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Short Communication

Role of Extracorporeal Membrane Oxygenation (ECMO) in PARDS

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Abstract

The successful use of ECMO in neonatal respiratory failure has stimulated its application in children and adults. In PARDS, ECMO may support systemic oxygen delivery while allowing lung-protective unloading of the injured lungs through a reduction in ventilatory intensity. However, implementation of ECMO requires appropriate institutional infrastructure as well as specialized personnel resources. In 2009, during the H1N1 influenza pandemic, approximately 2,000 pediatric ECMO cases were registered worldwide (see also the website of the Extracorporeal Life Support Organization, ELSO). Over the subsequent five years, the number of pediatric ECMO cases increased substantially and has remained consistently just above 3,000 cases per year since 2014 [1]. Approximately half of these cases were performed for respiratory support, and the other half for cardiac support.

Introduction

During the COVID-19 pandemic, ECMO was increasingly utilized as a rescue therapy for adult patients with severe COVID-19–associated ARDS refractory to conventional lung-protective ventilation strategies. Early reports raised concerns due to high mortality rates and the unprecedented strain on ICU resources. In response, the Extracorporeal Life Support Organization (ELSO) issued interim guidance emphasizing strict patient selection, treatment in experienced centers, and careful resource allocation in order to maintain acceptable outcomes and avoid inappropriate ECMO initiation during periods of limited capacity.

Subsequent analyses from the international ELSO Registry suggested that outcomes of ECMO-supported COVID-19 patients were comparable to those historically reported for ECMO in non-COVID severe ARDS, particularly when applied in high-volume centers and in carefully selected patients. However, later phases of the pandemic demonstrated variability in outcomes across regions, likely influenced by evolving viral variants, patient demographics, delayed referral, and differences in center experience [2]. The use of ECMO rose dramatically in adults but not in pediatric patients. Survival to hospital discharge in pediatric hypoxemic respiratory failure has remained stable at approximately 60%, although it varies by diagnosis from 32% (pertussis) to 88% (asthma). Viral pneumonias are associated with a slightly better prognosis than bacterial pneumonias, and infants exhibit more favorable outcomes than toddlers or school-aged children. Prognosis in patients on ECMO with existing underlying diseases may have poorer outcomes. In pediatric respiratory failure, veno-venous (VV) ECMO is generally preferred over veno-arterial (VA) ECMO when cardiac function is adequate, because it provides effective respiratory support (oxygenation and CO_2 removal) while preserving native cardiac output and avoids arterial cannulation. Compared with VA ECMO, VV ECMO is associated with a lower risk of neurologic injury and embolic complications (e.g., carotid artery-related stroke), less hemodynamic disturbance, and fewer vascular access–related complications (including limb ischemia and carotid ligation), while still enabling ultra–lung-protective ventilation and lung rest. Looking into the ELSO registry in PARDS, the mode of ECMO support was veno-arterial in up to 40% of cases and veno-venous in 60%. Whereas roller pumps are most commonly used in neonates,

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centrifugal pumps are now used almost exclusively in pediatric patients.

In adults, ECMO use has increased even more markedly compared with children, and the Conventional Ventilation or ECMO for Severe Adult Respiratory Failure (CESAR) trial demonstrated that ECMO was cost-effective, as it resulted in improved survival without severe disability at six months [3]. The subsequent ECMO to Rescue Lung Injury in Severe ARDS (EOLIA) trial, however, did not demonstrate a mortality benefit of ECMO compared with conventional ventilation [4]. In contrast to the well-established benefit of ECMO in neonates with respiratory failure, evidence from clinical trials supporting ECMO in PARDS is currently lacking. In a cohort study published in 2018, children treated with ECMO were compared with matched non-ECMO controls, and no significant reduction in mortality was observed among ECMO-treated patients [5].

In cases of severe, refractory respiratory failure, ECMO may be initiated prior to transfer or during interhospital transport to facilitate safe referral to an experienced ECMO center. Mobile ECMO retrieval teams have been established in many regions and allow for cannulation and stabilization at the referring hospital, followed by transport under ongoing extracorporeal support. This approach may reduce the risks associated with transport under maximal conventional ventilation, particularly in patients with critical hypoxemia or severe ventilator-induced lung stress. Safe transport requires predefined logistics, specialized personnel, and standardized protocols, as complication risk (e.g., circuit failure, bleeding, hemodynamic instability) remains relevant during retrieval and transfer. With regard to utilization, ECMO has been applied considerably more frequently in adults than in children, particularly since the 2009 H1N1 pandemic and again during the COVID-19 pandemic. The expansion in adult ECMO reflects the high incidence of severe ARDS in adults, a greater absolute number of eligible patients, and the widespread establishment of adult ECMO programs. In contrast, pediatric ECMO volumes remain substantially lower and are mainly concentrated in specialized tertiary centers. In children, the need for ECMO is comparatively less frequent and patient populations are more heterogeneous, including respiratory and cardiac indications as well as neonatal cases; these factors limit overall case numbers and contribute to pronounced variability in center experience and practice patterns. An ELSO Registry report by Tonna JE et al. summarizes global ECMO activity and outcomes through 2022, highlighting that the registry has surpassed 100,000 survivors and providing updated epidemiology and survival benchmarks across ECMO indications and age groups. This report demonstrated that in 2022 about 10 percent of pediatric patients were transported on ECMO whereby the rate in adults was higher with 15% of the ECMO patients [6]. The main German ECMO center Mannheim during the last 5 years 40 pediatric patients were transferred for the therapy option ECMO, but none was on ECMO during transport and only 7 patients went on ECMO (6 VV ECMO and one VA ECMO).

In conclusion ECMO may be used in PARDS when adequate gas exchange can only be achieved with Plateau pressures exceeding recommended limits may become unavoidable. Prompt initiation of ECMO is indicated in cases of acute hypoxemia, i.e., $PaO_2 < 50$ mmHg despite maximal mechanical ventilatory support. Later initiation of ECMO during the course of ARDS may be considered in patients with a persistently high oxygen requirement ($FiO_2 > 0.8$ for more than 5 days). However, prior to ECMO initiation, a thorough and repeated reassessment is essential to determine whether stabilization may still be achievable with conventional therapy and appropriate adjunctive measures. Furthermore, in the event of a decision to proceed with ECMO, there should be a realistic expectation of disease reversibility or, alternatively, lung transplantation may represent a potential therapeutic goal.

Weaning of ECMO versus discontinuation of therapy

All patients diagnosed with ARDS have a high risk of mortality, even in cases in which ARDS improves rapidly and diagnostic criteria are no longer met by treatment day 2 (affecting approximately one fifth of cases). In adults, the use of higher tidal volumes correlates with persistence of ARDS. Patients with severe ARDS on day 2 represent a high-risk group [7]. In the absence of multi-organ failure or relevant pre-existing disease, the likelihood of rapid recovery from ARDS is greatest. Recovery from ARDS (cessation of inflammation at the alveolar–capillary membrane and regression of interstitial edema) is reflected by an improvement in pulmonary compliance. This is initially manifested by higher tidal volumes at an unchanged pressure gradient on the ventilator. In parallel, oxygenation improves. On chest radiography, infiltrates begin to resolve, and the weaning phase can subsequently be initiated (typically once OI < 8), with transition to non-invasive ventilation (NIV) where appropriate. In PARDS patients receiving ECMO (most commonly veno-venous ECMO), ventilator settings are reduced to safely lung-protective parameters, as the membrane oxygenator provides oxygenation and eliminates carbon dioxide. With improvement in compliance and radiographic appearance, ECMO flow can—under favorable conditions—be reduced after only a few days; however, flow must be maintained above a minimum threshold to prevent thrombosis. The feasibility of ECMO separation is assessed in VV ECMO by discontinuing (“clamping”) the sweep gas to the membrane lung. If ventilation is possible with an $FiO_2 < 0.50$ while maintaining adequate carbon dioxide elimination, ECMO can be discontinued and ventilator weaning continued. Strategies to prevent prolonged mechanical ventilation and potential weaning failure include early interruption of sedation and repeated spontaneous breathing trials in order to facilitate early extubation. NIV is a particularly effective approach in hypercapnic patients. Prolonged weaning is most commonly attributable to respiratory muscle weakness of various etiologies, often aggravated by comorbidities. Tracheostomy can reduce the work of breathing by up to 20%. In adults, tracheostomy is performed frequently and early in some centers; however, clear algorithms have not been

published and an effect on mortality has not been demonstrated. In children with PARDS, tracheostomy is rarely used and is generally an individualized decision. This should be made within a shared decision-making process with the parents. In cases of conflict between clinicians and parents, a clinical ethics committee may be consulted to support decision-making with consideration of long-term prognosis and the child's expected quality of life.

Outlook for future research directions

Due to the limited evidence base for therapeutic interventions, management of PARDS remains highly variable. The recommendations of the PALICC2 guideline summarized by Papazian et al. may facilitate improved standardization of PARDS therapy [8]. A former survey conducted in 2013 demonstrated frequent use of adjunctive therapies: 80% of respondents reported using inhaled nitric oxide (iNO) in PARDS, approximately three quarters routinely applied prone positioning, and half would administer surfactant [9]. However, robust evidence supporting these adjunctive treatments remains scarce. The question of the benefit of ECMO should be addressed using a risk-based approach focusing on the subgroup of severe ARDS associated with high mortality, as mild and moderate ARDS have comparatively low mortality and likely do not require adjunctive therapies. Epidemics or pandemics such as the 2009 H1N1 influenza season or the COVID-19 pandemic since 2020 may pose a major burden on intensive care services due to an increased incidence of ARDS requiring advanced supportive therapies. Fortunately, COVID-19 has rarely led to ARDS in children compared with adults. Early in the pandemic (April 2020), a European cohort study including 582 children with a positive PCR test reported that 62% were hospitalized; 8% of the overall cohort required intensive care; 4% were intubated and received mechanical ventilation for a mean duration of 7 days. One child received ECMO. Four children died; only 25% had pre-existing comorbidities, and the highest risk was observed in young infants [10].

Early consultation with experienced centers may be beneficial to optimize PARDS management and, in the event of disease escalation, to enable timely transfer. In addition, future research should more specifically evaluate the effects of different therapeutic interventions on post-PARDS morbidity (e.g., pulmonary function, cognitive impairment, and quality of life).

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