Ventricular Assist Devices for Neonates and Infants

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Heart transplant waitlist survival in pediatric patients has been substantially improved since the introduction of pediatric-specific ventricular assist device. In neonates and infants, however, the waitlist mortality remains very high. The only long-term device currently approved for use in the United States is the Berlin Heart EXCOR, but this device has several important limitations because of the paracorporeal, pulsatile nature of the underlying technology. We reviewed Stanford ventricular assist experience on patients less than 1 year old since 2004. It shows overall 1-, 3-, and 5-year survival were 68%, 62%, and 49%, respectively. There are statistically significant differences in survival among cardiomyopathy group, end-stage congenital heart disease group and single ventricle group. In order to improve outcomes in this extremely high risk group, modifications were made to anticoagulation protocols, cannulation strategy in hypertrophic cardiomyopathy patients, and preferential use of continuous flow pumps in a single ventricle patients. The long-waited PumpKIN trial testing the Jarvik 2015 is about to start with the first human implant.
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Introduction

Mortality of Neonates and Infants During the Ventricular Assist Device Era

Since the introduction of the Berlin Heart EXCOR, and the simultaneous expansion of the use of adult ventricular assist devices (VADs) in children over the past decade, the heart transplant waitlist survival in pediatric patients has significantly improved. Zafar et al reported the pediatric heart transplant waiting list mortality in the era of VAD in all pediatric candidates (aged ≤18 years).[1] In the pre-VAD era (1999-2004), 1 year survival was 74%, compared with 86% in the post-VAD era (2005-2012). However, in a subgroup analysis, infants in the recent cohort actually showed higher mortality compared with older cohorts (21% vs 14%), and it was clear that infants have derived less benefit from VAD support as compared with larger patients.

A patient who received PediMag assist device after bilateral pulmonary banding during the neonatal period.

Central Message

Outcomes of ventricular assist device for neonates and infants are far from satisfactory. New devices, flexible utilization of existing equipment, and sophisticated management are essential to achieving good outcomes.

Long-Term Use of Ventricular Assist Device in Neonates and Infants

As of April 2017, the VADs that are available for use in infants and children remain limited. For long-term use, the only device approved by the US Food and Drug Administration is the Berlin Heart EXCOR.[2] This paracorporeal pneumatic pulsatile pump has various cannula (5 mm, 6 mm, 9 mm, and 12 mm) and pump sizes (10 mL, 15 mL, 25 mL, 30 mL, 50 mL, and 60 mL), and we can choose appropriate size cannulas and pump, depending on the size of a patient. This technology can apply to even neonates whose body weight is less than 3 kg, although

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outcomes in this size population remain extremely challenging.[3] Owing to the nature of the paracorporeal pump, its great advantage is that we can increase pump sizes as a patient grows. This is especially beneficial for neonates and infants, whose body weight can double while waiting a long period for transplant. However, because of the lack of portability of the Berlin Heart EXCOR console, a patient with this VAD cannot leave the hospital. The patient and family are required to stay in the hospital until transplant, which is extremely expensive and has a negative impact upon the quality of life. Additionally, the 2 cannulae that emerge from the upper abdomen can be a nidus of bacterial invasion and pose an ongoing risk of infection.

Outcome of Berlin Heart EXCOR in Neonates and Infants

Conway et al reviewed all children who received the Berlin Heart EXCOR from 2007 to 2010 in a total of 47 pediatric centers in the United States and Canada and reported the outcome of Berlin Heart EXCOR on patients weighing less than 10 kg, compared with larger-sized cohorts. Survival in this cohort at 6 months was barely 30% compared to 80% in larger patients. The outcome of patients weighing less than 5 kg is even worse, with 6 months survival below 20%. The most common cause of death was neurologic events, followed by respiratory, bleeding, and multisystem organ failure. Jordan et al also reported the high incidence of neurologic events in small children and noted that many of the neurologic events occurred early in the course of support.[4] These rates are substantially higher than the reported rates of neurologic events ranging from 8% to 17% in recent adult continuous-flow VAD trials.[5,6]

Emergence of Temporary Circulatory Support

Because of the inferior outcome of Berlin Heart EXCOR in neonates and infants, there is a recent trend to use short-term continuous flow pump devices as bridge to transplant in small children. Even here, the variety of short-term devices that fit neonates and infants are limited. Currently, the Levitronix PediMag and Maquet Rotaflow are the only 2 devices with operational flow ranges even lower than 1 L/min, which is often required for infant support. The Levitronix PediMag is the pediatric counterpart of the adult CentriMag, and can support flow rates up to 1.5 L/min. The pump is fully levitated magnetically which affords a theoretical advantage with respect to hemolysis and thrombosis.[7] The PediMag is mainly used in extracorporeal membrane oxygenation (ECMO) circuits,[7] but its use as temporary circulatory support ventricular device has been growing. The Rotaflow ranges from 0 to 10 L/min in flow and can support neonates to adult size patients. This is a centrifugal pump that features a 1-point sapphire bearing which lowers friction substantially.[8] Beside these 2 devices, adult size centrifugal pumps can be used by modifying the circuit, typically by inserting a bridge to divert excess flow back to the device. Monge et al reported a series of successful support for small children using the TandemHeart, an adult-size device. They limited the flow to the patient by creating a shunt between the inflow and outflow circuit.[9] It is worth noting that although there are successful support case reports of bridge to transplant by temporary circulatory devices in neonates and infants, there exists no substantial evidence that temporary circulatory support outperforms the Berlin Heart EXCOR.

Stanford Experience

Patient Demographics

From July 2004 to April 2017, at Lucile Packard Children's Hospital Stanford, 29 patients less than 1 year of age underwent VAD, intended as bridge to transplant. Instances of short-term VAD support in which the intent was to bridge to recovery, were excluded. Mean body weight was 6.0 kg (3.0-9.2) and mean age was 164 days (1-360). Seventeen patients were male. Nine patients were on ECMO before VAD implant. Median duration of support time was 71 days (1-206). Underlying diagnoses and support types are summarized in Figure 1. Twenty-five patients were biventricular anatomy and 4 patients were single ventricle. Among the biventricular group, 20 patients (80%) had cardiomyopathy. Within the cardiomyopathy group, 7 patients (35%) received biventricular assist device (BiVAD). Our indication for BiVAD is failure of weaning of cardiopulmonary bypass after left ventricular assist device (LVAD) or incessant hemodynamically significant arrhythmia. To monitor LVAD function and right ventricular function, we placed left and right atrial pressure monitoring catheters as needed. Five patients needed BiVAD due to depressed right ventricle function in dilated cardiomyopthy, 1 patient due to bilateral hypertrophic cardiomyopathy, and 1 patient due to incessant ventricular arrhythmia. In end-stage congenital heart disease group, all patients received Berlin Heart 10 mL LVAD due to left-sided systolic or diastolic dysfunction. In the single ventricular group, after early experience with the Berlin Heart EXCOR implant was unsuccessful, our preference changed to use extracorporeal centrifugal continuous flow. Due to the complexity of the physiology and the variability of age, our approach in the single ventricle group has evolved over the study period. All patients in the single ventricle group were diagnosed as hypoplastic left heart syndrome. One patient was born with severely depressed cardiac function and underwent bilateral pulmonary artery banding immediately after birth and subsequent PediMag VAD placement. Another patient was born with intact atrial septum and brought to the catheter laboratory right after birth for atrial septal defect stent. The stent perforated the left atrium and the patient developed cardiac tamponade. After 2 weeks of ECMO, the patient underwent PediMag VAD placement. One patient was status post Norwood procedure with severely depressed function and underwent bidirectional Glenn with 10-mL Berlin Heart with take down of right ventricle to pulmonary artery conduit. Another patient was status post Glenn and underwent take-down of Glenn with BT shunt and centrifugal pump (Revolution, Sorin, Arvada, CO, USA).

Outcome and Follow-Up

Median follow-up period is 26.3 months. Eighteen patients were successfully transplanted (62%). Two patients out of 18