Changes in End-Organ Function in Patients With Prolonged Continuous-Flow Left Ventricular Assist Device Support

Daisuke Yoshioka, MD, Hiroo Takayama, MD, PhD, Paolo C. Colombo, MD, Melana Yuzefpolskaya, MD, Arthur R. Garan, MD, Veli K. Topkara, MD, Jiho Han, BS, Paul Kurlansky, MD, Yoshifumi Naka, MD, PhD, and Koji Takeda, MD, PhD

Divisions of Cardiothoracic Surgery and Cardiology, Columbia University Medical Center, New York, New York

Background. **Few studies have evaluated the long-term effects of continuous blood flow with reduced pulsatility on end-organ function.**

Methods. **Between May 2004 and December 2015, 469 patients underwent continuous-flow left ventricular assist device (LVAD) implantation at our center. Our study included 59 (13%) patients who were supported with an LVAD for a minimum of 3 years. We evaluated postoperative renal function and hepatic function at 1 and 6 months, and 1, 2, and 3 years after implantation in those 59 patients.**

Results. **The patients' mean age was 63 ± 13 years, 81% were male, 53% had an ischemic cause of heart failure, and 68% underwent LVAD implantation as destination therapy. All laboratory determinations showed significant improvements at 1 month after the procedure. Hepatic values remained in a normal range for up to 3 years, although renal function improvement was predominantly transient. One month after implantation, the mean estimated glomerular filtration rate (eGFR) was improved from 58.2 ± 27.9 to 77.7 ± 33.5 mL/min/1.73 m^2. However, 46 (78%) patients showed a gradual decline in eGFR to only 1.7% above the preoperative value after 3 years ($p = 0.67$ vs baseline). The risk factors for impaired renal function after long-term support were age 60 years or older, ischemic cause, and late right heart failure.**

Conclusions. **Continuous-flow LVAD improves renal and hepatic functions in patients with advanced heart failure. However, in most, the initial improvement in renal function is largely transient and returns to baseline after a prolonged support period.**

(Ann Thorac Surg 2017;103:717–24)

Use of a left ventricular assist device (LVAD) has become standard therapy for end-stage congestive heart failure [1]. However, continuous-flow (CF)-LVADs are preferred to pulsatile-flow LVADs because they are smaller, have lower rates of adverse events, and have better long-term durability [2].

For severe heart failure patients, who often have impaired end-organ function because of insufficient blood flow, an LVAD provides sufficient blood flow, improving end-organ function. However, contemporary CF-LVADs do not reflect physiologic blood flow, and the effects of low pulsatility on end-organ function remain to be elucidated. Several studies have indicated that medium-term support with a CF-LVAD does not have detrimental effects on organ function and can improve clinical conditions [3–5]. However, those analyzed patients received an LVAD as bridge to transplantation (BTT) within a 1-year period. After approval for destination therapy (DT), the duration of LVAD support has been increasing, although limited data regarding the effects of long-term CF-LVAD support on end-organ function are available. Here, we assessed end-organ function in patients with CF-LVAD support for at least 3 years of follow-up.

Patients and Methods

Patients

Our institutional review board approved this study. We retrospectively reviewed patients treated at Columbia Presbyterian Medical Center between January 2004 and December 2015, including 469 patients with end-stage heart failure who underwent implantation of a CF-LVAD as BTT or DT. Of those, we analyzed end-organ function in 59 patients who survived with CF-LVAD support for at least 3 years.

Accepted for publication Dec 8, 2016.

Address correspondence to Dr Takeda, 177 Ft Washington Ave, New York, NY 10032; email: kt2485@cumc.columbia.edu.

Dr Naka discloses a financial relationship with Thoratec Corp.

0003-4975/$36.00
http://dx.doi.org/10.1016/j.athoracsur.2016.12.018

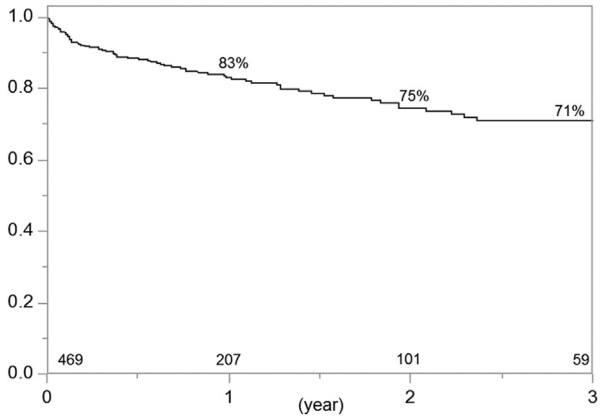

Fig 1. Kaplan-Meier analysis of on-device survival in entire 469 patients.

Device Insertion, Concomitant Procedures

The LVAD implantation procedures were conducted as previously reported [6]. In patients with mild or greater aortic insufficiency, aortic valve repair or tissue valve replacement was performed. In most, the aortic valve was repaired by approximating the raphe of each leaflet. Mitral valve repair was performed in patients with severe functional mitral regurgitation at the discretion of the surgeon. A tricuspid valve procedure was generally performed in cases of moderate or greater tricuspid regurgitation. The decision regarding concomitant right ventricular assist device (RVAD) insertion was made at the surgeon's discretion.

Postoperative LVAD Management

Antiplatelet therapy with aspirin (81 mg for HeartMate II, Thoratec, Pleasanton, CA; 325 mg for HeartWare, HeartWare, Framingham, MA) was implemented and maintained. Anticoagulation therapy was maintained at the target international normalized ratio of 2 to 2.5 for HeartMate II and 2.5 to 3.0 for HeartWare. The volume status in each patient was medically optimized before discharge. Patients received follow-up examinations 1 week after initial discharge and monthly thereafter, unless an issue necessitated more frequent visits.

Data Collection and Follow-Up

All clinical data were collected by review of medical records, with preoperative variables retrospectively collected for each patient. Those included baseline demographics (age, sex, body surface area, body mass index, device purpose, cause), comorbidities (diabetes mellitus, peripheral vascular disease, chronic obstructive pulmonary disease, cerebral vascular accident), laboratory values (aspartate transaminase, alanine transaminase, total bilirubin, blood urea nitrogen, serum creatinine, total protein, albumin, hemoglobin), and echocardiographic and hemodynamic determinations. Postoperative renal and hepatic data were collected at 1, 6 months and 1, 2 and 3 years. The estimated glomerular filtration rate (eGFR) was calculated by use of the following equation: $eGFR = 186 \times (\text{serum creatinine} / 88.4)^{-1.154} \times (\text{age})^{-0.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if African American})$. A model for end-stage liver disease (MELD)-XI score was generated for each patient by use of the following equation: $\text{MELD-XI} = 5.11 \times \ln(\text{serum bilirubin}) + 11.76 \times \ln(\text{serum creatinine}) + 9.44$. To avoid negative scores, serum bilirubin and creatinine levels below 1.0 mg/dL were set at 1.0 mg/dL. The eGFR and MELD-XI scores were calculated at each data collection time point.

Major Adverse Events Definition

Major adverse events requiring readmission during LVAD support were also recorded, including major bleeding events, such as gastrointestinal tract bleeding and significant epistaxis; device-related events, such as pump thrombi and driveline injury; major cerebral events; late right heart failure (RHF); cardiac arrhythmia; and infection related to the LVAD.

Major cerebral events were defined as events accompanied by at least one obvious cerebral lesion in neuroimaging. Late RHF was defined as right heart failure

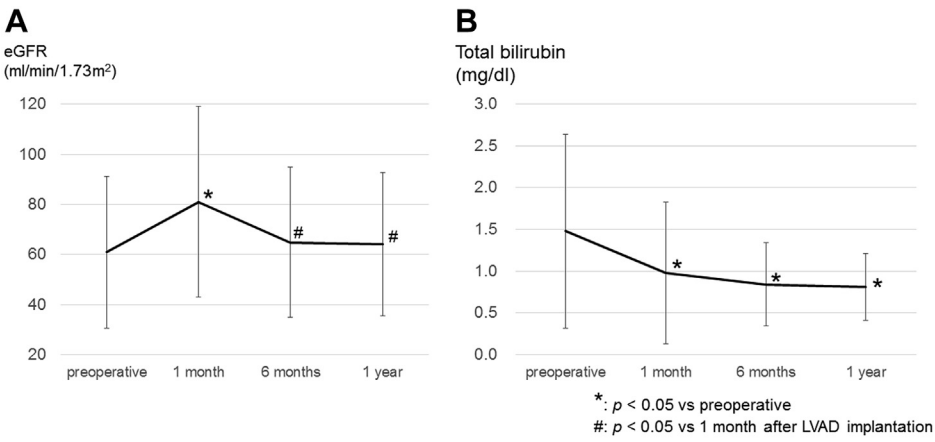

Fig 2. Changes in (A) estimated glomerular filtration rate (eGFR) and (B) serum total bilirubin in entire cohort. (LVAD = left ventricular assist device.)