Clinical Experience With the MEDOS HIA-VAD System in Infants and Children: A Preliminary Report

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Background. The need of pediatric cardiac assist is growing because of the complexity of the congenital conditions operated on and the increasing number of pediatric transplantations. We evaluated the newly developed pediatric MEDOS HIA-VAD ventricular assist device.

Methods. The pneumatic paracorporeal ventricular assist device has three left ventricular sizes (10-, 25-, and 60-mL maximum stroke volume) and three right ventricular sizes (9, 22.5, and 54 mL) and can be operated effectively with up to 180 cycles/min. We used this device in 6 consecutive pediatric patients. Intention of treatment was to bridge to transplantation in 3 patients and to aid in recovery from a cardiac operation in 3. Age ranged from 5 days to 8 years.

Results. Two children died during assist, 2 were weaned from the system and discharged home, and 2 had successful transplantation. During assist, laboratory variables indicative of impaired renal, hepatic, or pulmonary function normalized or showed a trend toward normalization. Both deaths were related to infection.

Conclusions. With the new MEDOS HIA-VAD ventricular assist device system, pediatric mechanical cardiac assist can be performed successfully. It requires timely implantation, careful monitoring, and adequate size-matched devices.

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Mechanical circulatory assist with ventricular assist devices (VADs) in infants and children is still evolving. Although the need of pediatric cardiac assist is growing because of the complexity of the lesions operated on today and because of the success of pediatric cardiac transplantation, a pediatric support system covering the wide demands of this heterogeneous patient group was not available until very recently. We evaluated the newly developed pediatric MEDOS HIA-VAD in 6 consecutive patients.

Material and Methods

Device

The pneumatically driven MEDOS HIA-VAD system was developed by one of us (H.R.) at the Helmholtz Institute, Aachen, Germany [1]. After extensive laboratory in vitro [2, 3] and in vivo [4, 5] testing, we started a clinical trial with mechanical circulatory assist in children.

The system is available in three left ventricular sizes of 10-, 25-, and 60-mL maximum stroke volume (Fig 1). Ventricles that are 10% smaller, namely, 9, 22.5, and 54 mL, are intended for right ventricular support if the need of biventricular support should arise. The ventricles are made of polyurethane with a double-layer inner, displacement membrane and are pneumatically driven. The polyurethane three-leaflet valves are incorporated seamlessly, and the ventricles are totally transparent to allow visual control of filling and emptying and observation of any air during installment of the system or clot formation during prolonged pumping. The design of the ventricles was optimized by the demands of fluid dynamics, and the valve design follows valvular geometry and physical demands. This led to leaflets 0.2 mm thick and allows very low opening and closing pressures [2]. Systolic transvalvular gradients are low, and rapid closure of the valve minimizes regurgitant flow. The ventricles are intended for paracorporeal use.

Cannulas of the appropriate size are available for each ventricle (Fig 2). The atrial inlet cannula has a wide bore, is wire reinforced, and is bendable at the tip, which allows optimal routing within the chest. An inlet cannula for left ventricular apical access is also available. The outlet cannula has a vascular graft at the tip that can be trimmed and sewn to the appropriate artery. Currently, this is a polytetrafluoroethylene graft, but an outlet cannula with a gelatin-sealed Dacron graft is under investigation. The middle part of all cannulas is covered with Dacron felt to permit rapid ingrowth of host tissue and sealing of the skin at the cannula insertion site.

The drive unit (Fig 3) can be operated by external power, pressure, and vacuum sources as well as by an

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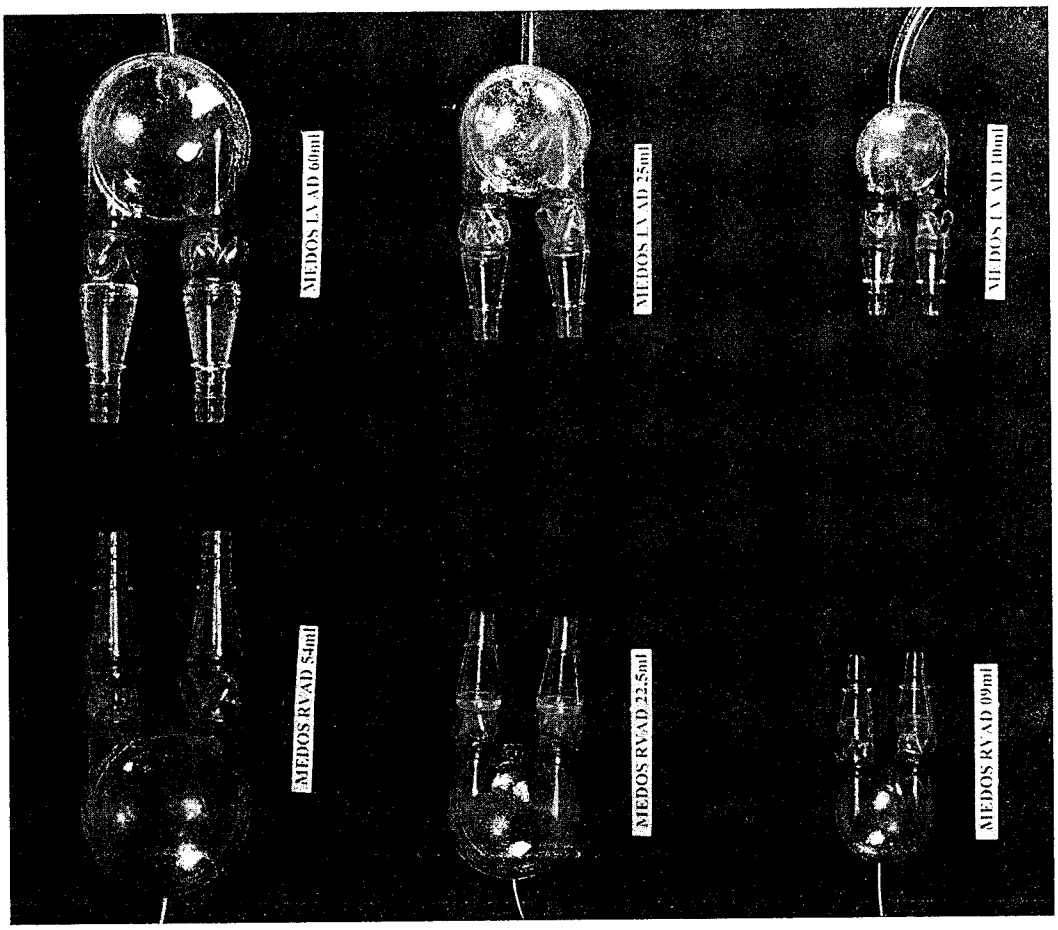

Fig 1. The available sets of ventricles for left and right heart support. (LVAD = *left ventricular assist device;* RVAD = *right ventricular assist device.)*

internal battery (2 hours) and compressor. It generates up to 300 mm Hg positive pressure and to −80 mm Hg negative pressure at rates up to 180 beats/min. It can be used in fixed rate or electrocardiogram-triggered rate, and the pump systole can be adjusted to the cardiac cycle allowing 1:1, 1:2, or 1:3 counterpulsation. The drive unit is operated by an interactive touch screen monitor displaying the operational status of the pump.

Patient Population

From March 1, 1994, to February 29, 1996, 2,497 cardiac patients including 388 pediatric patients underwent operation at our institution. In a clinical trial, we used the MEDOS HIA-VAD system in 16 patients, 6 of whom were children. These 6 patients comprise the study cohort. The intention of treatment was immediate or delayed postcardiotomy support in 3 and bridging to transplantation in 3. The demographic data and the status prior to device use are shown in Table 1. All patients were in profound cardiac failure under maximum inotropic support.

Surgical Techniques

A midline sternotomy was used in all patients. For left ventricular support, the outflow cannula was sewn to the aorta and exteriorized through a stab incision in the left epigastrium. Then the inflow cannula was placed through the right superior pulmonary vein, secured with two pursestring sutures, and exteriorized through the right epigastrium. With the patient in deep Trendelenburg's position, the cannulas were thoroughly deaired. With meticulous care, the ventricle was filled with Ringer's solution to remove all air. This step can be easily verified, as the ventricles are totally transparent. Sometimes it is advisable to let the ventricle perform some strokes immersed in a large bowl filled with Ringer's solution. The ventricle was then connected to the tubing, and several single strokes were performed slowly to control for any residual air. When implantation of the device takes place with the patient on a heart-lung machine, the surgical team should be sure that the heart is completely deaired and already filled with blood and that flow from the heart-lung machine has been decreased. After another careful check for any air in the tubing and the ventricle, pumping was initiated, and after the heart-lung machine was discontinued, the ventricle was set to the desired level of support. In the postcardiotomy patients, the chest was closed only temporarily. When edema was present or cannula placement

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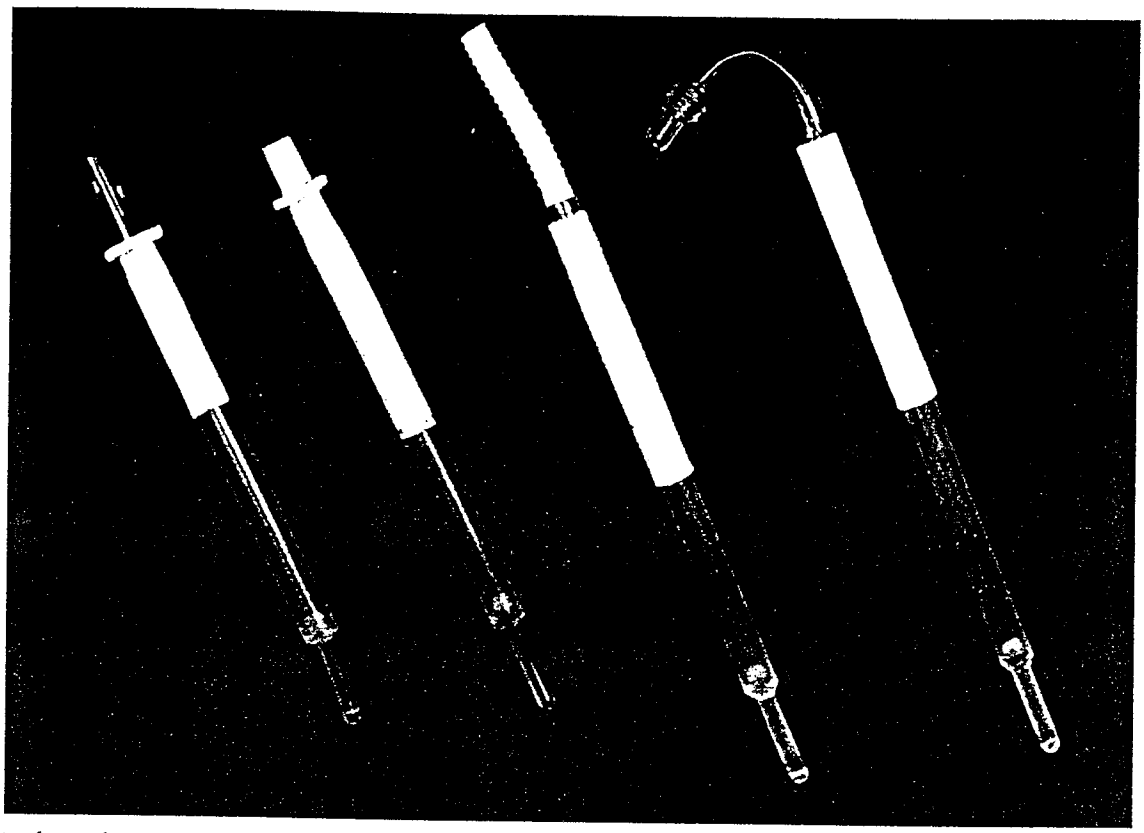

Fig 2. Sets of cannulas: atrial and apical inlet cannulas and aortic or pulmonary outlet cannula with a mounted polytetrafluoroethylene graft.

was shown to compromise the heart, a sheet of Gore-Tex Surgical Membrane (W. L. Gore and Associates, Flagstaff, AZ) was used; otherwise, the skin edges were simply approximated. In all patients being bridged to transplantation, the sternum was wired and the wound closed in layers.

Anticoagulation and Antibiotics

Only nonheparin-bonded systems were used. When the implantation was done with the patient on a heart-lung machine, heparin sodium was partially neutralized with protamine sulfate to an activated clotting time of 200 seconds. In the other patients, heparin was administered before placement of the outflow cannula. The Hepcon System (Medtronic HemoTec, Minneapolis, MN) has proved to be extraordinarily sufficient in properly regulating dosages of heparin and protamine. During the first postoperative hours, no heparin was added until chest drainage decreased; then heparin was administered to keep the activated clotting time at 180 to 220 seconds. In the longer runs, acetylsalicylate, 5 mg $\cdot$ kg^{-1} $\cdot$ day^{-1}, was added after removal of the chest tubes.

Antibiotic treatment consisted initially of routine institutional postcardiotomy treatment with penicillin. On the basis of blood and urine cultures and wound, tracheal, throat, or fecal swabs, the regimen was changed later. The exit points of the VAD tubing were dressed daily under sterile conditions with povidone-iodine ointment.

Respirator Treatment and Supportive Measures

As soon as bleeding from chest tubes ceased and hemodynamic stability was maintained, patients were weaned

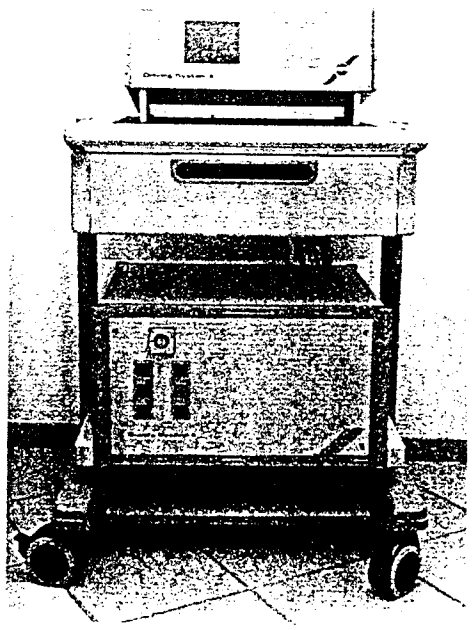

Fig 3. The drive unit with interactive touch screen monitor.

Table 1. Demographics and Clinical Status Before Device Use

Patient No.	Age	Sex	Weight (kg)	Diagnosis	Cardiac Status	End-Organ Failure
1	5 y	F	13.0	DCM	Dobutamine, 20 $\mu g \cdot kg^{-1} \cdot min^{-1}$; dopamine, 3 $\mu g \cdot kg^{-1} \cdot min^{-1}$	Renal, hepatic
2	3 mo	M	4.0	BWG	Unable to wean from CPB	None
3	2 y	F	10.5	Redo TOF	Unable to wean from CPB	None
4	5 days	M	3.1	HLHS	Low cardiac output; Epinephrine, 0.4 $\mu g \cdot kg^{-1} \cdot min^{-1}$; dobutamine, 10 $\mu g \cdot kg^{-1} \cdot min^{-1}$; dopamine, 3 $\mu g \cdot kg^{-1} \cdot min^{-1}$	Renal, hepatic, pulmonary
5	5 mo	F	5.2	DCM	Low cardiac output on ventilator; epinephrine, 0.2 $\mu g \cdot kg^{-1} \cdot min^{-1}$; dobutamine, 20 $\mu g \cdot kg^{-1} \cdot min^{-1}$; dopamine, 3 $\mu g \cdot kg^{-1} \cdot min^{-1}$	Renal
6	8 y	M	20.5	DCM	Dobutamine, 20 $\mu g \cdot kg^{-1} \cdot min^{-1}$; dopamine, 3 $\mu g \cdot kg^{-1} \cdot min^{-1}$	Renal, hepatic

BWG = Bland-White-Garland syndrome; CPB = cardiopulmonary bypass; DCM = dilated cardiomyopathy; HLHS = hypoplastic left heart syndrome; TOF = tetralogy of Fallot.

from respiratory support. Sufficient breathing was obtained and extubation accomplished even with the wound only temporarily closed.

For older children, sitting in bed and walking in the room were strongly recommended. Infants were allowed to be on the parent's or nurse's arm after extubation, and breast feeding was recommended, when appropriate.

Results

Duration of support ranged from 8 hours to 17 days. Two infants died, 1 during bridging to transplantation on postoperative day 17 and 1 5-day-old baby with hypoplastic left heart syndrome whose condition deteriorated on the third day after an initially uneventful Norwood repair. Recoarctation was excluded by echocardiography and heart catheterization, and in a desperate attempt to save the neonate, we started VAD support, which was able to stabilize his condition for only a short time.

The VAD sizes, duration of support, survival, and complications are summarized in Table 2. Anticoagulation was maintained with heparin with the aim of a partial thromboplastin time higher than 50 seconds; or an activated clotting time in the range of 180 to 220 seconds. Bleeding requiring reexploration, thromboembolic complications, or both occurred in 2 patients. One 5-year-old patient required several reexplorations during support and underwent successful transplantation after 5 days. The other patient, a 5-month-old infant, sustained a transient minor stroke 15 days after implantation of the device. One day earlier, the leukocyte count increased and the desired activated clotting time could not be reliably maintained, which resulted in an increased need of heparin. Thrombi were visible in one sinus of the outflow valve, which prompted a change in the ventricle and increased anticoagulation. One day later, massive retroperitoneal bleeding led to surgical exploration, and a bleeding site at the femoral artery from a previous pressure-monitoring line was identified. The child died of profound bleeding 1 day later.

Despite an aggressive antibiotic regimen, 3 patients had an infection. Two of them died. In 1, infection was clinically evident at the time of implantation and probably was responsible for inadequate recovery on the device. The other had had a long stay in the intensive care unit of another institution and was brought by air ambulance to our hospital for mechanical support. Clinically an infected central venous line without laboratory evidence of infection was present. Table 3 shows the

Table 2. Summary of Device-Related Data

Patient No.	VAD Size and Type	Implantation on CPB	Mean Flow Through Device (L/min)	Duration of Support (days/h)	Alive	Support-Related Complications
1	25 mL, LVAD	Yes	2.8	5/4	Yes	Bleeding
2	10 mL, LVAD	Yes	1.0	0/8	Yes	None
3	22.5 mL, RVAD	No	1.8	2/16	Yes	None
4	9 mL, SVAD	No	0.8	2/16	No	None
5	9 mL, LVAD	No	1.0	17/5	No	Bleeding, TE
6	25 mL, LVAD	No	2.2	9/8	Yes	None

CPB = cardiopulmonary bypass; LVAD = left ventricular assist device; RVAD = right ventricular assist device; SVAD = single ventricular assist device; TE = thromboembolism; VAD = ventricular assist device.

Table 3. Leukocyte Count Before and During Assist and Antibiotic Regimen

Patient No.	Leukocyte Count				Antibiotic Regimen	Infection
	Before	1 Day	3 Days	Explantation		
1	8.1	13.6	19.3	17.3	Piperacillin and cefofaxim	No
2	6.5	NA	NA	6.5	Azlocillin and oxacillin	No
3	9.5	7.4	NA	10.0	Piperacillin and cefofaxim	No
4	24.0	10.0	NA	15.1	Azlocillin and oxacillin	Yes
5	8.1	8.0	14.0	20.0	Imipenem, cilastatin, and vancomycin; imipenem, cilastatin, and teicoplanin	Yes
6	15.3	28.1	23.0	21.9	Vancomycin; imipenem, cilastatin, and gentamicin	Yes

NA = not applicable.

leukocyte counts and the antibiotic regimens for the 6 patients..

Respiratory treatment was aimed toward early extubation. Two infants were maintained on the respirator during the whole run. The infant with anomalous origin of the left coronary artery from the pulmonary artery showed evidence of early recovery, which prompted explantation of the VAD after 8 hours. The other baby died on the system after initial stabilization; the cause of death was multiorgan failure including dysfunction of the lungs, heart, liver, and kidneys. Changes in arterial oxygen saturation before and after implantation of the support system, duration of mechanical ventilation, and postextubation activities are shown in Table 4, and Table 5 contains some renal, metabolic, and hepatic data before and during VAD operation.

Comment

The recently available MEDOS HIA-VAD permits support of small babies as well as adults by offering a variety of ventricular sizes that can be matched to the needs of the patient. The system has some unique features. In small patients requiring small VAD ventricles and high pump rates, mechanical valves may be undesirable because of their closing and opening properties. These drawbacks are avoided by the unique design of the polyurethane valves, which are seamlessly incorporated into the VAD. The special design of the sinus portion in regard to optimal opening and closing as well as "washing flow" has been documented in extensive studies by Reul and colleagues [2]. They were also able to show low gradients and negligible low energy loss over the valves. Another valuable feature of the VAD is its total transparency. This allows visual control of filling and emptying and of thrombus generation on the inner surface of the device. In this series, thrombus generation at the outflow valve prompted the change of a ventricle in 1 patient, which was easily managed in the intensive care unit.

In infants and children, extracorporeal membrane oxygenation has been shown to be more successful than in adults [6]. However, ECMO requires a complex setup, a variety of monitoring lines, and most often endotracheal intubation and allows no ambulation or other physical activity [7–9]. Continuous surveillance by trained personnel is mandatory. These limitations seem undesirable, especially in infants who are bridged to transplantation. Other systems that have been used in infants and children include centrifugal pumps for univentricular and biventricular support [10]. However, with full unloading of the heart, they do not permit pulsatile flow. Loss of pulsatility has been blamed for capillary leakage during prolonged pump runs [11, 12], and recovery of the heart

Table 4. Respiratory Status Before and During Support

Patient No.	Arterial Oxygen Saturation (%)					Respirator (days/h)	Postextubation Activities
	Before	6 Hours	1 Day	3 Days	Explantation		
1	84	99	99	99	97	0/20	Sitting in bed
2	87	99	NA	NA	99	Implantation to explantation	NA
3	100	100	98	100	100	0/21	Sitting in bed
4	61	74	79	47	30	Implantation to explantation	NA
5	63	97	97	99	92	2/1	Out of bed, mother's lap, breast feeding
6	94	98	98	98	98	2/10	Sitting in bed, ambulation in ICU

ICU = intensive care unit; NA = not applicable.

Table 5. Selected Variables of Renal, Metabolic, and Hepatic Function Before and During Support[a]

Patient No.	Before Implantation					6 Hours of Implantation					Before Explantation or Death				
	Crea	BUN	Lactate	AST	ALT	Crea	BUN	Lactate	AST	ALT	Crea	BUN	Lactate	AST	ALT
1	138	35.3	1.8	0.8	1.4	58	36	1.9	1.3	0.5	26	18.1	1.2	1.2	0.6
2	26	4.0	0.8	0.2	0.3	...	...	...	...	...	25	4.5	1.6	1.3	0.3
3	22	...	1.0	0.7	0.4	37	...	4.9	1.1	0.53	21	...	1.0	1.0	0.5
4	112	13.8	21.8	8.8	9.5	105	11.4	28	33	7.9	120	12.0	16	24.8	5.1
5	66	3.3	0.9	1.8	0.7	50	4.1	0.9	1.8	0.7	70	10.7	8	1.4	0.2
6	96	4.1	22	0.6	1.4	72	4.3	2.4	1.3	0.9	62	1.5	2.0	0.7	0.3

[a] All data are shown in micromoles per liter.

ALT = alanine aminotransferase; AST = aspartate aminotransferase; BUN = blood urea nitrogen; Crea = serum creatinine.

may be improved by electrocardiogram-trigged counterpulsation of the device [13].

In addition, patients on centrifugal pumps are confined to bed. It would be difficult to mobilize and transport babies and small infants while they require a centrifugal pump. This can be accomplished much more easily when the pump is close to the body and wearable, as with pneumatically driven paracorporeal assist devices. Pneumatically driven paracorporeal pumps are in clinical use with the Thoratec system, but it is currently available only for adults. The pediatric MEDOS HIA-VAD described here is a commercially available system applicable to infants and allows matching the VAD size to the patient's need. The use of adult or intermediate-sized pneumatic ventricles in infants and children is associated with low pump rates and large stroke volumes. Slow operation of the pump, however, increases the thromboembolic risk [14].

Death in our series occurred only in combination with infection. Probably in 1 infant, infection triggered coagulation abnormalities resulting in thromboemboli and subsequent bleeding. This pathophysiologic pathway has been described previously by Didisheim and associates [15] and recently by Copeland and co-workers [16] in a patient with an implantable artificial heart. Because infection was the most common cause of death in that series, we increased microbiologic surveillance, and now we isolate and monitor these patients as we do transplant patients. The longest support time for a survivor was 9 days 8 hours, after which the child underwent successful transplantation. In longer runs, prevention of infection and adequate anticoagulation require utmost attention. This is very important, as patients who do not recover after a few days may become transplant candidates.

In this small study, we have shown that pediatric left VAD or right VAD support for postcardiotomy failure or as a bridge to transplantation can be performed in infants and children with a reasonable salvage rate. The system described has some unique features, including VAD sizes that can accommodate small babies as well as adults. Further clinical research and application of the system for biventricular support are in progress.

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