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Outcome of cardiac transplantation in patients requiring prolonged continuous-flow left ventricular assist device support

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OBJECTIVE: This study assessed the early and late outcomes after cardiac transplantation in patients receiving long-term continuous-flow left ventricular assist device (CF-LVAD) support.

METHODS: Between April 2004 and September 2013, 192 patients underwent HeartMate II (Thoratec, Pleasanton, CA) CF-LVAD placement as a bridge to transplant at our center. Of these, 122 (63%) successfully bridged patients were retrospectively reviewed. Patients were stratified into 2 groups according to their waiting time with CF-LVAD support of <1 year or ≥ 1 year.

RESULTS: The study cohort was a mean age of 54 $\pm$ 13 years, 79% were male, and 35% had an ischemic etiology. The mean duration of CF-LVAD support before transplantation was 296 days (range, 27–1,413 days). The overall 30-day mortality was 4.1%. Overall post-transplant survival was 88%, 84%, 78% at 1, 3, and 5 years, respectively. The 32 patients (26%) with ≥ 1 year of CF-LVAD support (mean, 635 days) were more likely to have blood type O, a larger body size, and to have been readmitted due to recurrent heart failure and device failure requiring exchange than those with <1 year of CF-LVAD support. Patients who required prolonged support time also had worse in-hospital mortality (16% vs 6.7%, $p = 0.12$) and significantly lower survival at 3 years after transplantation (68% vs 88%, $p = 0.049$).

CONCLUSIONS: The overall short-term and long-term cardiac transplant outcomes of patients supported with CF-LVAD are satisfactory. However, patients who require prolonged CF-LVAD support may have diminished post-transplant survival due to adverse events occurring during device support.

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Continuous-flow left ventricular assist devices (CF-LVADs) have rapidly become standard care for advanced heart failure patients.[1,2] The bridge-to-transplant (BTT) strategy is especially reasonable in patients listed for transplantation who are expected to have an extended waiting time due to blood type, a large body size, or a high degree of allosensitization. However, in contrast to the increasing number of CF-LVADs being implanted, there are a limited number of donors, which remains a nationwide issue. This discrepancy has led to longer waiting times to transplant spent on CF-LVAD support.[3] Currently, almost 50% of BTT patients are alive and on CF-LVAD support after 1 year.[4]

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Transplant outcomes in patients bridged with CF-LVAD appear similar to those of patients bridged with pulsatile-flow LVAD or who receive an allograft without BTT.[5]

However, limited data are available on the post-transplant outcomes of patients receiving CF-LVAD support for more than 1 year. There have been concerns regarding the negative effects of post-transplant hemodynamics in patients who required longer durations of CF-LVAD support.[6] Moreover, such patients can be exposed to an increased risk of device-related morbidities, including infection and device thrombosis, before transplantation.[3,7–9] These factors may affect short-term and long-term post-transplant outcomes. Given the continuously improving outcomes achieved with CF-LVADs as destination therapy,[10] the optimal timing of cardiac transplantation after the initiation of LVAD support requires clarification. In this long-term follow-up study, we reviewed our single-center experience of BTT with CF-LVAD.

Methods

The Columbia Presbyterian Medical Center Institutional Review Board approved this study. We retrospectively reviewed our experiences with CF-LVAD at the Columbia Presbyterian Medical Center between April 2004 and September 2013. During this period, 192 consecutive patients with advanced heart failure underwent the insertion of a HeartMate II (Thoratec, Pleasanton, CA) as a BTT, and 122 (63%) of these successfully bridged patients were included in this study. Patients were stratified by waiting time with CF-LVAD support into 2 groups: Group 1, support <1 year or Group 2, support ≥ 1 years.

Device implantation

All patients received the HeartMate II LVAD at our center. The details of the device and surgical implantation have been described before.[1,2]

Post-implant device management

After device implantation, all patients received a standardized medical regimen, including a neurohormonal antagonist, diuretics, and anti-arrhythmic agents, if needed. Anti-coagulation therapy with aspirin and warfarin was implemented. The target international normalized ratio range was 2 ± 0.5. After discharge, anti-coagulation was managed by nurse practitioners with the repeat testing frequency dictated by the ease or difficulty of maintaining the patient within the target range. Anti-coagulation therapy was withheld in the event of bleeding and resumed once bleeding stopped. Patients were followed up at 1 week after the initial discharge and monthly thereafter unless an issue necessitating more frequent visits arose. The frequency of clinic visits varied among patients depending on individual medical issues and travel distances. A shared-care program was established in 2012, and currently, 2 community health care providers are available for sharing patient care.

Desensitization therapy

The panel reactive antibody (PRA) test was used to screen for allosensitization. Patients with global sensitization, defined as a PRA greater than 10%, were treated with intravenous immunoglobulin (IVIg) therapy, with or without cyclophosphamide, before transplantation.[11]

Transplant procedures and post-operative immunosuppression

All patients underwent cardiac transplantation with bicaval anastomosis. All patients received standard therapy with calcineurin inhibitors, cyclosporine or tacrolimus, mycophenolate mofetil, and prednisone. Patients received 4 mg/kg azathioprine pre-operatively, and 500 mg Solu-Medrol (Pfizer, New York, NY) intraoperatively. Post-operatively, patients received 125 mg Solu-Medrol every 8 hours for 3 doses. Mycophenolate mofetil was started at a dose of 1,500 mg twice daily. High-dose oral prednisone was started at 100 mg daily and tapered to 30 mg daily by 2 weeks. Induction therapy using interleukin-2 receptor antagonists was administered within 24 hours after transplantation.[12] Patients with active infections did not receive induction therapy. Patients who were highly sensitized pre-operatively received cyclophosphamide for 4 to 6 months after transplantation and then were treated with mycophenolate mofetil.[13]

Post-operative endomyocardial biopsy

Endomyocardial biopsies were performed regularly.[11] The degree of cellular rejection on the specimen was graded according to International Society for Heart Transplantation criteria.[14] Antibody-mediated rejection was defined as histologic evidence of acute capillary injury and Ig and/or C4d deposition identified by immunofluorescence.

Post-transplant follow-up

Patients were regularly monitored by a cardiologist after transplantation. The follow-up examinations were completed on September 30, 2013, and the follow-up period lasted from 0.025 to 8.1 years (median, 2.1 years; interquartile range, 0.98–3.6 years). Clinical follow-up was completed in 98% of patients.

Data collection

All clinical data were collected thorough a review of electronic medical records. For each patient, pre-operative variables that might correlate with survival were retrospectively collected for each procedure (i.e., LVAD implantation and transplantation). These data included baseline demographics, medical histories, laboratory values, hemodynamic parameters, medications, and donor demographics.

Intraoperative variables included concomitant procedures at the time of LVAD implantation and ischemic time, cardiopulmonary bypass time, blood product use, dosage of vasoactive drugs, and nitric oxide use at the time of transplantation. Early post-operative data included complications that occurred between the operation and hospital discharge. Severe primary graft dysfunction (PGD) was defined as a need for mechanical circulatory support within 24 hours of completion of surgery.[15]

Major adverse events requiring readmission during the waiting time on LVAD support were also recorded. These included major bleeding events, such as gastrointestinal tract bleeding and significant epistaxis; device-related events, such as pump malfunction, thrombi, and infection; and major cerebral events, recurrent