Long-term outcome of patients on continuous-flow left ventricular assist device support

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Objectives: Recent advances in technology and improved patient management have enabled the use of mechanical circulatory support for unexpected long-term periods. Improved long-term outcomes may facilitate the use of device therapy as an alternative to heart transplantation. However, there are scarce data about the long-term outcomes of continuous-flow left ventricular assist devices. This study sought to evaluate the long-term outcomes in patients receiving continuous-flow left ventricular assist devices.

Methods: Between March 2004 and June 2010, 140 patients underwent continuous-flow left ventricular assist device insertion as a bridge to transplantation or a destination therapy. These patients' charts were retrospectively reviewed.

Results: The initial strategy for continuous-flow left ventricular assist device therapy was bridge to transplantation in 115 patients (82%) and destination therapy in 25 patients (18%). Of those, 24 (17%) died on left ventricular assist device support, 94 (67%) were successfully bridged to transplantation, and 1 (0.71%) showed native heart recovery. Twenty-four patients (17%) had been on continuous-flow left ventricular assist device support for more than 3 years (mean, 3.9 years; range, 3.0-7.5 years). Estimated on-device survival at 1, 3, and 5 years was 83%, 75%, and 61%, respectively. Rehospitalizations due to bleeding, cardiac events, and device-related issues were common. The freedom from rehospitalization rates at 1 and 3 years was 31% and 6.9%, respectively. A total of 14 patients (10%) required device exchange.

Conclusions: Current continuous-flow left ventricular assist devices can provide satisfactory long-term survival. However, rehospitalization is frequently required. (J Thorac Cardiovasc Surg 2014;148:1606-14)

Continuous-flow left ventricular assist devices (CF-LVADs) have become an essential therapeutic option in the standard of care for patients with end-stage heart failure.[1] Clinical outcomes continue to improve through better patient selection, surgical techniques, and perioperative management.[2,3] Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) data showed that 1- and 2-year survival in patients receiving these devices reach 80% and 70%, respectively.[4] These favorable midterm results encourage the use of CF-LVADs both as a bridge to transplantation (BTT) and as a destination therapy (DT). The number of DT implants, as a permanent therapy, dramatically increased to more than 40% of the total LVAD implants in the United States in 2012.[4]

For BTT, because of the persistent donor organ shortage, the wait time on the device support for cardiac transplantation has increased,[5] and in clinical settings, we occasionally encounter patients who require unexpected long-term device support, depending on blood type, body size, and allosensitization. Consequently, long-term CF-LVAD therapy has become a more important option for the treatment of end-stage heart failure. Furthermore, with the current 1-year survival of this therapy being almost equivalent to that of cardiac transplantation, the topic on whether mechanical circulatory support could play a role of replacement for heart transplantation in patients with stage D heart failure is being actively discussed.[6-8] However, compared with transplantation, more clinical data from long-term follow-up studies are necessary to evaluate the risks and benefits of CF-LVADs. In this study, we reviewed our single-center experience with CF-LVADs through a long-term follow-up study.

METHODS

The institutional review board of the Columbia University Medical Center approved this study. We retrospectively reviewed our experience with the CF-LVAD at the Columbia Presbyterian Medical Center between March 2004 and June 2010. During this period, 140 consecutive patients with end-stage heart failure who underwent the insertion of a CF-LVAD were included in this study. Preoperative variables that may correlate with survival were retrospectively collected for each patient. Most of these variables were selected on the basis of previous LVAD risk scores.[9] The cohort consisted of 111 men with a mean age of 55 years. The initial

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Abbreviations and Acronyms

AI	= aortic insufficiency
BTT	= bridge to transplantation
CF-LVAD	= continuous-flow left ventricular assist device
DT	= destination therapy
GI	= gastrointestinal
INTERMACS	= Interagency Registry for Mechanically Assisted Circulatory Support
LVAD	= left ventricular assist device
RVAD	= right ventricular assist device
TR	= tricuspid regurgitation

strategy for LVAD insertion was BTT in 115 patients (82%) and DT in 25 patients (18%). The baseline patient characteristics are shown in Table 1.

Devices and Concomitant Surgery

LVAD support was provided by 117 HeartMate II devices (Thoratec Corp, Pleasanton, Calif), 9 VentrAssist devices (Ventracor Ltd, Chatswood, NSW, Australia), 8 DuraHeart devices (TerumoHeart, Ann Arbor, Mich), and 6 DeBakey devices (MicroMed Technology, Inc, Houston, Tex). Various concomitant procedures were performed during LVAD insertion (Table 2). Of note, 39 patients (28%) underwent tricuspid annuloplasty (suture annuloplasty in 2, ring annuloplasty in 37), and 13 patients (9.2%) underwent aortic valve repair. Two patients (1.4%) in whom severe right ventricular failure developed in the operating room required concomitant right ventricular assist device (RVAD) insertion with a CentriMag system (Thoratec Corp).

Postimplant Anticoagulation and Follow-up

After device implantation, a standardized anticoagulation therapy with aspirin and warfarin was implemented. In patients receiving the HeartMate II device, a target international normalized ratio (INR) range was 2 ± 0.5. After discharge, patients' anticoagulation was managed by nurse-practitioners with repeat testing frequency dictated by ease or difficulty in maintaining the patient within target INR range. Anticoagulation therapy was held in the event of bleeding and resumed once bleeding stopped. Patients were followed up at 1 week after initial discharge and then monthly unless there was an issue. There was no shared-care center during this study period. The frequency of clinic visits varied among patients depending on medical issues and the distance from a patient's home.

Follow-up and Postoperative Data Collection

The follow-up examinations were completed in June 30, 2013, and extended from 0 to 8.5 years (median, 3.6 years; interquartile range, 2.1-4.8 years). Clinical follow-up was completed in 98% of patients. To evaluate the early and late outcomes of patients during on-device support, all clinical data were collected until the patient reached 1 of 3 end points (death, transplant, or device explant for recovery). Late adverse events requiring rehospitalization included major bleeding events, such as gastrointestinal (GI) tract bleeding and significant epistaxis; device-related events, such as pump malfunction, thrombi, and infection; major cerebral events; recurrent heart failure; cardiac arrhythmia; infections not related to LVAD; and other various reasons. For patients receiving BTT, follow-up data after the cardiac transplantation also were collected.

To assess the time course of end-organ function after LVAD insertion, biochemical data, including blood urea nitrogen, creatinine, total and direct bilirubin, alanine aminotransferase, and aspartate aminotransferase levels, were collected at 1 and 6 months and at 1, 2, and 3 years after the LVAD insertion.

Echocardiographic reports were retrospectively reviewed to assess the time course of the left ventricular dimension, aortic insufficiency (AI) severity, and tricuspid regurgitation (TR) severity. AI and TR severities were graded as none to trace, mild, mild-to-moderate, moderate, moderate-to-severe, and severe. AI and TR were considered to be significant if the grades were mild-to-moderate or greater.[10] The data before; at 1 and 6 months after; and at 1, 2, and 3 years after LVAD insertion also were collected.

Statistical Analysis

The data represent frequency distributions and percentages. Continuous variables are expressed as mean $\pm$ standard deviation and compared using 2-sample t tests. Categoric variables were compared using the chi-square test. Kaplan–Meier analysis was used to calculate survival along with a log-rank P value when comparing groups. Patients were censored for transplantation and native heart recovery to calculate estimated on-device survival. Patients were stratified by preoperative variables, including age, cause of heart failure, implant era (before or after approval of the HeartMate II device by the Food and Drug Administration), device type (HeartMate II or others), and the HeartMate II Risk Score profiles.[11] Logistic regression was used to identify correlates of overall mortality during LVAD support. Continuous variables were dichotomized using the median value. Because of the small number of patients reviewed and lack of sufficient power, multivariate analysis was not performed. For multiple group comparison, mixed maximum likelihood regression models with log-transformed values were used.

RESULTS

Early and Late Clinical Outcomes

Early and late mortality and morbidity rates are listed in Table 3. The in-hospital mortality rate was 7.9% (n = 11). Seven patients (5.0%) had major stroke events, 2 of whom died. During hospitalization, 5 patients required delayed RVAD insertion for refractory right ventricular failure at 1 to 60 days after LVAD insertion. Of the 7 patients who eventually required RVAD support, 4 died (3 of multiorgan failure, 1 of a hemorrhagic stroke) and 3 were successfully bridged to transplantation. There were 13 late deaths during LVAD support after discharge. The leading cause of late death was device-related issues (device thrombus requiring device exchange in 1 case, sudden device malfunction in 3 cases, and operator error in battery exchange at home in 1 case). Overall, 24 patients (17%) died on LVAD support during a mean duration of 1.2 years (range, 0.011-7.5 years). Kaplan–Meier analysis showed an estimated on-device survival at 1, 3, and 5 years of 83%, 75%, and 61%, respectively (Figure 1, *A*). There were no statistically significant differences in in-hospital mortality and 1-year on-device survival among patients when stratified by preoperative variables including age, cause of heart failure, implant era, device type, and the HeartMate II risk score (Table 4).

Table 5 demonstrates the risk factor analysis of overall mortality during LVAD support. Preoperative use of