Levitronix CentriMag to Berlin Heart Excor: A "Bridge to Bridge" Solution in Refractory Cardiogenic Shock

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Levitronix CentriMag is a third generation bearingless temporary rotary pump designed for short-term mechanical support. The device, combined with Berlin Heart cannulas, was implanted in 30 patients suffering from acute cardiogenic shock with biventricular failure. Fifteen patients were successfully bridged to long-term Excor support due to lack of myocardial recovery. The approach produces good results, avoiding the risks of repeated sternotomy and cardiopulmonary bypass and reducing the costs involved. *ASAIO Journal* 2009; 55:465–468.

Refractory acute cardiogenic shock remains a leading cause of death in patients hospitalized and prediction of outcome is still an unsolved question. For many of these patients, mechanical circulatory support (MCS) as a bridge to recovery or transplantation (Htx) remains the only means of survival. Prognosis is poor in those patients in multiple organ failure (MOF) despite maximal medical therapy (including the use of intraaortic balloon pump, multiple inotropes, and pressors). Tremendous progress has been made in the management of acute cardiogenic shock with the use of mechanical assist devices. The two options available for such patients are 1) ventricular assist devices (VAD) or 2) extracorporeal membrane oxygenation (ECMO).

A cost-effective short-term MCS system is beneficial and can even be implanted in a nontransplanting center. In patients with organ recovery without myocardial recovery long-term MCS is necessary to bridge to Htx or as a permanent support. We report our approach consisting of using the cannulas of a paracorporeal long-term device, Berlin Heart Excor (Berlin Heart GmbH, Berlin, Germany), in combination with a novel short-term rotary pump, Levitronix CentriMag (Levitronix LLC, Waltham, MA), that unloads the failing heart and provides adequate organ perfusion. The goal is to support the heart until it recovers. If it does not recover, although multiorgan dysfunction resolves and no neurologic deficits can be seen under mechanical support, the short-term device can be switched to a long-term assist device in the intensive care unit (ICU) or operating theater (OR) without repeat sternotomy and the use of cardiopulmonary bypass (CPB). However, most of these patients can be saved only by Htx, and therefore we restricted VAD implantation to those patients who possibly qualified for Htx.

Patients and Methods

Patients

Between December 2006 and November 2008, 55 patients were supported with Levitronix CentriMag at the Deutsches Herzzentrum Berlin. A biventricular configuration was established in 30 patients (20 men; age 50.8 ± 13.4 years, range: 24–73 years). Indications were postcardiotomy cardiogenic shock in 16 cases (previous valvular surgery in eight patients, coronary artery bypass grafting in seven patients, and adult Fallot correction in one patient) (group A) and bridge to decision regarding transplantation or permanent support in 14 cases (nine idiopathic dilated cardiomyopathy, three acute myocardial infarction, and two fulminant myocarditis) (group B). Berlin Heart Excor cannulas were placed in traditional fashion in combination with the CentriMag circuit.

The remaining 25 patients underwent CentriMag placement (mostly initial insertion of CentriMag pump at our institution) with different cannulas (Medtronic) for other indications, including right ventricular failure after long-term or permanent implantable left VAD, primary CentriMag left VAD placement, or different strategy with the CentriMag pump exchanged for the Cardiowest total artificial heart (due to extensive myocardial tissue compromise, *e.g.*, after massive myocardial infarction).

All 30 patients initially had evidence of severe biventricular failure with MOF, requiring mechanical ventilation and intravenous infusion of inotropes and vasopressors. Twenty-five patients received intraaortic balloon pump support. Indications for VAD placement and particularly the choice of biventricular support followed our institutional algorithms.[2,3]

Technique

Median sternotomy for initiation of CBP was performed in traditional fashion after anticoagulation based on activated clotting time-guided heparinization. In patients with postcardiotomy cardiogenic shock, the previously established CPB was continued. The right atrial and left apical ventricular inflow and pulmonary and aortic outflow cannulas from an extracorporeal, pneumatically driven Berlin Heart Excor assist device (Berlin Heart GmbH, Berlin, Germany) were implanted in traditional fashion. The choice of cannula size was custom-

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ized to the patient's body surface area.[1] The cannulas were brought through the diaphragm and the skin below the costal arch as described elsewhere.[1] Next, the CentriMag pump heads and tubing were prepared and primed extracorporeally. The tubes were then divided within the operating field and appropriately connected to each Berlin Heart Excor cannula, carefully avoiding letting any air into the system and using appropriately sized titanium connectors (Berlin Heart GmbH, Berlin, Germany), thus reducing platelet aggregation activity on site. Once the CentriMag pump fully supports the circulation, the patient was weaned from CPB, and CPB was stopped. The heparin was reversed using protamine, the mediastinal tubes were inserted, and the sternotomy was closed in traditional manner. Anticoagulation therapy with heparin was started 8 hours after cessation of bleeding, and the anticoagulation management was performed in accordance with our institutional protocol.[2]

To assess any myocardial recovery, echocardiographic studies were performed daily, and MCS weaning was performed by reduction of the flow by 0.5 L every 30 minutes until 2 L/min was achieved. The hemodynamic situation was considered stable if, under minimal inotropic drug support, no increase or only a slight increase in wedge and central venous pressures and no decrease in perfusion pressure or cardiac output occurred. If during the first 2 weeks of support the weaning attempts were unsuccessful, it was evaluated whether the patient was a candidate for long-term assist device support. The evaluation took into consideration age, neurologic status, signs of systemic infection, organ function, and social situation. If the patient was a suitable candidate for long-term MCS, clinical consent was obtained, and pump exchange was performed in the ICU or in the OR. The Berlin Heart pumps were primed with sterile saline solution and connected to the drive console. A heparin bolus of 5,000 IE was administered intravenously before pump stop. During the procedure, the patient was slightly sedated with a short-acting hypnoticum. After disinfection of the skin and cannulas, the CentriMag assist device was stopped, the left-side inflow and outflow cannulas clamped, and the connectors and the CentriMag pump removed from the Berlin Heart cannulas. In the next step, the Berlin Heart pump was connected to the cannulas, the clamps removed, and the Berlin Heart assist device started. Next, the same procedure was performed for the right side.

The pump exchange for each side takes approximately 2–3 minutes. If necessary, catecholamines were given intravenously as a bolus to maintain stable arterial pressure and cardiac output. The frequency of the counterpump was always slowed during the exchange procedure. After the pump exchange, the patients were mobilized and weaned from the ventilator. Anticoagulation management on Excor support was performed following our institutional protocol already described.[2]

Statistical Analysis

All values are expressed as means ± standard deviation. Differences in hemodynamic and end-organ function were compared using one-way repeated analysis of variance. All analyses were performed using SPSS for Windows Release 11.5 (SPSS Inc., Chicago, IL).

Table 1. Hemodynamic Characteristics and End-Organ Functional Status Before and at the End of CentriMag (Levitronix LLC, Waltham, MA) BVAD Support in Survived Patients Before Exchange for Excor Support (Berlin Heart GmbH, Berlin, Germany)

	Before Support	On Last Day of Support	One-Way ANOVA, *p*
mAP (mm Hg)	67.0 ± 9.8	78.7 ± 13.7	0.03
mPAP (mm Hg)	44.3 ± 12.2	33.0 ± 8.1	0.07
CVP (cm H_2O)	17.1 ± 3.9	13.7 ± 2.7	0.05
White blood count (cells × $10^3/\mu l$)	15.2 ± 7.4	13.2 ± 6.8	0.99
Hemoglobin (mg/dl)	11.1 ± 2.5	10.1 ± 1.0	0.20
Hematocrit (%)	32.3 ± 7.4	29.8 ± 3.4	0.33
Platelet count (cells × $10^3/\mu l$)	133.7 ± 69.9	116.9 ± 69.9	0.52
Blood urea nitrogen (mg/dl)	49.4 ± 31.4	42.5 ± 16.3	0.47
SCr (mg/dl)	2.27 ± 0.9	1.67 ± 1.3	0.08
AST (U/L)	937 ± 1123	251 ± 292	0.23
ALT (U/L)	962 ± 1201	87 ± 94	0.05
ALP (U/L)	103.7 ± 67.9	65.7 ± 22.6	0.04
Total bilirubin (mg/dl)	2.85 ± 2.8	1.96 ± 1.1	0.008
Albumin (U/L)	2.7 ± 0.3	2.5 ± 0.5	0.38
INR	1.9 ± 1.2	2.0 ± 1.6	0.90
PTT (s)	59.7 ± 31.9	73.2 ± 39.8	0.31
Serum lactates (μmol/L)	8.3 ± 5.2	3.8 ± 3.7	0.008

ANOVA, Analysis of variance; mAP, mean systemic arterial pressure; mPAP, mean pulmonary arterial pressure; CVP, central venous pressure; SCr, serum creatinine; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; INR, international normalized ratio; PTT, prothrombin time.

Results

At the time CentriMag support began, three patients (group B) with acute myocardial infarction were unresponsive, with a Glasgow Coma Scale score of 3; the rest of the patients in group B had no severe impairment of neurologic responsiveness, similar to the patients in group A before the cardiac surgery procedure. Cardiac arrest before VAD placement occurred in four patients (n = 2 in group A; n = 2 in group B).

Mean support time on the CentriMag VAD was 8.1 ± 7.9 days (range: 1–39 days). Overall, 30-day mortality was 50% due to MOF. Ten patients who died were in group A (62.5%) and five in group B (35.7%). Two cases in group B had fatal cerebral hemorrhage. All surviving patients were judged to be candidates for Excor because there was no myocardial recovery during CentriMag support. Surviving patients included nine patients (60%) of group B (six idiopathic dilated cardiomyopathy, one acute myocardial infarction, and one fulminant myocarditis) and six patients (40%) of group A (four valvular surgery patients and two coronary artery bypass grafting patients). Hemodynamic characteristics and end-organ functional status before and at the end of CentriMag BVAD support in survived patients before exchange for Excor support is shown in **Table 1**. There were no significant differences in end-organ function assessment between survivors and nonsurvivors in our study. The average plasma-free hemoglobin, hemolysis marker during CentriMag support was 8.7 mmol/L (range, 1.4–210 mmol/L). Among survivors, the average plasma-free hemoglobin was 7.8 mmol/L (range, 1.4–211 mmol/L), whereas for nonsurvivors, it was 12.3 mmol/L (range, 1.4–210 mmol/L).

Pump exchange was performed without resternotomy with patients slightly sedated in the ICU at the beginning of our experience and then in the majority of cases in the OR to provide more clinical security and sterility during the pump changing procedure. The conversion was performed after 7.4 ± 3.8 days (range: 1–16). Although on Excor support, one patient (group B, idiopathic dilated cardiomyopathy) received successful transplantation 6 months after implantation. Overall, 12 patients (40%) were discharged home and three (group B, idiopathic dilated cardiomyopathy) of them are currently waiting for a suitable organ. One patient (group A, valvular surgery patient) is on support permanently due to noneligibility for Htx for age reasons. One patient on support died of MOF and a second died of sepsis after 130 and 88 days, respectively (group A, coronary artery bypass grafting patients). End-organ functional recovery maintenance was achieved in the remainder of the patients by Berlin Heart Excor support. Neither minor nor major cerebral events occurred on Excor VAD. Coagulation management on Excor followed our institutional protocol.[2] At the latest follow-up, mean duration of support is 245 ± 93.6 days (range: 89–450 days).

Discussion

In most of our patients with acute cardiogenic shock in biventricular failure, we showed that temporary biventricular CentriMag circulatory support improved end-organ function and allowed full neurologic recovery; 50% of them became candidates for long-term Excor implantation. Our approach allowed the recovery of many patients otherwise ineligible for Excor implantation, with good early and mid-term survival.

As the use of MCS in patients with heart failure increases, and as options increase for mechanical assistance, the indications for implantation of each device need to be clarified. Although individual patients continue to benefit from this life-saving technology, the cost-benefit ratio of implantable support therapy certainly does not justify its use in all potential recipients.

In critically ill patients suffering from acute cardiogenic shock, MOF, prior cardiac arrest, and neurologic dysfunction, the mortality rate after direct long-term or permanent VAD insertion is dramatically high. Such patients consequently benefit from temporary support first. Short-term VADs include the widely used Abiomed BVS 5000 (Abiomed Inc., Danvers, MA), Bio-Medicus systems (Medtronic Bio-Medicus, Inc., Minneapolis, MN) and the percutaneous devices such as Tandem Heart (CardiacAssist Inc., Pittsburgh, PA).[4,5] In addition, ECMO is also useful.[6] However, disadvantages of these modalities of support include the limited support duration and the need for pump exchanges at short intervals of time, a high incidence of complications with increasing duration of support, the need for fairly stringent anticoagulation, lower leg ischemia in percutaneous support modalities, and the requirement of an experienced team of personnel to allow for their safe use.

In our study, by using biventricular CentriMag support in 30 patients with refractory acute cardiogenic shock and MOF, we achieved an overall 30-day survival of 50% (the worst outcome was in the postcardiotomy group). The use of the recently introduced third generation bearingless CentriMag system[7–9] allowed rapid assessment of ventricular recovery, weaning, and potential explanation. The CentriMag system's durability is also much greater than that of any other temporary circulatory assist device currently available. The cutoff timing of CentriMag support that we fixed at the beginning of our experience was 15 days, in accordance with the CE mark approval and statement. In the meantime, we can prolong the support for up to 30 days. An additional advantage with CentriMag support is the absence of stringent requirements for anticoagulation.

Our policy at the Deutsches Herzzentrum Berlin for such patients allows recovery of the renal, hepatic, and respiratory systems during the support period. These patients can also be weaned from the ventilator and even extubated if their condition warrant (as achieved in 50% of our patients on BVAD CentriMag support presented). Nursing and physiotherapy staff are encouraged to partially mobilize the patient and perform initial rehabilitative therapy.

Traditionally, in patients who benefited from a temporary mechanical support and required conversion to long-term support, the conventional technique involves repeat sternotomy and the use of CPB, with consequently increased risk for infection. Second, exchange of the cannulas causes additional trauma of the fragile myocardium with increased risk for bleeding. Avoiding these procedures by using the approach presented here, already described elsewhere with the Abiomed device[10] and similarly proposed by Maat et al.,[11] in infants after hemodynamic stabilization by means of initial ECMO support may lead to significant reduction of life-threatening postoperative complications. Furthermore, the larger size of the Berlin Heart inflow cannulas increases the blood flow provided by the CentriMag device.

The exchange of CentriMag pumps for Berlin Heart pumps also saves costs (for operating room, CPB, additional personnel, and equipment). To conclude, the approach described could even be applied in nontransplanting centers or those using Thoratec VAD cannulas with an option for subsequent transfer to a hub center where the conversion to a long-term assist device can be performed.

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