Prolonged continuous-flow left ventricular assist device support and posttransplantation outcomes: A new challenge

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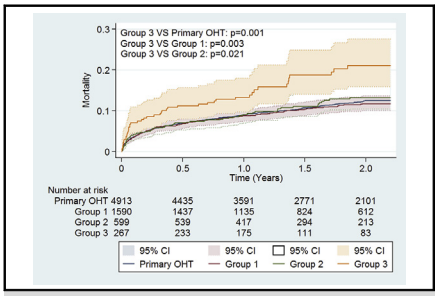
ABSTRACT

Objective: To assess outcomes after cardiac transplantation in patients receiving long-term continuous-flow left ventricular assist device (CF-LVAD) support.

Methods: The United Network of Organ Sharing Database was used to identify 7808 heart transplant recipients between January 2011 and March 2014, 2456 (31.5%) of whom were bridged with CF-LVAD. Recipients were stratified by CF-LVAD duration: group 1, <1 year (n = 1590; 64.7%); group 2, 1 to 2 years (n = 599; 24.4%); and group 3, >2 years (n = 267; 10.9%).

Results: Compared with patients in groups 1 and 2, patients in group 3 spent more time as status 1A, had a greater body mass index and higher serum creatinine level, more often received blood transfusions and antibiotics, and more often developed device-related infection and life-threatening arrhythmia before transplantation. Kaplan–Meier analysis revealed statistically significant lower survival rates in group 3 compared with groups 1 and 2, at both 30 days (92.9% vs 96.4% vs 95.5%; group 1 vs group 3, $P = .009$) and 2 years (78.9% vs 88.2% vs 86.3%; group 1 vs group 3, $P = .001$) posttransplantation. Multivariable analyses identified duration of CF-LVAD support as a significant factor for 2-year posttransplantation mortality (hazard ratio, 1.16; 95% confidence interval, 1.01-1.34; $P = .040$).

Conclusions: A bridge-to-transplant (BTT) strategy with a CF-LVAD has become standard care for patients with advanced heart failure. Duration of CF-LVAD support is associated with increased midterm mortality, warranting early transplantation in the modern BTT era. (J Thorac Cardiovasc Surg 2016;151:872-80)



Posttransplantation mortality up to 2 years based on device support duration.

Central Message

Prolonged device support is associated with increased midterm posttransplantation mortality.

Perspective

The number of patients supported with a continuous-flow left ventricular assist device, as well as the duration of device support, have been steadily increasing. However, prolonged device support is associated with decreased midterm posttransplantation survival, likely due to multifactorial causes, warranting early transplantation strategy in the modern bridge-to-transplant era.

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Supplemental material is available online.

Heart transplantation today remains the gold standard for end-stage heart failure refractory to medical management. Owing to a nationwide scarcity in donor organs, there has been a rapid growth in the field of mechanical circulatory support (MCS). Specifically, the bridge-to-transplant (BTT) strategy with a continuous-flow ventricular assist device (CF-LVAD) has played a major role in providing temporary support for patients with end-stage heart failure.[1] In more recent years, BTT patients with a CF-LVAD have shown increasingly improved survival while awaiting transplantation.[2,3] In addition, the duration of device support before transplantation, as well as the proportion of BTT patients among transplant recipients, have been steadily increasing owing to a number of factors, including patient blood type, body size, and a high degree of allosensitization, in addition to the continuing organ shortage.[3]

Despite the benefits that CF-LVADs have provided to patients with advanced heart failure, concerns remain regarding the negative effects of prolonged continuous-

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Abbreviations and Acronyms

BMI = body mass index
BTT = bridge to transplant
CF-LVAD = continuous-flow left ventricular assist device
CI = confidence interval
CVA = cerebrovascular accident
DRC = device-related complication
ECD = expanded-criteria donor
ECMO = extracorporeal membrane oxygenation
HR = hazard ratio
IABP = intra-aortic balloon pump
MCS = mechanical circulatory support
OPTN = Organ Procurement and Transplantation Network
OR = odds ratio
PRA = panel reactive antibody
RHF = right heart failure
RVAD = right ventricular assist device
UNOS = United Network for Organ Sharing

flow device support. These negative effects have been seen in the form of worse posttransplantation hemodynamics[2,4,5] and an increased risk of device-related complications (DRCs) before transplantation.[4,6]

Although CF-LVADs are not without potential complications, currently there is a paucity of data examining the impact of prolonged CF-LVAD support on outcomes in patients after heart transplantation. The present study was designed to determine whether the duration of CF-LVAD support impacts patient outcomes following transplantation using the United Network for Organ Sharing/Organ Procurement and Transplantation Network (UNOS/OPTN) registry.

METHODS

Data Collection/Study Population

A retrospective review of deidentified data from the UNOS Thoracic Registry identified a total of 7808 heart transplant recipients between January 6, 2011, and March 31, 2014. Of these, 2456 patients (31.5%) were BTT recipients with a CF-LVAD, whereas 4913 (62.9%) were non-BTT recipients. Patients who underwent multiorgan transplant were excluded from the analysis. The study period was chosen because the UNOS registry began routinely recording the date of CF-LVAD implantation in all patients after January 6, 2011, enabling the acquisition of device support duration in each recipient. Among those who received multiple CF-LVADs, the date of initial device implantation was used to calculate cumulative support duration. The distribution of device support duration in each individual appeared to be positively skewed, with many outliers at the high end (1-1934 days). This strong positive skewness of the distribution was confirmed by a quantile-quantile plot of expected versus observed device support duration (data not shown). These patients were stratified into 3 groups based on the duration of CF-LVAD support (group 1, <1 year [n = 1590; 64.7%]; group 2, 1-2 years [n = 599; 24.4%]; group 3, >2 years [n = 267; 10.9%]). Follow-up ended on March 5, 2015.

DRCs in each group were also provided within the dataset and were included for the analysis. OPTN policy defines DRCs in 5 categories: thromboembolism, device infection, mechanical failure, life-threatening ventricular arrhythmias, and others. For the present study, posttransplantation survival was defined as absence of death from any cause. The UNOS dataset uses the Karnofsky performance score[7] (KPS) to determine the functional status of a recipient. In brief, the KPS increases by 10 points from 0 to 100 as the level of independence improves and the symptoms of disease resolve. Functional status in each patient was categorized corresponding to a KPS of 80 to 100 (no assistance), 50 to 70 (some assistance), and 10 to 40 (total assistance). The Columbia University Institutional Review Board approved all aspects of the present study and waived informed consent, because the database is deidentified and publicly available.

Statistical Analysis

Continuous variables are expressed as mean ± standard deviation. Categorical variables are presented as proportion and absolute number. Differences between groups were detected using the χ^2 test or Fisher's exact test for categorical variables and the Student *t* test, Mann–Whitney *U* test, or 1-way analysis of variance with the Bonferroni post hoc test for continuous variables. Survival data were compared using Kaplan–Meier survival analysis and the log-rank test. Spearman's correlation coefficient was used to characterize the degree of correlation between 2 variables. For regression modeling, missing variables were imputed using a multiple imputation technique.[8,9] All missing data (Table E1) were imputed 10 times, resulting in 10 imputed datasets. All subsequent analyses were performed for each imputed dataset separately and then combined to produce a final single set of parameter estimates.

Clinical parameters before transplantation were analyzed to identify factors contributing to posttransplantation mortality, using logistic regression for 30-day mortality and Cox proportional hazards models for 2 year-mortality following transplantation. For multivariable analyses, variables with a P value $\leq .25$ on univariate analysis were included into a final multivariable model (Tables E2 and E3). Identical analyses were performed separately using the device support duration symmetrized by the base-10 logarithmic transformation, to minimize the influence of outliers. Results are presented as odds ratio (ORs) or hazard ratios (HRs) with corresponding 95% confidence intervals (CIs). A P value $< .05$ was considered statistically significant. All P values were the result of 2-tailed tests. All statistical analyses were performed using SPSS version 22.0 (IBM, Armonk, NY).

RESULTS

Current Trends in CF-LVAD Use as a BTT in Transplant Recipients

Figure 1 shows the annual distribution of CF-LVAD–supported BTT patients in the entire cohort between 2011 and 2013. The annual proportion of those patients, as well as the respective mean duration of CF-LVAD support, increased gradually each year (2011: 28.8%, 310.0 ± 254.0 days; 2012: 29.9%, 351.5 ± 288.2 days; 2013: 36.5%, 367.3 ± 315.3 days; $P < .001$ for all). The distribution of implanted CF-LVAD brands is summarized in Table 1.

Patient Demographics

Recipient characteristics. Patient demographic data and clinical characteristics for each group are shown in Tables 1 and E4. In addition, status justification at time of transplantation in each group is further displayed in Table E5.