Korean J Thorac Cardiovasc Surg 2013;46:391-401 □ Review □
ISSN: 2233-601X (Print) ISSN: 2093-6516 (Online) http://dx.doi.org/10.5090/kjtcs.2013.46.6.391

Pediatric Mechanical Circulatory Support

Ivan Wilmot, M.D.[1], Angela Lorts, M.D.[1], David Morales, M.D.[2]

Mechanical circulatory support (MCS) in the pediatric heart failure population has a limited history especially for infants, and neonates. It has been increasingly recognized that there is a rapidly expanding population of children diagnosed and living with heart failure. This expanding population has resulted in increasing numbers of children with medically resistant end-stage heart failure. The traditional therapy for these children has been heart transplantation. However, children with heart failure unlike adults do not have symptoms until they present with end-stage heart failure and therefore, cannot safely wait for transplantation. Many of these children were bridged to heart transplantation utilizing extracorporeal membranous oxygenation as a bridge to transplant which has yielded poor results. As such, industry, clinicians, and the government have refocused interest in developing increasing numbers of MCS options for children living with heart failure as a bridge to transplantation and as a chronic therapy. In this review, we discuss MCS options for short and long-term support that are currently available for infants and children with end-stage heart failure.

Key words: 1. Heart failure
2. Pediatric
3. Ventricular assist device
4. Extracorporeal membranous oxygenation
5. Cardiac transplantation

INTRODUCTION

Mechanical circulatory support (MCS) has a long-standing history in the adult heart failure population. Hall is credited with implanting the first ventricular assist device (VAD) in 1963 and only a year later, the US government began funding of adult MCS. The result is that adult MCS has evolved to the standard of care for adults with end-stage heart failure and to date twelve Food and Drug Administration (FDA) approved devices are available for adult heart failure patients. In contrast, the first monies given for the development of pediatric MCS by the US government was nearly 40 years later in 2004, explaining the very limited history of pediatric MCS for infants, and neonates.

Pediatric specific VADs were only made available for compassionate use in North America in 2000. Although few implants were performed in the first 4 years (n=4), it was in 2004 that the number of Berlin Heart EXCOR device implants, as a bridge to transplant (BTT) grew significantly. It has been increasingly recognized that there is a rapidly expanding population of children living with heart failure. It has been estimated that approximately 16,000 pediatric heart fail-

Departments of [1]Cardiology and [2]Congenital Heart Surgery, The Heart Institute, Cincinnati Children's Hospital Medical Center, University of Cincinnati College of Medicine
Received: October 29, 2013, Revised: October 29, 2013, Accepted: October 29, 2013
Corresponding author: Ivan Wilmot, Division of Pediatric Heart Failure & Transplant, Department of Cardiology, The Heart Institute, Cincinnati Children's Hospital Medical Center, The University of Cincinnati College of Medicine, 3333 Burnet Avenue, MLC 2004 Cincinnati, OH 45229, USA
(Tel) 1-513-803-4534 (Fax) 1-513-803-4493 (E-mail) ivan.wilmot@cchmc.org

ure hospitalizations occur per year in the United States [1]. Additionally, there has been a reported increase of greater than 30% in pediatric hospitalizations for heart failure over a 3 year period [1]. Improved recognition of children living with cardiomyopathy, and improved surgical outcomes for children with congenital heart disease (CHD) is credited as contributors. The traditional therapy for children with end stage heart failure has been heart transplantation. Heart transplantation is a significantly limited resource given the limited donor population, and is also associated with potential morbidity. The outcomes utilizing extracorporeal membranous oxygenation (ECMO) as a BTT with prolonged wait times have yielded poor results [2]. As such, industry and science have combined to develop increasing numbers of MCS options for children living with heart failure. The Berlin Heart EXCOR was approved by the FDA in December 2011 specifically for use in children and infants. The National Heart, Lung, and Blood Institute (NHLBI) have supported the drive for additional MCS options in children with the Pumps for Kids, Infants, and Neonates (PumpKIN) trial. In this review of pediatric MCS we discuss indications and timing of support, contraindications, device selection, operative concerns, and post-operative care and outcomes.

INDICATIONS AND TIMING OF SUPPORT

Patient selection and timing of MCS is critical to successful outcomes. Several unique limitations exist in the selection and timing of MCS in children. Children with heart failure often compensate very well when compared to their adult counterparts, and thus very often present with late onset symptoms and severe ventricular dysfunction. Additionally, children with CHD and heart failure are often challenging with regards to anatomy, eligibility of MCS, and timing of support. Unlike most large adult centers, many pediatric centers are just beginning to develop their MCS programs with evolving selection/evaluation criteria and clinical protocols.

Our institutions current indications for MCS have matured over several years. Patients with heart failure requiring an inotrope are evaluated for MCS if the circulation remains suboptimal resulting in evidence of end-organ dysfunction (e.g., neurologic: altered mental status; respiratory: intubated; gastrointestinal: inability to tolerate enteral feeds; renal: rising creatnine; musculoskeletal: inability to ambulate).

Special consideration is given to small infants and patients with CHD because of limited device options and a higher morbidity profile for these patients. An understanding of the unique pathological features in children with CHD is required prior to initiating MCS. Cannulation in this population can be particularly challenging. Consideration of how the patients may be cannulated, and into which vessels and or chambers these cannulae may connect. Also, consideration of patients with abnormal situs further challenges how these cannulae may attach to the assist device. Additional concerns with regards to internal anatomy are raised with septal defects, hypoplastic chambers, and anomalous systemic and venous connections, as well as extra-cardiac anatomy. Aorto-pulmonary shunts, both surgically created (i.e., Blalock Taussig shunt) and pathological (i.e., aorto-pulmonary collateral arteries) can be challenging as one must supply greater than normal cardiac output. It is with these complexities in mind that MCS results in children with CHD must be interpreted. In children with single ventricles VAD support has been more successful at the Glenn stage than any other of the two stages. A trial of adequacy of the Glenn shunt for oxygenation can be attempted with placement of a systemic VAD (SVAD) using a temporary centrifugal pump (common atrium and aortic cannulation). If the patient is well supported in this fashion then one can return to place a more long-term device (i.e., Berlin Heart EXCOR). The failing Fontan patients are a sub-group of the single ventricle patients who often present for MCS. Past results of VAD support in the failing Fontan population have been inconsistent. It is only in those who show features of isolated systemic ventricular failure (i.e., high end diastolic pressures >15 mmHg) in which SVAD therapy is effective [3]. Should Fontan failure be due to other hemodynamic complications, the patient is not a candidate for Fontan conversion and the patient has a body surface area (BSA) of >1.7 m^2, then total artificial heart (TAH) is an option. TAH has also been used in complex CHD patients and may represent a preferable option in settings where there is poly-valvular disease and or multiple residual abnormalities. Technical considerations due to anatomical constraints should be considered

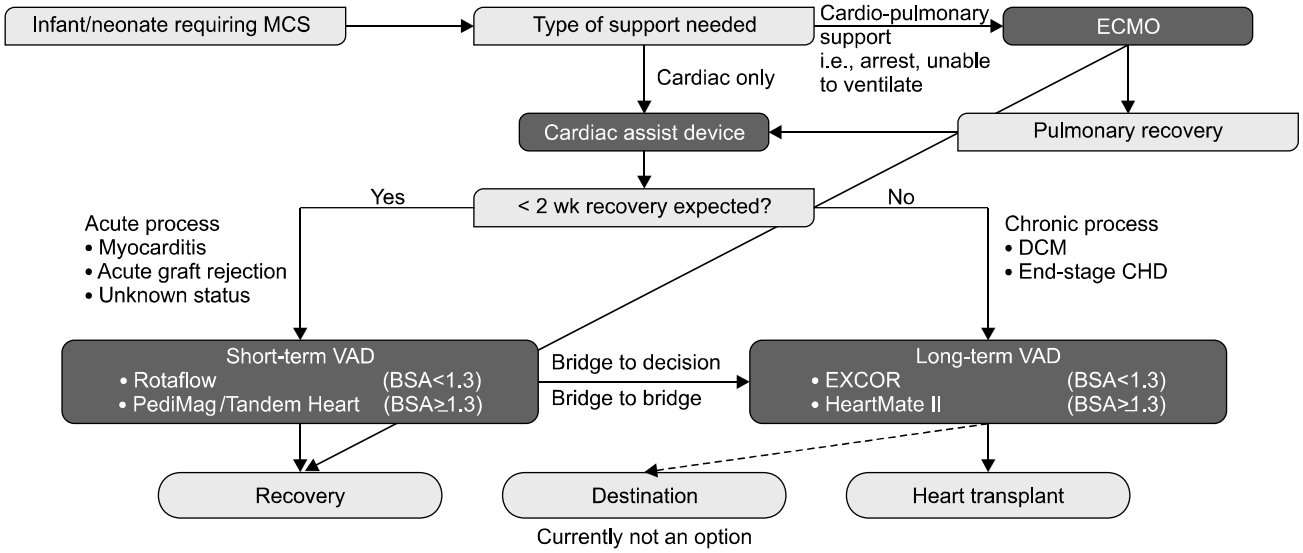

Fig. 1. Protocol for device selection; name of the devices used in the figure are authors' preference for each device type.

in the placement of TAH in patients with complex anatomy (i.e., CCTGA and Fontan variations) [4].

CONTRAINDICATIONS TO MCS

Extreme prematurity, very low birth weight (< 1.5 kg), significant neurologic damage, a constellation of congenital anomalies with poor prognosis, and chromosomal aberrations are generally accepted as contraindications for MCS. Multisystem organ failure is a relative contraindication, however hemodynamic improvement may reverse end-organ dysfunction in some cases. Both hepatic and renal dysfunction have been shown to improve with VAD related improved hemodynamics [5,6].

Indications and contraindications for initiation of MCS vary greatly based on a program's level of experience. It is well known that programs in their infancy are cautious and highly selective with initiation of MCS, this sometimes leads to immature programs initiating mechanical support late, making the patient high risk and propagating their fear of MCS. Experienced programs tend to be more aggressive in selecting patients early, leading to an improvement in results. The Berlin EXCOR USA trial clearly demonstrated this very marked difference in mortality, as renal and liver function were compromised even at the moderate range. Evolution of VAD availability for children has also significantly affected patient selection and choice of optimum device.

DEVICE SELECTION

Device selection can be divided into what cardiorespiratory site requires support, namely the systemic ventricle, pulmonary ventricle, respiratory system, or a combination thereof. Additionally, device selection is dependant on length of anticipated support: short- (< 2 weeks) or long-term and on device strategy: acute bridge to recovery, chronic BTT, or destination therapy (DT), and devices available. Devices options in children are limited and often dictate device selection. Devices may be categorized into their expected length of support as short-term or long-term MCS. Fig. 1 illustrates the device selection protocol in authors' current practice. Table 1 describes commonly used VADs for children in North America. There are several additional devices that are currently in development as part of a multi-institutional NHLBI funded trial, the PumpKIN trial, which are not yet available for clinical use.

There are currently three investigational devices funded by the PumpKIN trial. Two of which are ECMO systems. The first is the pCAS or Ension, a pump and oxygenator controlled by a touch screen console being developed as a small

Table 1. Commonly used ventricular assist devices for children in North America

Device	Position	Pump type	Flow type	Flow generation	SV (mL) or speed (rpm)	Flow range (l/min)	Body surface area (m^2)	Ambulation
Short-term MCS								
RotaFlow	EC	Rotary, radial	Continuous	Electromagnetic	0–5,000 rpm	0–10	No minimum	No
PediMag	EC	Rotary, radial	Continuous	Electromagnetic	0–5,500 rpm	< 1.5	< 0.5	No
Tandem heart	EC	Rotary, radial	Continuous	Electric	3,000–7,500 rpm	< 5	> 1.3	No
Long-term MCS								
EXCOR	EC	Volume displacement	Pulsatile	Pneumatic	10, 25, 30, 50 mL[a)]	Variable	0.2–1.3	Yes
PVAD/IVAD	EC/IC	Volume displacement	Pulsatile	Pneumatic	65 mL	Up to 7	> 0.7	Yes, possible discharge
TAH	EC	Volume displacement	Pulsatile	Pneumatic	70 mL	Up to 9.5[b)]	> 1.7	Yes, possible discharge
HVAD	IC	Rotary, radial	Continuous	Electromagnetic	2,400–3,200 rpm	Up to 10	> 1.0	Yes
HeartMate II	IC	Rotary, axial	Continuous	Electric	6,000–15,000 rpm	> 2.5	> 1.4	Yes, possible discharge

MCS, mechanical circulatory support; EC, extracorporeal; IC, intracorporeal; TAH, total artificial heart; SV, stroke volume.
[a)]60 and 80 mL pumps are also available but in Europe only. [b)]Through both ventricles.

unit for mobility. The second is the PediPL with a Levitronix pump and oxygenator, which is portable and small. Although two VAD's were initially funded in this program, the PediaFlow (Pittsburgh) program has ended secondary to a lack of an industry partner. The Jarvik Pediatric 2000 VAD is incredibly small with a priming volume of only 1 mL and sits inside the ventricle wall. These three devices continue to be developed with clinical trials anticipated in the next few years.

ECMO is only considered if the patient needs cardiac and pulmonary support. It is well documented that prolonged ECMO support is fraught with significant morbidity and mortality. As such, ECMO support is a bridge to other forms of MCS upon recovery of pulmonary function or weaned off in the setting of cardiopulmonary recovery. Should pulmonary function remain intact, then VAD therapy is preferred and is determined based on anticipated length of support. This can be in the form of short-term VAD (< 2 weeks) or long-term VAD (> 2 weeks). Should anticipated 'recovery' be longer than 2 weeks then transition from short-term to long-term VAD is recommended.

DT is the term used to describe long-term support of patients who are deemed not to be candidates for heart transplantation and whose cardiac function is also not felt to be amenable to recovery. DT has been successful in pediatric institutions but is rare and currently FDA approved destination devices are for adult sized patients. Currently the HeartMate II is the DT device that can be used in the larger adolescent or adult for this purpose. The HeartWare device and Syncardia are currently under trial and if successful should soon be approved for this indication.

1) SHORT-TERM MECHANICAL CIRCULATORY SUPPORT

(1) Extracorporeal membranous oxygenation: An ECMO circuit comprises the following: centrifugal or roller pump, hollow fiber membrane oxygenator, oxygen blender, and pump console and heat exchanger. Although ECMO was once commonly used as the sole form of MCS in the pediatric population secondary to unavailability of other devices to support pediatric patients, increasing development of pediatric VADs has shown a decreased trend in ECMO use. Some centers continue to use ECMO due to limited experience with or availability to pediatric VADs and other upcoming smaller adult VADs.

ECMO support should remain limited to patients with severe cardiac and respiratory failure. The use in isolated heart failure is no longer warranted. ECMO can be quite beneficial: 1) in patients who are arresting (ECMO cardiopulmonary resuscitation); 2) in scenarios where institutions who do not have a VAD program can use ECMO for stabilization and transport to a center with a VAD program; and 3) in those

Fig. 2. (A) RotaFlow: pump head and drive unit (Courtesy of MAQUET Cardiovascular). (B) Thoratec PediMag: pump (Courtesy of Thoratec Co.). (C) Tandem Heart: pump (Courtesy of Cardiac Assist Inc.).

patients with progressive cardiac failure who were not able to be intervened upon before the development of secondary pulmonary decompensation requiring maximal ventilatory support. To aid in the improvement in lung function secondary to cardiac disease, a direct vent in the left atrium is essential. Prolonged ECMO support is associated with up-regulation of the inflammatory cascade, embolic events, hemorrhage, and the need for circuit replacement. As the length of ECMO support increases, these factors can have significant negative effects on patient outcomes. These effects can be seen even after successful bridge to cardiac transplant as published by Davies in which transplanted patients supported with ECMO showed a higher mortality than those who had VAD support irrespective of diagnosis [7]. Additional studies utilizing a national database where ECMO was used even after being transitioned to a VAD was associated with a significantly worse survival (40%) compared to the use of VAD only (84%) [8]. Similar results are seen in a study of MCS in children with myocarditis [9]. Also, the use of ECMO as a bridge to 'salvage VAD,' a VAD after a failed congenital palliation, has consistently been shown to yield very disappointing survival results of approximately 27% [8]. Thus ECMO use in patients with isolated heart failure should be avoided.

(2) Jostra ROTAFLOW Centrifugal Pump (MaQUET Cardiovascular, Wayne, NJ, USA): A temporary VAD used to support all sizes, from the neonate to the adult patient. It is a centrifugal extracorporeal pump (50 mm in diameter made of polycarbonate material) requiring 32 mL of priming volume to flow at 0 to 10 L/min. The pump is powered via an electromagnetic mechanism with the circuit levitated in three magnetic fields with one point bearing, which produces laminar flow. This levitated mechanism reduces mechanical friction, hemolysis, and overall wear. A membrane oxygenator can be attached should an ECMO circuit be required (Fig. 2A).

Rotaflow is indicated in patients of all sizes where recovery is anticipated in <2 weeks. Central cannulation via sternotomy in the left atrium and the aorta without going onto cardiopulmonary bypass (CPB) is recommended to provide optimal circuit flow, and the ability to transition to a long-term device if recovery is not successful.

(3) Thoratec PediMag (formerly Levitronix PediMag/ CentriMag; Thoratec Co., Pleasanton, CA, USA): The PediMag is a pediatric specific VAD that is magnetically levitated. It has no points of contact limiting friction, and blood damage. The device is capable of flowing at up to 1.5 L/min, and has been implanted in more than 650 pediatric patients world-wide mostly in an ECMO circuit, but over the past three years its use as a temporary VAD continues to expand. The PediMag is indicated for patients as low as 3 kg in weight with a BSA of less than 1.3 m^2, and anticipated recovery of less than 2 weeks. It is also applied through central cannulation via sternotomy off CBP, and may be used for transition to a long-term device. The larger CentriMag is indicated for adults with BSA of greater than 1.3 m^2 (Fig. 2B).

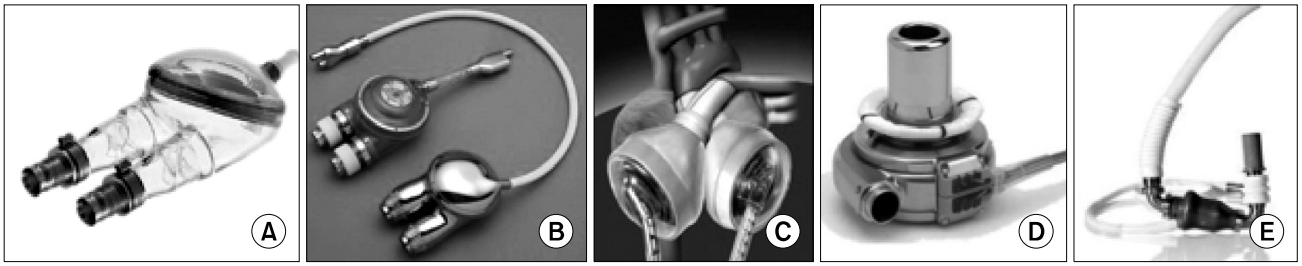

Fig. 3. (A) Berlin Heart EXCOR pump (Courtesy of Berlin Heart Inc.). (B) Thoratec IVAD/PVAD (Courtesy of Thoratec Co.). (C) TAH (Courtesy of SynCardia Systems Inc.). (D) HeartWare HVAD (Courtesy of HeartWare Systems). (E) Thoratec HeartMate II (Courtesy of Thoratec Co.).

(4) Tandem Heart (Cardiac Assist Inc., Pittsburgh, PA, USA): The Tandem Heart is used in patients ＞40 kg (BSA＞1.3) and is a percutaneously placed device. The hydrodynamic fluid bearing supports a spinning rotor in a device placed percutaneously through the femoral vessels. The transeptal extended flow cannula is placed through the femoral vein in the catheterization laboratory via a transeptal puncture into the left atrium. The arterial limb is placed in the femoral artery. For children under 70 kg a vascular graft sewn onto the femoral artery is recommended to preserve the native femoral vessel and prevent limb ischemia. The Tandem Heart is indicated where recovery is anticipated in less than 2 weeks (Fig. 2C).

2) LONG-TERM MECHANICAL CIRCULATORY SUPPORT

(1) Berlin Heart (Berlin Heart Inc., Berlin, Germany): The Berlin Heart EXCOR is the most commonly used pediatric VAD throughout the world with over 1,600 implants worldwide and over 500 implants in the United States. It is the only long-term FDA approved VAD available for neonates and infants in the United States. The Berlin heart is a paracorporeal device with pulsatile flow used solely for BTT. The Berlin Heart EXCOR is powered by a pneumatic IKUS driver unit currently. However, the new EXCOR Active driver unit, which is currently being tested, will allow for discharge of patients to home (Fig. 3A).

Although it has been widely used in Europe for decades, it has only been consistently used by major centers since 2004 and now its use has spread to even more centers after its approval in Northern America following the FDA approval in the United States in December 2011. It has the advantage of being used as a left VAD (LVAD), right VAD (RVAD), or BiVAD. Additionally, it is able to support neonates, children, and adolescents as pump sizes varying from 10 to 60 mL (10, 25, 30, 50, 60 mL).

(2) Thoratec VAD (IVAD/PVAD; Thoratec Co., Pleasanton, CA, USA): The Thoratec IVAD (implantable) and PVAD (paracorporeal) are similar in design, with the IVAD being slightly smaller weighing 70 grams less and having a smooth titanium exterior, and the PVAD having a polysulfone exterior. The Thoratec VAD is a pneumatic pulsatile VAD with a 65 mL stroke volume and a maximum flow of 7 L/min. The device may be used in the left, right, or biventricular assist position. These pumps are powered by a mobile driver, TLC-II Plus, for possible future home discharge. Their primary use in a pediatric program is for biventricular support in an adult size patient who is not a TAH candidate (Fig. 3B).

(3) Total Artificial Heart (SynCardia Systems Inc., Tucson, AZ, USA): The TAH is an implantable biventricular device that anatomically replaces both ventricles at implant. Although it has only been available as a 70mL pump in each chamber for patients with a BSA of 1.7 or greater in the past, a 50 mL pump for patients with a BSA of 1.2 to 1.7 is soon to be released for Investigational Device Exemption (IDE) trials in the United States. One can also use 3-dimensional computed tomography (CT) imaging and post-processing software to pre-operatively determine if the TAH can fit in smaller patients who do not meet the standard rule of needing 10 cm anterior posterior diameter at T10 vertebral body on CT (Fig. 3C).

It has been implanted in over 1,200 patients worldwide,

with a BTT rate up to 79% [10]. The TAH has been utilized successfully in patients with chronic rejection post orthotopic heart transplant, failing Fontan circulation, and in patients with multiple congenital defects that would require surgical correction prior to VAD placement (i.e., CHD with ventricular septal defect, aortic insufficiency, right ventricular [RV] to pulmonary artery [PA] conduit). The TAH has several distinct advantages over LVADs or BiVADs as it eliminates right heart failure, valvar regurgitation, cardiac arrhythmias, ventricular clots, intraventricular communications, and low blood flow.

Children with rejection post orthotopic heart transplant may benefit most from TAH implant, as it precludes the need for continuous aggressive immunosuppression. In chronic rejection with restrictive physiology and small ventricular cavities the TAH may also be of significant benefit. It also affords a very different state for end-organ recovery than does a VAD in that it not only gives supra-physiologic cardiac output but in the setting of low central venous pressures.

(4) HeartWare HVAD (HeartWare Systems, Framington, MA, USA): An intracorporeal third-generation centrifugal continuous flow VAD receiving FDA approval for BTT in November 2012, and currently under IDE approved clinical trial for DT. This device is implantable in the pericardial space and smaller in size and thus does not need a VAD pocket. It has been used in small patients down to BSA of 0.7 m^2 although caution is advised for patients with BSA under 1.5 m^2 [11,12] (Fig. 3D).

(5) HeartMate II (Thoratec Co., Pleasanton, CA, USA): The HeartMate II is a rotary, axial flow pump with FDA approval for both BTT and DT. It is the most commonly used LVAD in adult patients with over 10,000 implants worldwide. As a continuous flow device it is significantly smaller than a comparable pulsatile device, with no valves, has only one moving component thus reducing its complexity. It can be used in adolescent patients probably down to a BSA $\geq$ 1.3 m^2 as a BTT, and for chronic therapy (Fig. 3E).

PERIOPERATIVE CONCERNS

1) ANESTHESIA

Preoperative assessment of children with heart failure requires a thorough understanding of the unique associated pathologic features in this population. Children often present with heart failure symptoms late in their clinical course, which can often be associated with end organ dysfunction, namely liver and kidney injury. Hemodynamic stabilization prior to surgery is not always possible given the timing and degree of presentation. Optimizing patients prior to surgery often requires pharmacologic and positive pressure ventilation in the intensive care unit. Stressors (tachycardia, hypercarbia, loss of sinus rhythm, sudden alterations in volume status, hypotension) may contribute to hemodynamic abnormalities and should be addressed promptly.

Children with CHD have several unique considerations. In this population medication used to reduce afterload, promote diuresis, prevent arrhythmia and control heart rate is common. Use of such medications (aldosterone antagonists, angiotensin converting enzyme [ACE] inhibitors, amiodarone, B-blockers, diuretics, digoxin) can result in significant vasodilation and pose significant hemodynamic challenges in the post bypass period. Thus it is largely accepted to withhold diuretics in the immediate pre-operative period to avoid hypovolemia and electrolyte imbalances. Similarly, withholding ACE inhibitor therapy in the pre-operative period may avoid significant vasodilation and the associated hemodynamic challenges.

Operative anesthetic care in these children should minimize additional myocardial depression and account for potential pre-existing organ compromise. Thus medications associated with cardiac depression and increased myocardial oxygen demand should be avoided. Pharmacologic regimens such as Etomidate induction and Remifentanyl infusion for maintenance have proven useful. A variety of combinations have been used, but the core principle remains ensuring adequate analgesia and amnesia without reducing systemic vascular resistance or myocardial contractility.

The right heart remains an important factor in the operative management and if supported well can decrease the risk of needing a BIVAD. Elevated pulmonary vascular resistance and RV failure should always be considered and treated promptly in the presence of unexplained hypotension. In such settings, interventions to improve RV function include maintaining a mildly alkalotic environment, use of phosphodiesterase inhibitors (milrinone), diuretics, and inhaled nitric oxide

(iNO) or additional pulmonary vasodilators. Appropriate ventilation in such settings is essential; especially using appropriate peak exhaled expiratory pressure to maintain functional residual capacity minimizing pulmonary vascular resistance (PVR). In addition to routine hemodynamic monitoring for any cardiovascular surgery, trans-esophageal echocardiographic (TEE) monitoring is routine during VAD implantation. TEE allows for accurate assessment of anatomic variations and pathologies prior to implantation, appropriate positioning of cannulas, adequate de-airing of the device with implantation, and examining for adequate decompression and RV function following implantation.

2) OPERATION

Children with CHD pose anatomic operative challenges in cannulation for MCS (e.g., single ventricle, abnormal location of aorta and PA, prior surgical procedures with extensive fibrosis), as well as physiologic challenges (e.g., systemic-pulmonary shunts, disconnected vena cava in Glenn or Fontan operation). A thorough understanding of the unique pathologic features of pediatric heart failure is essential to a successful implantation of MCS. Special consideration with regards to central versus peripheral cannulation, device implantation, and operative features used in avoiding limb ischemia are discussed below.

3) Implantable devices

Median sternotomy incision is used to gain exposure for almost all the devices except in the rare occasion when a temporary device is required in a patient where mediastinal access is to be avoided as in these rare patients an LVAD can be placed via a thoracotomy. It is important to choose your aortic cannulation site prior to CPB so one can appreciate the right shoulder of the heart when it is full, this is especially true of the EXCOR whose cannula is non-compliant. Once this has been chosen, cannulation of the aorta should be determined keeping in mind with the smaller children one always has the option of sewing a graft into the innominate artery at time of implant or heart transplantation. We do not arrest the heart but to close a patent foramen of ovale and even then will restart it as quickly as possible to avoid arrest time which can have deleterious effects on the RV. One should remember that CPB is usually a time when these children are experiencing the best cardiac output they have seen in months to years and one should also take advantage to do aggressive ultrafiltration while on CPB. The latter has clearly been shown to improve right heart function. Also, the left heart in children is almost always full even when on CPB with the right side completely emptied so we also place a left heart vent via the left atrial appendage which also allows you to control level of blood when you have opened the left ventricular. We will not describe the implantation techniques of each device we use but in general we do an apical cannulation except for temporary VADs and use 12 plegetted sutures and Tisseel once tied down. The aortic cannula if a graft is placed in standard fashion and for the EXCOR cannula we use purse strings and an inkwell technique. Regardless of technique one must avoid bleeding and with proper timing and meticulous technique post-operative bleeding and transfusion can be avoided. We do the majority of our VADs with no use of post-operative blood products. We wean all patients off CPB on iNO, epinephrine, and milrinone. It is important as you wean off CPB that you do not allow the right ventricle to descend so I rapidly increase LVAD support as I come off CPB.

4) POSTOPERATIVE CARE

Successful post-operative care relies on a multi-disciplinary approach with other subspecialties (i.e., hematology, infectious disease, nephrology, psychiatry, family support). Anticoagulation in children with heart failure managed on MCS poses several unique challenges. Children have an evolving coagulation cascade until approximately 5 to 7 years. Anticoagulation regimens in children vary as it is unclear what is optimal. Initial management 24 to 48 hours following implantation and minimal bleeding ($<$2 mL/kg/day) consists of initiating heparin infusion. Should bleeding remain minimal 48 hours post implantation then transition to low molecular weight heparin may occur. Only, when the patient's condition has fully stabilized (no evidence of bleeding, stable hemodynamics, tolerating an enteral nutrition) is transition to vitamin K antagonist therapy made. Routine monitoring of platelet function with the use of platelet function assays and Thrombelastography (TEGs) aid in determining

need for initiation of aspirin and persantine therapy.

Children with heart failure are often fluid overloaded, and as such their pre-device fluid status and renal function guides postoperative diuresis. In most cases diuresis is achieved by good renal perfusion and use of diuretics, however patients with impaired renal function sometimes require hemodialysis. Assessment of filling pressures (proximal to the inflow cannula) and systemic pressures (distal to the arterial cannula) are essential for diagnosing and treating hemodynamic changes. LVAD filling is contingent on the adequacy of preload and RV function. As such, in patients with diminished LVAD flow evaluation for arrhythmias, increased PVR, and right heart failure should take place. Intensive care unit teams should be familiar with the management of right heart failure and or pulmonary vascular disease with therapies such as iNO, milrinone, prostacyclin, and sildenafil.

The determination of when to wean a patient from device is individualized and dependent on the pre-device goals, the particular device, and the patient's current status. The MCS settings are slowly decreased to allow the ventricle to fill and eject. If the patient has a BIVAD, current practice is to wean the RVAD. Hemodynamic assessment including TEE, arterial tracings, and filling pressures, provides necessary information to determine if the patient will maintain adequate perfusion if weaned from support. If there is no recovery and transplant or DT is not an option, withdrawal may need to be considered. Withdrawal may also need to be considered if there is a devastating complication such as severe neurologic injury. The multidisciplinary team and family must maintain a realistic outcome expectation in the treatment of these critically ill children. Continued honest and frequent communication between physician, patient, and family is essential in this endeavor.

OUTCOMES

Little is known with regards to the long-term outcomes of pediatric MCS patients. In the first multi-institutional prospective trial of a pediatric VAD (Berlin Heart EXCOR) reported by Fraser et al. [13]., 92% had a favorable outcome (transplant, recovery or alive on device) at around 6 months for both cohorts (<0.7 m^2 and 0.7 to 1.5 m^2). This was significantly better than matched ECMO groups. In this study, side effects including bleeding, infection, and stroke remained concerns. In these cohorts bleeding was noted in 42% and 50%, infection in 63% and 50%, and stroke in 29% and 29%. This was not dissimilar to other reported studies in which adolescent children were managed on adult MCS devices [14,15]. In several reported adult studies these complications although less frequent, remain significant concerns [16,17]. It must be noted that the study reported by Fraser includes only the 48 patients who met inclusion criteria for the IDE study, and not the complete North American experience with the Berlin Heart EXCOR. Almond et al. [18] reviewed all 204 patients who underwent Berlin Heart EXCOR implant in the US since the start of the study, which included VAD implants under compassionate use (40%). Mortality on EXCOR support in this study was 25% for the entire cohort with significantly higher mortality in the compassionate use group (36%) compared to the IDE group (18%). This mortality difference may be explained in the different characteristics in the two groups with the compassionate group more likely to have CHD, be on ECMO, have severe renal disease, and higher bilirubin levels at implant. Risk factors for death on the wait list included patients with CHD, ECMO pre-implant, age <1 year, weight <5 kg, severe renal dysfunction and higher bilirubin levels [18].

Pediatric MCS use, development, and experience is growing rapidly. Only a single device is currently FDA approved for infants, and young children but several devices are approved for adolescents and young adults. In adult studies, continuous-flow LVAD support (e.g., HeartMate II LVAD) has been associated with improvements in quality of life, functional capacity, and survival [19]. In pediatrics these devices may provide similar benefits, and also provide both temporary support for those with acute reversible myocardial injury and the potential for chronic support for those with continued irreversible myocardial insults. MCS use in acute fulminant myocarditis has been shown to provide acute hemodynamic support while allowing for myocardial inflammation to subside with promising results [9,20,21]. Similarly MCS has been used in pediatric heart transplant patients with acute graft rejection to allow for hemodynamic support while immunosuppressant modifications take effect,

and also as a bridge to retransplant [22]. Additionally, novel use of MCS in patients with chronic myocardial insults such as seen in Duchene Muscular Dystrophy have been reported. Recent reports measuring quality of life (QOL) in this population, may allow for future quantitative improvement in their QOL through the use of MCS therapy [23]. MCS has been used successfully in both acute myocardial injury such as myocarditis, and also in chronic injury with reverse remodeling [24-26]. Our current protocol for device selection (Fig. 1) relies on early identification of patients with medically refractory heart failure, short-term support for those felt to have an acute reversible injury with the transition to long-term support beyond 2 weeks, and initial long-term support for those with a chronic myocardial injury allowing for both BTT and DT. Early identification of medically refractory heart failure and initiation of MCS improves survival [27]. Early recognition and initiation of MCS should limit the need for BiVAD support, which has been associated with increased morbidity and mortality in children [28]. For the smallest of children, namely infants and neonates, MCS options remain limited. The PumpKIN trial is anticipated to add to this repertoire.

CONCLUSION

Although limited experience exists with regards to long-term outcomes of pediatric MCS, current outcomes are promising. Despite positive outcomes several significant side effects remain including bleeding, infection, and stroke. Patient selection, timing of support, device selection and perioperative care remain critical components in a successful outcome for these patients.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Rossano JW, Zafar F, Graves DE, et al. *Prevalence of heart failure related hospitalizations and risk factors for mortality in pediatric patients: an analysis of a nationwide sampling of hospital discharges.* Circulation 2009;120:S586.
2. Jeewa A, Manlhiot C, McCrindle BW, Van Arsdell G, Humpl T, Dipchand AI. *Outcomes with ventricular assist device versus extracorporeal membrane oxygenation as a bridge to pediatric heart transplantation.* Artif Organs 2010; 34:1087-91.
3. Morales DL, Adachi I, Heinle JS, Fraser CD Jr. *A new era: use of an intracorporeal systemic ventricular assist device to support a patient with a failing Fontan circulation.* J Thorac Cardiovasc Surg 2011;142:e138-40.
4. Morales DL, Khan MS, Gottlieb EA, Krishnamurthy R, Dreyer WJ, Adachi I. *Implantation of total artificial heart in congenital heart disease.* Semin Thorac Cardiovasc Surg 2012;24:142-3.
5. Helman DN, Addonizio LJ, Morales DL, et al. *Implantable left ventricular assist devices can successfully bridge adolescent patients to transplant.* J Heart Lung Transplant 2000;19: 121-6.
6. Rose EA, Moskowitz AJ, Packer M, et al. *The REMATCH trial: rationale, design, and end points. Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure.* Ann Thorac Surg 1999;67:723-30.
7. Davies RR, Russo MJ, Hong KN, et al. *The use of mechanical circulatory support as a bridge to transplantation in pediatric patients: an analysis of the United Network for Organ Sharing database.* J Thorac Cardiovasc Surg 2008; 135:421-7, 427.e1.
8. Morales DL, Zafar F, Rossano JW, et al. *Use of ventricular assist devices in children across the United States: analysis of 7.5 million pediatric hospitalizations.* Ann Thorac Surg 2010;90:1313-8.
9. Wilmot I, Morales DL, Price JF, et al. *Effectiveness of mechanical circulatory support in children with acute fulminant and persistent myocarditis.* J Card Fail 2011;17:487-94.
10. Copeland JG, Smith RG, Arabia FA, et al. *Cardiac replacement with a total artificial heart as a bridge to transplantation.* N Engl J Med 2004;351:859-67.
11. Padalino MA, Bottio T, Tarzia V, et al. *HeartWare ventricular assist device as bridge to transplant in children and adolescents.* Artif Organs 2013 Oct 3 [Epub]. http://dx.doi.org/10.1111/aor.12185.
12. Miera O, Potapov EV, Redlin M, et al. *First experiences with the HeartWare ventricular assist system in children.* Ann Thorac Surg 2011;91:1256-60.
13. Fraser CD Jr, Jaquiss RD, Rosenthal DN, et al. *Prospective trial of a pediatric ventricular assist device.* N Engl J Med 2012;367:532-41.
14. Cabrera AG, Sundareswaran KS, Samayoa AX, et al. *Outcomes of pediatric patients supported by the HeartMate II left ventricular assist device in the United States.* J Heart Lung Transplant 2013;32:1107-13.
15. Reinhartz O, Keith FM, El-Banayosy A, et al. *Multicenter*

experience with the thoratec ventricular assist device in children and adolescents. J Heart Lung Transplant 2001;20:439-48.
16. Miller LW, Pagani FD, Russell SD, et al. *Use of a continuous-flow device in patients awaiting heart transplantation.* N Engl J Med 2007;357:885-96.
17. Slaughter MS, Tsui SS, El-Banayosy A, et al. *Results of a multicenter clinical trial with the Thoratec Implantable Ventricular Assist Device.* J Thorac Cardiovasc Surg 2007; 133:1573-80.
18. Almond CS, Morales DL, Blackstone EH, et al. *Berlin Heart EXCOR pediatric ventricular assist device for bridge to heart transplantation in US children.* Circulation 2013; 127:1702-11.
19. Slaughter MS, Rogers JG, Milano CA, et al. *Advanced heart failure treated with continuous-flow left ventricular assist device.* N Engl J Med 2009;361:2241-51.
20. Duncan BW, Bohn DJ, Atz AM, French JW, Laussen PC, Wessel DL. *Mechanical circulatory support for the treatment of children with acute fulminant myocarditis.* J Thorac Cardiovasc Surg 2001;122:440-8.
21. Reiss N, El-Banayosy A, Arusoglu L, Blanz U, Bairaktaris A, Koerfer R. *Acute fulminant myocarditis in children and adolescents: the role of mechanical circulatory assist.* ASAIO J 2006;52:211-4.
22. Khan MS, Mery CM, Zafar F, et al. *Is mechanically bridging patients with a failing cardiac graft to retransplantation an effective therapy?: analysis of the United Network of Organ Sharing database.* J Heart Lung Transplant 2012;31: 1192-8.
23. Uzark K, King E, Cripe L, et al. *Health-related quality of life in children and adolescents with Duchenne muscular dystrophy.* Pediatrics 2012;130:e1559-66.
24. Young JB. *Healing the heart with ventricular assist device therapy: mechanisms of cardiac recovery.* Ann Thorac Surg 2001;71(3 Suppl):S210-9.
25. Madigan JD, Barbone A, Choudhri AF, et al. *Time course of reverse remodeling of the left ventricle during support with a left ventricular assist device.* J Thorac Cardiovasc Surg 2001;121:902-8.
26. Levin HR, Oz MC, Chen JM, Packer M, Rose EA, Burkhoff D. *Reversal of chronic ventricular dilation in patients with end-stage cardiomyopathy by prolonged mechanical unloading.* Circulation 1995;91:2717-20.
27. Meliones JN, Custer JR, Snedecor S, Moler FW, O'Rourke PP, Delius RE. *Extracorporeal life support for cardiac assist in pediatric patients: review of ELSO Registry data.* Circulation 1991;84(5 Suppl):III168-72.
28. Morales DL, Almond CS, Jaquiss RD, et al. *Bridging children of all sizes to cardiac transplantation: the initial multicenter North American experience with the Berlin Heart EXCOR ventricular assist device.* J Heart Lung Transplant 2011;30:1-8.