Optimizing Outcomes in Extracorporeal Membrane Oxygenation Postcardiotomy in Pediatric Population

Ahmad Salha[1] Tasnim Chowdhury[1] Saloni Singh[2] Jessica Luyt[3] Amer Harky[4,5]

[1] Department of Medicine, St George's Hospital Medical School, London, United Kingdom
[2] School of Medicine, University of Central Lancashire, Preston, United Kingdom
[3] Department of Paediatric Intensive Care, Alder Hey Children's Hospital, Liverpool, United Kingdom
[4] Department of Cardiac Surgery, Alder Hey Children Hospital, Liverpool, United Kingdom
[5] Department of Cardiothoracic Surgery, Liverpool Heart and Chest Hospital, Liverpool, United Kingdom

Address for correspondence Amer Harky, MRCS, MSc, Department of Cardiothoracic Surgery, Liverpool Heart and Chest Hospital, Liverpool, United Kingdom (e-mail: aaharky@gmail.com).

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Abstract

Extracorporeal membrane oxygenation (ECMO) is a rapidly emerging advanced life support technique used in cardiorespiratory failure refractory to other treatments. There has been an influx in the number of studies relating to ECMO in recent years, as the technique becomes more popular. However, there are still significant gaps in the literature including complications and their impacts and methods to predict their development. This review evaluates the available literature on the complications of ECMO postcardiotomy in the pediatric population. Areas explored include renal, cardiovascular, hematological, infection, neurological, and hepatic complications. Incidence, risk factors and potential predictors, and scoring systems for the development of these complications have been evaluated.

Keywords
- extracorporeal membrane oxygenation
- complications
- outcomes
- intervention

Introduction

Extracorporeal membrane oxygenation (ECMO) is a rapidly emerging advanced life support technique used to provide cardiac and respiratory support in cardiorespiratory failure refractory to other treatments. The first successful use of the technique in an adult was reported in 1972 (Hill et al),[1] which is followed soon after in 1974 by the first use in a pediatric patient.[2] Since then, the use of ECMO in children has been increasing with more than 55,000 pediatric patients[3] since 1990. The majority of patients comprise of neonates, accounting for >50% of reported cases.[3]

There have been notable recent advancements made in ECMO technology, though complications still remain prevalent and can lead to significant morbidity and mortality. With increasing popularity, there has been an influx in the number of studies concerning ECMO. However, there is still a paucity in the literature relating to complications, impacts of these factors, and methods to predict their development.

This review aims to discuss the complications that may arise from the use of ECMO in pediatric population postcardiotomy including their incidence, risk factors, and predictors of complications.

Use of Extracorporeal Membrane Oxygenation

ECMO should be considered in patients where conventional maneuvers and therapies have failed, reversible pathology is

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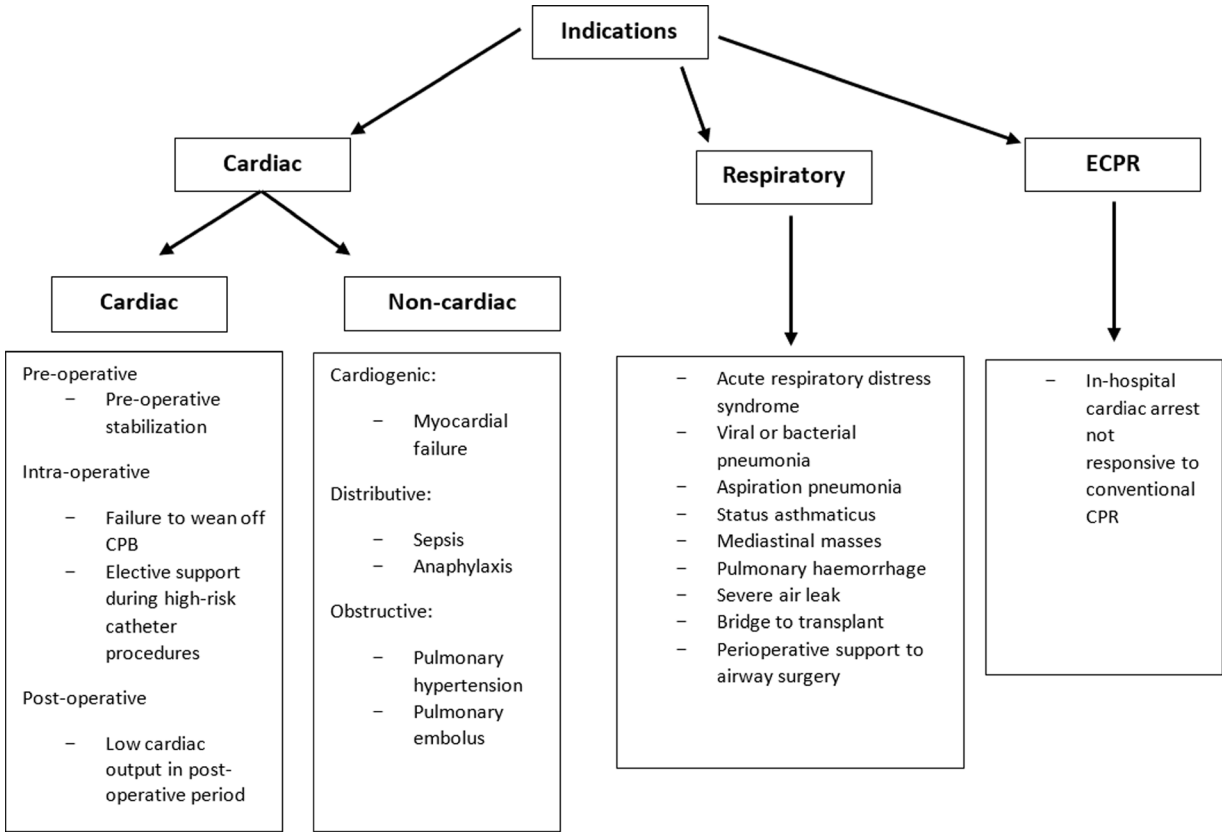

Fig. 1 Indications for extracorporeal membrane oxygenation in pediatric population.

suspected, and the benefits of the procedure outweigh the risks. Decision to initiate ECMO is made on a case-by-case basis, based on patient condition, expert senior advice, and institutional experience.

The indications for ECMO can be categorized as cardiac, respiratory, and extracorporeal cardiopulmonary resuscitation (ECPR). Cardiac indications are further subclassified into cardiac surgery: preoperative, intraoperative, and postoperative or noncardiac surgery. Within the pediatric population, we can classify relating to common indications for use in neonates (<30 days) and pediatric (>30 days to ≤ 18 years), summarized in ►**Fig. 1**.

The two main forms of ECMO are veno-venous (VV-ECMO) and veno-arterial (VA-ECMO). The indication for ECMO, among other factors, will determine the form utilized. The most common indication for VV-ECMO in the pediatric population is severe respiratory failure and for VA-ECMO is cardiac surgery.[4] Dalton et al[5] found that in a cohort of 2,036 pediatric patients, VA-ECMO was used for respiratory failure in 64% of patients and almost exclusively (>99%) in cardiac causes and ECPR.

The ECPR describes the process of initiating ECMO during active CPR in patients suffering refractory cardiac arrest. It is utilized when cardiac arrest is confirmed to be of cardiac origin. ECPR has become more widely available and is commonly utilized in both adult and pediatric populations.[6] ECMO implantation during cardiac arrest relatively common, comprising 36% of neonatal implantations and 13% of pediatric ECMO implantations, according to the 2016 Extracorporeal Life Support Organization (ELSO) report.[6] The successful initiation of ECPR in pediatric patients requires prompt access to state-of-the-art facilities, with the highest survival rates post-ECPR being identified in those who are postcardiotomy and already within a PICU or catheter laboratory setting.[7] ECPR has been proven to be an effective means of improving survival to hospital discharge postcardiopulmonary arrest in both pre- and postoperative cardiac pediatric patients. Rapid initiation is a key to success.[8]

Indications and Contraindications of ECMO Postcardiotomy

Extracorporeal membrane oxygenation is a well-established treatment for complication in the postoperative period for children with congenital heart disease (CHD). Indications for VA-ECMO in these patients include failure to wean off cardiopulmonary bypass, postoperative low cardiac output syndrome, thrombosis of shunt in univentricular circulations, intractable arrythmias, and cardiac arrest.[9] In addition to these, ECMO postcardiotomy can be used as a bridge therapy, where a patient is awaiting a cardiac transplantation.[10]

The contraindications of postcardiotomy ECMO are relative and involve decision-making on a case-by-case basis balancing the benefits and risks of the procedure. The relative contraindications to be considered include age and size of patient, preexisting conditions affecting patient quality of life, and conditions incompatible with life post-ECMO and futility.[11]

Complications

The ECMO complications can be divided into various categories including renal, cardiovascular, hematological, infection, neurological, and hepatic. A summary of studies assessing complications of ECMO in pediatric population postcardiotomy is shown in ►**Table 1**. The incidence and risk factors of various complications of ECMO in pediatric and adults are summarized in ►**Table 2**.

Renal

Acute kidney injury (AKI) is a commonplace in pediatric patients receiving ECMO therapy postcardiac surgery, with incidence in various studies[12–15] ranging from 30 to 90%. In-hospital mortality was also significantly increased in two of the four studies ranging from 77 to 83%. Typically, AKI occurs within 48 hours of initiating ECMO support.[16] It is known that there is an increased morbidity and mortality associated with a single episode of AKI. Hence, the focus should be aimed at prevention, early detection, and intervention in at risk patients.

Patients may already have significant renal injury prior to the initiation of ECMO due to infection, ischemia, or hemodynamic instability. Patients receiving ECMO therapy are shown to have worsening AKI with fluid overload[17] and increasing duration of therapy,[18,19] conferring a decreased survival benefit in pediatric cardiac patients. A review by Jenks et al[20] recommended fluid restriction, diuretics, peritoneal dialysis, and continuous renal replacement therapy as treatment options to assist in the management of AKI and fluid overload after ECMO.

Guo et al identified renal failure as a prominent feature in 54.5% ($n = 6$) of pediatric ECPR-assisted patients; of these six patients, four died.[21] Longer hypoperfusion times are associated with renal failure; however, it confers no association with other complications.[21] Another study identified non-survivors of pediatric ECPR therapy as being more likely to have received renal replacement therapy compared to survivors (35.5 vs. 10.8%).[22] Despite this, early initiation of ECPR is recommended to preserve optimal renal perfusion and reduce morbidity as a result of ECPR.[23]

Cardiovascular

Cardiovascular complications are a major cause of mortality in ECMO patients. In pediatric population, this predominantly comprises hypertension, myocardial dysfunction, arrhythmias, cardiac arrest, and thromboembolic events. Children with at least one cardiovascular complication have been shown to have reduced survival rates post-ECMO.[24]

VA-ECMO can give rise to specific complications such as cardiac thrombosis and cerebral or coronary hypoxia. This is due to the retrograde blood flow through the aorta when the femoral artery and vein are cannulated. Stasis can occur in the left ventricle leading to thrombus formation.[25] Fully oxygenated blood entering through the femoral artery will preferentially perfuse the lower extremities, whereas the heart will perfuse the coronary circulation, brain, and upper extremities. This leads to a greater proportion of oxygenated blood perfusing lower extremities compared to blood supplying the heart and brain.[26] For this reason, oxygen saturation should be monitored in the right upper extremity, in light of potential need for intervention.

Thrombotic events occurred in 34.8% of patients postcardiac surgery in one cohort.[27] Thromboembolic events may give rise to ischemic bowel, infarction of the kidney, or ischemia of the extremities, noted in 14% of cases in a 20-year long and retrospective review of pediatric ECMO patients.[28]

One study found hemolysis measured by plasma free hemoglobin (pFHb) occurred in 57.5% of patients and was prognostic for the development of thrombotic complications.[27] Another study found hemolysis to predict acute renal failure and mortality.[29] Thrombotic risk, among other complications, may be decreased with closer coagulation management of pediatric ECMO patients including 24-hour laboratory support.[30]

Thiagarajan et al[31] found the rate of thrombus formation did not differ between survivors and nonsurvivors of ECPR; however, rates of arrhythmias and CPR during ECMO support were higher in nonsurvivors.

Harlequin syndrome, also known as "North–South syndrome," is another known potential complication of VA-ECMO support with an incidence of 8.8%.[32] It describes oxygen-rich blood leaving the ECMO circuit reaching body parts supplied by the descending aorta and the distal aortic arch only to supply abdominal organs and legs. Inadequate oxygenation of blood via the lungs inhibits retrograde movement of oxygenated ECMO blood toward the aortic arch resulting in upper body hypoxia and cerebral hypoxemia.[33] Strategies to oppose combat the development of Harlequin syndrome include altering the cannulation site.[34,35]

Hematological

Bleeding in ECMO patients can manifest in various different formats, including blood loss from surgical sites, pulmonary hemorrhage, intracranial hemorrhage, gastrointestinal and genitourinary bleeding, and blood loss from laboratory sampling. Bleeding events were identified as occurring in 78.2% of one pediatric patient cohort.[27] Bleeding complications are associated with reduced survival in neonatal patients. However, this trend has not been identified in the pediatric population according to ELSO registry data.[5] Bleeding was identified as the most common complication in 54.5% of patients ($n = 6$).[21] The severity of which required re-exploration in this cohort. Of those patients who experienced bleeding as a complication, 83.3% ($n = 5$) died.[21] Key risk factors associated with hemorrhage include young age, pre-ECMO severity of illness, and increased surgical risk.[36] These risk factors may aid in identification of high-risk patients prior to initiation of ECMO therapy.

An important aspect of management in mechanical circulatory support such as ECMO is the balance of anticoagulation and bleeding. ELSO 2020 guidelines[37] recommend the use of unfractionated heparin (UFH) prior to cannulation as the primary method of anticoagulation in ECMO. However, a known complication of heparin is

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Table 1 Summary of studies assessing complications of extracorporeal membrane oxygenation in pediatric patients

Study (Year)	Study design	Cohort number	Population	Venoarterial ECMO (%)	Key outcome measures
Azizov et al (2019)[4]	Single-center retrospective observational cohort study	45	Pediatric patients (age < 18 y)	N/A	Prolonged duration on ECMO support might aggravate irreversible cardiopulmonary failure.
Dalton et al (2015)[5]	Multicenter retrospective observational cohort study	2,036	Pediatric patients (age < 19 y)	N/A	Survival to discharge was 56%. For every 10 hours of ECMO, the risk of complications and death increased.
Selewski et al (2017)[17]	Multicenter retrospective observational cohort study	756	Pediatric patients (age < 18 y) with ECMO for greater than or equal to 24 h	71.4	Fluid overload occurs commonly and is independently associated with adverse outcomes including increased mortality and increased duration of ECMO.
Fleming et al (2016)[18]	Multicenter retrospective observational cohort study	832	Pediatric patients (age < 18 y)	73.1	AKI present in 60–74% post-ECMO. AKI has a significant association with increased duration of ECMO support and increased adjusted odds of mortality at hospital discharge.
Kumar et al (2010)[19]	Single-center retrospective observational cohort study	58	Pediatric patients (age < 18 y)	N/A	AKI is associated with increased duration of ECMO. Longer duration of ECMO and AKI are associated with mortality.
Dalton et al (2017)[27]	Multicenter prospective observational cohort study	514	Pediatric patients (age < 19 y)	N/A	Bleeding events occurred in 70.2% of cohort. Thrombotic events occurred in 37.5% of patients.
Gupta et al (2012)[28]	Single-center retrospective observational cohort study	951	Pediatric patients (age < 18 y)	N/A	Thromboembolic events may give rise to ischemic bowel, infarction of the kidney, or ischemia of the extremities.
Hervey-Jumper et al (2011)[40]	Multicenter retrospective observational cohort study	Total: 33,100 Pediatric: 23,421	All ages, pediatric patients classified as <16	N/A	Intracranial hemorrhage occurred in 7.4% of children treated with ECMO. The incidence of ECMO associated ICH is higher both in children compared with adults and in neonates compared with older children.
Werho et al (2015)[36]	Retrospective review of the Extracorporeal Life Support Organization Registry (2002–2013)	21,845	Pediatric patients (age < 18 y)	79.2%	Key risk factors associated with hemorrhagic risk include young age, pre-ECMO severity of illness and increased surgical risk. Long ECMO duration, surgical exploration of the mediastinum prior to ECMO support, cannulation <24 h after surgery, and long bypass time of ≥282 min are risk factors for hemorrhage post-ECMO. Hemorrhagic complications are associated with a significant mortality risk.

Table 1 (*Continued*)

Study (Year)	Study design	Cohort number	Population	Venoarterial ECMO (%)	Key outcome measures
Abbasi et al (2008)[66]	Single-center retrospective observational cohort study	211	Neonates (<30 d)	N/A	Longer duration of ECMO and ECMO complications are more likely in those patients developing cholestasis.
Dohain et al (2019)[74]	Single-center retrospective observational cohort study	30	N/A	N/A	Patients with single ventricle physiology and repaired truncus arteriosus may benefit less from ECMO support and have higher mortality risk. Capillary leak on extracorporeal membrane oxygenation could be a risk of mortality in patients after pediatric cardiac surgery.
Baslaim et al (2006)[75]	Single-center retrospective observational cohort study	26	N/A	N/A	Patients who develop renal failure, stroke and DIC during ECMO support have a high mortality

Abbreviations: AKI, acute kidney injury; DIC, disseminated intravascular coagulation; ECMO, extracorporeal membrane oxygenation; ICH, intracranial hemorrhage.

heparin-induced thrombocytopenia (HIT), and thus, an alternative method of anticoagulation may be appropriate in some patients.

A review by Taylor et al[38] explored the use of bivalirudin as an alternative to heparin in mechanical circulatory support. Primarily, studies comparing the use of bivalirudin to heparin in pediatric population have been carried out based on need, where an alternative had been necessary, such as heparin resistance or a diagnosis of HIT. Advantages of bivalirudin over heparin seen in these studies included shorter time to therapeutic anticoagulation and lower number of significant bleeding events.[38] However, the literature on this topic is few and limited by their retrospective nature, and thus, further studies are required to determine safety, efficacy, and the most effective dosing strategies for use of bivalirudin in ECMO.

A study looking at ECPR-ECMO found bleeding requiring re-exploration in 44% in one cohort.[39] Severely low cardiac output for a prolonged period of time prior to cardiac arrest may lead to a significant metabolic acidosis and elevated lactate post-ECMO initiation. This is associated with a failure to wean off ECMO and increased mortality.[23,40] Patients may have benefited from better quality CPR or earlier initiation of ECPR. In addition, early correction of causes of poor perfusion and clearance of lactic acidosis may prevent severe organ injury.[23]

Infection

Nosocomial infections are common as a result of ECMO therapy. Studies have found sepsis to occur in 21 to 31% of children in postcardiotomy ECMO.[41,42] Another study by Lou et al[43] found culture-proven infection in 42% of their cohort. Nosocomial infections are associated with longer duration of ECMO therapy and increase mortality.[44]

Risk factors for nosocomial infections include long duration of ECMO therapy, bleeding complications on ECMO, and mechanical complications such as oxygenator failure or pump malfunction.[44] The use of prophylactic antimicrobial and antifungal therapy and surveillance cultures is suggested to be of value in reducing the incidence of nosocomial infection.[44] Lack of evidence and consensus has resulted in varying practices across centers regarding antimicrobial prophylaxis and infection surveillance.[45]

Rapid cannulation is crucial in improving outcomes in ECPR and reducing hypoxic injuries. However, with this, it becomes difficult to perform a clean procedure in a timely manner. Indwelling medical devices, such as those used in ECMO, central lines and arterial lines, can also act as a risk factor for the development of infection. Nosocomial infections were not associated with increased mortality in ECPR,[31] although one study found multidrug resistant pathogens to be associated with higher mortality.[46]

Inflammation

A potential complication of ECMO is the onset of an immediate complex inflammatory response described as similar to that seen in systemic inflammatory response syndrome when blood is exposed to the extracorporeal circulation.[47]

Table 2 Incidence of complications in pediatric extracorporeal membrane oxygenation and associated risk factors

Complication	Incidence in pediatrics (%)	Incidence in adult (%)	Associated risk factors
Acute kidney injury	8–78	4–68.8	Longer duration of ECMO[18,19]
Sepsis/infection/ bacteremia	9–56	7–58	Duration of ECMO, mechanical complications, hemorrhagic complications and use of VA- and central ECMO are associated with increasing risk of nosocomial infection.[19,45]
Liver dysfunction	5–28	3.9	Hemolysis, prolonged fasting, and total parenteral nutrition and diuretic use during ECMO[65]; associated with increased risk of liver dysfunction Longer duration of ECMO is associated with cholestasis.[64]
Bleeding	9–65	2.9–91	Heparin effect or overdose, coagulopathy, thrombocytopenia, platelet dysfunction, acquired von Willebrand syndrome, and hyperfibrinolysis.[82] Overall risk of hemorrhage is 5–10%, possibly greater among those requiring support for cardiac indications.[7] An analysis of the ELSO registry revealed age >1 y, long ECMO duration, surgical exploration of the mediastinum prior to ECMO support, cannulation <24 h after surgery, and long bypass time of ≥282 min as risk factors for hemorrhage.[36] Total amount and number of intravascular volume administration is linked to the development of intracranial hemorrhage during VA-ECMO treatment.[60]
Central nervous system complications	4–51	3.2–29	Overall risk of acute seizures is 5–10%, possibly greater among those requiring support for cardiac indications.[7] Lower gestational age, birth weight <3 kg, prior CPR or those with sepsis, acidosis, coagulopathy or an inotropic requirement, neonates requiring VA-ECMO.[7] Metabolic acidosis (arterial blood pH < 7.2) pre-ECMO and during ECMO.[35]

Abbreviations: CPR, cardiopulmonary resuscitation; ECMO, extracorporeal membrane oxygenation; ELSO, extracorporeal life support organization; VA, venoarterial.

Activation of the contact and complement systems cause massive cytokine release. This response is clinically concerning as it can potentially lead to endothelial injury and end-organ dysfunction.[48] A number of technologies have been proposed to combat this inflammatory response including cytokine adsorption.[49] Combined use of ECMO and adsorption technologies has been used successfully in pediatric populations to reduce inflammatory markers and prevent multiorgan failure.[50]

COVID-19 Pandemic

ECMO has been utilized extensively throughout the COVID-19 pandemic in both adult and pediatric populations. The ELSO registry as of May 10, 2021 indicates that 6,662 confirmed cases of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) patients had been supported by ECMO.[51] There has been much discrepancy in survival outcomes associated with ECMO use globally in patients with COVID-19; however, this has been attributed to many factors including differences in patient cohorts, virulence variability, and preexisting morbidity.[52] The use of ECMO in management of patients with COVID-19 has not been associated with any increased risk of mortality compared to patients with acute hypoxemic respiratory failure treated without ECMO.[53] While pediatric populations have generally experienced reduced disease severity associated with SARS-CoV-2 infection, there have been cases of multisystem inflammatory syndrome in children (MIS-C) requiring pediatric intensive care admission.[54,55] MIS-C is defined by the Centers for Disease Control and Prevention as presenting in individuals less than 21 years of age with fever, laboratory evidence of inflammation, and clinically severe illness requiring hospitalization with organ damage in more than two organs. These same individuals are required to have had current or recent SARS-CoV-2 infection within 4 weeks of symptom onset.[56] ECMO support has successfully been utilized in the management of MIS-C in pediatric populations.[57]

Neurological

Neurological complications include intracerebral hemorrhage, seizures, infarction, and brain death; which can have serious lasting implications on patient morbidity. A study[58] looking at 1,602 patients undergoing surgery for CHD found that stroke or intracranial hemorrhage occurred in 14% of children undergoing ECMO. Independent predictors of these neurological events included weight under 3 kg, pre-ECMO pH, and CPR prior to initiation of ECMO.

A study by Chow et al[59] found 22% of their cohort had short-term neurological sequalae while hospitalized post-ECMO, of which 40% had seizures. Another study[60] found the rate of seizures to be 7% in both neonates and pediatrics, while ICH was higher in neonates, 11.1% compared to 4.9%. Neurological impairment resulting in seizures and status

epilepticus have been identified as having a negative impact on survival of pediatric patients.[4] Neonates treated with ECMO who have seizures have increased cognitive delay and decreased IQ compared to those without.[61] Despite this, patients treated with ECMO are not associated with increased risk of neurological disease when compared to patients treated without ECMO.[60]

The initiation of ECPR in pediatric patients is associated with increased neurological morbidity compared to pediatric patients receiving ECMO therapy only. The ELSO database identified 22% of neonates and children who received ECPR as experiencing an acute neurological injury.[7] Efforts to decrease the incidence of neurological injury following ECPR may include therapeutic hypothermia to increase the likelihood of recovery, and the routine use of head ultrasound examinations to identify early bleeding.[23]

Hepatic

Patients on ECMO are often in a compromised hemodynamic condition. Consequently, they are at risk of hepatic ischemia resulting in hepatic dysfunction and failure.[62] Hepatic dysfunction is associated with poor prognosis in critically ill patients, particularly those with cardiac failure.[63] Evaluation is by elevation in bilirubin, alanine aminotransferase, alkaline phosphatase, and γ-glutamyl transferase.

The 2019 international summary by the ELSO reported an incidence of 4.7% of hyperbilirubinemia in the pediatric population post-ECMO.[64] Hyperbilirubinemia has been shown to be increased in nonsurvivors post-ERCP.[31]

Hyperbilirubinemia and biliary calculi may develop as a result of hemolysis, prolonged fasting and total parenteral nutrition (TPN), and the use of diuretic therapy during ECMO.[65] Direct hyperbilirubinemia and raised hepatic enzymes usually resolve after ECMO support withdrawal.[66,67] Plasma exchange transfusion may be used to rapidly reduce bilirubin levels.[68] Fluids and electrolytes (potassium, magnesium, phosphorus, and ionized calcium) should also be carefully monitored.[68]

The Role of Ultrasound Imaging in Postcardiotomy ECMO

Echocardiography plays a fundamental role in predicting complications and improving outcomes in ECMO postcardiotomy, providing information on patient selection, guiding cannula insertion and placement, detecting complications, and aiding the weaning and decannulation process.[69] The use of echocardiography can be divided broadly into three categories: pre-ECMO, during ECMO, and post-ECMO (i.e., weaning off ECMO). ELSO have published guidelines on the use of echocardiography for ECMO.[70]

Pre-ECMO echocardiography is crucial in understanding the patient's underlying cardiac anatomy, the patient's hemodynamic condition, and to determine the best ECMO modality.[69] During cannulation, venous cannula size plays an important role in determining blood flow in the ECMO circuit, hence measuring diameter via echocardiogram aids selection of the largest possible venous cannula size.[69] Although transthoracic echocardiography is firstline for imaging pre-ECMO,[70] transesophageal echocardiography may be required where there is not sufficient spatial resolution.[71]

Routine echocardiography should be performed on all patients during ECMO to monitor cardiac function and screen for complications. There should be routine monitoring of cannula position to identify those at increased risk of decannulation. Complications such as bleeding are more common due to systemic anticoagulation utilized in ECMO and may lead to effusions which can be identified on imaging.[69] Cannula thrombus formation is also a known complication during ECMO.[72]

The decision of when to wean off ECMO should be a clinical decision based on comprehensive assessment of the patient. The findings of echocardiography play an important role in helping the decision-making process, especially in VA-ECMO. Aissaoui et al[73] showed that patients more hemodynamically stable during ECMO support reduction had more successful wean of ECMO. They recommended that successful weaning in VA-ECMO should be expected when LV ejection fraction, lateral E/Ea ratio, velocity time integral, lateral strain, and strain rate increase while gradually decreasing the level of mechanical support.

Risk Factors and Predictors of Complications

Time on ECMO is a widely agreed risk factor for the development of complications and poor outcomes post-ECMO. One study found for every 10 hours of ECMO, the risk of complications and death increased (relative risk [RR]: 1.005; 95% confidence interval [CI]: 1.003–1.007; RR: 1.005; 95% CI: 1.003–1.007, respectively).[5]

Reversibility of the cause of the cardiorespiratory failure requiring ECMO is an important factor to consider when deciding to initiate ECMO support. A study performed in 2014 revealed that newborn infants with reversible causes of cardiac arrest requiring ECPR, such as respiratory failure and cardiac disease, had significantly better odds of survival with reduced incidence of multisystem organ failure.[31]

Predictors of mortality and risk factors for complications may be used to design patient selection criteria for ECMO and guide discontinuation. A study performed in 2006 revealed that higher mortality is associated with the development of renal failure, stroke, and disseminated intravascular coagulopathy during ECMO support. It also concluded that those with single ventricle physiology and repaired truncus arteriosus may benefit less from ECMO support and have higher mortality risk.[74] This is supported by another study, where patients requiring ECMO after pediatric cardiac surgery were less likely to survive to hospital discharge, if the surgical procedure had been single ventricle palliation compared to biventricular repair (16.66 vs. 55.55%). Similarly, patients with higher serum creatinine and alanine aminotransferase enzymes levels before commencing ECMO tended to have worse survival rates ($p = 0.012$ and 0.03, respectively).[75]

Another study revealed that arterial blood pH less than 7.2 during ECMO was associated with increased risk of neurological injury and mortality (odds ratio: 2.23, 95% CI:

1.23–4.06). Moreover, presence of metabolic acidosis pre-ECMO and during ECMO also increased mortality rate, as this suggests insufficient circulatory support. However, 12% of the patients who survived after ECMO also had pH <7.2. Therefore, it could not be used as a criterion to withhold ECMO support but should be considered carefully in these patients.[31]

Factors such as elevated levels of lactate during the first 72 hours, high inotrope score when initiating ECMO and ECMO support duration of more than 3 days can be used to determine the discontinuation of ECMO support.[75]

Currently, there are no tools developed to predict mortality in children undergoing ECMO postcardiotomy. A number of risk stratification tools to predict mortality for patients receiving respiratory ECMO support have been developed in recent years. These can be divided into neonatal and pediatric tools. A summary of predictors of mortality and scoring systems is shown in ►**Table 3**.

The neonatal prediction tools include the Pittsburgh index for pre-ECMO risk (PIPER)[76] and the neonatal risk estimate score for children using extracorporeal respiratory support (neo-RESCUERS),[77] which both utilized data from the ELSO registry, a registry of 298 centers. The PIPER tool predicts mortality based on seven pre-ECMO variables and revealed a 15% increase in mortality per PIPER quartile. This study also went on to add on-ECMO complications and length of time on ECMO to produce a PIPER+ score, which had increased sensitivity and specificity for hospital mortality in these patients. A limitation of the PIPER tool is that the dataset this was derived from only included neonates on VA-ECMO, and therefore, this cannot be applied to those using VV-ECMO. The neo-RESCUERS tool utilized 10 variables to produce a pre-ECMO risk of in-hospital mortality in neonates and was validated with an internal cohort.

The Pediatric Risk Estimate Score for Children Using Extracorporeal Respiratory Support (PedRESCUERS)[78] and Pulmonary Rescue with Extracorporeal Membrane Oxygenation Prediction (P-PREP)[79] Score are both tools predicting mortality in pediatric ECMO patients also derived from the ELSO Registry. Both tools only include pre-ECMO variables and although the PedRESCUERS was internally validated, the P-PREP score was the only tool to be validated with an external cohort aiding its generalizability.

These tools allow risk stratification of patients, which is particularly important when dealing with high cost, high-risk therapies such as ECMO that also pose technical and ethical issues. They are also helpful in discussions with parents regarding the risks and benefits of ECMO therapy prior to initiation.

There are a number of limitations applying to all five prediction tools previously mentioned. Firstly, these tools have all been developed for respiratory failure ECMO and therefore cannot be applied to cases, where ECMO has been indicated for cardiac causes and ECPR. Second, all of the

Table 3 Predictors of mortality postextracorporeal membrane oxygenation and scoring systems

Study (Year)	Outcome
Dalton et al (2015)[5]	The duration of ECMO; risk of death and complications increases every 10 hourly.
Thiagarajan et al (2007)[35]	For patients on ECPR, those with irreversible causes of the cardiorespiratory failure had worse odds of survival. Arterial blood pH less than 7.2 and metabolic acidosis prior to and during ECMO.
Dohain et al (2019)[74]	The development of renal failure, stroke, disseminated intravascular coagulopathy during ECMO. Single ventricular physiology and repaired truncus arteriosus are associated with higher mortality risk as they may benefit less from the ECMO support.
Baslaim et al (2006)[75]	Single ventricle palliation has worse survival rates compared to biventricular repair for pediatric patients requiring ECMO during surgery.
Maul et al (2016)[76]	Risk stratification tool "PIPER": The Pittsburgh index for pre-ECMO risk. The tool acts as a pre-ECMO risk index to predict mortality in neonates receiving VA-ECMO for respiratory failure. Each PIPER quartile linked to a 15% increase in mortality.
Barbaro et al (2016)[77]	Risk stratification tool "neo-RESUERS": The neonatal risk estimate score for children using extracorporeal respiratory support. A risk adjustment score to predict mortality for neonates receiving ECMO in respiratory failure.
Barbaro et al (2016)[78]	Risk stratification tool "PedRESCUERS": pediatric risk estimate score for children using extracorporeal respiratory support. risk-adjustment tool predicting mortality in children (29 d–18 y) receiving respiratory ECMO support.
Bailly et al (2017)[79]	Risk stratification tool "P-PREP": pulmonary rescue with extracorporeal membrane oxygenation prediction an externally validated tool for predicting in-hospital mortality among children (7 d–18 y) with respiratory failure receiving ECMO support.

Abbreviations: CDH, congenital diaphragmatic hernia; ECPR, extracorporeal cardiopulmonary resuscitation; ECMO, extracorporeal membrane oxygenation; VA, venoarterial.

aforementioned tools have been developed by using ELSO data and therefore may not generalize to non-ELSO ECMO centers. Furthermore, variables used in these prediction tools were limited to those in the ELSO dataset, and hence, missed variables such as severity of illness, markers of renal function (e.g., urine output and creatinine), and neurological status (e.g. pupil response and seizures). Finally, these tools do not take into account the influence of ECMO center characteristics such as varying infrastructure and ability to deliver timely interventions and advanced treatments to high-risk patients. Future work is needed to incorporate a larger population, specifically postcardiotomy and ECPR, and to explore variables not already used. This will allow development of more accurate prediction tools in pediatric and neonatal ECMO.

Summary

Despite great advancement in ECMO technology, with positive outcomes in patients who are refractory to conventional therapies, there are still high rates of complications which can have significant effects on patients' short- and long-term morbidity and mortality. The majority of complications of ECMO following cardiac surgery are renal, infective, and bleeding related. Other causes include thromboembolic, neurological, and hepatic complications. Risk factors for the development of complications include longer duration on ECMO, cardiac indications for procedure, and hypocapnia. There is a lack of scoring systems in the literature to predict mortality following ECMO in this patient population. Further work is needed to help predict and minimize complications of this procedure in pediatric population.

Conclusion

ECMO is an advanced life support technique that is used to provide support in cardiorespiratory failure refractory to other treatments. Complications associated with its use in pediatric population postcardiotomy is common, include renal, cardiovascular, hematological, infection, neurological, and hepatic causes, and associated with morbidity and mortality. However, there are methods available to reduce their occurrence. Risk stratification tools such as PIPER, neoRESCUERS, pre-ECMO, and on-ECMO have been developed to predict mortality for pediatric patients on ECMO based on the various risk factors for the development of these complications. Further work is needed in order to earlier predict complications of ECMO in pediatric population and optimize outcomes in these patients.

Conflict of Interest
None declared.

References

1 Hill JD, O'Brien TG, Murray JJ, et al. Prolonged extracorporeal oxygenation for acute post-traumatic respiratory failure (shock-lung syndrome). Use of the Bramson membrane lung. N Engl J Med 1972;286(12):629–634
2 Bartlett RH, Gazzaniga AB, Fong SW, Burns NE. Prolonged extracorporeal cardiopulmonary support in man. J Thorac Cardiovasc Surg 1974;68(06):918–932
3 Thiagarajan RR, Barbaro RP, Rycus PT, et al; ELSO member centers. Extracorporeal life support organization registry international report 2016. ASAIO J 2017;63(01):60–67
4 Azizov F, Merkle J, Fatullayev J, et al. Outcomes and factors associated with early mortality in pediatric and neonatal patients requiring extracorporeal membrane oxygenation for heart and lung failure. J Thorac Dis 2019;11(Suppl 6):S871–S888
5 Dalton HJ, Garcia-Filion P, Holubkov R, et al; Eunice Kennedy Shriver National Institute of Child Health and Human Development Collaborative Pediatric Critical Care Research Network. Association of bleeding and thrombosis with outcome in extracorporeal life support. Pediatr Crit Care Med 2015;16(02): 167–174
6 Barbaro RP, Paden ML, Guner YS, et al; ELSO member centers. Pediatric extracorporeal life support organization registry international report 2016. ASAIO J 2017;63(04):456–463
7 Robinson S, Peek G. The role of ECMO in neonatal & pediatric patients. Pediatr Child Health 2015;25(05):222–227
8 Wolf MJ, Kanter KR, Kirshbom PM, Kogon BE, Wagoner SF. Extracorporeal cardiopulmonary resuscitation for pediatric cardiac patients. Ann Thorac Surg 2012;94(03):874–879, discussion 879–880
9 Cooper DS, Jacobs JP, Moore L, et al. Cardiac extracorporeal life support: state of the art in 2007. Cardiol Young 2007;17 (Suppl 2):104–115
10 Almond CS, Singh TP, Gauvreau K, et al. Extracorporeal membrane oxygenation for bridge to heart transplantation among children in the United States: analysis of data from the Organ Procurement and Transplant Network and Extracorporeal Life Support Organization Registry. Circulation 2011;123(25):2975–2984
11 General Guidelines for all ECLS Cases August, 2017 [Internet]. 2017 [cited 12 May 2021]. Accessed 2021 at: https://www.elso.org/Portals/0/ELSO%20Guidelines%20General%20All%20ECLS%20Version%201_4.pdf
12 Kolovos NS, Bratton SL, Moler FW, et al. Outcome of pediatric patients treated with extracorporeal life support after cardiac surgery. Ann Thorac Surg 2003;76(05):1435–1441, discussion 1441–1442
13 Gbadegesin R, Zhao S, Charpie J, Brophy PD, Smoyer WE, Lin JJ. Significance of hemolysis on extracorporeal life support after cardiac surgery in children. Pediatr Nephrol 2009;24(03): 589–595
14 Ricci Z, Morelli S, Favia I, Garisto C, Brancaccio G, Picardo S. Neutrophil gelatinase-associated lipocalin levels during extracorporeal membrane oxygenation in critically ill children with congenital heart disease: preliminary experience. Pediatr Crit Care Med 2012;13(01):e51–e54
15 Elella RA, Habib E, Mokrusova P, et al. Incidence and outcome of acute kidney injury by the pRIFLE criteria for children receiving extracorporeal membrane oxygenation after heart surgery. Ann Saudi Med 2017;37(03):201–206
16 Cleto-Yamane TL, Gomes CLR, Suassuna JHR, Nogueira PK. Acute kidney injury epidemiology in pediatrics. J Bras Nefrol 2019;41 (02):275–283
17 Selewski DT, Askenazi DJ, Bridges BC, et al. The impact of fluid overload on outcomes in children treated with extracorporeal membrane oxygenation: a multicenter retrospective cohort study. Pediatr Crit Care Med 2017;18(12):1126–1135
18 Fleming GM, Sahay R, Zappitelli M, et al. The incidence of acute kidney injury and its effect on neonatal and pediatric extracorporeal membrane oxygenation outcomes: a multicenter report from the kidney intervention during extracorporeal membrane oxygenation study group. Pediatr Crit Care Med 2016;17(12): 1157–1169

19 Kumar TKS, Zurakowski D, Dalton H, et al. Extracorporeal membrane oxygenation in postcardiotomy patients: factors influencing outcome. J Thorac Cardiovasc Surg 2010;140(02):330–336.e2

20 Jenks C, Raman L, Dhar A. Review of acute kidney injury and continuous renal replacement therapy in pediatric extracorporeal membrane oxygenation. Indian J Thorac Cardiovasc Surg 2021; 37(Suppl 2):254–260

21 Guo Z, Yang Y, Zhang W, et al. Extracorporeal cardiopulmonary resuscitation in children after open heart surgery. Artif Organs 2019;43(07):633–640

22 Shakoor A, Pedroso FE, Jacobs SE, et al. Extracorporeal cardiopulmonary resuscitation (ECPR) in infants and children: a single-center retrospective study. World J Pediatr Congenit Heart Surg 2019;10(05):582–589

23 Alsoufi B, Awan A, Manlhiot C, et al. Results of rapid-response extracorporeal cardiopulmonary resuscitation in children with refractory cardiac arrest following cardiac surgery. Eur J Cardiothorac Surg 2014;45(02):268–275

24 Becker JA, Short BL, Martin GR. Cardiovascular complications adversely affect survival during extracorporeal membrane oxygenation. Crit Care Med 1998;26(09):1582–1586

25 Slottosch I, Liakopoulos O, Kuhn E, et al. Outcomes after peripheral extracorporeal membrane oxygenation therapy for postcardiotomy cardiogenic shock: a single-center experience. J Surg Res 2013;181(02):e47–e55

26 Lo Coco V, Lorusso R, Raffa GM, et al. Clinical complications during veno-arterial extracorporeal membrane oxigenation in post-cardiotomy and non post-cardiotomy shock: still the achille's heel. J Thorac Dis 2018;10(12):6993–7004

27 Dalton HJ, Reeder R, Garcia-Filion P, et al; Eunice Kennedy Shriver National Institute of Child Health and Human Development Collaborative Pediatric Critical Care Research Network. Factors associated with bleeding and thrombosis in children receiving extracorporeal membrane oxygenation. Am J Respir Crit Care Med 2017;196(06):762–771

28 Gupta P, McDonald R, Chipman CW, et al. 20-year experience of prolonged extracorporeal membrane oxygenation in critically ill children with cardiac or pulmonary failure. Ann Thorac Surg 2012;93(05):1584–1590

29 Dufour N, Radjou A, Thuong M. Hemolysis and plasma free hemoglobin during extracorporeal membrane oxygenation support: from clinical implications to laboratory details. ASAIO J 2020;66(03):239–246

30 Hensch LA, Hui SR, Teruya J. Coagulation and bleeding management in pediatric extracorporeal membrane oxygenation: clinical scenarios and review. Front Med (Lausanne) 2019;5:361

31 Rupprecht L, Lunz D, Philipp A, Lubnow M, Schmid C. Pitfalls in percutaneous ECMO cannulation. Heart Lung Vessel 2015;7(04): 320–326

32 Rao P, Khalpey Z, Smith R, Burkhoff D, Kociol RD. Venoarterial extracorporeal membrane oxygenation for cardiogenic shock and cardiac arrest. Circ Heart Fail 2018;11(09):e004905

33 Al Hanshi S, Al Othmani F. A case study of Harlequin syndrome in VA-ECMO. Qatar Med J 2017;2017(01):39

34 Honore PM, Barreto Gutierrez L, Kugener L, et al. Risk of harlequin syndrome during bi-femoral peripheral VA-ECMO: should we pay more attention to the watershed or try to change the venous cannulation site? Crit Care 2020;24(01):450

35 Thiagarajan RR, Laussen PC, Rycus PT, Bartlett RH, Bratton SL. Extracorporeal membrane oxygenation to aid cardiopulmonary resuscitation in infants and children. Circulation 2007;116(15): 1693–1700

36 Werho DK, Pasquali SK, Yu S, et al; Extracorporeal Life Support Organization Member Centers. Hemorrhagic complications in pediatric cardiac patients on extracorporeal membrane oxygenation: an analysis of the Extracorporeal Life Support Organization Registry. Pediatr Crit Care Med 2015;16(03):276–288

37 Maratta C, Potera RM, van Leeuwen G, Castillo Moya A, Raman L, Annich GM. Extracorporeal life support organization (ELSO): 2020 pediatric respiratory ELSO guideline. ASAIO J 2020;66 (09):975–979

38 Taylor T, Campbell CT, Kelly B. A review of bivalirudin for pediatric and adult mechanical circulatory support. Am J Cardiovasc Drugs 2020;10:1–15

39 Santiago-Lozano MJ, Barquín-Conde ML, Fuentes-Moreno L, et al. Infectious complications in paediatric patients treated with extracorporeal membrane oxygenation. Enferm Infecc Microbiol Clin (Engl Ed) 2018;36(09):563–567

40 Hervey-Jumper SL, Annich GM, Yancon AR, Garton HJL, Muraszko KM, Maher CO. Neurological complications of extracorporeal membrane oxygenation in children. J Neurosurg Pediatr 2011;7 (04):338–344

41 Alsoufi B, Awan A, Manlhiot C, et al. Does single ventricle physiology affect survival of children requiring extracorporeal membrane oxygenation support following cardiac surgery? World J Pediatr Congenit Heart Surg 2014;5(01):7–15

42 El Mahrouk AF, Ismail MF, Hamouda T, et al. Extracorporeal membrane oxygenation in postcardiotomy pediatric patients-15 years of experience outside Europe and North America. Thorac Cardiovasc Surg2019;67(01):28–36

43 Lou S, MacLaren G, Clark J, et al. Safety of therapeutic hypothermia in children on veno-arterial extracorporeal membrane oxygenation after cardiac surgery. Cardiol Young 2015;25(07): 1367–1373

44 MacLaren G, Schlapbach LJ, Aiken AM. Nosocomial infections during extracorporeal membrane oxygenation in neonatal, pediatric, and adult patients: a comprehensive narrative review. Pediatr Crit Care Med 2020;21(03):283–290

45 Kao LS, Fleming GM, Escamilla RJ, Lew DF, Lally KP. Antimicrobial prophylaxis and infection surveillance in extracorporeal membrane oxygenation patients: a multi-institutional survey of practice patterns. ASAIO J 2011;57(03):231–238

46 Ko RE, Huh K, Kim DH, et al. Nosocomial infections in in-hospital cardiac arrest patients who undergo extracorporeal cardiopulmonary resuscitation. PLoS One 2020;15(12):e0243838

47 Millar JE, Fanning JP, McDonald CI, McAuley DF, Fraser JF. The inflammatory response to extracorporeal membrane oxygenation (ECMO): a review of the pathophysiology. Crit Care 2016; 20(01):387

48 Chen Q, Yu W, Shi J, et al. The effect of venovenous extra-corporeal membrane oxygenation (ECMO) therapy on immune inflammatory response of cerebral tissues in porcine model. J Cardiothorac Surg 2013;8(01):186

49 Datzmann T, Träger K. Extracorporeal membrane oxygenation and cytokine adsorption. J Thorac Dis 2018;10(Suppl 5):S653–S660

50 Rybalko A, Pytal A, Kaabak M, Rappoport N, Bidzhiev A, Lastovka V. Case report: successful use of extracorporeal therapies after ECMO resuscitation in a pediatric kidney transplant recipient. Front Pediatr 2020;8:593123

51 Extracorporeal Life Support Organization - ECMO and ECLS > COVID-19 [Internet]. Elso.org 2021 [cited 12 May 2021]. Accessed 2021 at: https://www.elso.org/COVID19.aspx

52 Huang S, Zhao S, Luo H, et al. The role of extracorporeal membrane oxygenation in critically ill patients with COVID-19: a narrative review. BMC Pulm Med 2021;21(01):116

53 Barbaro RP, MacLaren G, Boonstra PS, et al; Extracorporeal Life Support Organization. Extracorporeal membrane oxygenation support in COVID-19: an international cohort study of the Extracorporeal Life Support Organization registry. Lancet 2020;396 (10257):1071–1078

54 Riphagen S, Gomez X, Gonzalez-Martinez C, Wilkinson N, Theocharis P. Hyperinflammatory shock in children during COVID-19 pandemic. Lancet 2020;395(10237):1607–1608

55 Belhadjer Z, Méot M, Bajolle F, et al. Acute heart failure in multisystem inflammatory syndrome in children in the context

of global SARS-CoV-2 pandemic. Circulation 2020;142(05): 429–436
56 Archive HAN. - 00432 | Health Alert Network (HAN) [Internet] Emergency.cdc.gov. 2021 [cited 12 May 2021]. Accessed 2021 at: https://emergency.cdc.gov/han/2020/han00432.asp
57 Kaushik S, Ahluwalia N, Gangadharan S, et al. ECMO support in SARS-CoV2 multisystem inflammatory syndrome in children in a child. Perfusion 2020:267659120954386
58 Polito A, Barrett CS, Rycus PT, Favia I, Cogo PE, Thiagarajan RR. Neurologic injury in neonates with congenital heart disease during extracorporeal membrane oxygenation: an analysis of extracorporeal life support organization registry data. ASAIO J 2015;61(01):43–48
59 Chow G, Koirala B, Armstrong D, et al. Predictors of mortality and neurological morbidity in children undergoing extracorporeal life support for cardiac disease. Eur J Cardiothorac Surg 2004;26(01): 38–43
60 Mehta A, Ibsen LM. Neurologic complications and neurodevelopmental outcome with extracorporeal life support. World J Crit Care Med 2013;2(04):40–47
61 Snookes SH, Gunn JK, Eldridge BJ, et al. A systematic review of motor and cognitive outcomes after early surgery for congenital heart disease. Pediatrics 2010;125(04):e818–e827
62 Roth C, Schrutka L, Binder C, et al. Liver function predicts survival in patients undergoing extracorporeal membrane oxygenation following cardiovascular surgery. Crit Care 2016;20(01):57
63 Kramer L, Jordan B, Druml W, Bauer P, Metnitz PGHAustrian Epidemiologic Study on Intensive Care, ASDI Study Group. Incidence and prognosis of early hepatic dysfunction in critically ill patients–a prospective multicenter study. Crit Care Med 2007;35 (04):1099–1104
64 ELSO. ECLS Registry Report International Summary July, 2019 [Internet] 2019 [cited 2021 Jan 14]. Accessed 2021 at: http://www.elso.org/Portals/0/Files/Reports/2019/International%20Summary%20July%202019.pdf
65 Makdisi G, Wang IW. Extra corporeal membrane oxygenation (ECMO) review of a lifesaving technology. J Thorac Dis 2015;7 (07):E166–E176
66 Abbasi S, Stewart DL, Radmacher P, Adamkin D. Natural course of cholestasis in neonates on extracorporeal membrane oxygenation (ECMO): 10-year experience at a single institution. ASAIO J 2008;54(04):436–438
67 Walsh-Sukys MC, Cornell DJ, Stork EK. The natural history of direct hyperbilirubinemia associated with extracorporeal membrane oxygenation. Am J Dis Child 1992;146(10):1176–1180
68 Shakoor A, Streltsova S, Brewer MP, et al. Continuous double volume exchange transfusion is a safe treatment for ECMO-induced hemolysis. J Pediatr Surg Case Rep 2018;32:75–78
69 Bautista-Rodriguez C, Sanchez-de-Toledo J, Da Cruz EM. The Role of echocardiography in neonates and pediatric patients on extracorporeal membrane oxygenation. Front Pediatr 2018;6:297
70 Extracorporeal Life Support Organization. ELSO Guidelines. Accessed 2021 at: https://www.elso.org/Portals/0/Files/elso_Ultrasoundguideance_ecmogeneral_guidelines_May2015.pdf
71 Dolch ME, Frey L, Buerkle MA, Weig T, Wassilowsky D, Irlbeck M. Transesophageal echocardiography-guided technique for extracorporeal membrane oxygenation dual-lumen catheter placement. ASAIO J 2011;57(04):341–343
72 Ranasinghe AM, Peek GJ, Roberts N, et al. The use of transesophageal echocardiography to demonstrate obstruction of venous drainage cannula during ECMO. ASAIO J 2004;50(06): 619–620
73 Aissaoui N, Guerot E, Combes A, et al. Two-dimensional strain rate and Doppler tissue myocardial velocities: analysis by echocardiography of hemodynamic and functional changes of the failed left ventricle during different degrees of extracorporeal life support. J Am Soc Echocardiogr 2012;25(06):632–640
74 Dohain AM, Abdelmohsen G, Elassal AA, ElMahrouk AF, Al-Radi OO. Factors affecting the outcome of extracorporeal membrane oxygenation following pediatric cardiac surgery. Cardiol Young 2019;29(12):1501–1509
75 Baslaim G, Bashore J, Al-Malki F, Jamjoom A. Can the outcome of pediatric extracorporeal membrane oxygenation after cardiac surgery be predicted? Ann Thorac Cardiovasc Surg 2006;12 (01):21–27
76 Maul TM, Kuch BA, Wearden PD. Development of risk indices for neonatal respiratory extracorporeal membrane oxygenation. ASAIO J 2016;62(05):584–590
77 Barbaro RP, Bartlett RH, Chapman RL, et al. Development and validation of the neonatal risk estimate score for children using extracorporeal respiratory support. J Pediatr 2016;173:56–61.e3
78 Barbaro RP, Boonstra PS, Paden ML, et al. Development and validation of the pediatric risk estimate score for children using extracorporeal respiratory support (Ped-RESCUERS). Intensive Care Med 2016;42(05):879–888
79 Bailly DK, Reeder RW, Zabrocki LA, et al; Extracorporeal Life Support Organization Member Centers. Development and validation of a score to predict mortality in children undergoing extracorporeal membrane oxygenation for respiratory failure: pediatric pulmonary rescue with extracorporeal membrane oxygenation prediction score. Crit Care Med 2017;45(01):e58–e66
80 Lorusso R, Raffa GM, Alenizy K, et al. Structured review of post-cardiotomy extracorporeal membrane oxygenation: part 1-Adult patients. J Heart Lung Transplant 2019;38(11):1125–1143
81 Lorusso R, Raffa GM, Kowalewski M, et al. Structured review of post-cardiotomy extracorporeal membrane oxygenation: Part 2-pediatric patients. J Heart Lung Transplant 2019;38(11): 1144–1161
82 Thomas J, Kostousov V, Teruya J. Bleeding and thrombotic complications in the use of extracorporeal membrane oxygenation. Semin Thromb Hemost 2018;44(01):20–29