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Bridging the Gap Between Intensivists and Primary Care Clinicians in Extracorporeal Membrane Oxygenation for Respiratory Failure in Children
A Review

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IMPORTANCE Extracorporeal membrane oxygenation (ECMO) is a form of advanced life support that may be used in children with refractory respiratory or cardiac failure. While it is required infrequently, in the US, ECMO is used to support childhood respiratory failure as often as children receive kidney or heart transplants. ECMO is complex, resource intensive, and potentially lifesaving, but it is also associated with risks of short-term complications and long-term adverse effects, most importantly with neurodevelopmental outcomes that are relevant to all pediatric clinicians, even those remote from the child's critical illness.

OBSERVATIONS The 2009 influenza A(H1N1) pandemic, along with randomized clinical trials of adult respiratory ECMO support and conventional management, have catalyzed sustained growth in the use of ECMO. The adult trials built on earlier neonatal ECMO randomized clinical trials that demonstrated improved survival in severe perinatal lung disease. For children outside of the neonatal period, there appear to have been no respiratory ECMO clinical trials. Applying evidence from adult respiratory failure or perinatal lung disease to children outside the neonatal period has important potential pitfalls. For these children, the underlying diseases and risks of ECMO are different. Despite these differences, both neonates and older children are at risk of neurologic complications, such as intracranial hemorrhage, ischemic stroke, and seizures, and those complications may contribute to adverse neurodevelopmental outcomes. Without specific screening, subtle neurodevelopmental impairments may be missed, but when they are identified, children have the opportunity to receive therapy to optimize long-term development.

CONCLUSIONS AND RELEVANCE All pediatric clinicians should be aware not only of the potential benefits and complications of ECMO but also that survivors need effective screening, support, and follow-up.

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When children experience life-threatening respiratory failure despite optimal mechanical ventilation, extracorporeal membrane oxygenation (ECMO) may be used to correct hypoxemia and hypercapnia while facilitating lung-protective ventilation. This involves pumping venous blood outside of the body and through an artificial membrane lung, where oxygen is added, carbon dioxide is removed, and the blood is then returned to the patient.[1] The Extracorporeal Life Support Organization (ELSO) Registry, a 30-year-old international ECMO registry and the largest such repository in the world, currently counts approximately 30 000 children as having survived respiratory failure in the setting of ECMO support.[2] After complex and prolonged hospitalizations, these children and their caregivers turn to primary care clinicians to lead the next phase of their recovery.[3]

Pediatric acute respiratory distress syndrome (PARDS) and, more broadly, acute respiratory failure are characterized by a sudden life-threatening illness with diffuse alveolar damage, reduced compliance, and poor gas transfer.[4,5] In severe PARDS, more than 30% of children die.[6] Deciding that the potential life-saving benefits of pediatric respiratory ECMO support outweigh the risks of short-term complications and the potential long-term effects on neurodevelopmental outcomes is a vital decision for health care professionals and parents.

This review will define ECMO terminology, describe ECMO circuit components, consider ECMO risks and benefits, and assimilate the evidence relevant to supporting children with ECMO for severe respiratory failure. In addition, we will describe the general pediatric implications of ECMO, highlighting the risk of adverse neurodevelopmental outcomes associated with both ECMO and this degree of critical illness.

ECMO Terminology

Recently published international consensus statements clarified ECMO nomenclature (**Box**).[7,8] Extracorporeal life support (ECLS) is

Box. Extracorporeal Membrane Oxygenation (ECMO) Nomenclature[a]

Extracorporeal life support (ECLS): A broad term describing support of the failing heart or lungs through mechanical devices that provide blood flow, blood gas exchange, or both outside of the body.

ECMO: The use of at least a membrane lung, blood pump, and vascular cannulae to provide blood oxygenation and carbon dioxide removal.

Membrane lung: a device that receives a flow of oxygen gas and a flow of the patient's venous blood. The gas and fluid are separated by a semipermeable membrane, and the device oxygenates blood and removes carbon dioxide.

Blood pump: A mechanical device, usually a centrifugal pump (or possibly a roller pump), that actively withdraws blood from the body and pumps it back to the patient.

Respiratory ECMO: The use of ECMO to support a patient in respiratory failure.

Venovenous ECMO: Extracorporeal support delivered by drawing blood from the venous system, providing blood gas exchange and returning it into the venous system.

Venoarterial ECMO: Extracorporeal support delivered by drawing blood from the venous system, providing blood gas exchange and returning the blood into the arterial system, partially bypassing the heart.

Sweep gas: The gas delivered to the membrane lung; oxygen or a blend of oxygen and air (rarely, with carbon dioxide blended in).

Vascular cannulation: Often shortened to *cannulation* in the context of ECMO; refers to the placement of 1 or more large cannula into the vascular system for blood drainage and return.

Single-lumen cannula: A cannula with 1 lumen for either blood drainage or return of blood to the body.

Dual-lumen cannula: A cannula with 2 lumens, 1 used for blood drainage and 1 used for blood return.

ECMO blood flow rate: The volume of blood (expressed in liters) passing through the ECMO circuit in a minute.

ECMO circuit: The tubing and connected devices (at least a blood pump and a membrane lung) starting at the cannula withdrawing blood and ending at the cannula returning blood to the patient.

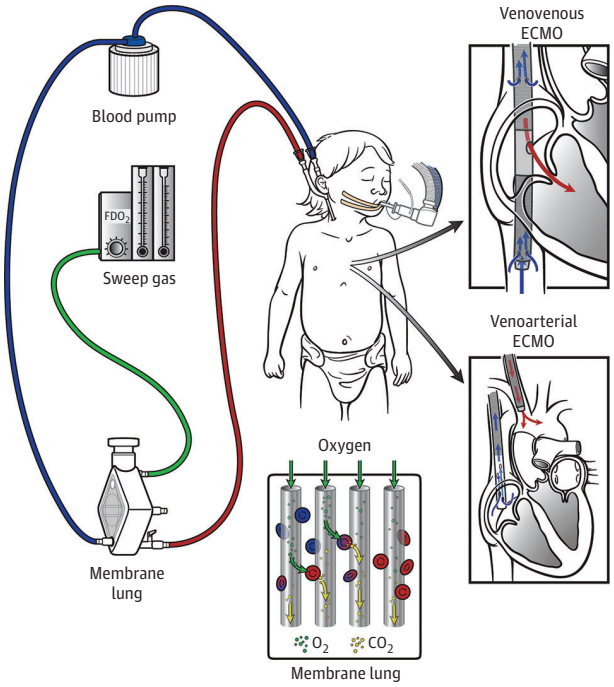
[a] Additional terminology may be used for more detailed description or more complex configurations of extracorporeal life support.[7,8]

a broader term that can refer to ECMO or extracorporeal carbon dioxide removal ($ECCO_2R$).[7] ECMO provides adequate blood flow rates to provide either full respiratory support or full cardiac support; $ECCO_2R$ operates at lower blood flow rates because it is designed to remove carbon dioxide alone without necessarily providing substantial oxygenation. While $ECCO_2R$ has been reported in pediatrics, it is much less commonly used and will not be a focus of this review.

Anatomy and Physiology of ECMO

Once the decision is made to initiate ECMO, a large vascular cannula is placed in a central vein. The vascular cannula is attached via tubing to a blood pump. The blood pump generates negative pressures, which extracts venous blood from the body. The blood pump then propels the venous blood to a membrane lung. The membrane lung functions to oxygenate the blood and remove carbon dioxide (just as in the human lung). The membrane lung is composed of thin, semipermeable, hollow fiber tubes (analogous to alveoli). Sweep gas, most frequently pure oxygen or a mix of oxygen and air (analogous to the air we breathe), is driven through the membrane lung and its hollow fiber tubes. The membrane lung's hollow fibers are bathed in flowing venous blood. Across this membrane (analogous to the interface between alveoli and alveolar capillaries), oxygenation and carbon dioxide removal occurs by diffusion (**Figure 1**).[9,10]

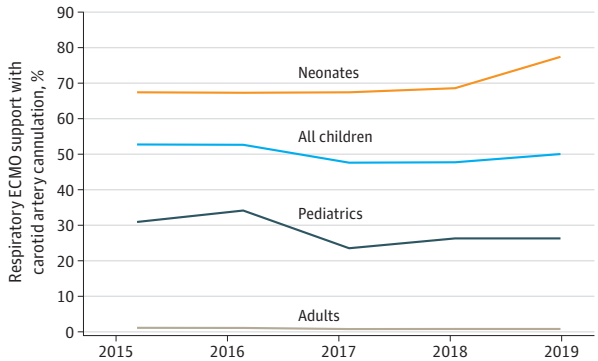
Figure 1. Anatomy and Physiology of Pediatric Extracorporeal Membrane Oxygenation (ECMO)



The blood pump withdraws venous blood from the child and propels through the ECMO circuit. The sweep gas flows from an oxygen-air blender to the membrane lung. In the membrane, lung blood surrounds hollow fibers as sweep gas is propelled through the fibers, allowing gas exchange with the blood. At top right, venovenous ECMO using a dual-lumen cannula; in this case, blood is withdrawn from the superior and inferior vena cava and reinfused into the right atrium. At bottom right, venoarterial ECMO using 2 cannulae; in this case, blood is withdrawn from the superior vena cava or right atrium and reinfused into the common carotid or brachoecepahlic artery. FDO_2 indicates delivered fractional oxygen percentage.

The principal determinant of carbon dioxide removal during ECMO is the rate of sweep gas flow. The faster the sweep gas moves through the membrane lung, the greater the diffusion gradient is, and as a result, more carbon dioxide is removed from the blood. ECMO oxygenation is determined almost entirely by the amount of oxygen that can be bound to hemoglobin. Generally, the higher the ECMO blood flow rate, the more deoxygenated the hemoglobin that is withdrawn from the body and made available to the device for oxygen uptake. However, other factors beyond the scope of this review can complicate that association.[11,12]

Figure 2. Proportion of Children With Carotid Artery Cannulation for Respiratory Extracorporeal Membrane Oxygenation (ECMO)



Patients, %

Neonates	68	67	67	68	77
All children	53	53	48	48	50
Pediatric	31	34	23	26	26
Adults	<1	<1	<1	<1	<1

Data are based on an Extracorporeal Life Support Organization Registry report (January 2020).[9] Neonates are those aged 0 to 28 days; pediatric patients are those aged 29 days to 17 years. All children includes both age ranges.

To initiate ECMO, clinicians must decide on which vessels to cannulate and choose the appropriate cannula size. The femoral vessels of children weighing less than 25 kg (or up to approximately 8 years old) are often too small to receive an ECMO cannula that is large enough to enable the necessary ECMO blood flow rate.[13] Consequently, most children have ECMO cannulae placed in the neck vessels. These children receive either a dual-lumen cannula in the right internal jugular vein for venovenous ECMO or a single-lumen cannula in the right internal jugular vein with a second single-lumen cannula placed in the right internal carotid artery for venoarterial ECMO.[2] From 2015 through 2019, most pediatric respiratory ECMO reported to the ELSO Registry was venoarterial ECMO: 69% in neonates (aged 0-28 days) and 28% in children aged 29 days to 17 years (**Figure 2**).[2]

Risks of ECMO Support and Conventional Management

Children receiving respiratory ECMO support may endure considerable complications (**Figure 3**).[2,14] A prospective observational study of 514 children receiving ECMO support demonstrated that bleeding and thrombotic rates are much higher in pediatric respiratory ECMO than the rates reported in adult studies.[1,2,14,15] For example, intracranial hemorrhage rates are reported to be 22.5% (n = 34 of 151) in neonates and 16% (n = 14 of 86) in children over 28 days, compared with 3% for adults in the ELSO Registry[16] and 2.4% (n = 3 of 124) in the ECMO to Rescue Lung Injury in Severe ARDS (acute respiratory distress syndrome) (EOLIA) Trial.[15] In addition, 338 of 514 children (65.8%) required a blood transfusion for bleeding.[17] Among 287 children, the median pre-ECMO platelet count of 172 × 10^3/μL (interquartile range, 111-248 × 10^3/μL) (to convert to platelets × 10^9 per liter, multiply by 1.0) declined to a platelet count while receiving ECMO of 89 × 10^3/μL (interquartile range, 51-130 × 10^3/μL) within 12 hours.[18]

However, outside of clinical trials, it is difficult to separate the complications that are the result of ECMO vs those attributable to critical illness itself. In the EOLIA trial,[15] short-term complications, such as hemorrhagic stroke, cardiac arrhythmias, cardiac arrest, pneumothorax, and kidney replacement therapy use, were all similar in the ECMO and conventional management groups, although bleeding and thrombocytopenia occurred more frequently in the ECMO group. A 7-year follow-up study[19] of neurodevelopmental outcomes in neonates randomized to ECMO or conventional care found no difference in neuromotor development outcomes, lower respiratory morbidity, and fewer behavioral problems in the ECMO group compared with the control group. These findings highlight that some of the complications often attributed to ECMO may in fact be due to the underlying critical illness.[20]

Reserving ECMO initiation until conventional therapies fail may avoid unnecessary ECMO, yet waiting too long risks the worsening of ventilator-induced lung injury, development of multisystem organ failure, or cardiac arrest.[4,5,21,22] In the absence of ECMO support, life and vital organ oxygenation is preserved by increasing the support from the mechanical ventilator.[23] However, the need for increasing ventilator pressures and volumes may exacerbate lung injury and induce a systemic inflammatory response, which in turn may contribute to multisystem organ failure, including worsening lung injury, and ultimately increased mortality.[4,5,21,22]

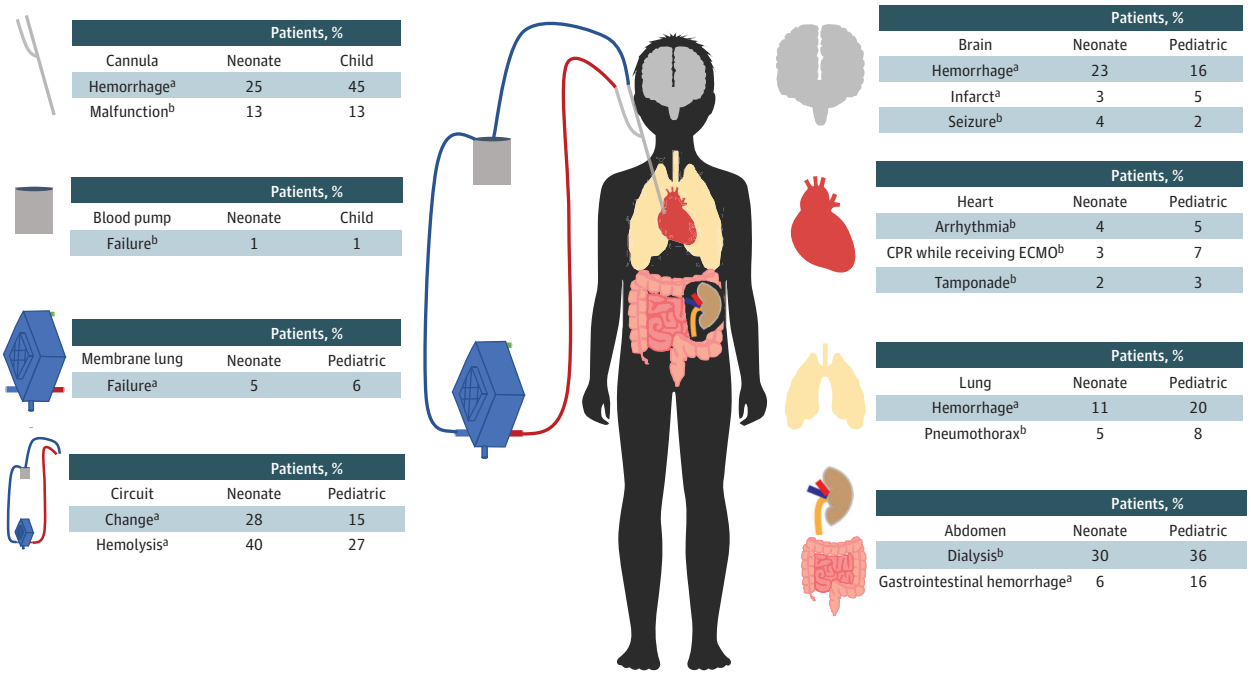
Evidence Relevant to Supporting Children With Respiratory ECMO

The growth of respiratory ECMO in all age groups stems from the demonstration that neonatal respiratory ECMO support reduced mortality in perinatal lung disease,[24] followed by advances in ECMO technology,[25] the 2009 influenza A(H1N1) pandemic,[26,27] and randomized clinical trials studying adult respiratory ECMO support.[15,28] Throughout the evolution of ECMO, this information and evidence has been purposefully disseminated through annual ECMO meetings.[29]

Severe Perinatal Lung Disease

The UK Collaborative ECMO Trial, a randomized clinical trial[24] of neonatal ECMO, randomized 185 neonates to ECMO or conventional management between 1993 and 1995. Enrollees were 35 weeks' gestational age or older and had birth weights of 2 kg or more, an age less than 28 days, and an oxygenation index of 40 or more or a $PaCO_2$ greater than 90 mm Hg for at least 3 hours, after having received less than 10 days of high pressure ventilation. Neonates who had been supported by ECMO had a mortality rate of 30 of 93 (32%), compared with a mortality rate of 54 of 92 (59%) among those who experienced conventional management. The relative risk of ECMO support was 0.55 (95% CI, 0.39-0.77; $P < .001$). Subsequently, inhaled nitric oxide was shown in 2 neonatal randomized clinical trials[30,31] to reduce the need for ECMO, and there has been a corresponding decline in the number of annual ECMO cases for neonatal respiratory failure.[32]

Figure 3. Complication Rates Reported in Children Supported With Respiratory Extracorporeal Membrane Oxygenation (ECMO)



Cannula	Patients, % Neonate	Child
Hemorrhage[a]	25	45
Malfunction[b]	13	13

Blood pump	Patients, % Neonate	Child
Failure[b]	1	1

Membrane lung	Patients, % Neonate	Pediatric
Failure[a]	5	6

Circuit	Patients, % Neonate	Pediatric
Change[a]	28	15
Hemolysis[a]	40	27

Brain	Patients, % Neonate	Pediatric
Hemorrhage[a]	23	16
Infarct[a]	3	5
Seizure[b]	4	2

Heart	Patients, % Neonate	Pediatric
Arrhythmia[b]	4	5
CPR while receiving ECMO[b]	3	7
Tamponade[b]	2	3

Lung	Patients, % Neonate	Pediatric
Hemorrhage[a]	11	20
Pneumothorax[b]	5	8

Abdomen	Patients, % Neonate	Pediatric
Dialysis[b]	30	36
Gastrointestinal hemorrhage[a]	6	16

Neonates are aged 0 to 28 days; pediatric patients are 29 days to 17 years old.[10] CPR indicates cardiopulmonary resuscitation.

[a] Complication rates are reported from December 2012 to September 2014 among 151 neonates and 86 pediatric cases.[14]

[b] Complication rates are based on Extracorporeal Life Support Organization reports from January 2014 to December 2018 among 4162 neonates and 3136 pediatric cases.[10]

Pediatric Acute Respiratory Failure and Severe PARDS

Outside of the neonatal period, there have been, to our knowledge, no pediatric randomized clinical trials of ECMO.[33] There have been 2 matched cohort studies of ECMO for respiratory support in children: 1 showing a benefit of ECMO[34] and 1 failing to demonstrate a difference in outcomes.[35] The later study,[35] a propensity score–matched analysis, found no difference in mortality. The study had 77% power to detect a 25% mortality difference, as previously observed,[24,27,28] but it had only 19% power to detect a 10% mortality difference, comparable with that observed in the EOLIA trial.[15,36] In other words, this study lacked the power to exclude a clinically meaningful difference, such as a mortality reduction of 10%.

Adult Acute Respiratory Failure and Severe ARDS

There have been 5 randomized clinical trials[15,28,37-39] of ECMO or $ECCO_2R$ vs conventional management in adult acute respiratory failure. The 2 contemporary ECMO trials[15,28] offer the most salient evidence. The Conventional Ventilation or ECMO for Severe Adult Respiratory Failure (CESAR) trial demonstrated a survival benefit of referral to a single ECMO center for consideration of treatment with ECMO.[28] However, limitations of the study included inconsistent delivery of standard ventilation parameters in the conventional arm, based on the pragmatic design of the study; also, 25% of the treatment group never received ECMO.[40] The EOLIA trial enrolled adults with very severe ARDS who were 18 years and older, had been receiving invasive mechanical ventilation for less than 7 days, and had evidence of severely impaired gas exchange as evidenced by the clinical criteria in **Table 1**. The EOLIA trial randomized patients to ECMO vs continued high-quality conventional care. The mortality in the ECMO group was 35% vs 46% in the conventional group (relative risk, 0.76 [95% CI, 0.55-1.04]; $P = .09$).[15] A high rate of crossover

Table 1. Thresholds for Initiating Extracorporeal Membrane Oxygenation (ECMO) in Randomized Clinical Trials of Neonates and Adults

Patient characteristic	UK neonatal trial	The EOLIA Trial
Severity of lung disease	Oxygenation index ≥40 or a $Paco_2$ >90 mm Hg for ≥3 h	Acute respiratory distress syndrome plus 1 of the following: Pao_2/FiO_2 <50 mm Hg with FIO_2 ≥80% for >3 h; Pao_2/FiO_2 <80 mm Hg with FIO_2 ≥80% for >6 h; or pH <7.25 (with $Paco_2$ ≥60 mm Hg) for >6 h
Duration of mechanical ventilation	With <10 d of high-pressure ventilation	Receipt of mechanical ventilation for <7 d
Age	<28 d	≥18 y
Exclusions	<35 wk gestational age, <2 kg birth weight	Pregnancy, BMI >45, long-term ventilatory insufficiency, cardiac failure requiring venoarterial ECMO, heparin-induced thrombocytopenia, cancer with life expectancy <5 y, coma after cardiac arrest not attributable to medications, moribund (simplified acute physiology score >90), inability to obtain vascular access for ECMO

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); EOLIA, Extracorporeal Membrane Oxygenation for Severe Acute Respiratory Distress Syndrome trial; FIO_2, fraction of inspired oxygen; Pao_2/FiO_2, ratio of partial pressure of arterial oxygen to fraction of inspired oxygen; $Paco_2$, partial pressure of arterial oxygen.

to ECMO, occurring in 35 of 125 patients (28.0%) assigned to conventional care at a median of 7 days after randomization, biased the results toward the null. The ECMO group received more transfusions and had more thrombocytopenia, but it also had fewer ischemic strokes and more days free of kidney failure. A subsequent post hoc bayesian analysis of the EOLIA Trial,[41] a meta-analysis of trials of ECMO for ARDS in adults,[42] and a network meta-analysis[43] each lend credible support to the existence of a survival benefit of ECMO in this context.

Applying the Evidence in Severe Perinatal Lung Disease

For children with perinatal lung disease, the evidence supports a trial of inhaled nitric oxide and, if appropriate, high-frequency oscillatory ventilation prior to proceeding to ECMO.[30,31] The evidence supports a threshold of an oxygenation index of 40 (Table 1).

Applying the Evidence in Very Severe PARDS

The threshold for initiating ECMO is not established for PARDS or acute respiratory failure.[44,45] Given the absence of evidence, the addition of ECMO to invasive mechanical ventilation is undertaken when clinicians believe the risk of progressive, ventilator-induced lung injury, multiple organ dysfunction syndrome, or life-threatening hypoxemia outweighs the risks of bleeding, thrombosis, and other potential complications in pediatric respiratory ECMO. In practice, observational reports find this transition occurs mostly at a median oxygenation index of approximately 40 and partial pressure of arterial oxygen to fraction of inspired oxygen (Pao_2/FiO_2) ratio of approximately 60 mm Hg.[46-48] A review of the literature indicated pediatric intensivists consider transitioning to ECMO when the Pao_2/FiO_2 ratio is sustained at less than 60 to 80 mm Hg or the oxygenation index is less than 40.[44,45] The lack of consensus has led to wide variation in ECMO initiation thresholds.[35]

Beyond Perinatal Lung Disease and Very Severe PARDS

Status asthmaticus and viral bronchiolitis are both associated with obstructive airway disease. There are numerous case series suggesting ECMO may be used to support children, with an observed survival rate of 80% in patients with asthma or bronchiolitis.[2,46,49] Although rare, ECMO support has also been deployed as a bridge to lung transplant in children older than the neonatal period.[50] In this setting, the goal is to reduce sedation and actively rehabilitate the patient receiving ECMO support prior to lung transplant.[50]

Implications for the General Pediatrician

For many survivors of pediatric respiratory ECMO, recovery is not complete until long after discharge from the hospital.[19] Late death, defined as death more than 90 days after termination of ECMO support, occurred in 13 of 193 neonates (6.7%) and 9 of 90 children (10%) aged 28 days to 17 years.[51] Late death after respiratory ECMO support was more common in children with complex medical conditions, such as congenital diaphragmatic hernia.[51,52]

In addition, children need identification and follow-up of neurodevelopmental impairment.[19,53,54] The ELSO guidelines[55] and the California Children's Services Manual of Procedures Standard 3.35[56] recognize this and explicitly call for ongoing care to aid recovery after hospital discharge. Moreover, these policy recommendations are aligned with parental preferences, ranking functional status after discharge as the most important outcome after survival.[57] Parents receiving ECMO-specific follow-up after hospital discharge found it helpful in 95% of cases; they identified receiving reassurance, anticipatory guidance regarding long-term ECMO effects, and referral to specialist services to address patient-specific needs as helpful aspects.[58]

After ECMO Support for Severe Perinatal Lung Disease

Neonatologists have a long-standing focus on the development of children beyond the neonatal intensive care unit,[59] and consequently, there is much better characterization of recovery after respiratory ECMO support for perinatal lung disease than there is in later childhood.[3] The 185 children participating in the UK Collaborative ECMO Trial have long-term outcomes reported among the 90% of children who had survived 7 years after the trial.[19] Although disability was reduced in some domains for children who had received ECMO support relative to those who had received conventional management, disability was prevalent in both groups. There was no difference in cognitive testing between the 2 groups, and 68 of 89 participants (76%) scored in the normal range. However, in tasks of spatial ability, such as constructing patterns or recalling designs, in both groups, 29 of 89 (26%) scored at less than the 10th percentile, and 35 of 89 (39%) scored at less than the 10th percentile in reading comprehension. Overall, 19 of 89 participants (21%) received special education services, and 8 of 89 (9%) had communication difficulties their teachers assessed as affecting learning. There was also no difference between the 2 groups in neuromotor development, although 39 of 89 (44%) had evidence of impairment.[1]

Respiratory morbidity, measured as intermittent wheezing in the last 12 months, was more common in the conventional care group (11 of 30 [32%]) than the ECMO group (6 of 43 [11%]).[19] Hospitalizations for respiratory disease occurred in 2 of 30 participants (6%) in the control group and 4 of 43 participants (9%) in the treatment group.[19] Parental reports of behavior problems were more common in the conventional group. Hyperactivity was the most common behavior problem among all study participants, occurring in 22 of 85 children (26%)[19]; 8 of 88 (9%) required specialist intervention for behavioral problems.[19]

In a longitudinal study of 178 survivors of respiratory ECMO for perinatal lung disease measured at 2, 5, and 8 years, intelligence remained stable, with mean (SD) IQs of 102 (18), 100 (17), and 99 (17), respectively.[60] Looking broadly at school resource needs, 101 participants (56.7%) attended regular education, 65 (36.5%) received extra help, and 13 (7.3%) attended special education schools. Children with congenital diaphragmatic hernia scored significantly lower on IQ testing than children with other perinatal lung diseases.[60] An earlier report from the same cohort reported deficits in concentration: working speed was "slow to very slow" in 86 of 123 participants (69.9%), and 48 of 123 participants (39.0%) had "low to very low" accuracy.[61]

After ECMO Support for PARDS and Acute Respiratory Failure

Beyond perinatal lung disease, much less is known about the long-term neurodevelopmental outcomes after pediatric respiratory ECMO use.[3] A 2018 systematic review identified no studies evaluating the long-term neurodevelopmental outcomes of children with

PARDS who had received ECMO support.[62] A 1-year post-ECMO follow-up of survivors of respiratory ECMO use reported outcomes on 22 children who received ECMO support after 28 days of life.[54] The study identified a parental report of behavioral abnormalities in 4 children (18%), and 8 children (36%) needed referral to a specialist.[54] Evidence in PARDS and acute respiratory failure is limited, but in perinatal lung disease, long-term risks of adverse neurodevelopmental outcomes after neonatal ECMO are well characterized[3] and a functional decline 6 months after pediatric critical illness has been characterized in pediatric acute respiratory failure (without ECMO support).[63] Consequently, experts have still advocated for systematic mandatory follow-up of older children.[3,64]

Parental Psychological Morbidity After ECMO Support

The long-term outcomes of pediatric critical illness and ECMO support are likely not only affecting child survivors, but also their families and caregivers.[65,66] In a clinical trial of caregivers of patients who were critically ill, 148 of 222 (66.7%) reported depressive symptoms, which persisted in 59 of 136 (43.4%) even 1 year after discharge.[67] Most parents of children receiving ECMO support felt that their child faced eminent death without ECMO, and many reported anxiety throughout the hospitalization.[68] At least 6 months after ECMO support, 11 of 52 families (21.1%) had symptoms consistent with posttraumatic stress disorder.[66]

Recommendations for Follow-up

There are no established evidence-based or consensus-based guidance on appropriate follow-up after ECMO. However, follow-up can identify problems that may improve with appropriate intervention and can provide support as well as reassurance for families.[58] The best available evidence suggests that children who receive respiratory ECMO support commonly experience deficits in neuromotor ability, reading comprehension, communication, and visual-spatial ability after ECMO support. Respiratory comorbidities and difficulty in school are also common after ECMO support.[19,69]

Ideally, follow-up care is part of a continuation of rehabilitative care that began during hospitalization. For example, a physical medicine and rehabilitation or developmental pediatrician consultation can identify neuromotor or neurocognitive deficits and apply physical, occupational, or speech therapy. When performed during the hospitalization, families can be taught to proactively monitor for changes in function and provide supportive and rehabilitative care for their children. They may also be educated about specific follow-up visits to address ongoing needs. When therapeutic relationships have not been established during the course of inpatient care, consultation with an appropriate specialist is indicated to perform an initial screening of motor and cognitive functioning prior to discharge or transfer. This will allow timely connections to appropriate outpatient care based on a child's deficits and local resources.

If an in-hospital assessment has not been made prior to hospital discharge, we recommend that the primary care clinicians screen the child using age-appropriate developmental screening tools. Primary care clinicians can use the Ages and Stages Questionnaire for younger children, and for older children, the National Institutes of Health Patient-Reported Outcomes Measurement Information System Cognitive and Mobility pediatric short forms may be useful. If there are concerns identified on these screening tools or on discussion regarding return to home and school environment, the child should be referred to an appropriate specialist, such as a physical medicine and rehabilitation or developmental pediatrician. In addition, given the prevalence of difficulties in reading comprehension and communication as well as school problems, screening and evaluation should consider if testing is needed to guide individualized educational plans for school-aged children.

ECMO is often delivered at referral hospitals far removed from the child's home, and pediatric subspecialty services may not be as readily available outside of the referral hospital providing ECMO. In this scenario, virtual care, such as video visits or remote subspecialty consultation, may be used to facilitate care and extend referral center resources to families living in remote locations.

Conclusions

Randomized clinical trials in respiratory ECMO support for perinatal lung disease have established ECMO as an evidenced-based practice. Long-term functional outcome studies after ECMO support for perinatal lung disease suggest that overall cognitive testing is likely to be normal for most survivors of ECMO support. However, deficits in visual-spatial ability, reading comprehension, and communication; behavioral problems; neuromotor deficits; and difficulties in school are common, and affected children may benefit from early identification and treatment. Among children receiving respiratory ECMO support after 28 days of age, there is a paucity of evidence characterizing children's long-term neurodevelopment or supportive service needs. Nonetheless, clinicians caring for children recovering after ECMO should be aware of the need to serially screen for neurodevelopmental problems. Neurodevelopmental problems may evolve over time, only become apparent when the child attends school, and require referral to specialty or pediatric allied health services to help optimize long-term outcomes.

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Drafting of the manuscript: All authors.
Critical revision of the manuscript for important intellectual content: Brodie, MacLaren.
Administrative, technical, or material support: Barbaro.
Supervision: Brodie, MacLaren.

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