

Experience with Magnetically-Levitated Centrifugal Flow Pump in Patients with Cardiogenic Shock (INTERMACS 1)

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ABSTRACT

Introduction

Short term use of magnetically-levitated ventricular assist devices offers hemodynamic stabilization of patients with refractory cardiogenic shock in INTERMACS level 1, enabling a therapeutic strategy.

Objective

The aim of this study was to assess in a single centre the results with second generation centrifugal flow pumps in patients with refractory cardiogenic shock.

Methods

Fifteen patients with Levitronix CentriMag® ventricular assist device implantation were retrospectively analyzed from 2006 to 2011. All patients presented refractory cardiogenic shock under two inotropic agents and 13 patients had intra-aortic balloon pump assistance prior to ventricular flow pump support. The indications were: end stage cardiomyopathy in 8 patients, viral myocarditis in 1 patient, postpartum cardiomyopathy in 1 patient, postcardiotomy cardiogenic shock in 3 patients and post heart transplantation graft failure in 2 patients.

Results

Mean age was 49 ± 13 years, and 66% (10/15) were men. Only 1 patient underwent left ventricular assist device implantation (LVA) and 14 patients underwent biventricular assistance (BVA). Mean support duration was 6 ± 4 days (2-19). Final post-implant therapeutic decision was bridge to heart transplantation in 12 patients (80%), bridge to recovery in 1 patient (7%) and bridge to decision in 2 patients (13%). One patient was successfully weaned from BVA due to ventricular function recovery and 8 patients were transplanted, with a survival rate of 60% (9/15). Reoperation due to bleeding was performed in 6 patients (40%) and 1 patient presented cannulae thrombosis. None of the patients had stroke or technical system failures. Six patients died while receiving circulatory assistance (40%) (5 BVA and 1 LVA), 1 patient due to sepsis, 1 patient due to coagulopathy and 4 patients due to multiple organ failure. Out of the 6 deaths, 2 patients were in postcardiotomy cardiogenic shock and 4 were on heart transplantation waiting list.

Conclusions

In this series, circulatory support with Levitronix CentriMag® centrifugal flow pump was effective in critical patients with a survival rate of 60%. Reoperation for bleeding was the most frequent complication.

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Key words >

Heart failure - Cardiogenic shock - Circulatory assistance - Heart transplantation

Abbreviations >

BVA	Biventricular assistance	LVA	Left ventricular assistance
ECMO	Extracorporeal membrane oxygenator	IABP	Intra-aortic balloon pump
INTERMACS	Interagency Registry for Mechanically Assisted Circulatory Support	PCCS	Postcardiotomy cardiogenic shock
		VAD	Ventricular assist devices

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INTRODUCTION

Despite therapeutic progress, refractory cardiogenic shock and end-stage heart failure have an unfavorable prognosis. Ventricular assist devices (VAD) are efficient for the treatment of stage D severe heart failure (patients with refractory symptoms at rest regardless of utmost medical treatment, who are hospitalized and require specialized interventions). (1) In recent years, short-term use of second generation centrifugal flow pumps has consistently improved outcomes, stabilizing the hemodynamic status of the patients and offering the opportunity of evaluating the clinical condition, generally associated with organ failure and the neurologic state, often difficult to assess in ventilated patients.

Use of these devices improves tissue perfusion and organ function in patients with refractory cardiogenic shock (INTERMACS 1 level), aiding in the decision of subsequent therapeutic conduct, either as bridge to decision, bridge-to-transplantation, bridge to recovery, or bridge to implantation of another long-term device (definitive therapy). (2)

The Levitronix CentriMag® centrifugal flow pump was approved in 2005 by the National Administration of Drugs, Food and Medical Technology (ANMAT) as circulatory support for up to 14 days, and is currently authorized as circulatory support for up to 30 days by ANMAT, the Food and Drug Administration (FDA)

and the European Medicines Agency (EMA), and implantations for up to 100 days have been performed. The Levitronix CentriMag® is a paracorporeal pump, based on a propelling system without fixed mechanical bearings thanks to the application of a new levitation and rotational technology generated by a magnetic field. This system may produce a maximum univentricular directional flow of 10 L/min eliminating zones of flow stasis, and decreasing shear and friction forces which damage blood corpuscles causing hemolysis and thrombus formation. It requires an adequate anticoagulation level with intravenous heparin, keeping an activated coagulation time of 200 s or KPTT of 60-80 s. Figure 1 shows details of the CentriMag device.

The purpose of this study is to report in a single centre the experience of a group of patients with cardiogenic shock requiring Levitronix CentriMag® centrifugal flow pump as bridge to subsequent therapy.

METHODS

Fifteen consecutive patients receiving ventricular assistance with Levitronix CentriMag® centrifugal flow pump implantation were retrospectively analyzed from January 2006 to December 2011. All patients were evaluated and treated at the Intrathoracic Transplantation Unit. Confidentiality was preserved on the reviewed data.

The study included patients with refractory cardiogenic shock in INTERMACS 1 level, presenting refractory hypotension with target organ hypoperfusion unresponsive to

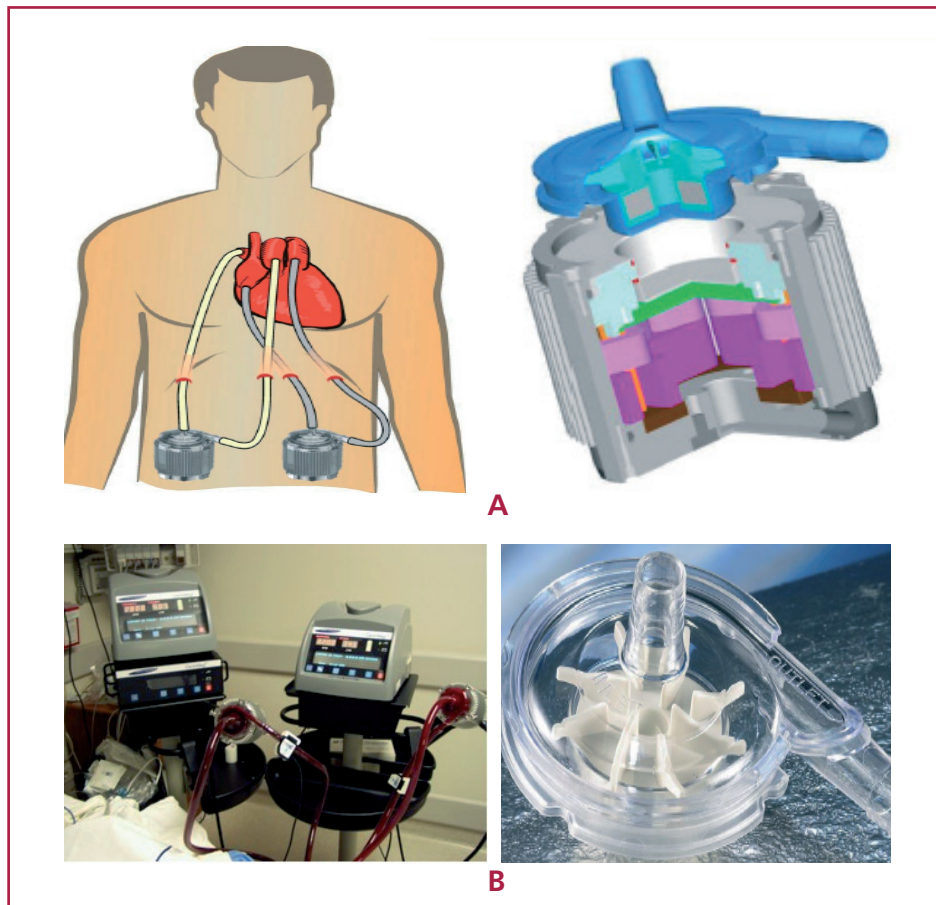


Fig. 1. A. Paracorporeal biven- tricular assist device and rotor pump. **B.** Console with two electromagnetic rotors and centrifugal pump

two inotropes at maximum dose (milrinone 0.75 gamma/kg/min and/or dobutamine 10 gamma/kg/min, and/or levosimendan and noradrenaline at variable doses according to mean arterial pressure). Thirteen patients had also received intra-aortic balloon pump (IABP) support prior to ventricular assist device implantation. All patients were potential candidates for cardiac transplantation or retransplantation without anatomical or clinical contraindications for mechanical assistance with centrifugal pump implantation

Underlying pathologies progressing to cardiogenic shock were: 8 patients had end-stage cardiomyopathies, 2 patients acute heart failure (peripartum cardiomyopathy or large cell myocarditis), 3 patients postcardiotomy cardiogenic shock (PCCS) due to difficult weaning from extracorporeal circulation or refractory low cardiac output in the immediate post-operative period, and 2 patients presented graft failure after heart transplantation (Figure 2).

All implantation procedures were performed in the operating room, with central cannulation by medial sternotomy.

The present study was approved by the institutional Teaching and Research Department. All patients or their relatives or legal representatives signed an informed consent to carry out the indicated surgical procedure after receiving appropriate information concerning the risks and benefits and answering all the procedure-associated questions and doubts.

RESULTS

Mean age was 49 ± 13 years (14-64) and 66% of patients were men (10/15). One patient (7%) received left ventricular assist device implantation and 14 patients (93%) biventricular support from the start and simultaneously due to severe biventricular failure in the operating room. Overall mean support time was 6 ± 4 days (2-19) and 8 ± 3 days (4-14) in the subgroup of patients that underwent emergency trans-

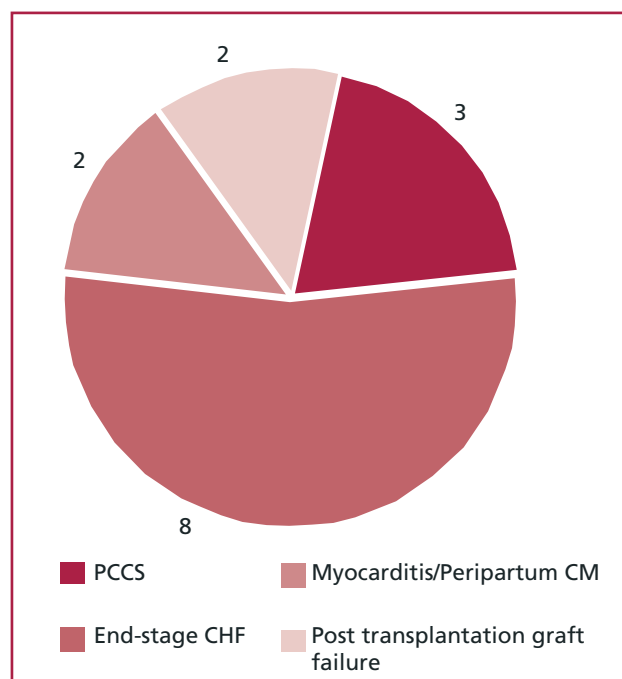


Fig. 2. Indications for circulatory support. CHF: Chronic heart failure. CM: Cardiomyopathy. PCCS: Postcardiotomy cardiogenic shock.

plantation. The final post-implant therapeutic decision was: bridge to heart transplantation in 12 patients (80%), bridge to recovery in 1 patient (7%) and bridge to decision in 2 patients (13%).

Biventricular assistance was weaned in 1 patient (7%) due to left ventricular function recovery and 8/12 patients (66%) were transplanted, with a survival rate of 60% (9/15) in this group of patients (Figure 3). The main complication was reoperation for bleeding in 6 patients (40%). Only one patient with peripartum cardiomyopathy required cannulae exchange due to thrombosis. None of the patients had stroke or embolic events. Neither were there system technical failures. Six patients died while receiving support resulting in an overall mortality rate of 40% (5 patients with BVA and 1 patient with IVA). The main causes of death were: sepsis in 1 patient, coagulopathy due to increased bleeding in another and multiple organ failure in 4 patients. The indications during ventricular support in the 6 deceased patients were: PCCS in 2 patients and decompensated end-stage heart failure in waiting list for transplantation in 4 patients.

DISCUSSION

In recent years, short-term use of VAD has been efficient to support critically ill patients with refractory cardiogenic shock and end-stage heart failure. These devices enable patient stabilization, recovery of tissue perfusion and organ function and the neurological reassessment of critical patients. (2, 3) Today, temporal paracorporeal circulatory assist pumps are the devices of choice as "bridge to decision". The potential candidates for short-term ventricular assistance are those with cardiogenic shock refractory to medical therapy, in whom one the following alternatives are posed: as bridge to recovery in patients with potentially reversible acute cardiomyopathy or PCCS with difficult weaning from extracorporeal circulation, as bridge to heart transplantation in end-stage and decompensated chronic cardiomyopathy patients and as bridge to bridge for patients requiring long-term support. (4, 5)

The prognostic factors considered in the decision of ventricular assist device implantation are: adequate patient evaluation, time of implant and appropriate device selection.

Cardiovascular evaluation must rule out presence of aortic regurgitation, patent foramen ovale, intracavitary thrombi, associated coronary disease, peripheral artery disease, and must assess right ventricular function. Evaluation must be completed with a general examination to rule out complications and contraindications to implantation. In our experience, we have used the selection criteria postulated by Wilson et al. for the management of these critically ill patients. (6)

The best moment for implantation has relevant prognostic value. The later the implantation decision is taken, the worse the prognosis. The clinical INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support) scale, initially designed within the framework of a multicentric registry of circulatory mechanical support, establishes seven levels as a function of clinical condition severity, and has

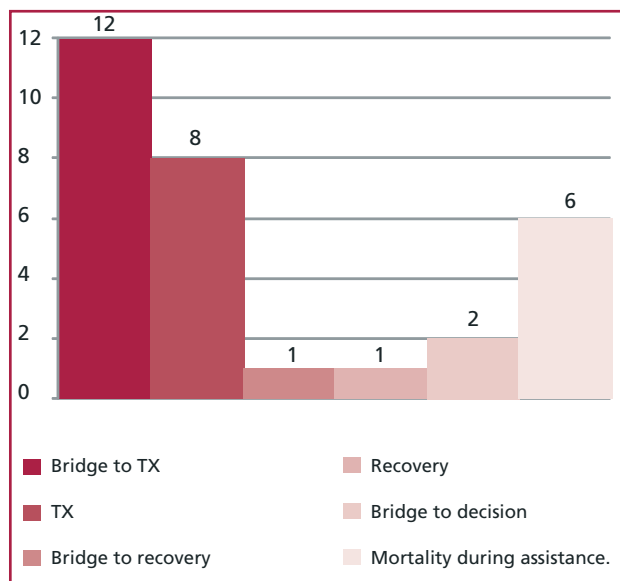


Fig. 3. Strategy and outcome. Tx: Transplantation

shown prognostic value in patients undergoing VAD implantation. (7) In the present study, the decision for device implantation was taken in the operating room in the case of 2 patients after at least two failed attempts at weaning from extracorporeal circulation. In the rest of the cases, the time elapsed between the medical indication and the effective support implantation varied in hours, even surpassing 24 hours. The longer delay in implantation was reflected in greater organ damage and higher mortality under support. This delay in the implantation time could be ascribed to the learning curve of logistics associated to a complex surgical procedure.

Device selection will depend on patient characteristics, whether there is univentricular or biventricular failure and the center's experience. (8) The most widely used short-term devices are: percutaneous assist devices (Tandem Heart, Impella), centrifugal flow pumps (Biomedicus, Jostra-Maquet Rotaflow, Levitronix CentriMag), pulsatile pumps (iVac 3L) and extracorporeal membrane oxygenator (ECMO).

Different studies have reported that use of the CentriMag pump is very efficient, as its implantation is not complex and provides immediate hemodynamic stability. (9) This support system with centrifugal flow pump allows a hemodynamic support of up to 10 L/min during 30 days with low risk of thromboembolic complications. It has been used either for univentricular or biventricular support in patients with refractory cardiogenic shock of different etiology. (10) In our center, we used the CentriMag flow pump as short-term univentricular or biventricular assist device in INTERMACS 1 patients. These patients were critically ill due to end-stage heart failure, postcardiotomy shock or post heart transplantation primary graft failure. Our implantation strategy was as "bridge-to-transplantation" in patients evaluated and previously

admitted in the waiting list who presented disease progression, or potential candidates with no contraindications at the time of implantation. In other patients the strategy was as "bridge to recovery" due to the potential reversibility of heart dysfunction, and finally, in another group of patients support was indicated as "bridge to decision", considering that at the time of implantation, the short-term strategy was uncertain.

In this series of severely ill patients, the therapeutic strategy was achieved safely and successfully in 9/15 patients: 1 patient was weaned from support due to biventricular function recovery and 8 patients in clinical emergency were recipients of heart transplantation. The mean waiting time of these emergency patients (including the period of IABP implantation plus the time under centrifugal flow pump support) was 12 ± 3 (1-17) days, which reflects that the possibility of organ procurement is not more than three weeks in our setting. The main cause of mortality was multiple organ failure (4 patients). We point out that 3 patients receiving biventricular circulatory support developed multiple organ failure with progressive hemodynamic impairment under inotropic and IABP support. In one case implantation was indicated owing to postcardiotomy shock 48 hours after surgery with reoperation for bleeding requiring multiple transfusions. The other two patients had non-coronary dilated cardiomyopathy. They were in national emergency waiting list for heart transplantation with IABP support (10 and 40 days) and evidenced progressive hemodynamic impairment and inflammatory response syndrome after implantation. The last patient was transplanted in emergency and weaned from centrifugal flow pump support. Twenty-four hours later, the patient progressed to cardiac graft failure requiring IABP, with subsequent acute arterial occlusion and right inferior limb necrosis, severe metabolic acidosis and multiple organ failure. We stress the importance of early implantation in INTERMACS 1 patients due to its impact and prognostic correlation.

The rate of complications during centrifugal pump support was low. The main complication, in agreement with other series, was reoperation for bleeding (40%). Only one patient presented severe sepsis followed by multiple organ failure leading to support discontinuation. In our experience all patients received antibiotic prophylaxis for 48 hours with subsequent treatment according to vigilance culture. We point out that there were no embolic complications. Only one patient with diagnosis of peripartum cardiomyopathy required cannulae exchange due to thrombi. All patients were treated according to the anticoagulation protocol recommended for this device. Mortality during support was 40% (6/15) in agreement with previous reports for high risk populations. (11, 12)

CONCLUSIONS

In our experience, circulatory support with the Levitronix CentriMag® centrifugal flow pump was an

effective therapeutic alternative in patients with refractory cardiogenic shock (INTERMACS 1) with a survival rate of 60%. Appropriate selection of candidates and early indication of short-term VAD are vital to optimize outcomes in critically ill patients.

RESUMEN

Experiencia con bomba centrífuga magnética en pacientes con shock cardiogénico (INTERMACS 1)

Introducción

El uso de dispositivos de asistencia ventricular a corto plazo con levitación magnética permite estabilizar hemodinámicamente a pacientes en shock cardiogénico refractario en estado INTERMACS 1 y definir la estrategia terapéutica.

Objetivos

Evaluar los resultados, en un único centro, del uso de bomba centrífuga de segunda generación en pacientes con shock cardiogénico refractario.

Material y métodos

Se analizaron retrospectivamente 15 pacientes con asistencia ventricular con bomba Levitronix CentriMag® desde 2006 a 2011. Todos los pacientes presentaban shock cardiogénico refractario con dos inotrópicos y 13 tenían balón de contrapulsación intraaórtico previo a la asistencia. Las indicaciones fueron miocardiopatías avanzadas en 8 pacientes, miocarditis viral en 1, miocardiopatía periparto en 1, shock cardiogénico poscardiotomía en 3 y falla del injerto postrasplante cardíaco en 2 pacientes.

Resultados

La edad media en adultos fue de 49 ± 13 años y el 66% (10/15) eran hombres. Se implantó asistencia ventricular izquierda (AVI) en 1 paciente y asistencia biventricular (ABV) en 14. El tiempo medio de asistencia fue de 6 ± 4 días (2-19). La decisión terapéutica final posimplante fue puente al trasplante cardíaco en 12 pacientes (80%), puente a la recuperación en 1 (7%) y puente a la decisión en 2 (13%). La asistencia (ABV) se explantó en 1 paciente por recuperación de la función ventricular y 8 pacientes recibieron trasplante, con una supervivencia del 60% (9/15). Requirieron reoperación por sangrado 6 pacientes (40%) y 1 presentó trombosis de las cánulas; ningún paciente presentó accidente cerebrovascular ni fallas técnicas del sistema. Fallecieron bajo asistencia 6 pacientes (40%) (5 ABV y 1 AVI): 1 por sepsis, 1 con coagulopatía grave y 4 por falla multiorgánica. De los 6 pacientes fallecidos, 2 se encontraban con shock cardiogénico poscardiotomía y 4 eran candidatos previos a trasplante cardíaco.

Conclusiones

En esta serie, el soporte circulatorio con bomba centrífuga Levitronix CentriMag® fue efectivo en pacientes críticos,

con una supervivencia del 60%. La complicación más frecuente fue la reoperación por sangrado.

Palabras clave > Insuficiencia cardíaca - Choque, cardiogénico - Corazón auxiliar - Trasplante de corazón

Conflicts of interest

None declared.

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