Implantable continuous-flow total artificial heart for newborns and small pediatric patients: First report of working model

Jamshid H. Karimov, MD, PhD,[a,b,c] Chihiro Miyagi, MD, PhD,[a] Taiyo Kuroda, MD,[a] Anthony R. Polakowski, BS, MEng,[a] Christine R. Flick, BS,[a] Barry D. Kuban, BS,[a] Kiyotaka Fukamachi, MD, PhD,[a,b,c] Tara Karamlou, MD,[b,d] Munir Ahmad, MD,[b,d] and Hani Najm, MD[b,d]

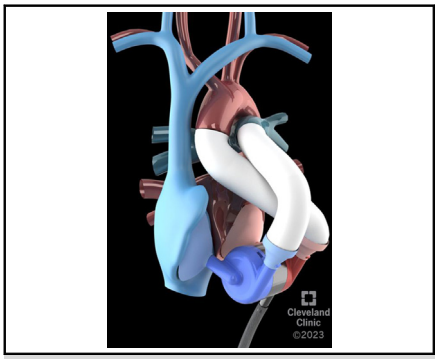
ABSTRACT

Objective: The need for safe and reliable mechanical circulatory support (MCS) for smaller children with severe heart failure (HF) is well defined. More specifically, in pediatric patients with advanced congenital HF, there is no implantable total artificial heart (TAH) device available for small patients. Herein, we report the development of the infant continuous-flow total artificial heart (I-CFTAH), a fully implantable in infants and newborns.

Methods: After extensive engineering analysis, we performed an unprecedented effort: reducing the I-CFTAH's displacement volume to be 14% of the adult CFTAH pump while simultaneously decreasing pump diameter (6.2 cm to 2.6 cm) and axial length (9.8 cm to 4.8 cm). Facilitated by these proportional reductions, for the first time, a durable total artificial heart device was successfully fit in the chest of infants and newborns (height of $\geq$50 cm).

Results: The functional I-CFTAH prototype demonstrated capability to support stable hemodynamics and desired device performance. The pump flow range (0.5-1.5 L/min) was confirmed in a mock circulatory testing loop. Within the tested flow range, the I-CFTAH can support small patients that could benefit from the intended cardiac output.

Conclusions: This successful effort demonstrated the feasibility of the miniature continuous-flow total artificial heart, intended for very small patient populations. I-CFTAH showed stable hemodynamics and could, therefore, become one of the few therapeutic options as a bridge to transplantation, aiming to enhance both the quality and duration of life for pediatric patients with advanced HF. (JTCVS Techniques 2024;28:124-31)



Implantable continuous-flow total artificial heart for newborns.

CENTRAL MESSAGE

In this early effort, we demonstrate the feasibility of the miniature continuous-flow total artificial heart, intended for very small patients.

PERSPECTIVE

The need for safe, reliable, and dischargeable mechanical circulatory support for smaller children with severe heart failure is well understood. The Cleveland Clinic I-CFTAH is a transformation of an ultraprecise scaling of established architecture, with all the inherent functionality, into a miniaturized, double-ended centrifugal pump, addressing an important clinical gap for infant patients.

From the [a]Department of Biomedical Engineering, Lerner Research Institute, [c]Kaufman Center for Heart Failure, Heart, Vascular, and Thoracic Institute, and [d]Department of Thoracic and Cardiovascular Surgery, Cleveland Clinic, Cleveland, Ohio; and [b]Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, Ohio.

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Address for reprints: Jamshid H. Karimov, MD, PhD, Department of Biomedical Engineering/ND20, Lerner Research Institute, Cleveland Clinic, 9500 Euclid Ave, Cleveland, OH 44195 (E-mail: karimoj.cc@gmail.com).

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Abbreviations and Acronyms

BHE	= Berlin Heart EXCOR Pediatric VAD
CFTAH	= continuous-flow total artificial heart
CF	= continuous flow
CHD	= congenital heart disease
FDA	= Food and Drug Administration
HF	= heart failure
HT	= heart transplant
I-CFTAH	= infant continuous-flow total artificial heart
MCS	= mechanical circulatory support
PVR	= pulmonary vascular resistance
SVR	= systemic vascular resistance
TAH	= total artificial heart
VAD	= ventricular assist device

▶ Video clip is available online.

The necessity for safe, reliable, and dischargeable mechanical circulatory support (MCS) for smaller children with severe heart failure (HF) is well recognized. Despite MCS having been established as a standard therapy for adult patients with end-stage HF,[1,2] in pediatric patients with congenital heart diseases (CHDs), the options for chronic MCS devices are limited, and no implantable devices are available at present for pediatric patient populations.[3,4] When compared with the normal anatomical heart, congenital anomalies in pediatric patients make it difficult to adapt corresponding types of adult ventricular assist devices (VADs) to sustain hemodynamics. Heart transplantation (HT) could be an option for end-stage HF; however, the availability of donor hearts limits this option in small children.[5] An implantable total artificial heart (TAH) may be considered for certain patients with complex cardiac anomalies, depending on individual clinical evaluations. The SynCardia 50 cc TAH (SynCardia Systems, LLC) is approved for pediatric patients with a body surface area of $\geq$1.2 m^2, which does not accommodate most of the smaller patients with CHD. Since 2011, the Berlin Heart EXCOR Pediatric VAD (BHE; Berlin Heart GmbH) has been the only durable VAD option approve by the Food and Drug Administration (FDA) for smaller children (available in 10, 15, 25, or 30 cc stroke volume).[6] A fully implantable, durable TAH with lower risk and potential for outpatient use remains unavailable for small children. In this effort our aim is to develop a durable, miniaturized continuous-flow (CF) TAH for newborns, infants, and small children (Figure 1) that would also enable their mobility while expecting an HT.

METHODS

Device and Hardware Development

By downsizing (scale factor = 0.455) the adult Cleveland Clinic CFTAH,[7] similar to the adult and much larger pediatric CFTAH,[8] this infant continuous-flow total artificial heart (I-CFTAH)[9] was envisioned with one motor and one rotating assembly supporting a hydrodynamic bearing[10,11] (Figure 2, Video 1). The pump was designed to produce 500 to 1500 mL/min of flow between 30 and 90 mm Hg and to self-regulate the balances between an atrial pressure difference of −5 to 10 mm Hg and between a systemic vascular resistance (SVR)/pulmonary vascular resistance (PVR), SVR/PVR of 2 to 15.

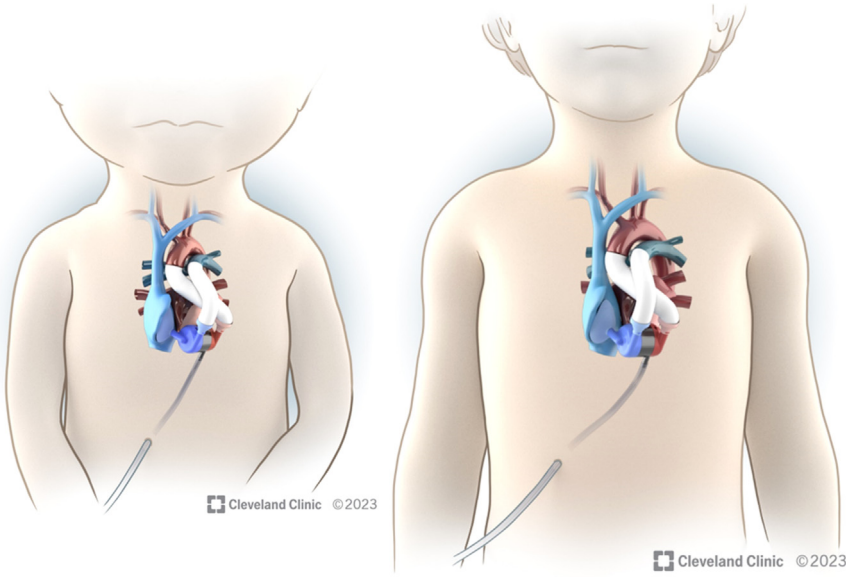

FIGURE 1. Implantable continuous-flow total artificial heart for newborns (*left*) and small pediatric patients (1-year old) (*right*).

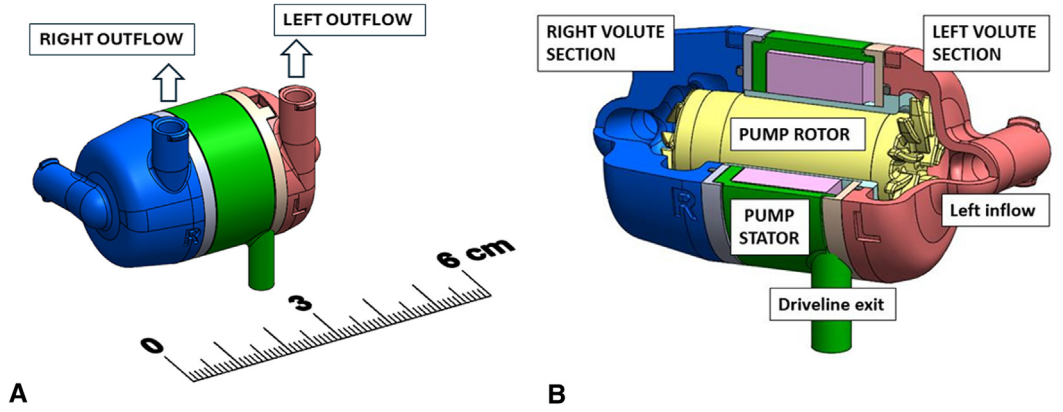

FIGURE 2. The assembled infant continuous-flow total artificial heart design view (A) and cross-sectional device architecture (B).

After initial analysis and refinement of the I-CFTAH pump design, the working model was fabricated for in vitro characterization of device performance and self-regulation (Figure 3). The magnetic assembly and stator windings were produced for the pump rotor and tested. Left and right volute housings and impeller for double-ended rotor were 3-dimensionally printed and postprocessed for close-tolerance at various lengths until proper pressure balance was achieved. I-CFTAH is extremely small, 4.8 cm (axial length) by 2.6 cm (pump body diameter), respectively. All 4 pump ports were enabled with Luer-type connectors (2 inflow ports and 2 outflow ports); altogether with driveline exist site, the prototype could volumetrically fit inside a chest cavity of infants and neonates (4.95 cm [longitudinal] × 4.57 cm [lateral, including ports] × 4.08 cm dimensions [diametric]). The miniature TAH model has undergone virtual fitting assessments for infants and newborns (height of ≥50 cm), as documented in previous research.[12]

The mock loop had a circulating volume of approximately 200 mL. The test fluid was filled with 80% water and 20% glycerin mixture at room temperature with a specific gravity of 1.060. Two modified 50-cc syringes (Becton Dickinson) were used as the filling reservoirs for both right and left pumps. Tygon tubing with an inner diameter of 7/32 inches was used to connect the pump to the reservoirs and the pump outlets to the reservoirs. The only compliance in the system was a result of the flexible tubing. Two clamps after the pressure measurement on the outlet of each pump were used to replicate vascular and pulmonary resistance Flow was measured with an ME 13 PXN inline flow probe monitored with a TS410 meter (Transonic System Inc). All pressures were monitored by fluid filled lines

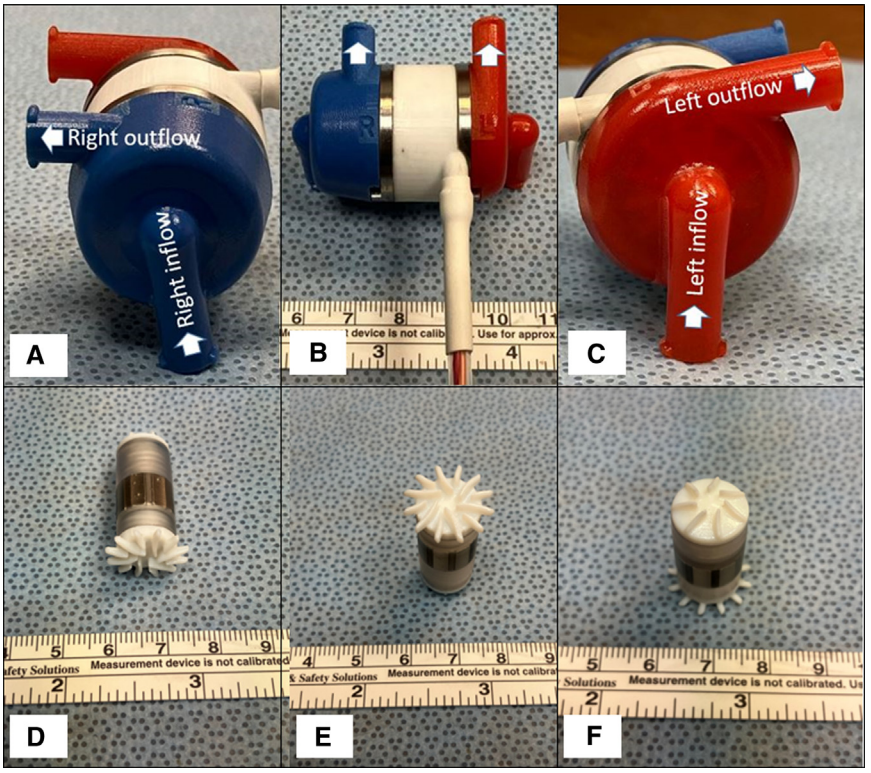

FIGURE 3. Lateral (A and C) and front (B) views of the infant continuous-flow total artificial heart working model. D, Pump rotor with asymmetric rotor design; E, left impeller; F, right impeller designed for device self-regulation and automatic pump aperture opening/closure.

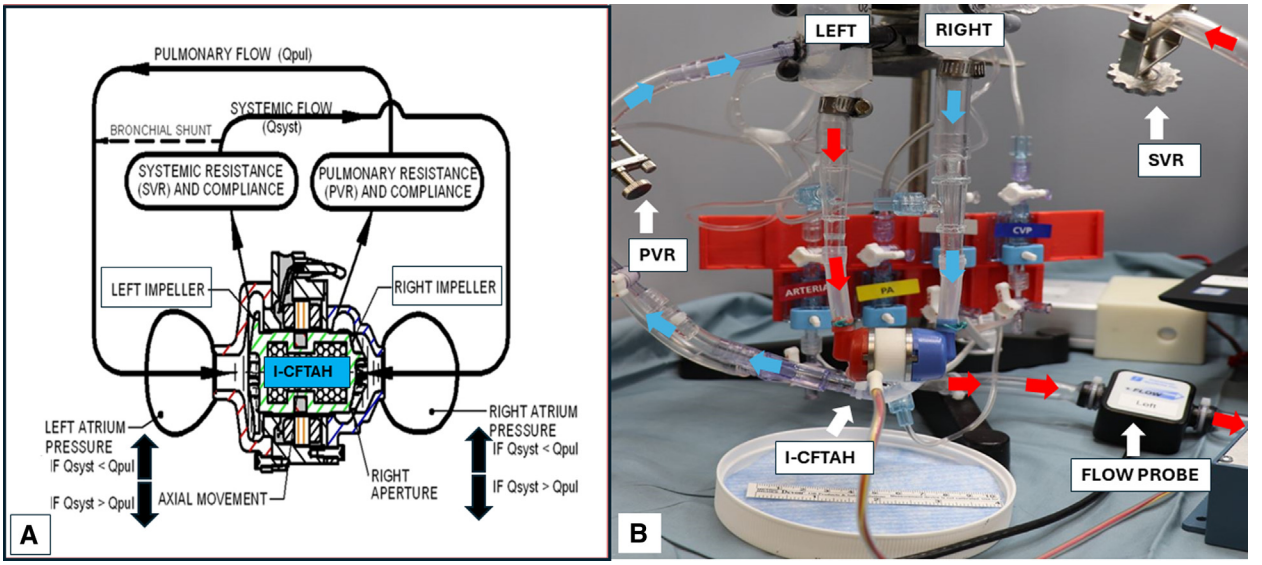

FIGURE 4. A, Schematic representation of the systemic and pulmonary circulation and hemodynamics supported by continuous-flow total artificial heart architecture. The blood pump cross-section shows impeller heads and device housings, as well as axial movement and pressurization of right atrial chamber, a key element in passive device self-regulation mechanism; B, I-CFTAH prototype placed on circulatory mock loop for mapping. *I-CFTAH*, Infant continuous-flow total artificial heart; *SVR*, systemic vascular resistance; *PVR*, pulmonary vascular resistance.

leading to pressure transducers (13-6615-50; Gould Electronics) and amplifiers (M21018; Honeywell viewed by PowerLab [ADInstruments]).

The pump was tested with a fixed-speed motor controller. The speed was set, and vascular and pulmonary resistance were changed while pressure and flow were recorded. The maximum speed tested was 7000 RPM.

Hemodynamic parameters of systemic and pulmonary circulation with related pressures, the deltaP (left atrial pressure – right atrial pressure, indicative of atrial balance), pump flow, in addition to parameters of speed and power, were recorded using real-time data acquisition in a miniature mock loop (water-glycerin mixture of specific gravity of 1.060) designed for testing the performance and self-regulation feature (mechanical, sensorless adjustment of atrial pressure balance by the pump) of the pump[13] (Figure 4, *A* and *B*) as shown in Table E1.

RESULTS

Preliminary Studies

The pressure–flow curves indicated a broad range of left pump flow. Figure 5 shows the left pump pressure–flow curves. The pump speed during ranged from 3000 RPM to 7000 RPM and the early performance data met the

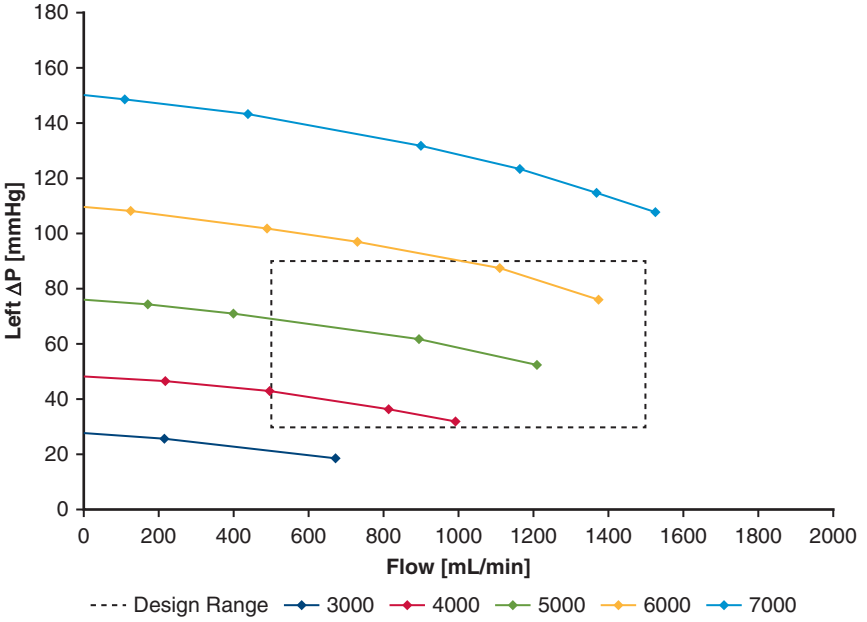

FIGURE 5. The left pump pressure–flow curve is based on pump performance data. The *box* indicates the pump performance within the design point.

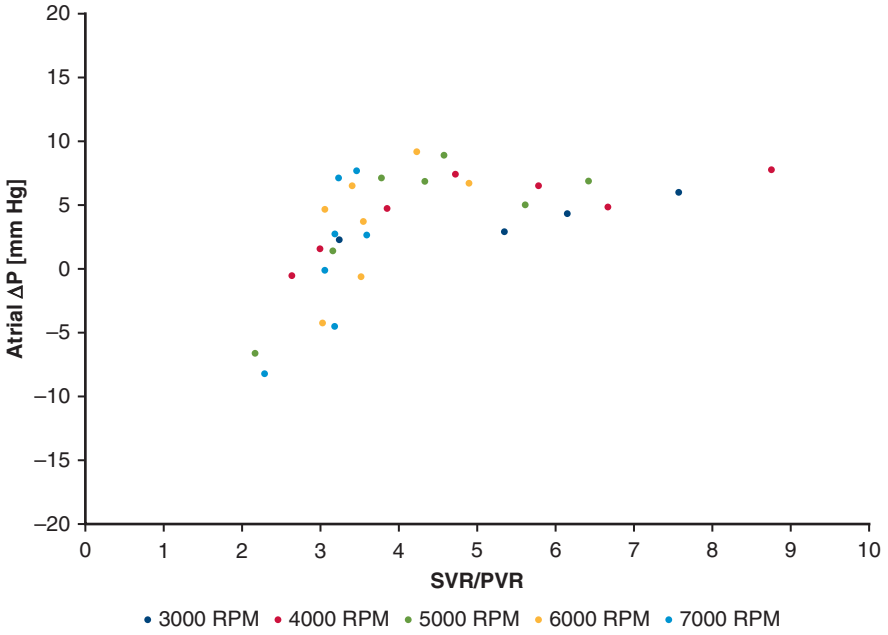

FIGURE 6. Atrial pressure balance with a wide range of SVR/PVR ratios. *SVR*, Systemic vascular resistance; *PVR*, pulmonary vascular resistance.

proposed design requirements for pump flow range of 0.5 to 1.5 L/min and were repeatable. During the pump operation at various speeds, the pump was able to produce more than 1200 mL/min at 60 mm Hg, with an overall total flow performance of 1800 mL/min achieved with the prototype at greater speeds (Figure 5). The left and right atrial pressure were well balanced, with the majority of points falling between the acceptable range (−5 to 10 mm Hg between an SVR/PVR of 2-15) without speed modulation. In Figure 6, the deltaP (left atrial pressure – right atrial pressure) shows the atrial balance. With a sinusoidal speed modulation, the physiologic, pulsatile pressure, and flow were simulated (Figure 7). The pump demonstrated operational stability, characterized by steady flow and consistent hemodynamic support. This stability is evidenced by the absence of flow fluctuations, pressure imbalances, and other indicators of unintended pump behavior. Throughout its entire run duration, the pump maintained a steady cardiac output,

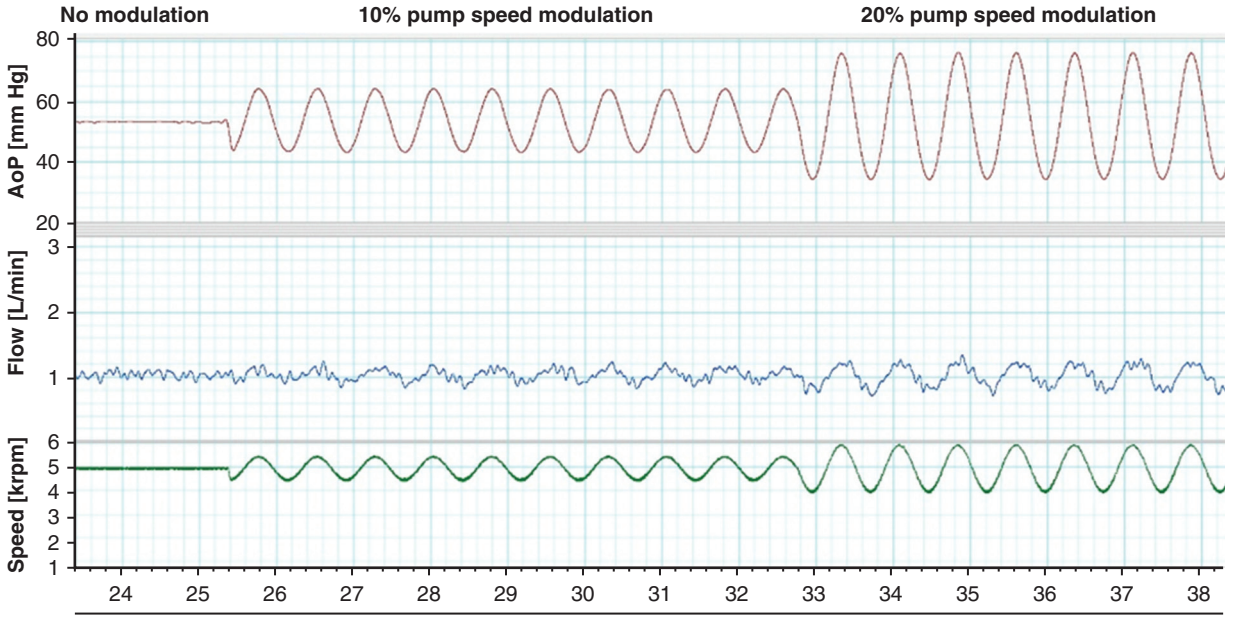

FIGURE 7. Pressure and flow waveforms of infant continuous-flow total artificial heart with pump speed modulation.

ensuring reliable performance. Pump motor currents at all tested speeds were stable, and no power elevations or mechanical failures occurred during these bench testing.

DISCUSSION

Pediatric MCS has been successfully used as a bridge to transplant for many children whom otherwise may have been unlikely to survive on the transplant waitlist. In many cases, it makes them better transplant candidates.[14] The most significant challenge is the lack of durable MCS for neonates and infants.[4] Advanced pediatric HF is terminal, and MCS options for smaller children are limited to older, paracorporeal pulsatile devices. These paracorporeal pulsatile devices, BHEs, prevent pediatric patients from being dischargeable postprocedure and necessitating prolonged hospital stays because of the equipment complexity and large size. CHD-related HF comprises nearly 70% of pediatric HF admissions in the United States.[15] In-hospital mortality for this group of children is among the greatest in all pediatric patients—with mortality rates of up to 50%. Approximately 1 in 5 children do not survive to hospital discharge.[15] On the basis of first-hand practical and clinical experience, the authors reiterate: because of scarcity of donor hearts, HT-waitlist mortality remains high, and waiting times to receive a donor heart are long and continually growing longer.

The Cleveland Clinic I-CFTAH is a transformation of an ultraprecise scaling of established CFTAH architecture, with all the inherent self-regulating functionality, into a miniaturized, double-ended centrifugal pump, addressing an existing clinical gap critically impeding the technological advancement of MCS for infant patients. In this effort, the I-CFTAH demonstrated promising preliminary feasibility of device performance and self-regulation by producing 500 to 1000 mL/min of flow between 30 and 90 mm Hg. The pump auto-regulation was successfully able to balance between an atrial pressure difference of −5 to 10 mm Hg and between an SVR/PVR of 2 to 15.

To our knowledge, the TAH of such a scaled-down, small size has never been developed. The pump was designed to provide a range of normal systemic and pulmonary circulations to the patient as a bridge to transplant or, possibly, as a destination therapy with next, larger device. The ultimate objective is to meet hemodynamic needs for infants while providing a means to eventually transition to larger CFTAH's; so that, a rapidly growing child can "graduate" into the next size-appropriate device.

In the United States, older children and adults have benefited from the HeartMate 3 left ventricular assist device (LVAD) (Abbott Laboratories), the only device approved by the FDA. Withdrawal of the Medtronic HeartWare Ventricular Assist Device System (Medtronic) from clinical use has created an increased demand for durable LVADs.[16] Both devices are too large to be used in newborns, infants, and small children (<15 kg). The present of state of technology further emphasizes the timely and critical need for MCS innovation for all advanced pediatric patients with HF. CHD remains a major cause of infant death during the first year of life, and the mortality of CHD is 30% to 50% of that by birth defects. Infant mortality accounted for ∼40% (69,252 deaths) of all mortality resulting from CHD.[17] Cardiac surgery for neonates and infants with CHD typically involves complex cardiac anomalies, such as hypoplastic left heart syndrome, transposition of the great artery, and different forms of the adult heart disease.

VIDEO 1. The 360° surgical view of the I-CFTAH implantation. Video available at: https://www.jtcvs.org/article/S2666-2507(24)00359-6/fulltext.

Despite the substantial strides the field of pediatric MCS has made over the last 15 years, the current options for MCS modalities remain rather limited: temporary extracorporeal membrane oxygenation, temporary extracorporeal centrifugal VAD, and BHE. The BHE VAD, a paracorporeal pneumatic pump, is currently the only device approved by the FDA available to provide long-term support to small children waiting for HT. The Infant Jarvik 2015 is an implantable pediatric LVAD[18] for 0.5 to 3.0 L/min support; device development of Jarvik 2015 has been challenging for several reasons.[18] It is currently being evaluated in the so-called Pump for Kids, Infants, and Neonates (PumpKIN) multicenter trial under the designation of "compassionate use."[19]

Scaling down a rotodynamic pump design by using conventional principles of dimensional similitude can be straightforward, but there are many challenges and innovative solutions are required. As we deal with smaller and more-delicate vasculature and cardiac tissues in newborns and infants, the miniaturization gain of the implantable blood pump size also expands towards the surgical necessity. Another important aspect of I-CFTAH is that pump speed is designed to create pulsatile flow and pressure, which is especially important in small compliance, fast-growing vasculatures to provide flow patterns that mirror "normal" as much as possible, ensuring more physiologic brain and multi-organ perfusion, and arterial pressure regulation.[20-25] The pulsatility in I-CFTAH is achievable through increase and decrease in speed (modulation) of its dual-centrifugal pump heads that could respond to

physiologic needs by various degrees of sinusoidal amplitude performance and. These would need to be further addressed more extensively to accommodate the dynamic clinical requirements in a growing patient. Acknowledging that motors and bearings scale differently than centrifugal pumps, a secondary challenge would be optimizing the motor and hydrodynamic bearing to optimize the pump performance, one of the ultimate goals of device scaling.

CONCLUSIONS

This early effort demonstrated the performance of miniature CFTAH intended for a very small patient population. The early I-CFTAH model showed stable hemodynamics and intended performance during bench testing and device mapping. Miniature TAH could, therefore, play a pivotal role as a therapeutic solution, particularly as a bridge to transplantation, aiming to enhance both the quality and duration of life for early age pediatric patients with advanced HF.

Conflict of Interest Statement

J.H.K., B.K., and K.F. and are coinventors of the I-CFTAH. All other authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: congenital heart failure, pediatric, mechanical circulatory support, total artificial heart

TABLE E1. A summary of hemodynamic parameters of pressures, pump flow, in addition to parameters of speed and power, and the miniature mock loop

Mean systemic flow	500 to 1500 mL/min
Speed modulation	Sinusoidal at an amplitude of up to ±25% average speed and 1.33 Hz (80 bpm)
Systemic pressure gradient	AoP–RAP: 40-120 mm Hg
Pulmonary pressure gradient	Mean PAP–LAP: 5-50 mm Hg, but with $1.5 \leq$ SVR/PVR ≤ 20
Maximum atrial pressure difference	-5 mm Hg $\leq$ (LAP-RAP) $\leq$10 mm Hg

bpm, Beats per minute; *AoP*, arterial pressure; *RAP*, right atrial pressure; *PAP*, pulmonary artery pressure; *LAP*, left atrial pressure; *SVR*, systemic vascular resistance; *PVR*, pulmonary vascular resistance.