Indian Journal of Pediatrics (May 2023) 90(5):501–509
https://doi.org/10.1007/s12098-023-04545-5

REVIEW ARTICLE

Advances in Extracorporeal Support Technologies in Critically Ill Children

Mahsun Yuerek[1] · Benjamin W. Kozyak[1] · Venkat R. Shankar[1]

Received: 16 December 2022 / Accepted: 28 February 2023 / Published online: 29 March 2023

Abstract
The field of pediatric heart failure is evolving, and the patient population is growing as survival after complex congenital heart surgeries is improving. Mechanical circulatory support and extracorporeal respiratory support in critically ill children has progressed to a mainstay rescue modality in pediatric intensive care medicine. The need for mechanical circulatory support is growing, since the number of organ donors does not meet the necessity. This article aims to review the current state of available mechanical circulatory and respiratory support systems in acute care pediatrics, with an emphasis on the literature discussing the challenges associated with these complex support modalities.

Keywords Ventricular assist device · Extracorporeal membrane oxygenation · Mechanical circulatory support · Heart failure · Intensive care medicine

Introduction

Improvement in specialized medicine and centralized care has led to higher survival rates in children with complex congenital heart disease, pulmonary hypertension, and acute cardiorespiratory failure. Extracorporeal support in critically ill children has developed to be a mainstay rescue modality in pediatric intensive care medicine.

For patients with acute respiratory and circulatory failure, venoarterial extracorporeal membrane oxygenation (VA-ECMO) is the modality commonly used to restore circulation and oxygen delivery. VA-ECMO can be implemented in neonates and children, and even sometimes in premature neonates, making this extracorporeal support modality available for most pediatric patients. In patients with expected longer recovery time, severe myocardial or respiratory dysfunction requiring longer duration of extracorporeal support, other support modalities may be required, since VA-ECMO has limitations with longer support times and appears to be a predictor for decreased survival in patients transitioning to long-term ventricular assist devices [1, 2]. Most of the equipment used for circulatory and/or respiratory failure is extrapolated from adult intensive care medicine, hence limiting the available support modalities for pediatric patients since weight and body surface area play a major in the decision-making process around choosing the ideal device for the individual patient.

The intention of this review is to assess the available extracorporeal circulatory and respiratory support technologies in children with acute respiratory and/or circulatory failure.

Veno-Arterial ECMO

Five decades ago, ECMO evolved from cardiopulmonary bypass to a now frequently used rescue therapy in severely ill children. The initial use of ECMO began in the 1970s for patients with severe acute pulmonary and / or cardiac failure [3–7]. Hill et al. described the successful use of ECMO in a 24-y-old man with acute respiratory failure [3]. Encouraged by this and additional reports on the use of ECMO in adults with respiratory failure, the National Institutes of Health sponsored a prospective, randomized trial of ECMO in adults with respiratory failure [8]. Unfortunately, the survival was poor in both groups and consequently the interest for the use of ECMO was greatly tempered. Without the continued effort of Dr. Bartlett et al., ECMO may have ended as an anecdote in medical history. Dr. Bartlett and his research team continued to focus their efforts on neonatal patients with respiratory

✉ Mahsun Yuerek
yuerekm@chop.edu

[1] Division of Cardiac Critical Care Medicine, Department of Anesthesiology and Critical Care Medicine, The Children's Hospital of Philadelphia, University of Pennsylvania, Perelman School of Medicine, Philadelphia, PA 19104, USA

distress syndrome showing improved survival in patients supported with ECMO compared to conventional ventilation therapies [7, 9]. Bartlett and his group performed a prospective randomized trial of ECMO *vs.* conventional therapy for severe neonatal respiratory distress syndrome. Their study enrolled 12 patients with 1 receiving conventional therapy and the remaining 11 receiving ECMO. All 11 ECMO patients survived and the 1 patient on conventional therapy died. Although this study was criticized for its randomization design, it demonstrated that ECMO could be successfully utilized in neonatal patients [10]. Further studies confirmed the utility of ECMO for neonatal respiratory failure and established ECMO as an important rescue modality in critically ill neonates and children [11, 12]. As seen on the registry of the Extracorporeal Life Support Organization, the number of runs per year and centers providing ECMO has at least quadrupled during the past decade. Adult intensive care units began to use ECMO more consistently for respiratory failure during the H1N1 pandemic, and usage spiked again during the SARS-CoV-2 pandemic [13].

ECMO has the advantage of being able to be deployed at the bedside in a quick fashion in most neonatal and pediatric patients who present in cardiac failure, cardiorespiratory failure, or cardiac arrest. There is increasing evidence supporting ECMO for pediatric patients with in-hospital-cardiac-arrest. Utilization of ECMO during cardiac arrest is also known as extracorporeal cardiopulmonary resuscitation (ECPR) [14].

VA-ECMO cannulation can occur through peripheral or central cannulation. Neck cannulation can be done in most neonatal and pediatric patients. Cannulation of the groin vessels is feasible in patients greater than 15 kg; however, limb ischemia with groin cannulation is a serious concern and can be mitigated by placement of a reperfusion cannula distally from the cannulation site [15]. Central cannulation is commonly used in patients with recent sternotomy as it allows quick access to the right atrial appendage and the ascending aorta. Central cannulation has shown some benefit in pediatric patients in septic shock as this allows larger cannulas to be placed, allowing higher flow rates [16–18]. Although ECMO provides right and left ventricular support in patients with biventricular circulation, it does not provide active decompression of the left ventricle. This may be necessary for the left ventricle to recover, especially in patients with primarily cardiac etiology for the cardiorespiratory failure. This situation may lead to left atrial hypertension and pulmonary hemorrhage as well as potentially impeding the recovery of a failing left ventricle because of high filling pressures and insufficient coronary perfusion pressure, respectively. Decompression of the left heart can be achieved through creation of an atrial communication in the cardiac catheterization laboratory or by placement of a left atrial cannula/vent or apical transventricular vent in patients cannulated centrally. In older children and teenagers, left atrial decompression can be achieved by interventional placement of a left atrial cannula through the femoral vein, as used for the TandemHeart. Experience in the use of Impella devices for active decompression of the left ventricle in teenagers has been recently published [19, 20]. There is no pediatric data suggesting a survival benefit of either strategy to decompress the left atrium and left ventricle, respectively [21]. However, publications in adult literature suggest a survival benefit of patients supported on VA-ECMO, who had an Impella device implanted for active decompression of the left ventricle [22, 23].

VA-ECMO is a useful tool to stabilize patients with acute decompensation who fail conventional medical management. By placing the patient on ECMO, sufficient end organ perfusion and oxygen delivery is usually readily reinstituted, preventing further end-organ injury. This strategy allows the treatment team to investigate the etiology of the acute decompensation and to assess the probable duration of the primary problem leading to the acute decompensation. VA-ECMO support also carries numerous risks, such as bleeding, thrombosis, and infection, making this mechanical circulatory and respiratory support device less favorable for long-term support of patients with an underlying primary cardiac disease. Large retrospective studies have shown poor survival rates in children bridged to heart transplant on VA-ECMO as opposed to children bridged with ventricular assist devices [2, 24]. There are, however, case reports of successfully bridging pediatric patients on VA-ECMO to heart transplant, and thus this strategy may be considered in certain patients or in resource limited situations [25, 26]. Most pediatric cardiac centers would transition patients after stabilization and end-organ recovery from VA-ECMO to either a temporary ventricular assist device or a durable ventricular assist device. The decision about the type of the device depends on the patient's size and cardiovascular anatomy, as well as on the expectations regarding the potential for myocardial recovery.

Veno-Venous ECMO and Paracorporeal Lung Support

In contrast to VA-ECMO, veno-venous-ECMO (VV-ECMO) has been increasingly used for bridging patients to lung transplant as Thompson et al. have shown in their recent publication [27]. Over the course of the study period, the percentage of lung transplant patients supported with pre-operative VV-ECMO increased from 0% in 2004 to 16.7% in 2018. Primary diagnoses included cystic fibrosis, pneumonia and/or acute respiratory distress syndrome, interstitial pulmonary fibrosis, and pulmonary hypertension. VV-ECMO is indicated in patients with primary lung disease, unable to sufficiently oxygenate blood with their

native lungs. Current technology allows VV-ECMO to provide supplemental gas exchange via a single, dual-lumen cannula, facilitating early mobilizition and mitigating pre-transplant deconditioning. In fact, "ambulatory ECMO" has become a standard of care in lung transplant centers [28]. Case reports of central cannulation strategies (right atrium inflow, right ventricle outflow) to facilitate early mobilization in children failing neck cannulation strategy have also been published [29].

It is important to note that VV-ECMO requires adequate right ventricular (RV)-function to pump the oxygenated blood through the diseased lungs. In patients with impending RV-failure due to pulmonary hypertension, "pumpless" paracorporeal lung support has been used to supplement gas exchange while simultaneously reducing right ventricular afterload. This support modality does not require an additional extracorporeal pump: by surgical placement of the inflow cannula into the pulmonary artery and the outflow cannula into the left atrium, the right ventricle continues to function as the "pump", perfusing the oxygenator and bypassing the native, high-resistance pulmonary vasculature [30]. This pumpless paracorporeal lung assist device has been successfully used in neonates and small children [31].

Percutaneous Ventricular Assist Devices

Patients with primary cardiac dysfunction may be temporarily supported using a percutaneous ventricular assist device, either as the primary support device or as a bridge to recovery after a period of ECMO support. Figure 1 and Table 1 depict the ventricular assist devices currently used in pediatric patients. Depending on the etiology of the cardiac function and on the size of the child, percutaneous temporary devices like the Tandem-heart or the Impella axial flow device may be used. In recent years, case reports about the successful usage of the Impella device in children with acute heart failure have been published [32–34]. The Impella device is available in 4 sizes: Impella 2.5 (flows as high as 2.5 L/min), Impella CP (flow rates of up to 4.3 L/min), Impella 5.0 (flow rates as high as 5.0 L/min) and Impella 5.5 (flow rates as high as 6.0 L/min. The Impella 2.5 and Impella CP can be placed percutaneously via femoral access, while the Impella 5.0 and 5.5 generally require surgical implantation via the axillary or subclavian artery.

The TandemHeart requires transseptal puncture of the atrial septum for placement of the inflow cannula into the left atrium. The outflow cannula is generally placed into the femoral artery, thus perfusing most end-organs by way of retrograde aortic blood flow, capable of providing flows as high as 5 L/min. Yarlagadda et el. investigated the usage of temporary circulatory support systems in the U.S from 2011 to 2015. Among 93 pediatric patients that were supported with temporary circulatory support, 18% received the TandemHeart for circulatory support with an average duration of 22 d (25^{th} to 75^{th} percentile range 9 to 33 d) [35]. Although the TandemHeart has been successfully used in pediatric patients, there have been only a few of case reports in the literature [36, 37].

Paracorporeal Continuous and Pulsatile Flow Ventricular Assist Devices

Options for long-term circulatory support of pediatric patients with severe ventricular dysfunction remain limited. Table 1 lists available devices used for long-term support as a bridge to either recovery or transplant. The ventricular assist devices can be classified as paracorporeal and implantable pumps. Paracorporeal ventricular assist devices include continuous flow devices with a centrifugal pump like the PediMag or Rotaflow, which are capable of delivering flows less than 1 L/min, which may be sufficient in neonates and infants. The PediMag can generate flows as high as 1.5 L/min. When higher flows are required, either the Rotaflow or the Centrimag, each of which have a max flow rate of approximately 10 L/min, can be used as paracorporeal ventricular assist device. Although the aforementioned paracorporeal continuous flow ventricular assist devices have been designed for short-term support, there are limited reports of using them successfully as long-term support in neonates, infants, and small children. Currently, the only device approved by the US Food and Drug administration for long-term support in infants and small children is the Berlin Heart EXCOR, which is a pneumatic pulsatile paracorporeal pump available in various pump sizes. In the smallest (10 ml) size, it is suitable for even small neonates with weights below 3 kg; however, mortality and morbidity in this age and weight group remains high [38, 39]. Recent outcome studies and single center studies have shown an increase in the use of paracorporeal continuous flow devices, though no device modality (paracorporeal pulsatile *vs.* paracorporeal continuous flow) has shown to be superior in terms of survival or morbidity [40–42]. In a recent publication, Sughimoto et al. report their single center experience with paracorporeal continuous flow devices and paracorporeal pulsatile flow devices. Their results suggest a survival disadvantage in patients supported with a paracorporeal continuous flow devices; however, the investigators point out that the difference in patient characteristics, like presence of congenital heart disease and lower weight in the patient group supported with paracorporeal continuous flow devices, may have influenced their findings [43]. There is institutional variance in which device is primarily used in neonates, infants and small children. Use of Berlin Heart cannulae

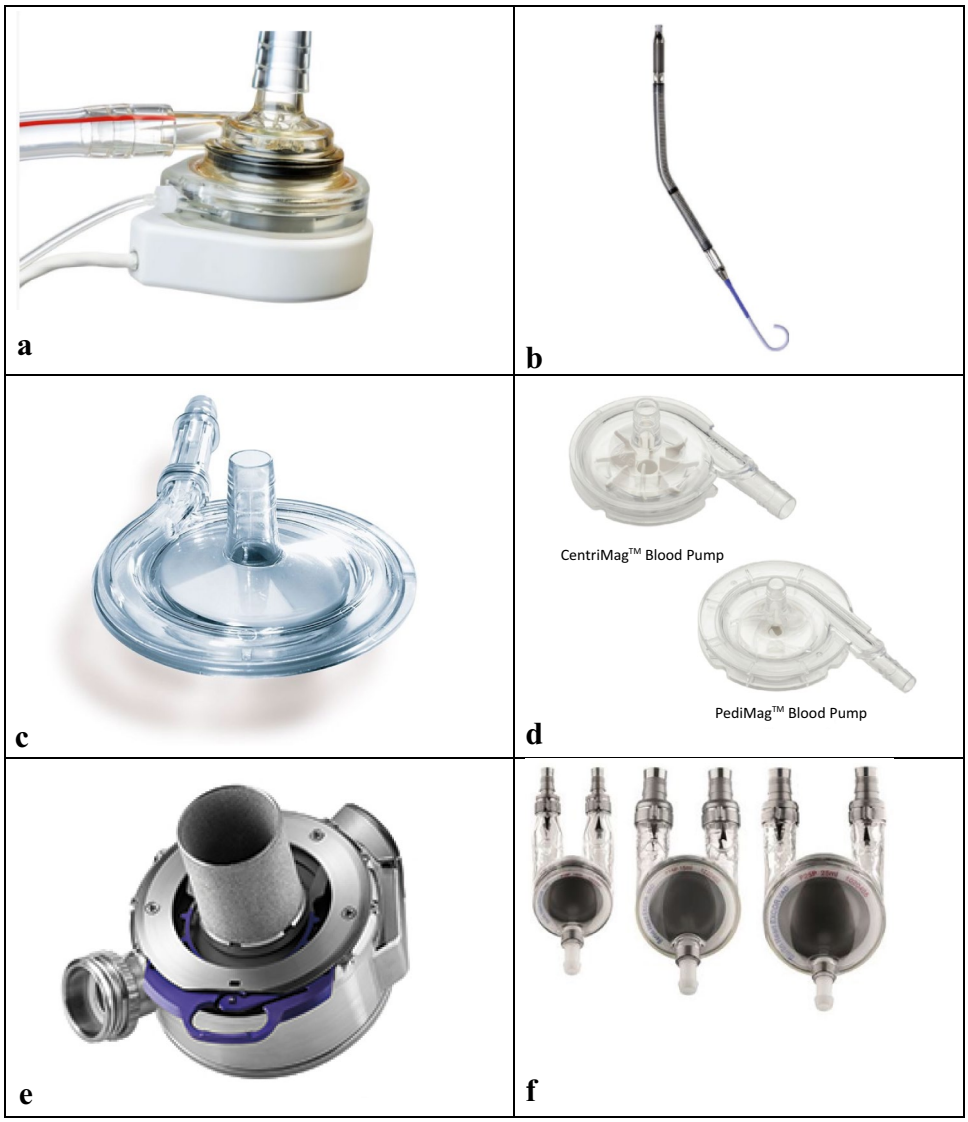

Fig. 1 **a** TandemHeart blood pump; **b** Impella; **c** Rotaflow blood pump; **d** CentriMag and PediMag blood pumps; **e** HeartMate3; **f** Berlin Heart EXCOR blood pump

as outflow and inflow cannulae allows transition between a pulsatile device and a continuous flow device without need for additional surgical intervention. Interchanging between a pulsatile and a continuous flow device could be required in situations where the paracorporeal pulsatile ventricular assist device may not provide sufficient ventricular unloading. Transition to a paracorporeal continuous flow device has the potential to unload the failing ventricle more effectively.

Early experience in patients with single ventricle physiology who were supported with paracorporeal ventricular assist devices was not promising. Placement of ventricular assist devices was associated with high mortality and morbidity. The recent increase in experience with usage of paracorporeal ventricular assist devices and novel cannulation strategies have revived the interest in offering this support modality to patients at high risk of failing single ventricle palliation. Case reports and small case series report successful bridge-to-transplant of this high-risk patient population with a pulsatile paracorporeal ventricular assist device, in combination with the hybrid palliation [44–47].

The paracorporeal ventricular assist devices have in common that the patients usually remain hospitalized until recovery and device explantation or until orthotopic heart transplantation. This may be disadvantageous in terms of quality of life and associated with increased costs. The Jarvik 2015 is the only implantable continuous flow ventricular assist device developed for infants and small children. Currently, the Jarvik 2015 pump is being evaluated in the so called "Pump for Kids, Infants and Neonates" trial (PumpKIN trial) and the results have not been published yet. Spinner et al. placed the Jarvik 2015 ventricular assist device in 2 patients with compassionate use authorization and describe their experience and challenges associated with that pump [48]. As the fields

Table 1 Overview of frequently used mechanical circulatory support systems

Device	Maximum flow rate	Type of flow	Placement	Suggested patient size
PediMag	1.5 L/min	Continuous/centrifugal	Sternotomy Paracorporeal	Neonates and infants
CentriMag	10 L/min	Continuous/centrifugal	Sternotomy Paracorporeal	Infants to adults
Rotaflow	10 L/min	Continuous/centrifugal	Sternotomy Paracorporeal	Neonates to adults
Impella[a]	2.5-6 L/min	Continuous/axial	Percutaneous/femoral artery or axillary artery Intracorporeal	Impella 2.5 might be feasible in patients with BSA of 0.89 m^2
TandemHeart[b]	5-8 L/min	Continuous/centrifugal	Percutaneous placement via femoral vessels or sternotomy Paracorporeal	Percutaneous placement limited by arterial (15 Fr and 17 Fr) and left atrial cannula (21 Fr) size
HeartMate3	10 L/min	Continuous/centrifugal	Sternotomy Intracorporeal	Report of placement in patient with BSA of 0.78 m^2, >19kg
Berlin Heart EXCOR	Variable with pump size	Pulsatile/pneumatic	Sternotomy Paracorporeal	Neonates to adults

BSA Body surface area

[a]maximum flow rate depending on size of Impella device

[b]maximum flow rate of 5 L/min with percutaneous placement, 8 L/min with surgical placement/sternotomy

of pediatric heart failure and cardiac intensive care medicine await the results of the PumpKIN trial, the optimal device selection for each patient will continue to be a case-by-case decision.

Durable Ventricular Assist Devices

During the past decade, usage of implantable durable continuous flow devices has been increasing in larger children and teenagers, who have been able to benefit from devices developed for adults, such as the HeartWare HVAD, HeartMate2 and HeartMate3. The HeartWare HVAD was removed from the market in June 2021, due to an the rates of thromboembolic stroke seen in adult patients supported with the device. Although this was not evident in pediatric patients, the device is no longer available for any population [49]. As a result, the choice of implantable devices for even larger children and teenagers is again somewhat limited. While there were reports of implantation of HeartWare HVAD devices in children with a body surface area as low as 0.56 m^2, the HeartMate3 is larger (HeartWare HVAD: 45 cc volume and 145 g *vs*. Heartmate3: 80 cc volume and 200 g) [50–52], with a smallest reported implantation in a 19 kg patient with a body surface area of 0.78 m^2 [53, 54]. Pre-implantation 3D fit studies may help in assessing the anatomic limitations for implantable continuous flow device placement [55, 56]. Younger children and teenagers have been discharged home with implantable continuous flow devices as bridge-to-transplant, bridge-to-recovery and occasionally as destination therapy.

Proposed Decision-Making Process for Device Selection

A crucial point in the decision-making process is the timing of implantation of circulatory and/or respiratory support device. Patients in cardiopulmonary arrest getting active chest compression or who present in cardiogenic shock and have hypoxemia secondary to respiratory failure should be placed on VA-ECMO if there is no absolute contraindication, such as irreversible severe neurological injury or fatal extracardiac/extrapulmonary disease. In many resuscitations, there is not sufficient time to evaluate for absolute contraindications, thus proceeding with VA-ECMO in those situations allows the medical team to stabilize the patient and define the further management plan afterwards.

The decision about mechanical circulatory support becomes more challenging if a child presents with primary cardiac failure without signs of cardiogenic shock. Although studies in adult patients have shown that early implantation of mechanical circulatory support devices is associated with improved outcomes, this approach has not transitioned to the management of children with acute heart failure given the size limitations of the patient population and the available devices. One common approach in the management of children with acute heart failure is to initiate mechanical circulatory support once medical therapy has failed; however, failure of medical therapy is poorly defined. Most clinicians would define failure of medical management as the need for inotropic support and signs of additional end-organ injury, like elevated renal function tests, elevated liver function

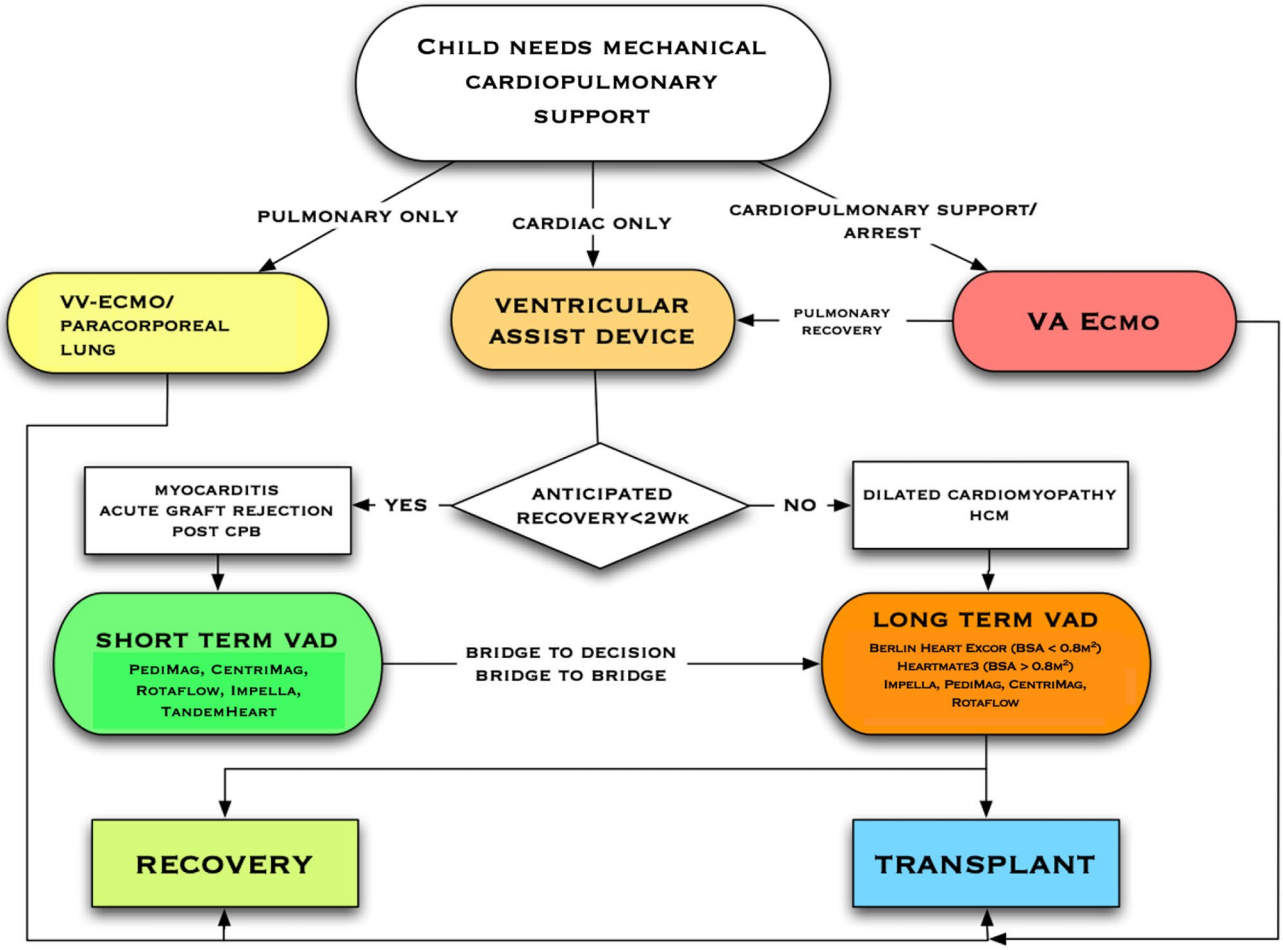

Fig. 2 Decision making algorithm. *BSA* Body surface area, *CPB* Cardiopulmonary bypass, *HCM* Hypertrophic cardiomyopathy, *VAD* Ventricular assist device, *VA ECMO* Venoarterial extracorporeal membrane oxygenation, *VV-ECMO* Venovenous extracorporeal membrane oxygenation, *Wk* Week

tests, inability to tolerate enteral nutrition or inability to wean from invasive ventilatory support. Once those criteria are fulfilled, most institutions would proceed with placement of mechanical circulatory support. In children less than 20 kg this usually means placement of central cannula for either paracorporeal pulsatile flow ventricular assist device (Berlin Heart Excor) or paracorporeal continuous flow ventricular assist device (PediMag, CentriMag, Rotaflow). Children weighing more than 20 kg, on the other hand, may be candidates for an implantable continuous flow ventricular assist device placed (HeartMate3). Certainly, the percutaneously placed ventricular assist devices, like Impella and TandemHeart, or any of the paracorporeal pulsatile/continuous flow ventricular assist devices, could be used in this size group as well; however, these are associated with lower quality of life, as discharge to home is not feasible with the paracorporeal or percutaneously placed ventricular assist devices. Time to recovery and the intent of device support also play an important role in the decision-making process. *For example*, larger children diagnosed with myocarditis and severe heart failure symptoms may show signs of recovery within a few weeks of presentation of illness. These patients may be adequately supported with an Impella device or TandemHeart, avoiding cardiopulmonary bypass exposure and sternotomy for implantation of a paracorporeal or implantable device.

The proposed decision-making algorithm is summarized in fig. 2.

Dedicated Highly Specialized Care Team

Centralizing care for this patient population with a dedicated team expert in the management of these complex patients and situations may have an impact on the morbidity and mortality. Pediatric and adult studies have shown that systematic and multidisciplinary approach improved outcome in this high-risk low volume population [50, 57, 58]. Management of the anticoagulation remains a crucial point in

Table 2 Overview of frequently used medications for anticoagulation and antiplatelet therapy; assays for therapeutic drug monitoring

Anticoagulant/ Antiplatelet medication	Assay for monitoring	Therapeutic drug monitoring
Unfractionated Heparin (UFH)	aPTT (Activated partial thromboplastin time)	• aPTT 60 to 80 s
	UFH-Anti-factor-Xa	• UFH-Anti-Xa: 0.3 to 0.7 U/ml
	ACT (Activated clotting time)	• ACT: 160-220 s
Bivalirudin	DTI (Direct thrombin inhibitor)	• DTI: 60 to 90 s
LWMH (Low Molecular Weight Heparin)	LWMH-Anti-factor-Xa	• LWMH-Anti-factor-Xa: 0.5 to 1.0 U/ml
Warfarin	INR (International normalized ratio)	• INR: 2.0-3.0
Aspirin	Platelet Mapping	• >70% of platelets inhibited by addition of arachidonic acid
	VerifyNow	• ARU (Aspirin Reaction Units): <550
Clopidogrel	Platelet Mapping	• Platelet inhibition tested by addition of adenosine diphosphate to specimen
	VerifyNow	• PRU (Platelet Reactivity Units): <194
Dipyridamole	Platelet Mapping	• >70% of platelets inhibited by addition of arachidonic acid

care of patients with ventricular assist device because of the high risk for cerebrovascular injuries related to both embolic stroke and intracranial bleeding. As the care teams for this patient population have evolved, the development of a specialized team for management of the anticoagulation has shown to impact the occurrence of cerebrovascular incidents [59]. In addition to anticoagulation recommendations from the manufacturer, many high volume centers have developed and published their anticoagulation strategy. Table 2 summarizes commonly used medications for antiplatelet therapy and anticoagulation along with their assays for therapeutic drug monitoring.

Conclusions

The field of pediatric heart failure is evolving, and the patient population is growing as survival after complex congenital heart surgeries is improving. The need for mechanical circulatory support is growing commensurately, since the number of organ donors does not meet the necessity. Further research in development of pumps suitable for neonates and infants, as well as in development of treatment algorithms, is needed to further optimize the care for this patient population.

Authors' Contributions All three authors contributed in the following order to various areas of the manuscript: MY, BWK and VRS. VRS will act as the guarantor for this manuscript.

Declarations

Conflict of Interest None.

References

1. Edelson JB, Huang Y, Griffis H, et al. The influence of mechanical circulatory support on post-transplant outcomes in pediatric patients: A multicenter study from the International Society for Heart and Lung Transplantation (ISHLT) Registry. J Heart Lung Transplant. 2021;40:1443–53.
2. Wehman B, Stafford KA, Bittle GJ, et al. Modern outcomes of mechanical circulatory support as a bridge to pediatric heart transplantation. Ann Thorac Surg. 2016;101:2321–7.
3. 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;286:629–34.
4. Hill JD, De Leval MR, Fallat RJ, et al. Acute respiratory insufficiency. Treatment with prolonged extracorporeal oxygenation. J Thorac Cardiovasc Surg. 1972;64:551–62.
5. Zapol W, Pontoppidan H, McCullough N, Schmidt V, Bland J, Kitz R. Clinical membrane lung support for acute respiratory insufficiency. Trans Am Soc Artif Intern Organs. 1972;18:553–60, 562.
6. Dorson W Jr, Meyer B, Baker E, et al. Response of distressed infants to partial bypass lung assist. Trans Am Soc Artif Intern Organs. 1970;16:345–51.
7. Bartlett RH, Gazzaniga AB, Jefferies MR, Huxtable RF, Haiduc NJ, Fong SW. Extracorporeal membrane oxygenation (ECMO) cardiopulmonary support in infancy. Trans Am Soc Artif Intern Organs. 1976;22:80–93.
8. Zapol WM, Snider MT, Hill JD, et al. Extracorporeal membrane oxygenation in severe acute respiratory failure a randomized prospective study. JAMA. 1979;242:2193–6.
9. Kirkpatrick BV, Krummel TM, Mueller DG, Ormazabal MA, Greenfield LJ, Salzberg AM. Use of extracorporeal membrane oxygenation for respiratory failure in term infants. Pediatrics. 1983;72:872–6.
10. Bartlett RH, Roloff DW, Cornell RG, Andrews AF, Dillon PW, Zwischenberger JB. Extracorporeal circulation in neonatal respiratory failure: a prospective randomized study. Pediatrics. 1985;76:479–87.

11. O'Rourke PP, Crone RK, Vacanti JP, et al. Extracorporeal membrane oxygenation and conventional medical therapy in neonates with persistent pulmonary hypertension of the newborn: a prospective randomized study. Pediatrics. 1989;84:957–63.
12. UK collaborative randomised trial of neonatal extracorporeal membrane oxygenation. UK Collaborative ECMO Trail Group. Lancet. 1996;348:75–82.
13. Barbaro RP, MacLaren G, Boonstra PS, et al. Extracorporeal membrane oxygenation for COVID-19: evolving outcomes from the international Extracorporeal Life Support Organization Registry. Lancet. 2021;398:1230–8.
14. Duff JP, Topjian A, Berg MD, et al. 2018 American Heart Association focused update on pediatric advanced life support: An update to the American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation. 2018;138:e731-9.
15. Kurkluoglu M, Hynes CF, Alfares FA, et al. Choice of peripheral venoarterial extra-corporeal membrane oxygenation cannulation site in patients above 15 kilograms. J Card Surg. 2015;30:461–5.
16. MacLaren G, Butt W, Best D, Donath S. Central extracorporeal membrane oxygenation for refractory pediatric septic shock. Pediatr Crit Care Med. 2011;12:133–6.
17. Butt WW, Chiletti R. ECMO for Neonatal Sepsis in 2019. Front Pediatr. 2020;8:50.
18. Ruth A, Vogel AM, Adachi I, Shekerdemian LS, Bastero P, Thomas JA. Central venoarterial extracorporeal life support in pediatric refractory septic shock: A single center experience. Perfusion. 2022;37:385–93.
19. Perri G, Trezzi M, Formigari R, et al. Use of transcarotid IMPELLA 2.5 axial-flow pump device for left ventricle unloading during VA-ECMO support in pediatric acute heart failure. World J Pediatr Congenit Heart Surg. 2021;12:542–6.
20. Sandoval Boburg R, Mustafi M, Magunia H, Kling S, Schlensak C, Popov AF. Left ventricular unloading with transaortic Impella 2.5 implantation in a pediatric patient supported by extracorporeal life support. Artif Organs. 2021;45:524–7.
21. Eastaugh LJ, Thiagarajan RR, Darst JR, McElhinney DB, Lock JE, Marshall AC. Percutaneous left atrial decompression in patients supported with extracorporeal membrane oxygenation for cardiac disease. Pediatr Crit Care Med. 2015;16:59–65.
22. Schrage B, Becher PM, Bernhardt A, et al. Left ventricular unloading is associated with lower mortality in patients with cardiogenic shock treated with venoarterial extracorporeal membrane oxygenation: Results from an international, multicenter cohort study. Circulation. 2020;142:2095–106.
23. Russo JJ, Aleksova N, Pitcher I, et al. Left ventricular unloading during extracorporeal membrane oxygenation in patients with cardiogenic shock. J Am Coll Cardiol. 2019;73:654–62.
24. Dipchand AI, Mahle WT, Tresler M, et al. Extracorporeal membrane oxygenation as a bridge to pediatric heart transplantation: effect on post-listing and post-transplantation outcomes. Circ Heart Fail. 2015;8:960–9.
25. Shudo Y, Wang H, Ha RV, Hayes AD, Woo YJ. Heart transplant after profoundly extended ambulatory central venoarterial extracorporeal membrane oxygenation. J Thorac Cardiovasc Surg. 2018;156:e7–9.
26. Gedik E, Ulas A, Ersoy O, Atar F, Camkiran Firat A, Pirat A. Venoarterial extracorporeal membrane oxygenation support as a bridge to heart transplant: Report of 3 cases. Exp Clin Transplant. 2016;14(Suppl 3):121–4.
27. Thompson K, Staffa SJ, Nasr VG, et al. Mortality after lung transplantation for children bridged with extracorporeal membrane oxygenation. Ann Am Thorac Soc. 2022;19:415–23.
28. Lehr CJ, Zaas DW, Cheifetz IM, Turner DA. Ambulatory extracorporeal membrane oxygenation as a bridge to lung transplantation: walking while waiting. Chest. 2015;147:1213–8.
29. Maeda K, Ryan K, Conrad CK, Yarlagadda VV. An alternative cannulation approach for venovenous extracorporeal membrane oxygenation in children for long-term ambulatory support. J Thorac Cardiovasc Surg. 2018;156:e13–4.
30. Maul TM, Nelson JS, Wearden PD. Paracorporeal lung devices: thinking outside the box. Front Pediatr. 2018;6:243.
31. Hoganson DM, Gazit AZ, Boston US, et al. Paracorporeal lung assist devices as a bridge to recovery or lung transplantation in neonates and young children. J Thorac Cardiovasc Surg. 2014;147:420–6.
32. Parekh D, Jeewa A, Tume SC, et al. Percutaneous mechanical circulatory support using impella devices for decompensated cardiogenic shock: A pediatric heart center experience. ASAIO J. 2018;64:98–104.
33. Bouhout I, Nguyen SN, Barry OM, Bacha EA, Goldstone AB. Transinnominate impella 5.5 insertion as a bridge to transplantation in a pediatric patient in refractory cardiogenic shock. JTCVS Tech. 2022;14:201–3.
34. Ankola AA, McAllister J, Turner ME, et al. Biventricular impella use in pediatric patients with severe graft dysfunction from acute rejection after heart transplantation. Artif Organs. 2020;44:100–5.
35. Yarlagadda VV, Maeda K, Zhang Y, et al. Temporary circulatory support in U.S. children awaiting heart transplantation. J Am Coll Cardiol. 2017;70:2250–60.
36. Ricci M, Gaughan CB, Rossi M, et al. Initial experience with the TandemHeart circulatory support system in children. ASAIO J. 2008;54:542–5.
37. Russell HM, Kulat B, Zingle N, Backer CL. Successful bridge to transplant using the TandemHeart(R) left ventricular assist device in a pediatric patient. World J Pediatr Congenit Heart Surg. 2012;3:249–50.
38. Conway J, St Louis J, Morales DLS, Law S, Tjossem C, Humpl T. Delineating survival outcomes in children <10 kg bridged to transplant or recovery with the Berlin Heart EXCOR ventricular assist device. JACC Heart Fail. 2015;3:70–7.
39. Fouilloux V, El Louali F, Gran C, et al. Berlin heart EXCOR paediatric ventricular assist device: does weight matter? Heart Lung Circ. 2021;30:585–91.
40. Morales DLS, Rossano JW, VanderPluym C, et al. Third annual pediatric interagency registry for mechanical circulatory support (Pedimacs) report: Preimplant characteristics and outcomes. Ann Thorac Surg. 2019;107:993–1004.
41. Rossano JW, VanderPluym CJ, Peng DM, et al. Fifth annual pediatric interagency registry for mechanical circulatory support (Pedimacs) report. Ann Thorac Surg. 2021;112:1763–74.
42. Rosenthal DN, Almond CS, Jaquiss RD, et al. Adverse events in children implanted with ventricular assist devices in the United States: Data from the pediatric interagency registry for mechanical circulatory support (PediMACS). J Heart Lung Transplant. 2016;35:569–77.
43. Sughimoto K, Pidborochynski T, Buchholz H, et al. Paracorporeal support in pediatric patients: the role of the patient-device interaction. Ann Thorac Surg. 2022;114:1442–51.
44. Mavroudis CD, Edelson JB, Wittlieb-Weber CA, O'Connor MJ, Maeda K. The innominate artery-to-pulmonary artery shunt as ventricular assist device outflow in hybrid stage one procedure with aortic coarctation. JTCVS Tech. 2022;14:204–6.
45. Philip J, Reyes K, Ebraheem M, Gupta D, Fudge JC, Bleiweis MS. Hybrid procedure with pulsatile ventricular assist device for hypoplastic left heart syndrome awaiting transplantation. J Thorac Cardiovasc Surg. 2019;158:e59–61.
46. Philip J, Powers E, Machado D, et al. Pulsatile ventricular assist device as a bridge to transplant for the early high-risk single-ventricle physiology. J Thorac Cardiovasc Surg. 2021;162:405–13.e4.
47. Bleiweis MS, Fudge JC, Peek GJ, et al. Ventricular assist device support in neonates and infants with a failing functionally univentricular circulation. JTCVS Tech. 2022;13:194–204.

48. Spinner JA, Tunuguntla HP, Tume SC, et al. "Compassionate" cases of the jarvik 2015 ventricular assist device. ASAIO J. 2021;67:1036–43.
49. Sert DE, Kocabeyoglu SS, Kervan U, et al. Cerebrovascular events in children on intracorporeal continuous-flow left ventricular assist devices. Artif Organs. 2020;44:1251–8.
50. Nelson McMillan K, Hibino N, et al. HeartWare ventricular assist device implantation for pediatric heart failure-a single center approach. Artif Organs. 2019;43:21–9.
51. Tuzun E, Roberts K, Cohn WE, et al. In vivo evaluation of the HeartWare centrifugal ventricular assist device. Tex Heart Inst J. 2007;34:406–11.
52. Bartoli CR, Hennessy-Strahs S, Gohean J, et al. A novel toroidal-flow left ventricular assist device minimizes blood trauma: Implications of improved ventricular assist device hemocompatibility. Ann Thorac Surg. 2019;107:1761–7.
53. O'Connor MJ, Lorts A, Davies RR, et al. Early experience with the HeartMate 3 continuous-flow ventricular assist device in pediatric patients and patients with congenital heart disease: A multicenter registry analysis. J Heart Lung Transplant. 2020;39:573–9.
54. Ranney DN, Habermann AC, Meza JM, et al. Implantation of a HeartMate 3 ventricular assist device in a 21-kg pediatric patient with Fontan failure. J Card Surg. 2020;35:3634–7.
55. Moore RA, Madueme PC, Lorts A, Morales DL, Taylor MD. Virtual implantation evaluation of the total artificial heart and compatibility: Beyond standard fit criteria. J Heart Lung Transplant. 2014;33:1180–3.
56. Van Puyvelde J, Jacobs S, Vlasselaers D, Meyns B. Heartmate 3 implantation in small patients: CT-guided chest diameter assessment. Interact Cardiovasc Thorac Surg. 2022;34:939–40.
57. Jorde UP, Shah AM, Sims DB, et al. Continuous-flow left ventricular assist device survival improves with multidisciplinary approach. Ann Thorac Surg. 2019;108:508–16.
58. Hawkins B, Fynn-Thompson F, Daly KP, et al. The evolution of a pediatric ventricular assist device program: The boston children's hospital experience. Pediatr Cardiol. 2017;38:1032–41.
59. Byrnes JW, Prodhan P, Williams BA, et al. Incremental reduction in the incidence of stroke in children supported with the Berlin EXCOR ventricular assist device. Ann Thorac Surg. 2013;96:1727–33.