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Pediatric Ventricular Assist Devices — First Steps for Babies

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Patients with severe cardiac failure who are candidates for heart transplantation may require temporary mechanical cardiac support to survive until a donor heart becomes available. This clinical observation is true of children as well as adults. Although the numbers of children may be much smaller than the numbers of adults thus affected, the potential number of years of life saved for each person is much greater for children.

Since the 1970s, the principal form of mechanical cardiac support for infants and children has been extracorporeal membrane oxygenation (ECMO). However, ECMO is designed for short-term support, and as waiting times for donor organs have grown progressively longer (especially for infants), the need for longer-term forms of support has become evident.

The development of ventricular assist devices for adults has been rapid over the past two decades. In contrast, the development of ventricular assist devices of appropriate size for children has been considerably slower. Nonetheless, it is clear that ventricular assist has advantages over ECMO in this population; in 2006, the Pediatric Heart Transplant Study Group reported an 86% rate of survival to transplantation in a group of 99 older children (median age, 13.3 years) who received a ventricular assist device,¹ a finding in stark contrast to the 39 to 75% survival rates among children receiving support with ECMO.^{2,3}

In response to the need for better ventricular-assist options for young patients, the National Heart, Lung, and Blood Institute in 2004 awarded five contracts for the development of novel circulatory-support systems for use in small

children.⁴ These devices will soon be ready for clinical trials through the Pumps for Kids, Infants, and Neonates (PUMPKIN) program. In the meantime, the Berlin Heart Excor Pediatric ventricular assist device, designed for children with a body weight as low as 3 kg, was made available in the United States on a compassionate-use basis. Multiple single-institution reports, as well as the combined retrospective North American experience, have cited survival rates between 70 and 86% among patients receiving this device as a bridge to transplantation, which is substantially better than the rates cited in many reports on the use of ECMO.⁵⁻⁸

These successes set the stage for the first prospective multicenter study of pediatric ventricular assist devices to be performed in the United States, sponsored by the Food and Drug Administration (FDA) Office of Orphan Product Development. The outcomes in 48 children who prospectively received the Excor Pediatric ventricular assist device are presented by Fraser et al. in this issue of the *Journal*.⁹ The children included in the trial were divided into two cohorts according to size; those in cohort 1 had a body-surface area of less than 0.7 m², and those in cohort 2 had a body-surface area of 0.7 to 1.5 m². The trial was designed to evaluate the safety and risk-benefit profile of this pump in both groups.

A randomized trial was not considered to be ethically feasible because of the mounting evidence of success with the device. Therefore, the decision was made to compare the prospective data with data from historical control groups of children who had received support with ECMO. The data on the patients in the ECMO control

groups came from a voluntary registry without set end points or information on adverse events; these children were not weight-matched or age-matched for cohort 2 (the larger children) and were likely to have differed substantially from the children who received the ventricular assist device. Although a comparison group was required by the FDA, using the ECMO registry complicated the study design and made specific comparisons between the groups more problematic.

The study showed that children in both cohorts survived longer than their counterparts who had received support with ECMO, validating the efficacy of the Excor ventricular assist device in supporting patients during long waiting times for transplantation. However, at the end of device support, there was no significant difference in the rate of a successful outcome (transplantation or successful weaning from the device) between the patients in cohort 1 and the matched ECMO group, with an absolute advantage of only 13 percentage points for the children who received the ventricular assist device. In contrast, a significant advantage of 25 percentage points was found for the larger children in cohort 2. It may be that the Excor Pediatric device is preferentially better for larger children because small children require lower flow rates, and there may be an inherent problem with miniaturizing a pulsatile system for such low flow rates.

The risk of any serious adverse event was 92% in cohort 1 (the smaller patients) and 79% in cohort 2 (the larger patients). Major bleeding and infection were frequent. The most worrisome outcome was neurologic complications, in 29% of children in each cohort; 17 strokes occurred in 14 of 48 children, and in 6 children, the strokes were severe enough that support was withdrawn. There were 46 pump exchanges in 48 patients, the majority of them for thrombus formation.

Do the strokes and pump thrombosis reflect suboptimal anticoagulation or a problem with low-flow pulsatile systems? For years, we touted the necessity of physiologic pulsatility for long-term support, but in adolescents and adults, the outcomes with continuous-flow devices have refuted this concept.¹⁰ Perhaps pediatric trials will show that small continuous-flow devices are effective, with lower complication rates. Perhaps different anticoagulation regimens will be more successful in preventing thrombosis, without unacceptable rates of bleeding. However, at present, given the rates of neurologic complications in

this well-managed trial, we must be cautious in extending the current practice in adults of early implementation of ventricular assist devices to children, particularly small children. Ventricular assist devices can save lives and successfully provide a bridge to transplantation for children, but they should remain, at present, a last resort in small children.

Fraser and colleagues have given us a thorough assessment of the Berlin Heart Excor Pediatric ventricular assist device, using rigorous standards and monitoring. The trial thus represents our first baby step toward prospective, evidence-based trials of devices in children. It is hoped that the PUMPKIN program will represent our next great step forward.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

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