



Infant miniaturized continuous-flow pumps and permanent support in Pediatrics

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“It’s the little details that are vital. Little things make big things happen.” —John Wooden

The use of ventricular assist device (VAD) has tremendously changed the management of advanced heart failure (HF) in the pediatric population, while continuously evolving technology and improved clinical strategies have ameliorated outcomes (1). The Third Annual Pediatric Interagency Registry for Mechanical Circulatory Support (1) documented a growing number of implantations, which are only expected to increase because of limited donors availability. In Europe and the USA, the swelling ranks of children in need of a transplant is resulting in a disproportionate number of waitlist deaths occurring in those weighing less than twenty-five kilograms (2). In North America, almost 50% of pediatric patients receive a heart transplant (HT) within the first six months of VAD implantation (3), while in Europe, only 33% of patients receives a transplant at six months and 38% patients at twelve months. These numbers also reflect an increased time of support (4).

Intracardiac (IC) continuous-flow (CF) VADs are currently the most commonly utilized VADs in pediatrics (1), accounting for one third of all VADs. The positive outcomes for the IC VADs exceed 90% at six months, suggesting an improvement in clinical management for both patient selection and timing of implantation. Their use has been restricted on the basis of size limitation. The paracorporeal (PC) devices are currently limited to support the most challenging pediatric patients: those weighing less than twenty kilograms and those with congenital heart

disease. These groups of children, when presenting with acute HF, have limited device options, leading to high morbidity and mortality. However, these devices require patients to be confined to the hospital until transplantation. Recently, a novel, durable and fully implantable, miniaturized axial flow pump, the Infant Jarvik 2015 (Jarvik Heart, Inc., New York) was implanted for the first time in Bambino Gesù Hospital in 2018 in a four-year-old girl (13 kg, body surface area 0.6 m²) (5). Since then, two more patients have received the implant at Bambino Gesù Hospital for compassionate use and nine other cases in the world, including five that were recruited for the PumpKIN trial in USA. We learned several specific lessons during day-by-day management. The first concerned the protocol of antithrombotic therapy. At the time of implantation, the optimal antithrombotic set-point for this small device was not established. Because of clotting complications despite the appropriate use of unfractionated heparin, the patient was switched to bivalirudin. In 2018, the US Food and Drug Administration (FDA) approved the Jarvik anti-thrombotic guidelines for the US Feasibility PumpKIN Trial, considering bivalirudin instead of unfractionated heparin. Another important lesson was the need to extend the controller’s power meter from six Watts to eleven Watts. Based on this case, the manufacturer and FDA agreed to extend the controller’s power meter up to eleven Watts.

The last surprising lesson was in regard to myocardial recovery. Over the time, all three of our patients with dilated cardiomyopathy, in which myocarditis was excluded, presented with substantial myocardial recovery and the

Infant Jarvik 2015 was successfully explanted. In all cases, ventricular function remained stable (>40%) after three months post-VAD removal. Overall, four out of all twelve patients (33%) treated with the Infant Jarvik 2015 showed this potentially beneficial effect of the CF pump and shed a new light about this subgroup of HF patients (6). To facilitate VAD removal in case of recovery, a special plug will be considered in the near future.

Also, in children weighing less than eight kilograms, the hybrid simulator of Infant Jarvik 2015 showed to maintain adequate patient hemodynamics (7) without back flow or suction.

Another growing field in the pediatric population with end-stage HF is the use of left VAD (LVAD) as permanent support. In selected adult patients with medically refractory HF who are not transplant candidates, LVAD has shown to have the same survival as HT one-year post-implantation (8).

In 2010, we considered LVAD implantation as destination therapy (DT) in a young boy for the first time. This case was a 15-year-old boy with end stage HF due to dilated cardiomyopathy and Duchenne Muscular dystrophy (DMD) (9). Since that time, the use of mechanical circulatory support as DT in DMD reached the clinical arena and case reports and small series have been described. Major causes of death included lung infection, tracheal bleeding and cerebral hemorrhage (10). However, the use of DT VAD in the DMD population carries some ethical concerns and opens the debate regarding patient selection and costs. A multidisciplinary approach with careful evaluation of frailty and co-morbidities is crucial in assessing the proper selection of DMD patients. Also, assessment of respiratory muscle weakness is mandatory before considering VAD placement. In our center, preliminary data on a group of nine DMD patients showed that DT LVAD was able to increase survival at one and five years (75% *vs.* 10% at one year; 32% *vs.* 0% at five years; $P=0.001$) when compared to a similar group in which VAD was not implanted, suggesting that DT LVAD is able to prolong life in DMD population. The longest period of support reached 78 months [unpublished data]. Further prospective studies are required.

LVAD as DT in DMD patients may be considered as a palliative “time-limited” therapy for the treatment of these patients with otherwise no therapeutic options and should be taken into account among all end of life management strategy. Preferences of patient, family and caregivers should be explored throughout management, not only in urgent situations, and a shared decision-making process is

essential.

In conclusion, the wide heterogeneity of end stage HF in the pediatric field requires continuously advancing technology and expanded considerations for therapeutic goals (bridge to transplant, recovery or decision).

Beyond innovative and technological progress in the field of VADs, the development of miniaturized pumps does not refer only to a dimension, as a unit of measure, but rather suggests a new approach, awareness and way of management. This is where the best success lies, as greatness begins with small change.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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