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REVIEW ARTICLE

Extracorporeal membrane oxygenation in children: A brief review

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With the advancement in technology and increasing familiarity, the use of extracorporeal membrane oxygenation (ECMO) has expanded in the past decade. Although ECMO can be lifesaving for critically ill children, it is an invasive therapy associated with complications that may necessitate rehabilitation and long-term follow-up. Paediatric clinicians play an essential role in managing these children, especially after the acute phase of their illness. This review provides an overview of ECMO and will provide a basic understanding of ECMO and its principles.

Key words: cost–benefit analysis; extracorporeal membrane oxygenation; review.

Extracorporeal membrane oxygenation (ECMO) is an advanced therapy used to manage critically ill patients with severe respiratory or cardiovascular dysfunction that is refractory to conventional management.

Over the last decade, the field of ECMO has expanded, requiring multidisciplinary involvement in the care of these complex patients. ECMO survivors need ongoing monitoring and rehabilitation after leaving the intensive care unit (ICU) setting and often long after discharge from hospital. Follow-up in this context often requires a multidisciplinary team including general paediatricians and physicians; however, as highlighted recently,[1] there is a knowledge gap with regards to ECMO and its long-term effects amongst follow-up care providers.

This review will attempt to fill that gap by providing a basic overview of ECMO, outlining its history, types and basic physiology, its indications, complications and outcomes, with a particular focus on paediatrics, in order to smooth the transition of care of ECMO survivors from ECMO centres to the general paediatrician.

Key points

1 Management of children on extracorporeal membrane oxygenation (ECMO) requires a multidisciplinary approach.
2 As ECMO survivors are at risk for developing neurodevelopmental delay, they should have a structured neurodevelopmental follow-up.
3 ECMO is complex and resource-intensive but can be cost-effective.

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History of ECMO

The successful use of ECMO was first described in 1972 in the management of post-traumatic respiratory failure in an adult patient.[2] In the same year, ECMO was successfully used in a neonate after Mustard operation for transposition of the great arteries.[3] This was soon followed by the management of severe meconium aspiration syndrome.[3] Despite early disappointments in adult critical care,[4] the use of ECMO continued to develop in neonatal and paediatric medicine in the late 20th century. The Extracorporeal Life Support Organization (ELSO) was formed in 1989 to support clinicians with guideline publication and education, ECMO research and registry data collection. An early randomised control trial of ECMO use in neonatal respiratory failure showed promising results,[5] and the Australian experience during the H1N1 influenza pandemic demonstrated the feasibility of widespread ECMO use.[6]

Today, there are 492 ECMO centres registered with ELSO, with a total of 151 683 ECMO runs to date, half of which have been in neonates and paediatric patients.[7]

ECMO technology has developed significantly over the decades. Surface modifications of the circuit tubing have reduced the risk of thrombosis.[8] The oxygenator has evolved from silicone membrane to polypropylene or polymethylpentene cross-flow systems to prevent clot formation and improve gas exchange.[9] Advances in technology have also allowed ECMO systems to become more compact and mobile. With these improvements, the safety, efficiency and longevity of ECMO continue to progress.

Types of ECMO

ECMO is broadly categorised into either veno-venous (VV) ECMO or veno-arterial (VA) ECMO. In both VV and VA-ECMO, deoxygenated blood is withdrawn from the venous circulation and passed through a membrane oxygenator for gas exchange. In VV-ECMO, this oxygenated blood is returned to the

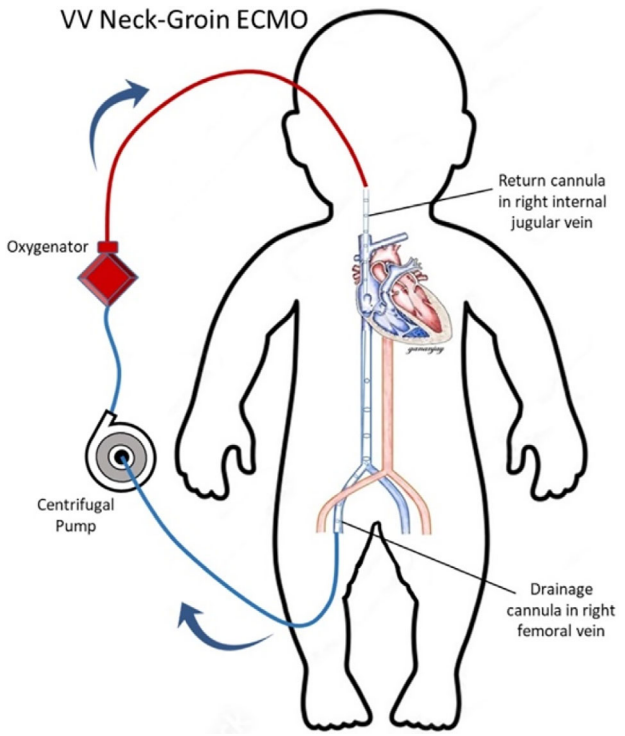

Fig. 1 Veno-venous (VV) ECMO. Blood is accessed via the femoral vein, passed through a membrane oxygenator which oxygenates the blood and eliminates carbon dioxide. This blood is returned to the internal jugular vein and requires the patient's native cardiac function to perfuse the systemic circulation. Thus VV-ECMO does not provide circulatory support. The figure demonstrates a peripheral circuit. ECMO, extracorporeal membrane oxygenation.

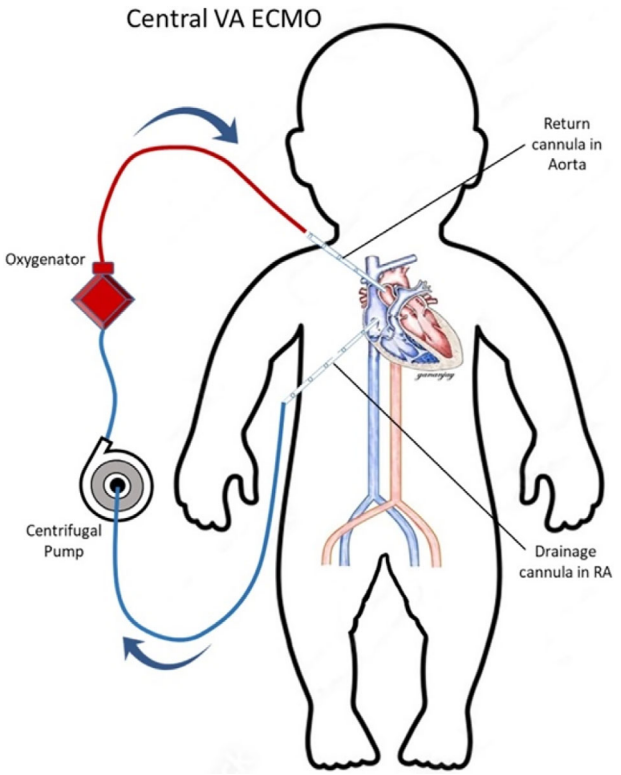

Fig. 2 Veno-arterial ECMO. Blood is accessed via the right atrium, passed through the membrane oxygenator and returned to the proximal aorta. Veno-arterial ECMO provides circulatory support in addition to respiratory support. This figure illustrates a central circuit. ECMO, extracorporeal membrane oxygenation.

systemic venous circulation (Fig. 1), augmenting the lung's gas exchange functions. In VV-ECMO, the patient's native cardiac function is required to deliver this oxygenated blood to the body. In VA-ECMO, blood is returned directly to the systemic arterial circulation (Fig. 2) and thus provides circulatory support in addition to respiratory support.

ECMO Configurations

Sites of vascular access can be central or peripheral. Central ECMO requires sternotomy with associated surgical risks, whereas peripheral ECMO can be established via percutaneous, surgical or hybrid techniques. Access in peripheral ECMO is established via an internal jugular vein (IJV) or femoral vein (FV).

In peripheral VV ECMO, both access and return of blood are via the femoral or internal jugular veins (Fig. 3a). Specialised dual-lumen cannulas such as the Avalon cannula (Fig. 3b) can allow single cannulation for both venous access and return, preventing the need for multiple cannulations. However, minor malpositioning can have deleterious effects on ECMO flow rates.

Recent advances have allowed central access for VV ECMO through sternotomy, with blood accessed via the right atrium (RA) or central vein and returned via the pulmonary artery (PA) (Fig. 3c). This helps reduce recirculation to improve the efficiency of ECMO oxygenation and offers support for isolated right heart failure.

Like peripheral VV ECMO, access for peripheral VA ECMO is established via femoral or internal jugular veins. However, blood is returned to the arterial circulation *via* the carotid, axillary or femoral arteries (Fig. 3d,e).

Access for central VA ECMO through sternotomy is via the RA. Blood is returned to the proximal aorta allowing stable blood supply to the ECMO circuit and reliable flow to the proximal aorta (Fig. 3f).

Indications and Contraindications

It is important to emphasise that ECMO is not a destination therapy but a bridge to recovery, decision-making, diagnosis, ventricular assist device (VAD), transplant or rarely, physiological support until organ donation. Over the last decade, indications for ECMO have rapidly expanded (Table 1).

Respiratory support with VV-ECMO can be provided for most respiratory pathologies. Short runs of ECMO can be used for difficult airway surgeries such as tracheal reconstruction and sliding tracheoplasty. ECMO can provide respiratory support in various pathologies such as asthma,[10] bronchopleural fistula,[11] and refractory hypoxaemia, such as in ARDS. Some common

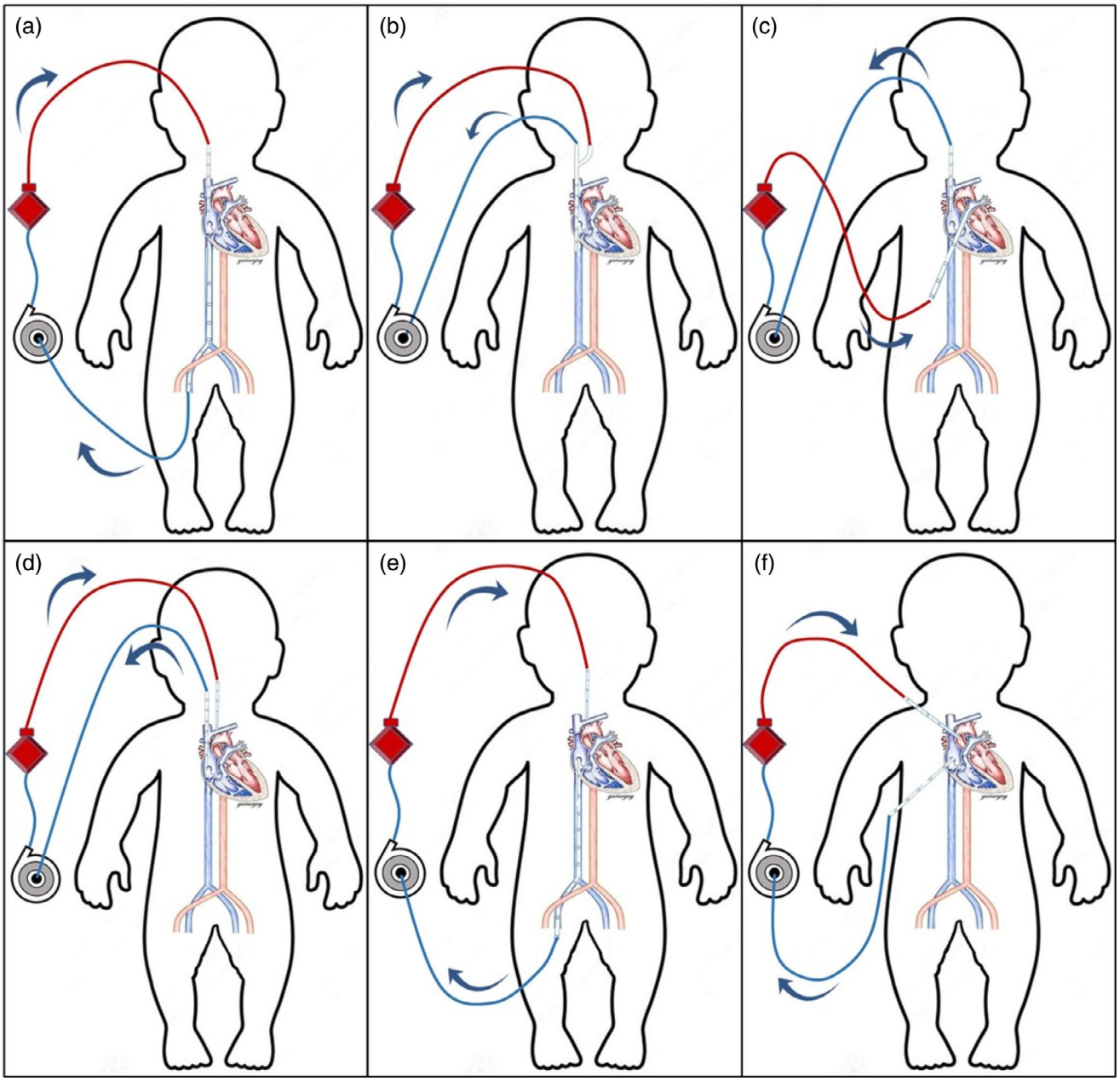

Fig. 3 Common ECMO Configurations. (a) Peripheral VV ECMO – Blood is accessed and returned via an internal jugular (IJ) or femoral vein. (b) VV ECMO via dual-lumen cannulae – A single cannula placed in the IJ vein provides both access and return. (c) Central VV ECMO – Blood is withdrawn via the right atrium or IJ veins and returned via direct cannulation of the pulmonary artery. (d, e) Peripheral VA ECMO – Blood is accessed via the IJ or femoral veins and returned via the carotid, axillary or femoral arteries. (f) Central VA ECMO – Blood is accessed via the right atrium and returned to the proximal aorta. ECMO, extracorporeal membrane oxygenation; VA, veno-arterial; VV, veno-venous.

respiratory indications in neonates are persistent pulmonary hypertension of the newborn, congenital pneumonia, meconium aspiration syndrome and congenital diaphragmatic hernia.

VA-ECMO for cardiovascular support is well-established post cardiothoracic surgery in the context of failure to wean from cardiopulmonary bypass, especially in children with congenital heart disease. Other common indications include cardiomyopathy or myocarditis as a bridge to recovery, VAD or transplant.

Favourable outcomes have been demonstrated with the use of ECMO in cardiac arrest,[12] which has led to its uptake as extracorporeal cardiopulmonary resuscitation (ECPR). The International Liaison Committee on Resuscitation recommends considering the use of ECPR in select paediatric patients with in-hospital cardiac arrests refractory to conventional therapy.[13]

The use of ECMO in the management of sepsis is controversial. Outcomes vary with age and clinical presentation, with neonates

Table 1 Indications for ECMO

Respiratory failure	Cardiac failure
1 Airway ○ Management of difficult airway ○ Airway obstruction ○ Sliding tracheoplasty 2 Lung ○ Bronchopleural fistula ○ Pneumonia ○ ARDS ○ Acute exacerbation of asthma ○ Inhalational injury ○ Pulmonary contusion ○ Alveolar haemorrhage 3 End-stage respiratory failure awaiting lung transplant 4 Neonatal respiratory failure ○ Meconium aspiration syndrome ○ Congenital diaphragmatic hernia ○ Congenital pneumonia	1 Failure to wean from cardiopulmonary bypass 2 Extracorporeal cardiopulmonary resuscitation 3 Cardiac failure ○ Cardiomyopathy ○ Myocarditis ○ Refractory arrhythmia ○ Massive pulmonary embolism ○ Severe cardiac contusion Other 1 Sepsis 2 Fulminant liver failure 3 Toxic ingestion 4 Organ support for organ donors

ARDS, acute respiratory distress syndrome; ECMO, extracorporeal membrane oxygenation.

faring better on ECMO,[14] and those with septic cardiomyopathy responding more favourably than those without.[15] VA ECMO with higher flow is associated with improved survival in paediatric sepsis.[16]

As indications for ECMO have expanded, there is also a reciprocal decline in absolute and relative contraindications (Table 2).

Organ-Specific Management During ECMO

ECMO requires careful monitoring and management of multiple organ systems for safe and efficient therapy.

Table 2 Contraindications for ECMO

Absolute contraindications	Relative contraindications
1 Catastrophic brain injury without prospect for recovery 2 Untreatable metastatic malignancy 3 End-stage organ failure without prospect for recovery or transplant	1 Severe multi-organ failure 2 Severe trauma with coagulopathy and haemorrhage 3 Severe immunocompromise 4 Extremes of age 5 Severe aortic regurgitation 6 Unfavourable vasculature such as aortic dissection

ECMO, extracorporeal membrane oxygenation.

Respiratory Management

The principle of respiratory management of an ECMO patient is to prevent further iatrogenic lung injury while allowing time for lung recovery. Lung-protective ventilation via 'Rest Settings' as suggested by the ELSO guidelines[17] forms the basis of management, minimising ventilator-induced lung injury.

Some degree of venous admixture is expected in VV ECMO, and as such, oxygen saturation of ≥80% should be acceptable for a patient on VV ECMO.[18]

Cardiovascular and Haematological Management

As with respiratory management, the goal of cardiovascular management of ECMO patients is to provide time to recover, whereas the ECMO circuit provides sufficient blood flow to support end-organ perfusion. Patients on VA ECMO are at risk of left ventricular (LV) distension which can lead to pulmonary oedema, further ischaemic injury, LV thrombosis and thromboembolism. Several LV unloading strategies are available (Table 3) and should be considered as soon as LV distension becomes evident.[19,20]

ECMO causes various haematological derangements, including both life-threatening bleeding due to circuit-induced coagulopathy and thrombosis and thromboembolism, which generally requires systemic anticoagulation. The circuit can induce haemolysis due to high shear forces, and this requires judicious titration of volume status and pump speed and may even necessitate oxygenator exchange.

Complications

ECMO is an invasive and complex therapy and is associated with significant complications. These complications can be divided into circuit or patient-related (Table 4). Circuit-related complications include cannula malpositioning and access insufficiency. Negative access pressures can cause air entrainment, leading to circuit failure, and there are reports of device entrainment, such as guidewires.[21] Circuit thrombosis and pump or oxygenator failure can occur.

Patient-related complications are numerous and can be categorised from a system-based approach. Haematological complications are the most common and can be either haemorrhagic or thrombotic.

Haemorrhage is often multifactorial, compounded by a coagulopathy both from anticoagulation and acquired von Willebrand syndrome and platelet dysfunction,[22] circuit-related fibrinogen consumption[23] and ECMO-induced reduction in factor VIII and XII.[24] Coagulopathy from the patient's critical illness may also contribute. Bleeding can be severe, necessitating massive transfusion, and can occur at the ECMO cannulation sites or can occur *de novo*, with intracranial haemorrhage (ICH) the most feared. Thrombotic complications are equally problematic and can lead to significant morbidity. ECMO causes a pro-thrombotic state due to blood exposure to non-physiologic surfaces and turbulent flow.[25]

Neurological complications occur in up to 30% of patients on ECMO[26] and can be catastrophic. The most common neurological complications are seizures, ischaemic stroke, and ICH.[27] The

Table 3 Strategies to decompress the left ventricle (LV) in LV distension

LV decompression strategies
1 Inotropes
2 Vasodilators
3 Titration of ECMO flow
4 Intra-aortic balloon pump
5 Impella ventricular assist device
6 Atrial septostomy
7 Percutaneous or surgical vent

ECMO, extracorporeal membrane oxygenation.

Table 4 Complications associated with the use of ECMO

Circuit-related complications	Patient-related complications
1 Access insufficiency	1 Haematological
2 Cannula malpositioning	○ Haemorrhage (gastrointestinal, pulmonary and intracranial)
○ Recirculation	○ Haemolysis
○ Differential hypoxaemia	○ Thrombosis and thromboembolism
3 Circuit rupture	2 Neurological
4 Air entrainment and embolism	○ Seizures
5 Pump failure	○ Ischaemic stroke
6 Oxygenator failure	○ Intracranial haemorrhage
7 Circuit thrombosis	○ Delirium
	3 Other
	○ Left ventricular distension (VA-ECMO)
	○ Nosocomial infection
	○ Limb ischaemia and compartment syndrome

ECMO, extracorporeal membrane oxygenation; VA, veno-arterial.

incidence of seizures in paediatric ECMO patients is approximately 20%.[27] Ischaemic stroke has been reported in up to 33% of neonates and children on ECMO, and the incidence of ICH ranges between 3.6 and 16%.[27]

There are complications specific to VA ECMO. In femoral VA ECMO, distal limb ischemia and compartment syndrome can occur due to the ECMO return cannula impeding blood flow distally, a complication more common in paediatric patients.[28] Appropriate selection of cannulation sites and monitoring of distal perfusion is critical. Augmentation of distal blood flow can be achieved by placing an antegrade distal perfusion catheter in the artery distal to the ECMO cannula.[29]

Weaning of ECMO Support

De-escalation from ECMO differs between VA-ECMO and VV-ECMO. In VA-ECMO, once recovery of cardiac function is observed, the ECMO flow is gradually reduced with monitoring of haemodynamics, markers of organ perfusion, and serial echocardiographic assessment. If successful, the patient can be weaned off ECMO support.

Weaning of VV-ECMO should be considered once lung recovery is evident. The fresh gas flow to the oxygenator is progressively reduced while ECMO blood flow is maintained. Without fresh gas flow, ECMO ceases to contribute to gas exchange, and the patient is wholly reliant on their own lung function. If this is tolerated, the patient can be decannulated.

Table 5 Neonatal and paediatric outcomes from the ELSO international summary[7]

	Total runs since 1990	Survived to discharge or transfer
Neonatal	33 400	73%
• Respiratory support	9651	43%
• Cardiac support	2244	42%
• ECPR	11 168	60%
Paediatric	13 945	53%
• Respiratory support	5630	42%
• Cardiac support		
• ECPR		

ECPR, extracorporeal cardiopulmonary resuscitation; ELSO, Extracorporeal Life Support Organization.

Outcomes

There is significant heterogeneity in neonatal and paediatric ECMO patients, and survival varies with the indication (Table 5). Due to recent improvements in survival,[30] attention should also be directed to long-term morbidity. Neuropsychological issues are present in quarter neonatal ECMO survivors with long-lasting effects on their academic performance.[31] Although their neurodevelopment seems favourable in the initial years, some of these children experience difficulties with memory, working speed and spatial ability tasks.[32] There are reports of poorer physical function at 36 months,[32,33] with a significant proportion of patients with learning difficulties.[34] A 5-year follow-up of neonates managed with ECMO revealed a substantial proportion had neurological, motor and cognitive difficulties.[35] In contrast, there was no difference in neurodevelopmental outcomes in a 7-year follow-up study of neonates randomised to ECMO or conventional care.[36] These findings may suggest that the underlying disease condition may be the significant factor determining long-term morbidity, rather than ECMO itself.[34,37]

Data is also limited with regards to long-term medical outcomes of neonatal ECMO survivors. Although most survivors seem to have normal physical growth, the risk of medical complications such as chronic kidney disease,[38] hearing loss[39] and reduced exercise tolerance[40] may be increased.

Ongoing Rehabilitation and Long-Term Follow-up

Based on current knowledge of long-term outcomes and the phenomenon that ECMO survivors may grow into their deficits,[41]

clinicians should plan for regular follow-up assessments covering both medical and neurodevelopmental domains.

The current ELSO guidelines suggest that all ECMO survivors should have long-term follow-up in a structured and standardised approach.[31] Long-term follow-up should be individualised depending on the availability of resources, indication for ECMO, nature of underlying disease and presence of other comorbidities. Some of these children will require more active investigation and intervention, and referral to other subspecialties such as neurology may be warranted.

Neonatal ECMO survivors should have their first follow-up within the first 3 months of discharge, followed by 6 months and 1 year.[31] Further follow-up through school age and adolescence should be individualised. Older paediatric ECMO survivors will also benefit from long-term follow-up.

The engagement of the parents of ECMO survivors is crucial for the success of an ECMO follow-up program. These parents should receive adequate education[1] about potential long-term sequelae to allow timely health-care access, monitoring and intervention.

Cost Efficacy

ECMO remains an expensive therapy, but numerous studies have demonstrated cost-efficacy. A US study estimated the average in-hospital costs of paediatric ECMO patients increased from $214 046 to $324 841USD for an average hospital length of stay of approximately 45 days.[30] A longitudinal Canadian study found a median inpatient hospital cost for paediatric ECMO patients of $119 197CAD, with a much shorter average length of stay of 26 days.[42]

For cost-efficiency, a UK-based study of ECMO for respiratory failure demonstrated a favourable cost-efficacy of £16 707 per life-year gained, and £24 775 per disability-free life-year gained.[43] The use of ECMO as rescue therapy post congenital heart surgery costs approximately $156 324USD for the inpatient stay, but with a favourable cost-efficacy of $24 386/Quality of Life-Year.[44]

Future Directions

Advances in ECMO have allowed runs up to 20 months with recovery in the patients' cardiopulmonary function,[45] and this has led to unique and challenging questions about patient selection for the initiation of ECMO. Decisions about ECMO candidacy should be based on patient, family and multidisciplinary team discussion and the ethical distribution of health-care resources.

With continuing improvements in technology, safety and circuit longevity, we are approaching the '3rd era' of ECMO.[46] Soon it may be possible for appropriate ECMO patients to be de-sedated and extubated with a gradual introduction of ambulation, facilitating rehabilitation to prevent deconditioning.[47]

Conclusion

As ECMO technology has advanced over the last decade, survival has increased, and the focus has shifted from a reduction in mortality to the prevention of long-term morbidity. Although ECMO remains an expensive therapy, it is a viable rescue therapy for our sickest patients. An understanding of the general principles of ECMO will aid paediatricians in their essential role in the multidisciplinary management and long-term follow-up of these patients.

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