Bridging patients after salvage from bridge to decision directly to transplant by means of prolonged support with the CentriMag short-term centrifugal pump

Saleem Haj-Yahia, BSc, MD, Emma J. Birks, MRCP, PhD, Mohammed Amrani, MD, PhD, Mario Petrou, FRCS, PhD, Toufan Bahrami, MD, Gilles Dreyfus, MD, PhD, and Asghar Khaghani, FRCS

Objective: Optimum strategy for salvage in patients with acutely decompensated end-stage heart failure and severe multiorgan dysfunction is complex. We present our experience with prolonged CentriMag (Levitronix, Waltham, Mass) support for transitioning patients after successful salvage from bridge to decision directly to transplant.

Methods: Records of patients who underwent salvage with a CentriMag as bridge to decision and later to transplant were reviewed. Between June 2003 and June 2008, 4 patients in cardiogenic shock from acute decompensated end-stage heart failure and multiorgan dysfunction underwent salvage with biventricular CentriMag as bridge to decision. Three were male. Mean age was 39.3 years (range 24–52 years). Three had dilated cardiomyopathy; 1 had ischemic cardiomyopathy. All had preoperative mechanical ventilation, large doses of multiple inotropes, and intra-aortic balloon support. All also had acute liver and renal failure and metabolic acidosis.

Results: After mean postimplant period of 43 days (range 7–70 days), patients had reversal of end-organ dysfunction; after mean waiting time of 31 days (range 21–67 days), all were transplant listed. Mean mechanical circulatory support was 87.7 days (range 26–105 days). No thromboembolic or neurologic events or mechanical failures occurred. Posttransplant mean ventilation and intensive care unit stay were 2 and 4 days (ranges 1–4 and 3–7 days), respectively. All patients were discharged home and remain alive and well.

Conclusion: CentriMag use as long as 3 months appears to be safe and cost-effective for bridging selected patients directly to transplant after salvage. Further clinical experience is still needed.

The CentriMag (Levitronix, Waltham, Mass) ventricular assist device (VAD) was initially used for short-term ventricular support in postcardiotomy failure after routine cardiac surgery, for primary graft dysfunction after heart transplant, and for salvage as a bridge to decision (BTD) in patients with severe decompensated end-stage heart failure (DESHF), as has previously been reported.^{1–6} In this report, we describe our experience with a subset of moribund patients who had initial salvage with this device as a BTD for longer than 3 months, leading directly to transplant.

MATERIALS AND METHODS

Eighty-patients received CentriMag VAD support at our institution between June 2003 and August 2008. We reviewed the records of patients with acute cardiogenic shock from advanced heart failure who underwent salvage with a CentriMag VAD as a BTD and later a direct bridge to orthotopic heart transplant.

From Cardiothoracic Transplantation and Mechanical Circulatory Support, Royal Brompton and Harefield Hospital, and the National Heart and Lung Institute, Imperial College for Science, Technology and Medicine, London, United Kingdom.

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Address for reprints: Asghar Khaghani, FRCS, Cardiothoracic Transplantation and Mechanical Circulatory Support, Royal Brompton and Harefield Hospital, Hill End Rd, Harefield, Middlesex UB9 6JH, UK (E-mail: S.Haj-Yahia@imperial.ac.uk).

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Between 2003 and 2008, a total of 80 patients received Levitronix CentriMag VAD support at our institution. Twenty-six patients (32.5%) had postcardiotomy failure, 15 (18.8%) had Levitronix CentriMag right VAD (RVAD) placement along with a long-term left VAD (LVAD), 16 (20%) had primary graft dysfunction after heart transplant, and 23 (28.8%) either had acute presentation for salvage procedure as a BTD or had deteriorating end-stage heart failure or acute heart failure with multiorgan dysfunction (MOD) and underwent salvage as a BTD. Three patients of this last group (3/23) had myocardial recovery and had the VAD explanted, 7 had upgrades to long-term LVAD (either HeartMate II [Thoratec Corp, Pleasanton, Calif] or Jarvik 2000 [Jarvik Heart, Inc, New York, NY]) with explantation of the RVAD, 10 patients died during support, and 4 (the subjects of this study) had prolonged Levitronix CentriMag support with subsequent bridging directly to transplant. This report focuses on the last subgroup.

All 4 patients had severe cardiogenic shock from DESHF, sepsis, and MOD, and all underwent salvage with the CentriMag biventricular VAD (BiVAD) as a BTD. Three were male and 1 was female. The mean age at presentation was 39.3 years (range 24–52 years). Three had dilated cardiomyopathy, and 1 had ischemic cardiomyopathy. The mean body mass index (BMI) was 22.5 kg/m² (range 18.7–25.2 kg/m²). All patients were in severe cardiovascular collapse and receiving large and multiple doses of inotropic support (more than two inotropes per patient). All patients had intra-aortic balloon pumps. Three patients also had cardiac cachexia. All were in respiratory failure and had mechanical ventilation. All had acute liver and renal failure and were in acute metabolic acidosis. Table 1 presents a summary of the preoperative hemodynamic and metabolic conditions. All patients underwent salvage with an off-pump CentriMag BiVAD as a BTD. In 1 case, the pump was inserted during cardiopulmonary resuscitation and open cardiac massage.

In all cases, an LVAD was first inserted, and nitric oxide was given to all the patients. If, however, hemodynamic and echocardiographic evidence of

Abbreviations and Acronyms

BMI	= body mass index
BiVAD	= biventricular assist device
BTB	= bridge to decision
DESHF	= decompensated end-stage heart failure
ICU	= intensive care unit
LVAD	= left ventricular assist device
MOD	= multiple-organ dysfunction
RVAD	= right ventricular assist device
VAD	= ventricular assist device

right ventricular dysfunction resulting in suboptimal LVAD flow to support BMI, rising central venous pressure, and a need for large dose of inotropes to support the right ventricle were observed, an RVAD was inserted. In this critically ill group of patients, we have a low threshold of BiVAD insertion rather than isolated LVAD support to allow optimal flow, reduce hepatic congestion, and secure good renal perfusion.

Surgical Technique

After the chest was opened through a median sternotomy, full heparinization (3 mg/kg) was given. The LVAD and RVAD inflow and outflow cannulas (32F single-stage malleable venous drainage cannula [Edwards Lifesciences, Irvine, Calif] for the inflow and 22F elongated 1-piece arterial cannula [EOPA; Medtronic, Inc, Minneapolis, Minn] for the outflow line) were introduced through separate skin incisions on the right upper abdominal quadrant for the LVAD and on the left upper abdominal quadrant for the RVAD. After preparation of double purse-string sutures, the LVAD inflow and outflow cannulas were placed and secured in the left atrium (intra-atrial groove) and ascending aorta, respectively. The RVAD inflow and outflow cannulas were placed in the right atrium and main pulmonary artery, respectively. The positioning of the inflow cannulas in the right and left atria was directed by transesophageal echocardiography.

Management of VAD and External Circuits

Throughout the period of mechanical circulatory support, the external circuits and the pump's head were arbitrarily changed every 4 weeks. Examination of a number of the first exchanged external circuits and pump heads did not, however, show clots or structural damage. We therefore decided that we could safely extend to 6 weeks the period of support without changing the pump head and external circuit. If any visible fibrin sediments were noted in the external circuit lines, an earlier exchange of the circuit was pursued.

Anticoagulation Protocol

Full heparinization was given preoperatively and was fully reversed after establishment of full flow on both VADs and before closure of the chest. Continuous intravenous heparin was restarted several hours postoperatively after at least 4 hours without a bleeding event. The dose was adjusted every 4 hours for a target activated partial prothrombin time of 60 to 100 seconds, other than during the period when the assessment of the heart function was made, with the pump flow lowered for few hours; then the target activated partial prothrombin time was 80 to 100 seconds.

Assessment of Cardiac Function During Support

First attempt at weaning from the VAD was performed at 14 postoperative days. The assessment of the cardiac function for potential early myocardial recovery was performed by recording such baseline hemodynamic data as mean blood pressure, heart rate, right heart pressures, mixed venous saturation, and urinary output during full support, followed by reducing the

TABLE 1. Preoperative hemodynamic and laboratory data

	Mean	Range
Blood pressure (mm Hg)		
Systolic	76	95–60
Diastolic	53	40–75
Heart rate (beats/min)	99	71–122
Central venous pressure (mm Hg)	17.6	14–21
Pulmonary arterial pressure (mm Hg)		
Systolic	82	NA
Diastolic	38	NA
Epinephrine ($\mu\text{g}/[\text{kg} \cdot \text{min}]$, 3/4 patients)	0.84	0–1.8
Norepinephrine ($\mu\text{g}/[\text{kg} \cdot \text{min}]$, 1/4 patients)	0.63	0–1.7
Dopamine ($\mu\text{g}/[\text{kg} \cdot \text{min}]$, 3/4 patients)	4.8	0–7.9
Dobutamine ($\mu\text{g}/[\text{kg} \cdot \text{min}]$, 1/4 patients)	6.4	0–7.3
Milrinone ($\mu\text{g}/[\text{kg} \cdot \text{min}]$, 2/4 patients)	0.33	0–0.43
Mechanical ventilation (no.)	4/4 (100%)	NA
Intra-aortic balloon pump (no.)	4/4 (100%)	NA
White blood cells (cells/mL, no.)	23,133	4300–54,200
Bilirubin (mmol/L)	79.2	18–197
Alkaline phosphatase (IU/L)	93.6	63–135
Alanine aminotransferase (IU/L)	422.8	53–1436
Sodium ion (mmol/L)	130.5	127–134
Potassium ion (mmol/L)	5.6	4.9–6.3
Urea (mmol/L)	13.18	9.2–22
Creatinine (mmol/L)	145	121–253

NA, Not applicable.

flow to a minimum of 1 L/min. During and after 6 to 8 hours of low flow without inotropes, the hemodynamic, right-heart pressure, and cardiac output studies were performed, as was transthoracic echocardiography.

Patient Management During Support

All patients were managed in the intensive care unit (ICU) by the ICU nursing team, supervised by the surgeons and mechanical circulatory support consultant and anesthetists. Continuous presence of the perfusionists in the ICU was not required. They did, however, review the patients in the ICU at least once a day to check the technical aspects of the pumps and were also present during physiotherapy and patient mobilization.

Once multiorgan function was restored with no remaining infection and the patients were self-ventilating, the patients were transferred to the ward under the VAD nurses' care, supervised mainly by the mechanical circulatory support cardiologist with surgical input as required. The exchange of the external circuits was performed electively by the perfusionists under surgeon supervision.

RESULTS

The mean duration of CentriMag BiVAD support was 87.7 days (range 26–105) days. The mean RVAD and LVAD flows were 4.9 and 5.4 L/min (range 4.6–5.5 and 4.5–6.7 L/min), respectively. No patient needed surgical re-exploration for postimplant bleeding. All patients were no longer receiving inotropes or intra-aortic balloon pulsation within the first 48 postoperative hours. Three patients were extubated within the first 48 postoperative hours. One patient needed longer-term ventilation through a tracheostomy because of general weakness and cachexia.

After a mean of 43 days (range 7–70 days) after BiVAD implantation, all patients showed good clinical recovery

and reversal of end-organ dysfunction, with no remaining infectious or neurologic complications. They were listed for and directly bridged to transplant. The mean waiting time for a donor heart was 31 days (range 21–67 days). Donor mean age was 27.2 years (range 18–40 years). Two donors were female, and 2 were male. All 4 donors had blood group O. One donor had died of intracranial bleeding after head injuries, 1 with Evans syndrome had died of relapsing myelitis, and 2 had died of subarachnoid hemorrhage related to arteriovenous malformation. The mean ischemic time was 180 minutes (range 135–220 minutes). The posttransplant mean duration of ventilation and ICU stay were 2 days (range 1–4 days) and 4 days (range 3–7 days), respectively. The posttransplant survival to home discharge was 100%. All patients remained alive and well at 4, 8, 14, and 25 months of follow-up.

No patients had sternal wound infection; in all cases, however, the VAD cannula exit sites were managed with surgical débridement and by using a vacuum-assisted closure dressing (KCI Medical Ltd, Kidlington, UK) until complete healing had been achieved. In 1 patient, a large abdominal wall defect caused by multiple cannula exit sites and chest drains needed a skin graft.

Gastrointestinal bleeding from peptic ulcers was seen in 1 patient during mechanical circulatory support, necessitating a large transfused volume of blood and blood products, repeated gastroscopies, and angiographic catheter embolization. During this period, the anticoagulation regimen was stopped for several days without any adverse effects.

There were no instances of pump mechanical failure, thrombosis, or thromboembolic events. No patient had neurologic complications. All patients underwent ambulation and mobilization from bed during support in the ICU and on the ward.

We compared the costs of this group of patients who had direct bridging to transplant after salvage with those of the group of patients who underwent salvage with the Levitronix CentriMag device and then upgrade to a long-term device (such as the HeartMate II) as a bridge to transplant. The immediate postoperative ICU stays were similar in these two groups; however, the cost of the Levitronix CentriMag device was significantly lower than that of the long-term device. The costs of an additional surgical procedure to perform the upgrade were also saved. We also managed to reduce the ICU stay substantially for patients who had prolonged Levitronix CentriMag support by encouraging early postoperative mobilization and by transferring them to the ward as soon as possible after reversal of MOD.

DISCUSSION

Our overall experience with CentriMag short-term VAD use as a BTM has been reported before.^{1–4} The indications for using the CentriMag in salvage for patients with acute decompensated end-stage heart failure, MOD, and infection

was influenced by the need for quick, and often off-pump, surgery with a simply operated and relatively inexpensive VAD that could support both sides of the heart for this very sick group of patients until there was evidence of the reversibility of end-organ dysfunction, particularly the neurologic condition. Moreover, the CentriMag had a satisfactory flow for high-BMI patients and provided adequate organ perfusion, which could effectively restore end-organ function, as defined at the point when the patients were self-ventilating with normal hepatic and renal function with no active infection. Once MOD had been reversed and there were neither serious neurologic damage, active sepsis, nor early signs of myocardial recovery, the decision was made to bridge these patients directly to transplant.

We consider this option to be a cost-effective and superior alternative to upgrading to a long-term VAD for this subgroup of patients, mainly because it avoids further surgical complications that might be associated with another device being inserted. It also allows a shorter bridging period, with reduced VAD-related complications. It avoids the risk of embolic complications during the removal of the VAD cannulas (particularly the left atrial cannula).

Because some time is needed for the patients to recover, however, and also because of the shortage of donor organs for transplant, our 4 patients needed longer than 3 months of mechanical circulatory support before they received a transplant. During this period, replacements of the single-use motor and external circuit of the VADs were successfully performed every 6 weeks in the ICU or the operating room without the need for sedation or surgical intervention.¹ This seemed to be a simple and well-tolerated procedure that allowed us to extend safely the length of mechanical circulatory support with this device. During this period, we saw high mechanical reliability, with no mechanical failures or thromboembolic events.

These patients cannot achieve full ambulation, but a policy of intensive physiotherapy and mobilization while they are in the ICU, and recently while they are on the ward, has been applied and shown to be effective. Our recent policy to allow transfer of these patients to the ward rather than keeping them in the ICU also has cost-effective implications.

In the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) trial, patients who were younger than 65 years did better than the older group of patients.⁶ Our study group was characterized by a relatively young age (mean age was 39.3 years, and the oldest was 52 years old), which may have had an impact on successful restoration of multiorgan function, capacity to ambulate and cooperate with the physiotherapy team, and potential to become viable transplant candidates. The groups of patients who survived and did not survive, however, were too small to draw conclusions.

Direct bridging to transplant after a prolonged period of mechanical circulatory support (as long as 3 months) proved

successful for these selected patients. This group of patients had relatively BMIs and common blood groups. For the patient who shows early signs of myocardial recovery after a few weeks of mechanical circulatory support or is unlikely to receive a transplant in the short term (such as a patient with high BMI, positive panel-reactive antibodies, or uncommon blood group), early consideration should be given to upgrading the short-term VAD to longer-term VAD support as soon as the MOD state has reversed with no active infection and the patient's nutritional and general conditions become suitable for further surgery.

CONCLUSIONS

Prolonged use of the Levitronix CentriMag VAD for as long as 3 months appears to be a relatively safe and cost-effective procedure for direct bridging of selected patients to transplant after salvage. Further clinical experience and evaluation are still needed.

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