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Review

Failure (at any stage) and the role of mechanical circulatory support in hypoplastic left heart syndrome

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ABSTRACT

Mechanical circulatory support (MCS) options in children with hypoplastic left heart syndrome (HLHS) may be limited due to size, anatomy, device and center limitations. This review aims to describe the various MCS options available to HLHS and other single ventricle heart failure patients, and review the outcomes of those devices in children after each stage of single ventricle surgical palliation.

1. Introduction: the scope of the problem

Heart failure in children with congenital heart disease carries a high rate of morbidity and mortality [1]. Those with hypoplastic left heart syndrome (HLHS) are certainly among those at risk for decompensated heart failure throughout their three-stage surgical palliations and beyond, as each of these stages includes a delicate balance between the pulmonary and systemic circulations that depends upon one functional pumping chamber (Fig. 1). An analysis of Single Ventricle Reconstruction (SVR) trial showed that heart failure develops in approximately 15% of children after the Norwood procedure by age 6 [2]. Consideration for advanced heart failure therapies in such children is often warranted.

Mechanical circulatory support (MCS) options in children with HLHS may be limited for several reasons. With respect to patient risk factors, these children may be small in size relative to the devices which are available, with complex anatomy and often multisystem organ dysfunction also stacked against them. The devices themselves come with an inherent risk of thrombosis, infection, and device malfunction [3]. There is also a learning curve that comes with new technologies, yet over half of the centers reporting data for the first Pediatric Interagency Registry for Mechanical Circulatory Support (PediMACS) Registry report had implanted 5 or fewer durable support devices between the years 2012–2015 [4]. Physiologically, most durable MCS devices do not directly address the problem of elevated central venous pressures that often plagues a failing single ventricle patient. Overall, ventricular assist device (VAD) support outcomes are worse in children with congenital heart disease as compared to children with cardiomyopathy, although similar between those with single ventricle and biventricular CHD physiology [5].

This review aims to describe the various MCS options available to HLHS and other single ventricle heart failure patients, and review the outcomes of those devices in children after each stage of single ventricle surgical palliation.

2. Types of mechanical circulatory support

The MCS options currently utilized in children are typically divided into short- and long-term devices, as shown in Table 1. Extracorporeal membrane oxygenation (ECMO) is widely available to provide short-term cardiorespiratory support when veno-arterial cannulation is utilized, but results in single ventricle patients are rather poor [6–8]. Percutaneous devices, such as the Abiomed Impella and TandemLife TandemHeart VADs, are short-term devices which can be deployed at bedside or in the cardiac catheterization laboratory to provide temporary ventricular support without membrane oxygenation. Paracorporeal continuous devices, such as the Maquet Rotaflow and Thoratec PediMag and Centrimag devices, were intended for short-term support but are increasingly utilized as a longer-term bridge to transplantation and now comprise about half of the VADs utilized in congenital heart disease patients [5].

More durable VADs include the Berlin Heart EXCOR, a paracorporeal pulsatile device that was the first to be FDA-approved for use in children. This device is available in a variety of pump sizes, allowing for implantation in children as small as 3 kg and as large as full-grown adults. While the only approved indication for the EXCOR was in children with cardiomyopathy, it also comprises about one quarter of the VADs used in children with CHD [5]. Another one fifth of VADs used in CHD are implantable continuous devices, such as the HeartWare HVAD and Abbott HeartMate 3 [5]. Some children with such

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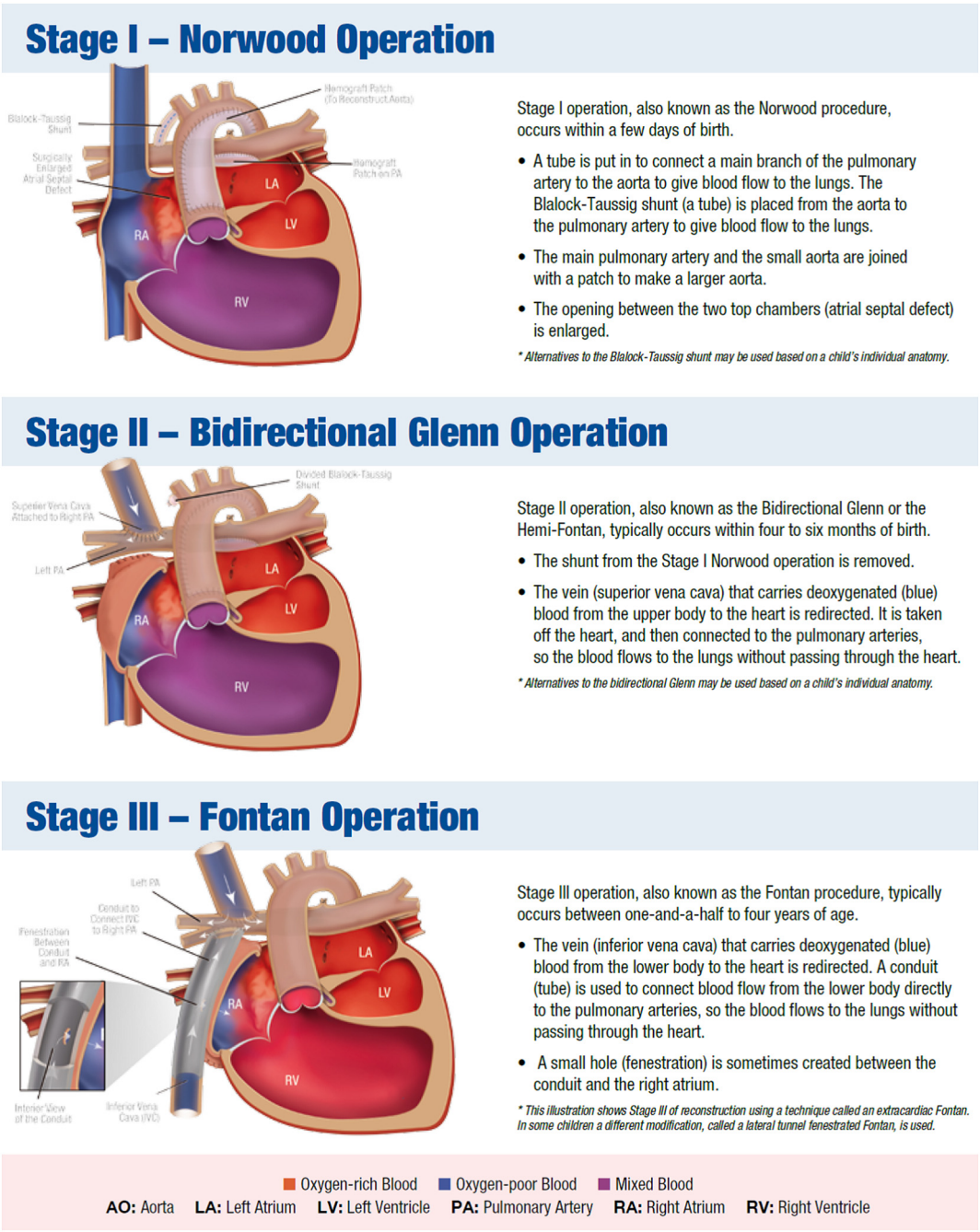

Fig. 1. Staged palliation surgeries for hypoplastic left heart syndrome.
Courtesy of the Children's Hospital of Philadelphia and available for download at www.chop.edu/treatments/staged-reconstruction-heart-surgery.

Table 1
Pediatric mechanical circulatory support options.

Short-term devices	Long-term devices
ECMO Paracorporeal continuous: PediMag/CentriMag, RotaFlow Percutaneous: Impella, Tandem Heart	Paracorporeal pulsatile: Berlin Heart EXCOR Implantable continuous: HeartWare HVAD, HeartMate III, Jarvik 2015 Biventricular: Syncardia TAH

ECMO, extracorporeal membrane oxygenator; TAH, total artificial heart.

implantable VADs have achieved discharge from the hospital setting with close outpatient monitoring, a considerable advantage in terms of quality of life and rehabilitation potential. However, many children are too small for these particular devices. The Infant Jarvik 2015 is the only device which has emerged from the PumpKIN (Pumps for Kids, Infants and Neonates) program and progressed to clinical trial as an implantable continuous flow device for small children. Finally, the Syncardia Total Artificial Heart (TAH) is the only VAD currently available to provide implantable biventricular circulatory support as a single device. The TAH has a portable driver that may allow for discharge

from the hospital, and a standard size that is intended for patients with a body surface area (BSA) of at least 1.7 m2.

3. Mechanical circulatory support after stage 1: limited options

For children who require advanced heart failure support after stage 1 single ventricle palliation, MCS options are severely limited due to small patient size. ECMO is the mainstay of MCS after stage 1. For such children, outcomes are better if the indication for ECMO support is a systemic to pulmonary artery shunt occlusion rather than circulatory collapse [9]. Stage 1 survival to hospital discharge when ECMO is needed is worst among the 3 staged palliation procedures at 31% [6]. A small but increasing number of paracorporeal continuous flow VADs are being used at earlier stages. In a recent PediMACS review of temporary VAD use in pediatrics, 11 such VADs were utilized in single ventricle patients after stage 1 surgery, with 7 (64%) achieving a positive outcome (4 recovered for VAD explant and 3 bridged to transplant) [10].

The published experience with a durable paracorporeal pulsatile VAD in children after stage 1 palliation has been discouraging. Only 1 of 9 neonates supported with an EXCOR device between the years 2007–2011 after stage 1 surgery survived, as reported in an analysis of the EXCOR Investigational Device Exemption study database [11]. Young age and small size certainly play a role in these disappointing results; there were no neonates (0 of 6) and only 25% of infants aged 30 days to < 1 year (4 of 16) who survived in a review of EXCOR support in congenital heart disease, while there was no significant difference in survival between single and biventricular CHD patients on EXCOR support [12]. Weight under 10 kg, presence of congenital heart disease, other end-organ dysfunction, and prior ECMO were all factors associated with poorer outcomes with EXCOR support [12,13].

4. Mechanical circulatory support after stage 2: options still limited

Size is likely still a limiting factor with respect to MCS options for most patients after stage 2 surgery. ECMO remains a short-term option after stage 2, but with only 42% survival to hospital discharge [7]. Paracorporeal continuous flow devices are also available; of 7 patients after stage 2 in a PediMACS report on temporary VADs in children, 3 (43%) had a positive outcome of either explant, bridge to durable VAD, or transplant from temporary VAD [10]. Outcomes for stage 2 patients supported with an EXCOR device between the years 2007–2011 were better than those in stage 1 patients, with 7 of 12 (58%) surviving to transplant [11]. Slightly higher age and size likely contribute to the better prognosis in this group [12,13].

The likelihood of persistent or even worsened hypoxemia along with a heavy systemic-to-pulmonary arterial collateral burden with VAD support in a stage 2 patient has led some to advocate for a “mechanically-assisted stage 3” procedure for children with a superior cavopulmonary connection who are limited by systolic dysfunction [14]. Such a procedure would likely be feasible only in children large enough for an implantable continuous flow VAD as well as Fontan completion surgery.

5. Mechanical circulatory support after stage 3: a broader palette

The larger size of most patients who have gone through a stage 3 Fontan surgery allows for a fuller array of MCS options if needed. VAD outcomes in single ventricle patients are clearly superior after stage 3 as compared with stage 1 and 2 [5]. ECMO is also widely available after Fontan, but yields only a 35% survival to hospital discharge [8]. A more recent series of 10 Fontan patients supported by the percutaneous Impella device showed an 80% survival to hospital discharge [15]. Short term devices, either paracoporeal or percutaneous, were infrequently used after stage 3 in the PediMACS report on temporary VAD use in children, with 2 of 2 Fontan patients (100%) reporting a positive outcome of either bridge to durable VAD or transplant [10].

Durable VAD support with a paracorporeal or implantable device is more often feasible in the larger stage 3 vs stage 1 or 2 patient. Systemic VAD filling depends upon passive flow of blood through the pulmonary circulation, and higher VAD outputs than are typically necessary for a similarly-sized biventricular patient may be required in order to account for any residual systemic-to-pulmonary arterial collateral burden. This can be a successful strategy with several different devices. Between the years 2007–2011, 3 of 5 (60%) Fontan patient supported with a single EXCOR VAD survived to heart transplantation [11]. In order to fit an intracorporeal device into patients with a body surface area as small as 0.6 m2, atrial cannulation and systemic atrioventricular valve excision has been reported as a successful strategy [16]. Successful use of the newest generation intracorporeal VAD, the Abbott HeartMate 3, was recently reported in an adult HLHS patient with failing Fontan physiology consisting of elevated central venous pressures, a low transpulmonary gradient, systemic ventricular dysfunction and atrioventricular valve regurgitation [17].

The paucity of subpulmonary MCS support options for the Fontan circulation has been a source of much consternation [18]. In clinical practice, biventricular support has been reported as a successful bridge to transplantation, either via two EXCOR devices [19] or a single TAH [20], and both requiring extensive reconstruction of the systemic venous pathway to the mechanical subpulmonary pumping chamber.

6. Smaller options on the horizon

Two devices are currently being studied in clinical trials that could directly benefit single ventricle patients with MCS needs. The Jarvik 2015 device is an implantable, continuous flow device designed for patients with a body surface area between 0.4 and 1.0 m2. A single arm feasibility study is now recruiting up to 10 subjects at 7 sites in the United States [21]. Syncardia has recently manufactured a second, smaller TAH device with 50 ml pumping chambers, designed to support patients down to a body surface area of 1.2 m2. This device has also shown encouraging early results in patients, including one with a Fontan circulation [22].

7. Current challenges and opportunities

MCS options after staged palliation surgeries in children broaden and outcomes improve with increasing size of the patient to be supported. After Stage 1 surgery, MCS options are limited to primarily short term devices, with ECMO most successful in those with an indication of hypoxemia rather than hypotension or circulatory collapse. Paracorporeal continuous flow devices are increasingly utilized in place of ECMO for longer durations after stage 1 and stage 2, and percutaneous devices are now feasible in many stage 3 patients for short-term support. Outcomes from durable VAD support with the Berlin EXCOR have been quite poor after stage 1 surgery, mixed at best after stage 2 surgery, and reasonable after stage 3 although increasingly supplanted by intracorporeal devices in such patients. Intracorporeal devices can provide systemic ventricular support for children with a BSA as low as 0.6 m2, and potentially lower if the Infant Jarvik 2015 trial shows successful outcomes. The total artificial heart may be an option for those with Fontan circulatory failure in whom both elevated central venous pressure and low systemic cardiac output must be addressed.

Smaller, more durable devices will be helpful at all stages of single ventricle palliation, as will an increase in the collective MCS experience in this special patient population. Meanwhile, the ideal means of mechanically supporting the pulmonary circulation for the failing single ventricle patient remains wide open for innovation and improvement.

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