

The Combined Use of Extracorporeal Life Support and the Berlin Heart Pulsatile Pediatric Ventricular Assist Device as a Bridge to Transplant in a Toddler

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Abstract: There is a very limited published material about experience with long-term pediatric mechanical circulatory support as a bridge to heart transplant. We report on a 2-year-old, 12 kg boy admitted with 2-week history of low-grade fever, ear pain, pulmonary edema, and congestive heart failure. Trans-thoracic echocardiography confirmed severe myocardial dysfunction with a left ventricular ejection fraction of 0.20 and percentage shortening of 13. After 2 days of ventilatory and inotropic support, the patient continued to deteriorate and subsequently required femoro–femoral extracorporeal life support (ECLS). This was later complicated by a progressive coagulopathy and massive bleeding. On day 17, a pulsatile pediatric paracorporeal biventricular assist device (VAD) (*Berlin Heart*) was implanted. The

patient's condition improved significantly with all coagulopathies corrected, and the patient was extubated 21 days later. After 109 days of bi-VAD support, the patient was successfully transplanted and discharged home 45 days post transplant. Our early experience with initial ECLS bridge to VAD and subsequently to transplant was encouraging. It allowed for additional time to select the ideal organ donor and optimize the recipient's comorbid condition and multiorgan failure. VAD provides an additional armamentarium of circulatory support in pediatric patients with severe heart failure. **Keywords:** cardiomyopathy, pediatric, pulsatile, ventricular assist device, heart transplantation. *JECT. 2004;36:158–161*

INTRODUCTION

Currently, the most common method of mechanical circulatory support for pediatric and neonatal patients with cardiopulmonary failure is extracorporeal life support (ECLS). This nonpulsatile support consists of a complex circuit requiring a high level of anticoagulation and constant monitoring by a perfusionist or a trained ECLS specialist. Unfortunately, this type of support may induce severe trauma to the blood elements and can stimulate an extensive inflammatory response that results in multiorgan dysfunction and marked coagulopathy with great po-

tential for sepsis. ECLS is, therefore, suitable for a limited period of time (7–10 days) at its current state (1–3).

There has been suggestion that ECLS, by itself, may not always be sufficient to support a patient in profound cardiopulmonary failure safely while waiting for a donor heart. This is particularly pertinent to pediatric patients in whom the waiting period might be prolonged to match the recipient with the proper organ size and blood type. In general, only 40% of pediatric patients undergoing cardiac ECLS will recover adequate myocardial function to be discontinued from ECLS and subsequently discharged home (Extracorporeal Life Support Organization [ELSO] registry data). In the remaining patients with myocardial function incompatible with life, but with still adequate neurologic function, ventricular assist device (VAD) can successfully keep patients alive long enough to bridge them to transplantation. We report our experience for a

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case using ECLS and a newly developed pulsatile pediatric VAD that successfully bridged (for a total of 126 days) a child who suffered from a severe dilated cardiomyopathy before orthotopic heart transplantation.

CASE REPORT

A 2-year-old boy weighing 12 kg, previously well, presented to the emergency room with a rapidly deteriorating cardiomyopathy and congestive heart failure. The child deteriorated with worsening heart failure and renal insufficiency despite escalating inotropic support and was placed on ECLS 4 days after admission. The circuit selected consisted of a centrifugal pump (Biomedicus BP-50, Medtronic, Minneapolis, MN), 1/4-inch *Carmeda*-coated tubing (Medtronic, Minneapolis, MN), silicone extended capacity membrane oxygenator (Model 1500, Medtronic, Minneapolis, MN), and a heat exchanger (Helios D-720C, Dideco, Mirandola, Italy). A femoro-femoral approach was chosen for this candidate to avoid sternotomy or cannulation of the carotid artery. A 12 Fr., (Biomedicus, Medtronic, Minneapolis, MN) cannula was inserted in a 7-mm *Gore-Tex* tube (W.L. Gore and Associates Inc, Flagstaff, AZ), which was anastomosed in an end-to-side fashion with the right femoral artery. This provided excellent distal flow to the limb, while perfusing the upper organs. The femoral vein was cannulated with a 12 Fr., (Biomedicus, Medtronic, Minneapolis, MN) cannula at the junction of the greater saphenous vein to allow for distal limb venous drainage. The ECLS circuit was first primed and debubbled with *Plasma-Lyte* solution (Baxter Corporation, Toronto, ON, Canada). After that, 150 mL of packed red blood cells, 100 mL of fresh frozen plasma, 50 mL of 25% albumin, 200 mg of calcium chloride, 10 Meq of sodium bicarbonate, and 1000 units of heparin were added to the circuit to replace the crystalloid solution. The ECLS was initiated at a flow of 80 mL/kg/min and immediate improvement in perfusion (mean arterial blood pressure between 60–80 mmHg), renal function and respiratory status was noted despite persistent left heart distention. Anticoagulation consisted of a heparin infusion (25–55 units/kg/h) titrated to achieve a target activated clotting time (ACT) of 180–200 sec (in a premembrane port). The negative pressure of the centrifugal pump was continuously monitored and kept in a range of –10 to –25 mmHg.

ECLS Complication

Despite meticulous hemostasis and strict control of ACT values, the patient developed marked coagulopathy and started to bleed at the cannulation site 16 hours after initiation of ECLS. During the course of ECLS, the child required surgical exploration of the groin on several occasions because of ongoing massive amounts of bleeding

without an identifiable source. This was locally managed with *Surgicel* (Ethicon, Somerville, NJ) and *Tissel* (Baxter AG, Vienna, Austria) application. On day 4, local tamponade temporarily interrupted the inflow for 30 minutes, requiring 13 minutes of CPR and volume resuscitation until surgical intervention at the cannulation site was performed. With time, numerous hemorrhagic episodes were encountered at different locations, including left thorax, nose, endotracheal tube, and cannulation site of the right groin. The heparin infusion was stopped on several occasions to control bleeding, but this resulted in thrombus formation in the silicone membrane oxygenator requiring emergency replacement of the circuit.

Our usual protocol had been to use a silicone membrane oxygenator for ECLS. However, in view of massive coagulopathic and thrombotic complications, the decision was made to use only *Minimax Carmeda*-coated hollow fiber oxygenator (Medtronic, Minneapolis, MN). This particular circuit and oxygenator selection allowed the child more prolonged ECLS without systemic heparinization.

VAD Implantation

After 17 days of difficult ECLS management, the *Berlin Heart* (Mediport Berlin Heart GmbH Kardiatechnik, Berlin, Germany) pulsatile pediatric VAD was implanted in the operating room with the support of a conventional cardiopulmonary bypass machine. The same femoral arterial and venous cannulas and a new right atrial cannula were used for CPB to completely drain the heart. The procedure was well tolerated, and heparin was reversed with protamine. The bleeding immediately improved, and the femoral vessels were decannulated and repaired. The pump time was 165 minutes. A 9-mm, 85° angled and a 9-mm, 60° angled cannula were sewn onto the ascending aorta and the pulmonary artery, respectively (Mediport Berlin Heart GmbH Kardiatechnik, Berlin, Germany). The right atrium was cannulated with a 25-mm basket-tip-type cannula, and the left ventricular apex was cannulated with a 6.4-mm cannula (Mediport Berlin Heart GmbH Kardiatechnik, Berlin, Germany). A 25-mL stroke volume chamber was used for right VAD, and a 30-mL chamber for the left VAD (Mediport Berlin Heart GmbH Kardiatechnik, Berlin, Germany). The parameters were adjusted in attempt to provide a cardiac output between 2.0–2.4 L/min, equivalent to a cardiac index between 3.5–4.0 liters/min/m². Adequate filling and emptying of the VADs were ensured by external examination. Anticoagulation (heparin) was restarted 12 hours post-VAD implantation to maintain an ACT level of 160–180 sec and a PTT of 60–80 sec. The patient was weaned from ventilatory support and full convalescence with nutritional support, and physiotherapy was initiated. On post-op day 21, patient was extubated. His renal and hepatic functions were noted to

have improved while on VAD. After 17 days of ECLS and 109 days of VAD support, orthotopic heart transplantation was successfully performed.

DISCUSSION

The growing need for long-term circulatory support for the pediatric population has led to research and development of VAD specially designed for pediatric patients. The success of pediatric cardiac transplantation has led to an increased number of pediatric patients awaiting donor organs. Although ECLS has been the most common method of circulatory support to bridge patients for heart transplant, the rate of complication greatly limits its duration. This is a major problem for pediatric patients because optimal donor hearts might be very difficult to find, and therefore, long-term support is often necessary. Efforts to scale down the pump size have met many difficulties. The reduction of pump size results in differences in the fluid dynamics sufficient to initiate clot formation caused by reduced wall shear stress and turbulence levels (4,5). Before the introduction of a pediatric pulsatile pneumatic paracorporeal VAD, a few trials had been conducted using adult size VAD to support pediatric patients (6–8). Unfortunately, oversized pumps could be hazardous because of a potential for clot formation in the large pumping chambers and a relatively large stroke volume delivered in each beat potentially too large to be accommodated by the small pediatric aorta (7). In fact, a retrospective analysis reported that 18% of the pediatric and adolescent patients supported with an adult VAD had hypertension requiring therapy (7).

The *Berlin Heart* is a suitable device to be used for all pediatric patient sizes. The *Berlin Heart* is not approved by the FDA or by Health Canada. After a multidisciplinary meeting and consultation with the family, ethical approval and permission from Health Canada (Medical Devices Bureau, Therapeutic Products Directorate) were obtained. The pediatric *Berlin Heart* VAD was then urgently imported from Germany, along with a technical expert, with the ultimate goal to maintain a small patient alive mechanically until transplantation.

The pediatric miniaturized pump system has been commercially available in Europe since 1992 in sizes of 10, 25, 30, 50, 60, and 80 mLs. These pump sizes allow neonates as well as adolescents to be supported for a short- or long-term period. The *Berlin Heart* smooth silicone cannulas are available in different sizes, with the middle portion surrounded externally by a *Dacron*-velours surface, which promotes tissue ingrowth, thus providing a shield against infection migration along the skin tunnel (9). The transparent chamber allows early detection of thrombotic deposits and evaluation of chamber filling and emptying

phases. The inner surface consists of polyurethane coated with heparin, according to the *Carmeda* method (Kanalvägen 3B, Upplands Väsby, Sweden) to improve antithrombogenicity further. The three-layer membrane construction ensures complete isolation of the blood and air chambers. The stationary drive system consists of three completely independent units that function to support the left and right VAD as well as a back-up system. The pressure and vacuum values can be adjusted to obtain optimal operation of the blood pump. Surveillance is minimal, and constant supervision is not required as in ECLS.

Most experience with the *Berlin Heart* has been reported in Europe. The overall survival rate in the largest series of patients supported with a pediatric device has been 40% (34 children, ages 6–16 years old) (9), and more recently approaching 50% (45 children, ages 2 days–16 years old) (8). With further improvement in technology, patient selection, and experience, these results will continue to improve (10). Early experiences suggest that pediatric pulsatile VAD can be safely applied to children of any age, despite its technical and engineering challenges.

Our current experience further confirmed that ECLS was associated with numerous complications that prevent its long-term use as a bridge to recovery or transplantation. Complete cessation of heparin was complicated by thrombus formation in the silicone membrane that was also associated with a more severe inflammatory response and coagulopathy. The *Carmeda*-coated oxygenator and circuit may provide a safety window should heparin need to be discontinued for a short period of time. Although we systemically heparinize all patients on ECLS, our experience with this patient and others have also confirmed the feasibility of reducing or even stopping the heparin temporarily (up to 24 hours) to control severe bleeding without signs of circuit thrombosis (11,12). This must be carefully monitored and the perfusionist must be prepared to replace any components rapidly should they become thrombosed. Without the combination of *Carmeda*-coated oxygenator and cessation of anticoagulation, it is our belief that ECLS would have been discontinued prematurely because of uncontrollable massive hemorrhage. The hollow-fiber oxygenator also lasted 5 days before plasma leakage became a problem. Over the 17 day period, the entire extracorporeal circuit, including the membrane oxygenator, was changed twice. The membrane oxygenator itself was changed on two additional occasions because of plasma leak.

Regarding the anticoagulation regimen for *Berlin Heart*, we noted that the use of antiplatelet therapy, in addition to heparin, was essential to prevent platelet and fibrin deposition in the circuit. This is more effectively controlled with *Clopidogrel* bisulfate rather than aspirin and should be used as an additional treatment in patients with pediatric *Berlin Heart* VAD.

ECLS AS A BRIDGE TO VAD

The selection of ECLS to provide immediate circulatory support to patients presenting with cardiac arrest or in extremis has been previously reported (13). This strategy allows the team to identify patients with clear contraindications to either long-term VAD and/or heart transplantation (e.g., neurologic status) (14). The ELSO registry suggests that only 47% of non-postcardiotomy patients bridged to transplant with ECLS were subsequently discharged from hospital. To the best of our knowledge, there has been no report on the use of prolonged ECLS, then VAD for bridge to transplant in the pediatric population. In a report from a selected high-risk group of adult patients presenting with cardiogenic shock, the author suggested that survival after left VAD support was similar to patients who were treated initially with ECLS then a VAD (14). In other words, the initial support using ECLS that allowed selection for optimal VAD candidates was not associated with an increase in mortality.

CONCLUSION

Long-term circulatory support using pulsatile pediatric VAD is feasible in the pediatric population (8,9). It is associated with fewer complications than using ECLS. The experience of bridge (ECLS) to bridge (VAD) to transplant in the pediatric population has not been reported in the literature. Our early experience suggests that it is feasible and may represent an additional tool for circulatory support in young patients with heart failure.

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