Ventricular Assist Device Support in Neonates and Infants with a Failing Univentricular Circulation

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Short title: VAD in Neonates and Infants with Single Ventricle

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Central Message

Extremely high-risk neonates with functionally univentricular hearts who are poor candidates for conventional palliation can be successfully stabilized with VAD while awaiting transplantation.

Perspective Statement

Our comprehensive strategy for neonates with functionally univentricular hearts includes (1) conventional neonatal palliation in standard risk patients, (2) hybrid approaches in neonates with elevated risk secondary to noncardiac etiology, and (3) neonatal palliation combined with insertion of a ventricular assist device in neonates with extreme elevated risk secondary to cardiac etiology.

Legend for our Central Picture

Palliation+VAD for HRHS with VAD and systemic-to-pulmonary shunt+/pulmonary arterioplasty

Keywords

ventricular assist device; functionally univentricular heart; hypoplastic left heart syndrome; hypoplastic right heart syndrome
I. Abstract

Some neonates with functionally univentricular hearts are extremely high risk for conventional surgical palliation. Primary cardiac transplantation offers the best option for survival of these challenging neonates; however, waitlist mortality must be minimized.

We have developed a comprehensive strategy for the management of neonates with functionally univentricular hearts that includes the selective use of conventional neonatal palliation in standard risk patients, hybrid approaches in neonates with elevated risk secondary to noncardiac etiology, and neonatal palliation combined with insertion of a single ventricular assist device (VAD) in neonates with elevated risk secondary to cardiac etiology. The purpose of this manuscript is to describe our selection criteria, technical details, management strategies, pitfalls, and current outcomes for neonates with functionally univentricular hearts supported with VAD. Our experience documents that extremely high-risk patients with functionally univentricular hearts who are poor candidates for conventional palliation can be successfully stabilized with concomitant palliation and pulsatile VAD insertion while awaiting transplantation.
II. Introduction

The survival of patients with congenital heart disease continues to improve after surgical palliation and repair; however, certain subsets of patients remain at high risk. We have developed a comprehensive strategy for the management of neonates and infants with functionally univentricular hearts that includes the selective use of conventional neonatal palliation in standard risk patients, hybrid approaches in neonates with elevated risk secondary to noncardiac etiology, and neonatal palliation combined with insertion of a single ventricular assist device (VAD) in neonates with elevated risk secondary to cardiac etiology (Figure 1 and Figure 2) [1, 2, 3, 4, 5]. Our unique strategy has resulted in improved survival of children with univentricular circulation. The purpose of this manuscript is to describe our selection criteria, technical details, management strategies, pitfalls, and current outcomes for neonates with functionally univentricular hearts supported with VAD.
III. Selection criteria

We have developed a comprehensive strategy for the management of neonates with functionally univentricular hearts, including neonates with both hypoplastic right heart syndrome (HRHS) and hypoplastic left heart syndrome (HLHS).

For neonates with HRHS (Figure 1):
- Standard risk patients undergo initial palliation with either a surgical or transcatheter approach.
- Neonates with elevated risk secondary to noncardiac etiology (e.g., necrotizing enterocolitis, stroke, genetic syndromes like Turner syndrome [4] and Kabuki syndrome, heterotaxy syndrome with asplenia) undergo transcatheter palliation.
- Neonates with elevated risk secondary to cardiac etiology (e.g., large coronary sinusoids/fistulas with concerning coronary circulation, cardiogenic shock, heart failure +/- associated end organ dysfunction, severe mitral regurgitation, severe ventricular dysfunction) undergo VAD insertion (Berlin EXCOR [Berlin Heart, Inc., Berlin, Germany]) along with initial surgical palliation (Palliation+VAD). The pathway for the patients who are candidates for Palliation+VAD is shown in the yellow boxes in Figure 1.

For neonates with HLHS or HLHS-related malformations (Figure 2):
- Standard risk patients undergo initial palliation with the Norwood (Stage 1) operation, typically with a right ventricle to pulmonary artery conduit. Neonates undergoing Norwood (Stage 1) operation with a dominant morphologic left ventricle (e.g., tricuspid atresia with transposed great arteries of double inlet left ventricle with transposed great arteries) will undergo placement of a systemic-to-pulmonary artery shunt as their source of pulmonary blood flow.
- Neonates with elevated risk secondary to noncardiac etiology (e.g., necrotizing enterocolitis, stroke, genetic syndromes like Turner syndrome [4] and Kabuki syndrome, heterotaxy syndrome with asplenia) undergo stage 1 hybrid palliation consisting of application of bilateral pulmonary bands, stent placement in the patent arterial duct, and atrial septostomy if needed.
- Neonates with elevated risk secondary to cardiac etiology (e.g., large coronary sinusoids/fistulas with concerning coronary circulation, cardiogenic shock, heart failure +/- associated end organ dysfunction, severe tricuspid regurgitation, severe ventricular dysfunction) undergo VAD insertion (Berlin EXCOR [Berlin Heart, Inc., Berlin, Germany]) along with stage 1 hybrid palliation consisting of application of bilateral pulmonary bands, stent...
placement in the patent arterial duct, and atrial septectomy if needed (Hybrid+VAD). The pathway for the patients who are candidates for Hybrid+VAD is shown in the yellow boxes in Figure 2.

Of note, it is possible to place bilateral pulmonary bands and maintain ductal patency with prostaglandin in neonates with HLHS (or HLHS-related malformations) and elevated risk secondary to noncardiac etiology, in order to allow the patient time to recover prior to undergoing the Norwood (Stage 1) operation after a few weeks on prostaglandin. This approach allows resuscitation of the high-risk neonate with pulmonary overcirculation in preparation for a Norwood (Stage 1) operation during the same hospitalization. We have not utilized this approach and prefer to place a ductal stent in these patients in preparation for a Comprehensive Stage 2.
IV. Technical details

A. Surgical Technique for Hybrid+VAD for HLHS

After performing a median sternotomy and pericardiotomy and evaluating the cardiac structures, the sub-rectus space, which will be used to tunnel the Berlin cannulae, is then created by dissecting the peritoneum off of the posterior aspect of the rectus muscles. The 6 mm VAD inflow cannula can be tunneled at this time, exiting on the right side, clear of the costal margin. The right-sided incision is placed so that the cannula will sit at the correct location in the right atrium, and the Teflon felt on the VAD inflow cannula is ultimately positioned at approximately its midpoint with respect to the skin incision. In a neonate or small infant, the exit site is often at or below the umbilicus to ensure adequate Teflon below the skin for incorporation. The tunnel is dilated serially up to the size of a 9 mm dilator, and the canula is then passed through the tunnel. Then, the cannula tip is then parked in the right pleural space for later insertion and use.

The patient is systemically heparinized. In preparation for cardiopulmonary bypass (CPB), cannulation is performed of the patent arterial duct (and/or the innominate artery), the superior vena cava, and the inferior vena cava. The right and left pulmonary arteries are banded using a cut ring of a 4-mm polytetrafluoroethylene (PTFE) graft. The bands are sized to around 3.75mm to allow room for growth while on the waiting list. (A 3.5-mm PTFE graft was previously used and is still occasionally used in smaller patients). A hemoclip is placed as a radiographic marker at the junction of the left pulmonary artery and the arterial duct in order to aid in the subsequent positioning of the ductal stent.

The right is atrium prepared with two pledgeted 5-0 polypropylene (Prolene, Ethicon, Somerville, New Jersey [https://www.jnjmedicaldevices.com/en-US/companies/ethicon]) pursestring sutures positioned at the cranial and caudal ends of the planned VAD inflow cannulation site. This VAD inflow cannulation site is positioned at the convexity of the right atrial free wall slightly inferior to the atrial appendage, in such a position as to allow the VAD inflow cannula to be positioned in the mid right atrial cavity facing postero-medially at an angle of approximately 45 degrees. CPB is then established, and the patent arterial duct is snared with a silk ligature, incorporating the arterial CPB perfusion canula. Caval snares are applied. The atrium is then opened and an atrial septectomy is performed if needed.
The previously placed 5-0 polypropylene pursestring sutures are passed through the cuff of the VAD inflow cannula, 180 degrees from each other. The VAD inflow cannula is inserted into the atrium through the atriotomy incision pursestrings, the needles of the pursestring sutures are kept in place, and the purse strings are tied. The VAD inflow cannula is then secured by anastomosing the atrial wall to the polyurethane cuff of the VAD inflow cannula, using continuous running suture with the same previously placed 5-0 polypropylene atrial pursestring suture. The VAD inflow cannula is connected to a pump sucker using a \( \frac{1}{4} \) inch connector in order to vent the common atrium.

The 5-6 mm outflow cannula of the 10ml Berlin EXCOR VAD is prepared by attaching an 8mm Dacron graft extension orthogonally using 4 cardinally placed 5-0 polypropylene simple sutures. The graft is then secured by tying a #1 silk ligature to engage the flange on the cannula. The main pulmonary artery is opened longitudinally and then the arteriotomy is enlarged slightly with a punch. The graft is then cut to length (usually at least 10mm), beveled at an angle optimal to flow, and anastomosed to the main pulmonary artery with 5-0 polypropylene. We make the outflow graft extension of the cannula at least 1cm so that we have the flexibility of placing the outflow canula in an optimal position within the chest. The medial skin incision is placed so that the VAD outflow cannula will be in the correct location in the chest, and the VAD outflow cannula is also sized to ensure that the Teflon felt on the cannula is positioned at approximately its midpoint with respect to the skin incision. The tunnel through the previously created sub-rectus plane is dilated serially up to the size of a 9 mm dilator, and the VAD outflow cannula is then passed through the tunnel and the medial skin incision. The Berlin Heart cannulas are connected to the VAD after adequate deairing, and the transition is made from CPB to VAD. Heparin is reversed, and the cannulas for CPB are removed.

As discussed below, this procedure can be safely performed in a Hybrid Operating Suite or sequentially by starting in the Operating Theater for the portion performed on CPB with subsequent intraoperative transfer to the cardiac catheterization laboratory for ductal stent placement under fluoroscopy. Under fluoroscopy, the right ventricle is cannulated via the modified Seldinger technique using a 21-gauge 2.5-cm Cook One-Part Percutaneous Entry Needle (Cook Medical LLC, Bloomington, Indiana). A 0.018-inch x 40 cm Nitinol Mandrel Guidewire (B. Braun Interventional Systems Inc., Bethlehem, PA) is advanced through the needle into the main pulmonary artery and across the arterial duct. The needle is exchanged for with a 4-French Micro-Introducer (B. Braun Interventional Systems Inc., Bethlehem, PA) followed by exchange of the wire for a 0.035 inch x 180 cm Boston Scientific Magic Torque™ Guidewire, (Boston Scientific, Marlborough, MA) that is advanced into the descending aorta. The Micro-Introducer is removed and exchanged for a 7-French
5.5-cm Cordis BRITE TIP™ Interventional Sheath Introducer (Cordis, Cardinal Health, Santa Clara, California). Angiography of the arterial duct is performed through the sheath and used to obtain measurements of the arterial duct for stenting. The arterial duct is visualized by contrast angiography on the lateral plane. The stent is chosen is typically one to two mm larger than the size of the descending thoracic aorta at the aortic isthmus. The length of the chosen stent is such that it would cover the entire span of the ducal tissue. The proximal end of the stent is marked by a hemoclip placed at the origin of the left pulmonary artery and the distal end extends just slightly past the junction of the aortic arch onto the arterial duct.

An appropriately sized Cook Zilver® 635™ Vascular Self-Expanding Stent (Cook Medical LLC, Bloomington, Indiana) is then deployed in the arterial duct. This stent is typically 7 to 9 mm in diameter and 20 mm in length. Postprocedure angiography is performed to confirm appropriate stent position, assess retrograde arch flow, and confirm adequate pulmonary artery banding. The sheath in the right ventricle is removed and hemostasis is achieved. Usually, delayed sternal closure is performed on the first day after VAD insertion. Figure 3 demonstrates the surgical strategy and shows a drawing of the configuration of the Hybrid+VAD for HLHS.
B. Surgical Technique for Palliation + VAD for HRHS

The technique for HRHS is identical to that used for HLHS, with the exception of these notable differences:

- The aorta is used for arterial cannulation for CPB, rather than the innominate artery or arterial duct.
- The aorta is used for the VAD outflow cannula.
- A source of pulmonary blood flow is established with either ductal stenting or the creation of a systemic-to-pulmonary artery shunt +/- pulmonary arterioplasty.
- The systemic-to-pulmonary artery shunt can originate from the ascending aorta or from the Dacron extension of the VAD outflow cannula, depending on the aortic dimensions and the surrounding anatomy. The decision is made to prevent kinking of the shunt or compression by the VAD outflow cannula, especially at the time of sternal closure.

Figure 4 and Figure 5 demonstrate the surgical strategy and show a drawing of the configurations of Palliation+VAD for HRHS. Figure 4 demonstrates the configuration of Palliation+VAD for with ductal stenting HRHS. Figure 5 demonstrates the configuration of Palliation+VAD for HRHS with the creation of a systemic-to-pulmonary artery shunt +/- pulmonary arterioplasty.
C. VAD Logistics – Location of the Procedure and Composition of the TEAM

Insertion of VAD in the neonate or infant can be safely performed in a Hybrid Operating Suite or sequentially by starting in the Operating Theater for the portion performed on CPB with subsequent intraoperative transfer to the cardiac catheterization laboratory for ductal stent placement under fluoroscopy. Management of the neonate and infant supported with VAD requires excellence from all member of the multidisciplinary team.

D. VAD Management

The VAD settings are titrated to achieve an initial cardiac index of 4 l/min/m². Target hemodynamic and physiologic parameters are similar to any other Stage 1 procedure. The VAD can be upsized from a 10ml Berlin EXCOR VAD to a 15ml Berlin EXCOR VAD, if necessary, secondary to growth of the patient while on the waiting list.

Bivalirudin is initiated on postoperative day 1. The VAD rate is gradually increased as needed to assure adequate cardiac output and systemic tissue perfusion. The patient is extubated as soon as possible. Appropriate weight gain and end-organ function are maintained on VAD support until transplantation.

E. Anticoagulation

During the first 24 hours after VAD insertion, no anticoagulation is given. The following anticoagulation protocol is then initiated:

- **Bivalirudin:** During hours 24 to 72, bivalirudin is titrated to a PTT of 50 to 70. After 72 hours, bivalirudin is titrated to a PTT of 70 to 100.

- **Aspirin:** Aspirin is started on day 5 on VAD at a dose of 5 mg/kg/day (divided into two daily doses) and is increased each week until a dose of 30 mg/kg/day is reached by week 4.

- **Dipyridamole:** Dipyridamole is started on week 5 on VAD at a dose of 2.5 mg/kg/day and is increased twice each week until a dose of 15 mg/kg/day is reached by week 6.

- **Omega-3 fatty acid:** Omega-3 fatty acid is typically started after 3 to 4 months on VAD.
V. Potential Pitfalls – Stroke while on VAD

In this analysis, a stroke is defined as any confirmed neurological deficit of abrupt onset caused by a disturbance in blood flow to the brain, when the neurologic deficit does not resolve within 24 hours and is associated with radiographic confirmation by computerized axial tomography. In our HLHS cohort, only two of nine patients supported with Hybrid+VAD have experienced strokes, and both of these strokes were after 150 days on VAD. In our HRHS cohort, two of six patients supported with Palliation+VAD have experienced strokes, one after 90 days on VAD and one after 10 days on VAD in a patient with Factor V Leiden in whom anticoagulation was stopped due to bleeding from the VAD cannula.

None of these strokes were life threatening or necessitated VAD removal. Although we did not use Clopidogrel in these nine patients, our program is considering augmentation of our current protocol of anticoagulation while on VAD, including potentially adding Clopidogrel after 120 days on VAD support. In the four patients with stroke, bivalirudin, and dipyridamole, were both stopped following diagnosis. Computerized axial tomography was then repeated three days after the stroke, and if no evidence of bleeding or progression of the stroke was documented, bivalirudin was restarted with an initial goal PTT of 50 to 70. Computerized axial tomography was again repeated five days after the stroke, and if no evidence of bleeding or progression of the stroke was documented, dipyridamole was restarted.
VI. Current Outcomes

Our current approach is based on the following principles:

- Some patients with HLHS or HRHS are extremely high risk for conventional surgical palliation.
- Primary cardiac transplantation offers the best option for survival of these challenging neonates; however, waitlist mortality must be minimized.

We have supported 15 high risk neonates and infants with HLHS or HRHS utilizing the approach described in this manuscript with Initial Palliation + VAD insertion in preparation for cardiac transplantation:

- 9 high risk neonates and infants with HLHS stabilized with a Hybrid+VAD utilizing VAD + Bilateral PA Bands + Ductal Stent +/- Atrial Septectomy
- 6 high risk neonates and infants with HRHS stabilized with initial Palliation+VAD utilizing VAD + Central Shunt or VAD + Ductal Stent.

The 9 patients with HLHS had the following anatomical and/or physiological features associated with increased risk for conventional univentricular palliation:

- 4 with unfavorable coronary anatomy (large fistulas) and signs of coronary ischemia
- 3 with heart failure (1 heart failure with severe tricuspid regurgitation, 1 late referral with heart failure and associated end organ dysfunction, and 1 with heart failure status post prior hybrid at another institution)
- 2 with cardiogenic shock (1 with cardiogenic shock needing ECMO and 1 cardiogenic shock with incessant arrhythmia)

The 6 patients with HRHS had the following anatomical and/or physiological features associated with increased risk for conventional univentricular palliation:

- 3 with unfavorable coronary anatomy (large fistulas) and signs of coronary ischemia
- 1 with signs of coronary ischemia without obvious fistulas
- 1 with cardiogenic shock
- 1 with cardiogenic shock and bridge from extracorporeal cardiopulmonary resuscitation (ECPR).
In this analysis, we utilize the definition of Operative Mortality that is utilized by The Society of Thoracic Surgeons. Operative Mortality is defined in all STS databases as “(1) all deaths, regardless of cause, occurring during the hospitalization in which the operation was performed, even if after 30 days (including patients transferred to other acute care facilities); and (2) all deaths, regardless of cause, occurring after discharge from the hospital but before the end of the 30th postoperative day.”.

Of 9 high risk neonates and infants with HLHS stabilized with a Hybrid+VAD, 7 were neonates and 2 were infants. During this same era, at University of Florida:

- 57 standard risk neonates underwent Norwood Operation with an Operative Mortality of 2 out of 56 = 3.5%
- 9 neonates with noncardiac risk factors (e.g., Turner syndrome [4], necrotizing enterocolitis) underwent Hybrid Approach "Stage 1" without VAD (8 are alive and 1 died after Comprehensive Stage 2)
- 3 patients were supported with prostaglandin while awaiting transplantation

Of 6 high risk neonates and infants with HRHS stabilized with a Hybrid+VAD, 4 were neonates and 2 were infants. During this same era, at University of Florida, 21 neonates and infants underwent initial conventional surgical palliation for HRHS (12 systemic-to-pulmonary artery shunts, 3 pulmonary artery bands, and 6 primary Glenn superior cavopulmonary connections) with an Operative Mortality of 1 out of 21 = 4.8%.

Median age at Palliation+VAD is 21 days (range = 4 - 143 days). Median weight at Palliation+VAD is 3.47 kilograms (range = 2.43 - 4.6). Eight patients with HLHS underwent Hybrid+VAD as their initial procedure. One patient with HLHS had undergone bilateral pulmonary banding, subtotal atrial septectomy, and ductal stenting at a different institution and underwent VAD placement with completion atrial septectomy and ductal stent revision.

Of these 15 high risk neonates and infants with HLHS or HRHS stabilized with a Hybrid+VAD, eight patients survive (53.3%) and seven patients died (46.7%). Of the eight survivors, 7 survivors are at home doing well after successful cardiac transplantation and 1 survivor is doing well in the ICU on VAD support awaiting transplantation. Of the 7 deaths, 1 death was after primary graft failure at time of transplant after 287 days on VAD.
Of note, of 13 high risk neonates with HLHS or HRHS stabilized with Palliation+VAD, eight patients survive (61.5%) and five patients died (38.5%). (Two infants with HLHS were managed with Hybrid+VAD and did not survive: one 100-day-old infant underwent VAD insertion and hybrid revision after failed hybrid procedure at another institution and one 143-day-old previously unpalliated infant with end organ dysfunction underwent Hybrid+VAD as bridge to decision.)

In fourteen patients no longer on VAD, the median length of VAD support was 120 days (range=30-287 days):

- In seven survivors no longer on VAD, median length of VAD support was 162 days (range=64-196 days).
- In seven non-survivors no longer on VAD, median length of VAD support was 98 days (range=30-287 days).

Only two of eight survivors (25%) required intubation more than 10 days after Palliation+VAD.
VII. Summary

Of these 15 high risk neonates and infants with HLHS or HRHS stabilized with Palliation+VAD, eight patients survive (53.3%) and seven patients died (46.7%). Of note, of 13 high risk neonates with HLHS or HRHS stabilized with Palliation+VAD, eight patients survive (61.5%) and five patients died (38.5%).

Our analysis of 15 patients with HRHS or HLHS supported with Palliation+VAD demonstrates that high-risk patients with functionally univentricular hearts who are suboptimal candidates for conventional palliation can be successfully stabilized with concomitant palliation and pulsatile VAD insertion while awaiting transplantation; these patients may be extubated and optimized for transplantation while on VAD. In patients with functionally univentricular hearts, we prefer pulsatile rather than continuous flow VAD because we believe that:

1. pulsatile VAD is more physiologic,
2. the management of patients on pulsatile VAD is more intuitive the healthcare team,
3. pulsatile VAD is associated with decreased risk of pulmonary overcirculation, and
4. pulsatile VAD is associated with improved renal function.

Clearly, not enough donor hearts exist to offer transplantation to all patients with HLHS, let alone all patients with functionally univentricular hearts. However, it is reasonable to offer transplantation to patients at high-risk for conventional staged palliation. Unfortunately, because of the shortage of donor organs, time on the waiting list for a heart can be long, leading to increasing concern about the potential for waitlist mortality. Because of these potentially long waiting times, it is also reasonable to stabilize these high-risk patients with functionally univentricular hearts with Palliation+VAD while awaiting transplantation [1, 1, 3]. This approach facilitates early extubation and optimization for transplantation while on VAD in this high-risk population.

Survival of patients weighing < 5 kg with functionally univentricular physiology supported with VAD is novel [6, 7, 8, 9, 10, 11]. In 2008, Pearce and colleagues reported successful cardiac transplantation after Berlin Heart insertion and bridging in a 15-month-old boy with a functionally univentricular heart (double-outlet right ventricle {S,D,D}, mitral valve atresia, D-malposition of the great vessels, status-post pulmonary artery band in infancy) and poor systemic ventricular function, using an aortopulmonary shunt as a supplementary source of pulmonary blood flow [6]. In 2014,
Weinstein and colleagues reported a retrospective review of the EXCOR Investigational Device Exemption study database that included VAD implants under the primary cohort and compassionate use cohort between May 2007 and December 2011 [7]. Twenty-six of 281 patients supported with a VAD in this analysis had univentricular physiology, including 15 with HLHS. Nine patients were supported after neonatal palliative surgery (systemic-to-pulmonary artery shunt or right ventricle to pulmonary artery conduit), 12 after superior cavopulmonary connection, and 5 after total cavopulmonary connection (TCPC). Eight of 9 patients with VAD implant after neonatal palliation died, all within 3 weeks of implantation (range, 0-17 days). The only survivor in this series after stage I palliation was a 17-month-old child (Damus-Kaye-Stansel procedure) who had a systemic-to-pulmonary artery shunt take down and insertion of biventricular VADs after pulmonary artery reconstruction [7].

Also in 2014, Conway and colleagues reported an analysis of all children weighing <10 kg who were enrolled in the sponsor's U.S. regulatory database and supported with the Berlin Heart EXCOR Pediatric VAD as a bridge to transplant between May 9, 2007 and December 31, 2010 [8]. A total of 97 children weighing <10 kg were included, and 33 of these children were weighed less than 5 kg. Outcomes for patients weighing <5 kg were significantly worse than those between 5 and 10 kg. Only 27.3% (9 of 33) of children weighing < 5 kg experienced a successful outcome (defined as transplantation or being weaned from the device with a good neurological outcome within 30 days of explant); 63.6% (21 of 33) died, and 9.1% (3 of 33) were weaned unsuccessfully. These findings were significantly different from those in patients weighing between 5 and 10 kg; 71.9% of this cohort achieved a successful outcome (p < 0.001), and there was a 25% mortality rate [8].

In 2019, Adachi and colleagues reported their single-center experience with centrifugal-flow VAD support in children: 40 implantations in 39 patients (28 with cardiomyopathy, 11 with congenital heart disease, including only 3 with univentricular physiology) [9]. Of the 3 with univentricular physiology, all had a systemic right ventricle, 2 had Glenn circulation and 1 had Fontan circulation. All patients with univentricular physiology were managed as outpatients and underwent cardiac transplantation at 5, 7, and 17 months of VAD support [9].

A 2021 publication from Puri and Adachi “reviewed the published literature in the form of database and registry reports as well as single-center studies to discuss the outcomes of Stage I and Stage II single ventricle congenital heart disease patients on VAD support” [10]. This analysis
documented that “The outcomes of Stage I and Stage II SV-CHD patients on VAD support from the Pedimacs database are poor, with less than 50% survival on VAD by the 3-month mark in both.” [10].

Also in 2021, the International Society for Heart and Lung Transplantation (ISHLT) published a consensus statement for the selection and management of pediatric and congenital heart disease patients on VADs [11]. This consensus statement was endorsed by the American Heart Association and provides the following key points regarding support strategies for single ventricle patients on VAD [11]:

- To support stage 1 patients with parallel circulations, VAD flows to achieve a higher cardiac index are often required and a balanced Qp/Qs is crucial.
- In stage 2 patients, converting to shunted or Fontan physiology at the time of SVAD implant may be considered for improved pulmonary blood flow.
- There is increasing experience and success using durable VADs to support Fontan patients with HF due to systemic ventricular dysfunction.

The techniques, strategies, and approach reported in this manuscript are novel as evidenced by the paucity of published literature regarding VAD support in neonates and infants with a failing univentricular circulation [6, 7, 8, 9, 10, 11].

**Limitations and Future Directions**

The major challenge of prolonged VAD support of neonates and infants is the prevention of thromboembolic complications and stroke. Our program is considering augmentation of our current protocol of anticoagulation while on VAD, including the possible addition of Clopidogrel after 120 days on VAD support.

**VIII. Conclusion**

Our experience documents that extremely high-risk patients with functionally univentricular hearts who are poor candidates for conventional palliation can be successfully stabilized with concomitant palliation and pulsatile VAD insertion while awaiting transplantation. These patients may be extubated, enterally nourished, and optimized for transplantation while on VAD. VAD facilitates survival on the transplant waiting list during prolonged wait times. VAD support allows survival
through potential crises while on the waiting list, including episodes of hemodynamic instability and sepsis. Strategies must be developed to prevent stroke in neonates and infants supported with VAD for prolonged periods of time.

This strategy of management described in this review is clearly in evolution. We believe that this approach maximizes the chance of survival of extremely high risk patients with functionally univentricular hearts who otherwise might die awaiting transplantation.
Figure 1. Comprehensive Approach to Patients with HRHS
Figure 2. Comprehensive Approach to Patients with HLHS

Patients with HLHS or HLHS-related malformation

- Standard Risk
  - Norwood Stage 1
- High Risk
  - Risk Factors other than Major Cardiac Risk Factors
    (e.g., necrotizing enterocolitis, stroke, Turner syndrome, Kabuki syndrome, Heterotaxy syndrome with asplenia)
  - Major Cardiac Risk Factors
    (e.g., large coronary sinusoids/istulas with concerning coronary circulation, cardiogenic shock, heart failure +/- associated end organ dysfunction, severe tricuspid regurgitation, severe ventricular dysfunction)
- Hybrid Stage 1 without VAD
- Hybrid Stage 1 + VAD
Figure 3. The configuration of PALLIATION+VAD for HLHS utilizing application of bilateral pulmonary artery bands, stent placement in the patent arterial duct, atrial septectomy if needed, and Berlin heart VAD insertion.
Figure 4. The configuration of PALLIATION+VAD for HRHS utilizing stent placement in the patent arterial duct, atrial septectomy if needed, and Berlin heart VAD insertion.
Figure 5. The configuration of PALLIATION+VAD for HRHS utilizing systemic-to-pulmonary artery shunt +/- pulmonary arterioplasty, atrial septectomy if needed, and Berlin heart VAD insertion.
Legends for Figures:

- **Figure 1** documents our pathway for decision making for neonates with hypoplastic right heart syndrome (HRHS). The pathway for the patients who are candidates for Palliation+VAD is shown in the yellow boxes in Figure 1.

- **Figure 2** documents our pathway for decision making for neonates with hypoplastic left heart syndrome (HLHS). The pathway for the patients who are candidates for Hybrid+VAD is shown in the yellow boxes in Figure 2.

- **Figure 3** documents the configuration of PALLIATION+VAD for hypoplastic left heart syndrome (HLHS) utilizing application of bilateral pulmonary artery bands, stent placement in the patent arterial duct, atrial septectomy if needed, and Berlin heart VAD insertion.

- **Figure 4** documents the configuration of PALLIATION+VAD for hypoplastic right heart syndrome (HRHS) utilizing stent placement in the patent arterial duct, atrial septectomy if needed, and Berlin heart VAD insertion.

- **Figure 5** documents the configuration of PALLIATION+VAD for hypoplastic right heart syndrome (HRHS) utilizing systemic-to-pulmonary artery shunt +/- pulmonary arterioplasty, atrial septectomy if needed, and Berlin heart VAD insertion. The systemic-to-pulmonary artery shunt may originate from the 8mm Dacron graft extension connecting the outflow cannula to the aorta (as shown in this drawing) or from the aorta itself.
References


HRHS: Shunt and VAD

Aortic Cannula

Atrial Cannula

Systemic-to-Pulmonary Artery Shunt +/- Pulmonary Arterioplasty

Please note: The shunt may also originate on the aorta
HLHS: Hybrid-VAD

- Bilateral PA Bands
- Atrial Cannula
- Aortic Cannula
- Berlin Heart Pump
HRHS: Hybrid-VAD

- Ductal Stent
- Aortic Cannula
- Atrial Cannula
HRHS:
Shunt and VAD

Aortic Cannula

Atrial Cannula

Systemic-to-Pulmonary Artery Shunt +/- Pulmonary Arterioplasty

Please note: The shunt may also originate on the aorta
Ventricular Assist Device: Recent Articles From AATS Journals


Commentary: Patience is a virtue: Recovery is only possible if given a chance to happen, but is this safe? Riggs KW, Morales DLS. *J Thorac Cardiovasc Surg.* 2019;157(4):1618-1619.