Results following implantation of mechanical circulatory support systems: The Montreal Heart Institute experience

Ismaïl El-Hamamsy MD¹, Frédéric Jacques MD¹, Louis P Perrault MD PhD¹, Denis Bouchard MD¹,
Philippe Demers MD¹, Michel White MD², Guy B Pelletier MD², Normand Racine MD²,
Michel Pellerin MD¹, Michel Carrier MD¹

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BACKGROUND: Mechanical circulatory support systems (MCSS) have been available in Canada since 1986. Accepted indications include bridging to transplantation or recovery. The present study reviewed the results following MCSS implantation at the Montreal Heart Institute (Montreal, Quebec).

METHODS: From September 1987 to September 2006, 43 MCSS were implanted (32 Thoratec [Thoratec Corporation, USA], nine CardioWest TAH [SynCardia Systems Inc, USA], two Novacor [WorldHeart Corporation, Canada]) in 43 patients (mean $\pm$ SD) age 44 ± 13 years; range 19 to 64 years). Indications for implantation included cardiogenic shock due to ischemic (n=19), viral (n=10) or other types of cardiomyopathies (n=14).

RESULTS: The mean ejection fraction before implantation was $17.6 \pm 6.5\%$ (range 10% to 45%). Before MCSS implantation, most patients showed signs of end-organ failure, including mechanical ventilation (77%), central venous pressure higher than 16 mmHg (44%), oliguria (35%) and hepatic dysfunction (19%). The mean duration of MCSS support was 22.8 ± 32.8 days (range one to 158 days). Survival to transplantation or recovery was 74%. Only one patient was successfully bridged to recovery. Complications were common during MCSS support. They included re-exploration for bleeding (47%), respiratory failure (44%), renal failure requiring temporary dialysis (40%), infection (33%) and neurological events (16%). Only one patient had device failure. In patients successfully bridged to transplantation, early actuarial survival (one month) following transplantation averaged $71 \pm 8\%$ and was $57 \pm 9\%$ at one year.

CONCLUSION: MCSS support with a left ventricular assist device or a total artificial heart provides an effective means of bridging terminally ill patients to transplantation or recovery. Early survival after transplantation shows satisfactory results. However, these results come at the expense of frequent device-related complications, and device failure remains a constant threat.

Key Words: Ventricular assist device

Les résultats suivant l'implantation de systèmes mécaniques d'assistance circulatoire : L'expérience de l'Institut de cardiologie de Montréal

HISTORIQUE : Les systèmes mécaniques d'assistance circulatoire (SMAC) sont offerts au Canada depuis 1986. Parmi les acceptations indiquées, soulignons le pont dans l'attente d'une greffe ou de la guérison. La présente étude visait à examiner les résultats suivant l'implantation de SMAC à l'Institut de cardiologie de Montréal (à Montréal, au Québec).

MÉTHODOLOGIE : De septembre 1987 à septembre 2006, 43 SMAC ont été implantés (32 Thoratec [Thoratec Corporation, États-Unis], neuf CardioWest TAH [SynCardia Systems Inc., États-Unis], deux Novacor [WorldHeart Corporation, Canada]) à 43 patients (moyenne d'âge $\pm$ ÉT) de 44 ± 13 ans, plage de 19 à 64 ans). Les indications d'implantation incluaient le choc cardiogène causé par une ischémie (n=19), une myocardiopathie virale (n=10) ou d'autres types de myocardiopathie (n=14).

RÉSULTATS : La fraction d'éjection moyenne avant l'implantation était de $17,6 \pm 6,5\%$ (plage de 10 % à 45 %). Avant l'implantation du SMAC, la plupart des patients présentaient des signes d'insuffisance de la plaque terminale, y compris la ventilation mécanique (77 %), une pression veineuse centrale supérieure à 16 mmHg (44 %), une oligurie (35 %) et un dysfonctionnement hépatique (19 %). La durée moyenne du soutien par SMAC était de $22,8 \pm 32,8$ jours (plage de un à 158 jours). La survie jusqu'à la greffe ou jusqu'à la guérison correspondait à 74 %. Un seul patient a réussi à faire le pont jusqu'à la guérison. Les complications étaient courantes pendant le soutien par SMAC. Elles incluaient une nouvelle exploration pour cause d'hémorragie (47 %), une insuffisance respiratoire (44 %), une insuffisance rénale exigeant une dialyse temporaire (40 %), une infection (33 %) et des événements neurologique (16 %). Un seul patient a présenté un échec du dispositif. Chez les patients ayant réussi à faire le pont jusqu'à la greffe, la moyenne de survie actuarielle précoce (un mois) suivant la greffe était de $71 \pm 8\%$, puis de $57 \pm 9\%$ au bout d'un an.

CONCLUSION : Le soutien par SMAC accompagné d'un dispositif d'assistance ventriculaire gauche ou d'un cœur artificiel total constitue un moyen efficace de faire le pont jusqu'à la greffe ou à la guérison pour les patients en phase terminale. La survie précoce après la greffe est satisfaisante. Cependant, ces résultats sont au détriment de fréquentes complications liées au dispositif, et l'échec du dispositif demeure une menace constante.

Mechanical circulatory support systems (MCSS) have been available in Canada since 1986 (1). Various devices have been developed in the past 25 years in an effort to maximize hemodynamic performance while reducing the incidence of complications

associated with ventricular support, namely thromboembolic, hemorrhagic and infectious complications. These devices vary from small centrifugal pumps (eg, DeBakey) to total artificial hearts (eg, CardioWest TAH; SynCardia Systems Inc, USA). Three different

¹Department of Cardiac Surgery; ²Department of Cardiology, Montreal Heart Institute and Université de Montréal, Montreal, Quebec

Correspondence: Dr Michel Carrier, Montreal Heart Institute, 5000 Bélanger Street East, Montreal, Quebec H1T 1C8. Telephone 514-376-3330

ext 3715, fax 514-376-1355, e-mail michel.carrier@icm-mhi.org

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TABLE 1
Preoperative patient characteristics

Characteristic	Thoratec* (n=32)	CardioWest† TAH (n=9)	Novacor‡ (n=2)	Overall (n=43)
Age [§] , years	44±13	44±15	39±3	44±13
Sex, n (male/female)	20/12	8/1	2/0	30/13
Ejection fraction [§] , %	17.5±6.8	17.9±5.5	20.0±7.1	17.6±6.5
Oliguria, %	28	67	0	35
CVP >16 mmHg, %	50	33	0	44
Repeat operation, %	16	11	50	16
Coagulopathy, %	22	11	0	19
Mechanical ventilation, %	75	78	100	77
Body mass index [§] , kg/m ²	25±4	26±2	34±4	26±4
Weight [§] , kg	72±16	82±12	112±17	76±17
Height [§] , cm	169±10	176±9	183±4	171±10

*Manufactured by Thoratec Corporation, USA; †Manufactured by SynCardia Systems Inc, USA; ‡Manufactured by WorldHeart Corporation, Canada; §Values expressed as mean ± SD. CVP Central venous pressure

devices were used in our experience: the Thoratec VAD (Thoratec Corporation, USA), the CardioWest TAH and the Novacor (WorldHeart Corporation, Canada).

Indications for left ventricular assist device (LVAD) implantation have evolved through the years. Bridging to recovery (2) and transplantation (3) are both accepted indications for patients meeting criteria for terminal heart failure and cardiogenic shock (class IV congestive heart failure symptoms, optimal medical therapy, cardiac output of less than 2.0 L/min/m² with a pulmonary capillary wedge pressure higher than 20 mmHg and one or more inotropes with or without intra-aortic balloon pump). In practice, strict adherence to these criteria is sometimes difficult due to various clinical presentations, and the decision to implant a device must precede the progression toward a state of irreversible hemodynamic compromise, often with multiorgan failure, in patients in whom experience predicts a limited prognosis for recovery and an unavoidable transplantation.

The present study reports the experience of the Montreal Heart Institute (Montreal, Quebec) with MCSS from the beginning of the program in 1987 until today. This experience, as opposed to literature from the United States or Europe, reflects the reality of such a program within our national health care system dictated by much rationalization in the use of such expensive technology. In most cases, patients were in cardiogenic shock at the time of MCSS implantation and operated on an emergent basis.

METHODS

Study population

From 1987 to present, 43 MCSS have been implanted (32 Thoratec VAD, nine CardioWest TAH, two Novacor) in 43 patients (male to female ratio 30:13). The CardioWest (formally called Jarvik) was first available in 1987. At the Montreal Heart Institute, the Thoratec VAD was introduced in 2000, then the Novacor in 2002. Mean (± SD) patient age was 44±13 years (range 19 to 64 years). Indications for implantation included terminal cardiac failure and cardiogenic shock despite maximal medical treatment as defined above. Etiologies were as follows: ischemic (n=19), viral (n=10), impossible weaning from cardiopulmonary bypass (n=5), idiopathic (n=7), postpartum (n=1) and other types of cardiomyopathies (n=1). The six patients who received LVADs due to an impossible weaning from cardiopulmonary bypass had undergone coronary artery bypass graft surgery before implantation.

Devices

At the Montreal Heart Institute, a conservative policy is the rule regarding uni- or biventricular Thoratec support. All patients are

initially placed on univentricular support only. The status of the right ventricle dictates the need for a biventricular device, which depends on its ability to generate enough output to ensure adequate filling of the left heart chambers. In the present series, no biventricular devices were necessary. The insertion technique of the Thoratec device was a standard median sternotomy with inflow cannulation of the left ventricular apex, as well as a woven Dacron outflow graft anastomosed to the ascending aorta and positioned paracorporeally. No inflow cannulations into the left atrium were performed. The Novacor device was implanted using the same approach, except that it was positioned in the intra-abdominal position.

The CardioWest TAH was selected in patients with a large habitus, sufficient anteroposterior chest wall diameter to provide enough room for placement of the device and clinical evidence of biventricular failure. Patients with the total artificial heart device were allowed to ambulate once their overall status enabled it. The implantation technique was similar to regular orthotopic transplantation. All patients were systematically anticoagulated using a combination of acetylsalicylic acid (325 mg daily), warfarin (target international normalized ratio of 2.5 to 3.5) and dipyridamole for patients with the CardioWest TAH device.

Preoperative patient selection

Preoperative patient characteristics are shown in Table 1. Risk factors evaluated were drawn from previous experience of the Columbia Presbyterian team, which established a screening scale identifying risk factors associated with decreased prognosis (4,5). The average ejection fraction at the time of implantation measured by echocardiography was 17.6±6.5%. One-third of patients had oliguria at the time of implantation. Mechanical ventilatory support was present in 77% of patients, 44% had elevated central venous pressure (higher than 16 mmHg), 16% were repeat operations and 19% suffered from hepatic dysfunction resulting in coagulopathy.

All patients had their devices as a bridge to subsequent transplantation. No implantations were performed as destination therapy. Bridging to recovery was a possibility for certain patients, but it did not prevent or delay placing these patients on the transplantation list. All patients were evaluated before active listing for transplantation. Assessment of neurological injury was a requirement for listing.

Data collection and analysis

Detailed records were prospectively maintained for all patients undergoing MCSS implantation by a team of nurse practitioners from the Transplantation Clinic. Several end points were followed in those patients following device implantation and after transplantation when applicable. MCSS survival was defined as survival to transplantation or explantation of the device.

RESULTS

Survival

Successful bridging to transplantation or explantation following implantation of a ventricular assist device was 74% (n=32). In patients surviving to transplantation, actuarial survival following transplantation was 71% and 57% after one month and one year of follow-up, respectively (Figure 1). One patient underwent successful explantation of a Thoratec LVAD one week after implantation for acute fulminant myocarditis.

The causes of death were multiorgan failure in 11 patients, surgical bleeding in three patients, primary graft failure in two patients, stroke in two patients, sepsis in two patients, and myocardial infarction and lung cancer in the other patients.

Device-related complications

Device-related complications are depicted in Table 2. The most commonly encountered complications were bleeding requiring surgical re-exploration (47%) and respiratory failure requiring prolonged intubation (44%), followed by acute renal failure requiring hemodialysis

Figure 1 Actuarial survival of patients undergoing heart transplantation at the Montreal Heart Institute (Montreal, Quebec) without previous mechanical support (gray line) and following left ventricular assist device implantation (black line). MCSS Mechanical circulatory support system

(40%) and infectious complications (33%). Neurological complications occurred in seven patients (16%), presumably secondary to thromboembolic events following device implantation. Neurological events were defined as either a stroke or a transient ischemic attack confirmed by a complete examination performed by a neurologist and a computed tomography scan when feasible. Device failure occurred in one patient on the Thoratec LVAD 41 days following implantation. Failure was linked to a dysfunctional power cable and was therefore corrected without requiring a return to the operating room. The patient evolved well thereafter and was successfully transplanted.

Transplantation-related complications

Seven patients died perioperatively within one month of transplantation. Three of those patients were put on extracorporeal membrane oxygenator assistance before death. One patient died of severe right ventricular failure intraoperatively, despite adequate cross-matching and an ischemic time of less than 4 h. One patient suffered refractory hemorrhage in the immediate postoperative period of heart transplantation, which did not respond to recombinant factor VII; despite reintervention, graft failure occurred in the operating room. Another patient died in the operating room of immediate graft failure. This young patient suffered from Crohn's disease, had hypothyroidism and several other autoimmune disorders, and received massive transfusions while on the CardioWest device for 154 days.

Among patients surviving beyond the first month (n=22), seven (28%) developed infections, mainly of the respiratory tract, which were treated with antibiotic therapy. Eight patients (31%) had acute renal failure requiring temporary venovenous hemofiltration, and three patients (15%) required tracheostomy for respiratory failure. Bleeding requiring re-exploration occurred in two patients, while neurological complications occurred in three patients.

Two patients (8%) showed grade 3A acute rejection on endomyocardial biopsy at follow-up (one episode each). These rejection episodes were treated according to a standard protocol and responded favourably.

DISCUSSION

MCSS have been available in Canada since the mid-1980s, when the first device was used in Ottawa (6,7). Since then, their use has been available to a total of eight centres in Canada (1). Use of these devices carries a heavy financial burden and poses many ethical questions,

TABLE 2
Outcomes related to ventricular assist devices

Outcome	Thoratec* (n=32)	CardioWest† TAH (n=9)	Novacor‡ (n=2)	Overall (n=43)
Duration of support, days (mean ± SD)	15±15	38±46	84±99	23±33
Successful bridging, n (%)	21 (66)	9 (100)	2 (100)	32 (74)
Successful explantation, n	1	0	0	1
Device malfunction, n	1	0	0	1
Bleeding, %	44	56	50	47
Infection, %	28	44	50	33
Thromboembolic event, %	16	22	0	16
Acute renal failure, %	41	33	50	40
Respiratory failure, %	47	44	0	44

*Manufactured by Thoratec Corporation, USA; †Manufactured by SynCardia Systems Inc, USA; ‡Manufactured by WorldHeart Corporation, Canada

explaining in part why it is limited to only a few centres nationwide (8,9). It is, therefore, of interest to review one's own experience with these devices and attempt to answer a number of critical questions: Are they used judiciously? Do they change the natural history of a patient's disease? And most importantly, should we still be using them?

The present study was a retrospective review of the experience with MCSS at the Montreal Heart Institute over the past 19 years since the first total artificial heart (CardioWest) was put in place in 1987. Overall, results have been favourable, and they justify the use of these devices. Patients were highly selected and were terminally ill, with a short life expectancy, usually in cardiogenic shock despite optimal medical care, including intra-aortic balloon pump support, vasopressors, inotropes and mechanical ventilation (10).

The experience of the Columbia Presbyterian team with 100 patients supported with LVADs before transplantation suggested that predictors of a worse outcome were high central venous pressure, coagulopathy, repeat surgery, mechanical ventilation and oliguria (4,5). In the present series, three-quarters or the majority of patients were under ventilatory support, almost one-half had high central venous pressure and one-third had depressed renal function.

Actuarial survival in heart transplant recipients following MCSS support was lower than that for transplant recipients without previous MCSS support (Figure 1). This difference in survival was not only accounted for by the initial drop in survival due to perioperative mortality. Rather, it persisted throughout their follow-up, with one-year actuarial survival dropping to 57%. This is in contrast to previous series in the literature reporting survival similar to non-LVAD-supported patients following transplantation. This difference could be due to the restriction of LVAD support for seriously ill patients in cardiogenic shock or an emergent basis. A bias related to the limited number of LVAD recipients in our series cannot be completely eliminated.

Bleeding complications requiring re-exploration were common during MCSS support, and the majority of patients received large amounts of blood-related products. Transfusions elicit an immune reaction, with antibody formation and potential allosensitization. However, as seen in other series, no problems were observed in terms of panel reactive antigen levels, which are prospectively performed on a routine basis, or in terms of rejection episodes following transplantation. Therefore, no mismatch between donors and recipients was encountered due to allosensitization.

Only one patient benefited from the device as a bridge to recovery in our experience (11), although it has been suggested that 10% to 15% of patients could be weaned from devices after various periods of support and weaning protocols.

Patients receiving the CardioWest device were usually large in terms of body weight and had evidence of biventricular failure. The

use of the total artificial heart explains, in part, our favourable experience with LVAD support in the presence of right ventricular failure in selecting the worse cases for this device.

Acute postcardiotomy failure remains a difficult clinical situation. In our experience, extracorporeal membrane oxygenator assistance is first attempted for one or two days, and an attempt at weaning or implantation of a longer range device for bridging for transplantation is performed. In selected patients undergoing high-risk surgical procedures, a preoperative evaluation for transplantation is performed, and a bridging device is used in case of failure of the primary procedure.

CONCLUSION

The present study reports the overall results in one of Canada's mechanical support programs. The Canadian reality imposes a strict selection process and parsimony in implanting MCS devices considering their high financial burden on the health care system. Therefore, the overall patient population is limited compared with larger programs in Europe and the United States. However, over a period of nearly 20 years, the use of these devices has proven to be beneficial in saving terminally ill patients' lives and successfully bridging them to transplantation, with survival results that are satisfactory, although not nearly as good as non-LVAD heart transplantations. With improving technology in the field of mechanical support, miniaturization and total implantation of the devices, combined with an ever-aging population, there will be an increased need for mechanical support as destination therapy, sparking a societal debate over the appropriateness of such a strategy. In these potential destination therapy patients, consideration should be given to earlier implantation (New York Heart Association functional class III) to avoid, when possible, the deleterious consequences of cardiogenic shock end-organ failure, and perhaps lessen postimplant morbidity and improve survival with or without transplantation.

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