Preclinical performance of a pediatric mechanical circulatory support device: The PediaFlow ventricular assist device

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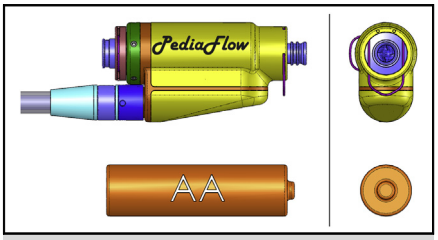
ABSTRACT

Objectives: The PediaFlow (HeartWare International, Inc, Framingham, Mass) is a miniature, implantable, rotodynamic, fully magnetically levitated, continuous-flow pediatric ventricular assist device. The fourth-generation PediaFlow was evaluated in vitro and in vivo to characterize performance and biocompatibility.

Methods: Supported by 2 National Heart, Lung, and Blood Institute contract initiatives to address the limited options available for pediatric patients with congenital or acquired cardiac disease, the PediaFlow was developed with the intent to provide chronic cardiac support for infants as small as 3 kg. The University of Pittsburgh–led Consortium evaluated fourth-generation PediaFlow prototypes both in vitro and within a preclinical ovine model (n = 11). The latter experiments led to multiple redesigns of the inflow cannula and outflow graft, resulting in the implantable design represented in the most recent implants (n = 2).

Results: With more than a decade of extensive computational and experimental efforts spanning 4 device iterations, the AA battery–sized fourth-generation PediaFlow has an operating range of 0.5 to 1.5 L/min with minimal hemolysis in vitro and excellent hemocompatibility (eg, minimal hemolysis and platelet activation) in vivo. The pump and finalized accompanying implantable components demonstrated preclinical hemodynamics suitable for the intended pediatric application for up to 60 days.

Conclusions: Designated a Humanitarian Use Device for ''mechanical circulatory support in neonates, infants, and toddlers weighing up to 20 kg as a bridge to transplant, a bridge to other therapeutic intervention such as surgery, or as a bridge to recovery'' by the Food and Drug Administration, these initial results document the biocompatibility and potential of the fourth-generation PediaFlow design to provide chronic pediatric cardiac support. (J Thorac Cardiovasc Surg 2018;■:1-9)



The PediaFlow pediatric VAD described in this article.

Central Message

The PediaFlow pediatric VAD has the potential to provide long-term cardiac support safely in pediatric patients.

Perspective

Limited options exist, associated with serious neurologic and coagulation-related adverse events, for pediatric patients (body surface area <1.5 m^2) requiring chronic MCS. The results of our PediaFlow design highlight the potential to safely provide long-term pediatric cardiac support using a magnetically levitated, fully implantable, CF RBP.

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MCS

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This work was supported by the National Heart, Lung, and Blood Institute under 2 contract awards – Pediatric Circulatory Support (N01-HV-48192; H.S.B. Principal Investigator) and Pumps for Kids, Infants and Neonates – Preclinical Program (N01-HV-00235; H.S.B. Principal Investigator); and National Institute of Child Health and Human Development award ''Development of the PediaFlow Pediatric Ventricular Assist Device'' (5RC1HD064041-02; P.D.W. – Principal Investigator). S.E.O. was supported in part by the National Institutes of Health T32-HL076124 Cardiovascular Bioengineering Training Program.

Received for publication April 28, 2016; revisions received March 23, 2018; accepted for publication April 11, 2018.

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0022-5223/$36.00

https://doi.org/10.1016/j.jtcvs.2018.04.062

Abbreviations and Acronyms

CF = continuous-flow
FDA = Food and Drug Administration
LV = left ventricle
MCS = mechanical circulatory support
NIH = normalized index of hemolysis
NHLBI = National Heart Lung and Blood Institute
PF3 = third-generation PediaFlow
PF4 = fourth-generation PediaFlow
RBP = rotary blood pump
RPM = revolutions per minute
VAD = ventricular assist device

Scanning this QR code will take you to the supplemental appendix, figures, tables, and video for this article.

HEART FAILURE IN ADULTS

Heart disease is the leading cause of mortality in adults internationally and domestically, responsible for 1 in every 7 deaths within the United States.[1] With circulatory assist device development spanning more than 5 decades for adults, multiple paradigm shifts from pulsatile total artificial hearts, to pulsatile (first generation) ventricular assist devices (VADs), to continuous-flow (CF) rotary blood pumps (RBPs) have revolutionized the field of mechanical circulatory support (MCS) in adults. By using centrifugal- or axial-flow designs with a single moving impeller, RBPs eliminate the flexible blood membranes, check valves, long cannulas, and tortuous blood paths required in prior pulsatile pumps. This increased simplicity allows for smaller blood-contacting surface area and reduced dead space, thereby reducing thrombosis potential and infection risks, in addition to decreasing the overall device size.[2] Likewise, controller size has been markedly reduced by the elimination of large percutaneous drivelines, compressors, vacuum pumps, solenoids, and large power supplies associated with positive-displacement VADs.[3] Supported by blood bearings/seals (second generation) or suspended by hydrodynamic or electromagnetic forces (third generation), RBPs are now the standard for chronic MCS support clinically.[3,4] With multiple adult CF VADs approved by the Food and Drug Administration (FDA) for bridge-to-transplant or destination therapy applications, these technologies have rescued thousands of adults with refractory end-stage heart failure with additional devices under development or in clinical trials.[5]

PEDIATRIC HEART FAILURE

Within the United States, 25% of all neonates born with a congenital heart defect will require invasive treatment within the first 12 months of life.[6] Approximately 1800 infants die of congenital heart disease each year, and an additional 350 develop cardiomyopathy.[7,8] Children weighing less than 15 kg listed for cardiac transplantation have the highest waiting list mortality rate (17%) in all solid-organ transplantation categories.[9] Cardiac transplantation remains the standard of care for refractory heart failure, but with limited donor availability, only 56% of infants listed received an organ over the last decade.[10] Although MCS has successfully decreased waiting list mortality and has been used as a bridge-to-recovery, availability of MCS devices for children remains limited.[11,12]

MECHANICAL CIRCULATORY SUPPORT FOR PEDIATRICS

Extracorporeal membrane oxygenation is used extensively for providing temporary cardiac support to children from neonates to adolescents. Although resource intensive, it is cost-effective, institutionally available, and rapidly initiated.[13] However, extracorporeal membrane oxygenation is indicated only for short durations requiring immobilization and sedation, and has a high complication rate related to bleeding and thromboembolism proportional to support length.[14] For adolescents with sufficient body surface area, the use of adult-indicated durable CF-VADs is supported by the PediMACs registry with a 6-month survival approaching 90% (n = 126) since inception in 2012.[15] The majority of CF-VADs were implanted in patients 6 years of age or older because of device size, although there is a growing off-label use of the smaller HeartWare HVAD (Framingham, Mass) typically implanted with an outflow graft constriction or operated at lower speeds (revolutions per minute [RPM]) to maintain pediatric-appropriate flow rates[15-17] in younger patients. Unlike adults, however, currently the only FDA-approved pediatric-specific bridge-to-transplant MCS device is the Berlin Heart EXCOR (Berlin, Germany), a paracorporeal, pneumatically driven, pulsatile VAD that provides extended support for the pediatric population through the use of varying volume-sized pumps coupled to a large pneumatic driver. The potential of the EXCOR as a lifesaving technology for children with heart failure is reflected in our center's experience since 2004.[18] However, the EXCOR has a substantial risk profile with approximately 80% of patients experiencing at least 1 significant adverse event, the majority (~50%) from severe bleeding or infection, and is associated with frequent pump exchanges due to device thrombosis around the valve leaflets.[19]