 (2)	0 (0)	0 (0)
Unknown	1	0	0	0
Age start ECMO, median (range), d	1 (0–23)	1 (0–10)	1 (0–11)	2 (0–23)
Hours on ECMO, median (range)	140 (24–369)	135 (24–288)	177 (63–369)	138 (53–288)
Mechanical ventilation, median (range), d	14 (3–68)	13 (6–32)	28 (7–68)	13 (3–40)
O ₂ post-ECMO, <i>n</i> (%)				
1 d–1 wk	87 (53)	51 (56)	9 (30)	27 (63)
>1 wk <1 mo	64 (39)	35 (39)	14 (47)	15 (35)
>1 mo	13 (8)	5 (5)	7 (23)	1 (2)
Unknown	14	6	6	2
CLD presence, <i>n</i> (%)				
Yes	39 (23)	18 (20)	16 (50)	5 (11)
No	129 (77)	74 (80)	16 (50)	39 (89)
Unknown	10	5	4	1
Abnormal CUS, <i>n</i> (%)				
Yes	17 (10)	6 (6)	2 (6)	9 (20)
No	159 (90)	91 (94)	33 (94)	35 (80)
Unknown	2	0	1	1

Lines that do not include percentages are unknown. CLD, chronic lung disease; CUS, cranial ultrasound; MAS, meconium aspiration syndrome; O₂ post-ECMO, extra oxygen supply postextubation; VA, venoarterial; VV, venovenous.

^a Other diagnoses were sepsis (*n* = 10), persistent pulmonary hypertension of the newborn (*n* = 30), pneumonia (*n* = 2), congenital cystic adenomatoid malformation of the lung (*n* = 1), pneumothorax (*n* = 1), and infant respiratory distress syndrome (*n* = 1).

^b Children with at least 1 nonnative Dutch parent.

<.05 was considered statistically significant.

RESULTS

Participants had a significantly higher birth weight than nonparticipants (mean ± SD birth weight: 3461 ± 552 g and 3294 ± 556 g, respectively; *P* = .02). No other clinical differences were found between participants and nonparticipants.

Developmental Trajectory of Intelligence

Intelligence fell within the normal range at 2, 5, and 8 years of age (Fig 2).^{13–15} Mauchly's test indicated that the assumption of sphericity had been violated (*P* < .001); therefore, Greenhouse-Geisser corrected tests are reported (ϵ = 0.01). Intelligence remained stable from 2, to 5, to 8 years of age (*P* = .15; *n* = 152). At 8 years of age, 6 children (3%) had low

IQ scores (<70), 39 children (22%) had below-average IQ scores (≤85), 103 children (58%) had average IQ scores (85–115), and 30 children (17%) had above-average IQ scores (≥115).

Outcome and Type of Education Intelligence

Thirty-seven percent (*n* = 65) of the ECMO survivors needed extra help at school at 8 years of age versus 20% of

TABLE 2 Outcome Based on Type of Education Attendance at 8 Years of Age

Education	MDI 2 y (<i>n</i> = 178)	IQ 5 y (<i>n</i> = 152)	IQ 8 y (<i>n</i> = 178)	Selective Attention 8 y (<i>n</i> = 148)
Regular education	105 ± 16	106 ± 14	104 ± 16	-1.50 ± 1.93
Regular education with help	100 ± 19	95 ± 17	95 ± 15	-2.54 ± 3.18
Special education	83 ± 19*	81 ± 15*	77 ± 15*	-2.91 ± 2.21

Mean ± SD mental developmental index (MDI)/IQ score and the mean z score of selective attention (as measured by working speed) are reported based on type of education. Mean z score: 0 ± 1. Mean population IQ score: 100 ± 15.

* Significantly different IQ score than the general population at $P < .001$.

TABLE 3 Neuropsychological Outcome Based on Diagnosis

Diagnosis	MDI 2 y	IQ 5 y	IQ 8 y	Selective Attention 8 y
MAS	104 ± 18	101 ± 14	100 ± 15	-1.60 ± 2.13
<i>n</i>	97	81	97	86
CDH	98 ± 18	98 ± 21	93 ± 20*	-3.48 ± 3.46*
<i>n</i>	36	32	36	30
Other	99 ± 18	99 ± 18	100 ± 19	-1.39 ± 1.88
<i>n</i>	45	39	45	32

Mean ± SD mental developmental index (MDI)/IQ score and the mean z score of selective attention (as measured by working speed) are reported based on diagnosis. Mean population IQ score: 100 ± 15. Mean z score: 0 ± 1. Other diagnoses include persistent pulmonary hypertension of the newborn, sepsis, cardinal respiratory insufficiency, persistent fetal circulation, and respiratory syncytial infection. CDH, congenital diaphragmatic hernia; MAS, meconium aspiration syndrome.

* Significantly different compared with other diagnostic groups at $P < .05$.

children in the general population.²⁴ Seven percent ($n = 12$) of children in our cohort attended special education at 8 years of age (Table 1), compared with 4.4% in the general population.²⁴ To gain a better understanding of the relatively high proportions of children receiving extra help and attending special education, we analyzed its relationship with intelligence. Children attending special education had significantly lower intelligence from age 2 years onward, whereas those attending regular education, irrespective of their need for extra help, had intelligence comparable to the general population (Table 2).

Selective Attention

The ECMO survivors who attended regular education without help performed significantly better on the selective attention task compared with those needing extra help or attending special education ($P = .02$). Selective attention did not significantly differ between the ECMO survivors attending special education and those needing extra help ($P = .75$) (Table 2).

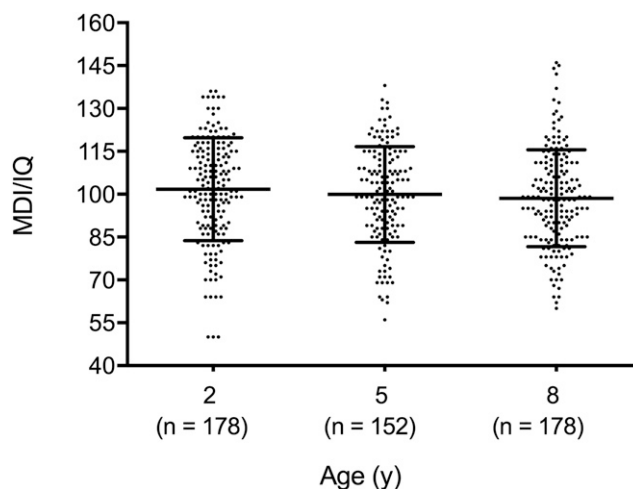
Diagnosis

Intelligence did not differ at 2 and 5 years of age between children with meconium aspiration syndrome, CDH, or other diagnoses. At 8 years of age, patients with CDH had a significantly lower IQ than those with other diagnoses ($P = .04$). Furthermore, significant differences were found on selective attention between the 3 diagnostic groups ($P = .007$), with the CDH group scoring lowest on the

selective attention task (Table 3).

Predictors of Outcome at 8 Years of Age

Low MEL increased the likelihood of having a lower IQ score at 8 years of age. In addition, children with higher IQ scores at 5 years of age were more likely to have higher IQ score at 8 years of age. Having a lower IQ score at age 5 years increased the likelihood of a poorer

**FIGURE 2**

Mean ± SD mental developmental index (MDI)/IQ scores were reported at 2, 5, and 8 years of age. The mean population IQ score was 100 ± 15.

TABLE 4 Predictors of Outcome at 8 Years

Predictor	IQ 8 y	Selective Attention 8 y
Demographic predictors		
Low MEL	$B = -4.72, P = .03$ (CI, -8.90 to -0.53)	$B = 0.04, P = .94$ (CI, -1.00 to 1.08)
Dutch ethnicity	$B = -1.80, P = .45$ (CI, -6.51 to 2.92)	$B = -1.10, P = .09$ (CI, -2.27 to 0.15)
MDI at 2 y	$B = 0.07, P = .22$ (CI, -0.04 to 0.18)	$B = -0.01, P = .54$ (CI, -0.04 to 0.02)
IQ at 5 y	$B = 0.75, P < .001$ (CI, 0.63 to 0.88)	$B = -0.07, P < .001$ (CI, -0.10 to -0.04)
Medical predictors		
CDH	$B = -5.02, P = .25$ (CI, -13.65 to 3.62)	$B = 1.31, P = .07$ (CI, -0.08 to 2.70)
MAS	$B = -0.43, P = .89$ (CI, -6.70 to 5.83)	$B = -0.01, P = .98$ (CI, -1.04 to 1.02)
Venoarterial ECMO	$B = 2.82, P = .49$ (CI, -5.21 to 10.84)	$B = -0.10, P = .87$ (CI, -1.27 to 1.08)
Mechanical ventilation, d	$B = -0.19, P = .19$ (CI, -0.46 to 0.09)	$B = 0.04, P = .06$ (CI, -0.00 to 0.09)

Multivariate regression analyses to assess the influence of demographic and medical characteristics on outcome at 8 years of age. Selective attention is measured by working speed given in seconds; a higher score represents slower working speed and vice versa. MEL ([Maternal Educational Level] high MEL versus low and moderate MEL; low MEL versus high and moderate MEL) and diagnosis (CDH [congenital diaphragmatic hernia] versus rest; MAS [meconium aspiration syndrome] versus rest) are dummy variables (yes = 1, no = 0). Ethnicity is Dutch (1) or non-Dutch (0). A P value $<.05$ was considered statistically significant. MDI, mental developmental index.

score on the selective attention task at age 8 years (Table 4). None of the medical characteristics were significantly related to outcome at 8 years of age.

DISCUSSION

To the best of our knowledge, this study is the first longitudinal assessment of IQ in a large group of children treated with neonatal ECMO. We showed that intelligence fell within the average range at 2, 5, and 8 years of age and remained stable. This outcome is in line with previous cross-sectional studies.^{2,3,7,8,21} Strikingly, a large group of children attending regular education needed extra help in school, despite average intelligence. We found that these school difficulties were related to selective attention problems. Because current follow-up protocols focus mainly on IQ, language, and visuomotor integration (domains that have been shown to remain intact after neonatal ECMO^{6,7,25-27}), those ECMO survivors at risk for school problems will not be identified. Our results underline the importance of a standardized, evidence-based, and problem-oriented neuropsychological follow-up after neonatal ECMO.

Despite the fact that the ECMO survivors included in the present study did not have severe neurologic

morbidity, twice as many children in our cohort needed extra help at regular education compared with the general population,²⁴ as previously found by our group.² However, all had average intelligence, which was similar to those who did not need help in school. In addition, a relatively high number of ECMO survivors attended special education compared with the general population.²⁴ These children had below-average intelligence. Interestingly, both the ECMO survivors needing extra help and the ones attending special education performed significantly worse on the selective attention task compared with the ECMO survivors not needing help in school. Our findings therefore allow us to identify 2 groups of neonatal ECMO survivors who (without overt neurologic deficits) are at risk for long-term school problems: (1) those with lower IQ and related neuropsychological impairments; and (2) those with average IQ but with isolated neuropsychological deficits. For children attending special education, poor selective attention is more in accordance with (and may be partly explained by) their below-average intelligence, the combination of which may lead to the need for special education. However, for those children needing extra help, isolated

neuropsychological deficits may prompt the need for educational support.

To identify those at risk for school problems, especially of the ECMO survivors with average intelligence, problem-oriented neuropsychological assessment that extends beyond testing global cognitive functioning with the use of an IQ test¹⁰ is essential. Attention and (working) memory have been shown to be overlapping constructs that share much of the same pathways in the brain.²⁸ The attention problems observed in our cohort could therefore be accompanied by (working) memory deficits. Indeed, earlier studies have shown that neuropsychological problems occur mainly in the attention and memory domains in these children.^{2-4,29} It is therefore highly recommended that in addition to intelligence, both attention and memory, or executive functioning altogether, are focused on after neonatal ECMO. Using the current guidelines, neonatal ECMO survivors at risk for school problems will not be identified.^{6,7,25-27} We therefore propose a problem-oriented revision of follow-up protocols.

Because neuropsychological impairments in neonatal ECMO survivors have been shown to emerge in childhood and to

persist even into adolescence,²⁻⁴ neuropsychological follow-up that extends beyond the age of 5 years is crucial.⁶ Neonatal follow-up of premature infants has revealed that early developmental assessments of high-risk infants are often imprecise, especially for those with milder impairments that at a later age do affect their school performance.³⁰ It is likely that this scenario is similar to neonatal ECMO follow-up. Moreover, neuropsychological testing beyond early childhood is important because these types of deficits at a later age may not only continue to hamper academic performance but also affect the ability to participate in society and thus lead a fulfilling life.⁴ However, because we have shown that intelligence at 5 years of age is highly predictive of IQ at 8 years, elaborate IQ assessments at both 5 and 8 years may be redundant. To make the most efficient use of time and resources, assessment of a full IQ can be considered at 5 years of age, and thus specified neuropsychological assessment can be conducted at age 8 years. At 8 years of age, IQ can be screened with the use of a few subtests, and a full IQ test can be administered only if needed. This problem-oriented approach will make risk stratification and early identification of those neonatal ECMO survivors at risk for school problems more feasible.

Finally, within follow-up of neonatal ECMO survivors, certain risk factors of impaired neurodevelopment should be taken into account. IQ at 8 years old and selective attention were lower in patients with CDH compared with children with other underlying diagnoses. These findings confirm earlier research showing that patients with CDH have generally worse outcomes.² Our proposal of problem-oriented and evidence-based neuropsychological follow-up

therefore seems even more critical for this particular patient group. None of the other clinical characteristics studied were found to predict outcome at 8 years of age, which is similar to previous findings.^{2,4} Low MEL significantly increased the likelihood of lower IQ at 8 years of age. Although this result is not specific to neonatal ECMO survivors,^{30,31} it is important to take into account during neonatal ECMO follow-up.

As noted earlier, this nationwide study is the first to longitudinally assess intelligence in a large group of neonatal ECMO survivors. We identified 2 specific groups of neonatal ECMO survivors who may be at risk for school problems (those with neuropsychological impairments despite having average intelligence and those with below-average intelligence and neuropsychological impairments). Because sources for educational support are available for all schools in the Netherlands, the number of children needing educational support or special education reported in this study is likely to be accurate. Furthermore, due to the high level of compliance, selection bias is highly unlikely. Nonetheless, our study has some limitations. First, a Dutch test measuring selective attention was used, which limits cross-sectional comparisons. However, we were able to compare our data to Dutch normative data. Second, 11% of children ($n = 31$) did not complete the neuropsychological assessment at 2 and/or 8 years of age due to cognitive or behavioral impairments ($n = 14$, seen elsewhere with severe cognitive impairment [ie, IQ <70]; $n = 11$, too tired or uncooperative at time of assessment; $n = 6$, tested elsewhere but had average IQ scores), which may have resulted in a bias. However, the percentage of dropouts due to severe cognitive

impairment was relatively low compared with the total number of participants, making significant bias unlikely. Third, ECMO technologies, especially the use of centrifugal pumps, a smaller priming volume, and new membranes with subsequently other adherence of commonly used drugs, are constantly changing and this may influence long-term outcomes. The current findings may thus not be generalizable to patients treated in recent years. Future studies should compare outcome between patients treated in different time periods to see what the effects of different treatment technologies are in the long term. Finally, at the time of data collection, our neuropsychological follow-up consisted only of intelligence and attention tests. Therefore, other cognitive functions that might be susceptible to impairment after neonatal ECMO, such as memory and executive functioning,⁴ were not evaluated. Future studies should include these cognitive functions when assessing long-term neurodevelopment in neonatal ECMO survivors.

CONCLUSIONS

Neonatal ECMO survivors have an overall average and stable IQ from 2, to 5, to 8 years of age. Despite this finding, a large group is at risk for school problems. In the majority of ECMO survivors at risk, these school problems were related to isolated selective attention deficits. IQ alone is therefore not a reliable predictor of school performance or even eventual participation in society. Because current neonatal ECMO follow-up protocols mainly focus on IQ and language and visuomotor integration, those children at risk will not be identified. Our findings emphasize the need for evidence-based, problem-oriented

neuropsychological follow-up, with a focus on attention and memory functioning after neonatal ECMO. Risk factors such as low MEL and/or a CDH diagnosis should be taken into account. Because neuropsychological impairments have been shown to emerge in childhood and persist into

adolescence, follow-up should extend beyond 5 years of age.

ACKNOWLEDGMENT

The authors thank Joost van Rosmalen, PhD, from the Department of Biostatistics, Erasmus MC, for statistical input and advice.

ABBREVIATIONS

CDH: congenital diaphragmatic hernia
ECMO: extracorporeal membrane oxygenation
MEL: maternal educational level

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FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: Ms Schiller was funded by the Sophia Stichting Wetenschappelijk Onderzoek (S14-213).

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

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Pediatrics 2016;138;

DOI: 10.1542/peds.2016-1313 originally published online October 6, 2016;

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