ORIGINAL CLINICAL SCIENCE

Aortic insufficiency in continuous-flow left ventricular assist device support patients is common but does not impact long-term mortality

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BACKGROUND: Aortic insufficiency (AI) is a significant long-term complication of continuous-flow left ventricular assist device (CF-LVAD) implantation. We sought to evaluate its impact on clinical outcomes and mortality in CF-LVAD recipients.

METHODS: We retrospectively analyzed 237 patients implanted with HeartMate II CF-LVADs at our institution from June 2005 through June 2013. We evaluated recipients' baseline characteristics and annual echocardiograms, grading AI severity as either none, trace, mild, moderate or severe. Only moderate or severe AI was considered clinically significant. Recipients who underwent concomitant aortic valve surgery or who had undergone previous prosthetic aortic valve implantation were excluded.

RESULTS: Moderate or severe AI occurred in 32 (15.2%) patients. Risk factors that significantly affected the development of AI included older age at the time of implantation, female gender, longer duration of LVAD support and destination therapy designation. Freedom from moderate or severe AI was 94%, 76% and 65% of patients at 1, 3 and 5 years, respectively. Overall cohort survival based on Kaplan-Meier analysis was 78%, 59% and 42% at 1, 3 and 5 years, respectively. There was no difference in survival between recipients who developed significant AI and those who did not (log-rank test, $p = 0.73$).

CONCLUSIONS: In this large, single-institution study, the overall rate of AI was low, but increased in frequency with longer duration of LVAD support. Although AI development remains a concern for patients on long-term CF-LVAD support, AI development does not appear to impact long-term mortality.

J Heart Lung Transplant ▮▮▮▮;▮:▮▮▮–▮▮▮

The use of continuous-flow left ventricular assist devices (CF-LVADs) in patients with end-stage heart failure has become a widely used and durable treatment strategy, both as a bridge to transplant (BTT) and as destination therapy (DT).[1] Despite these advances, the use of CF-LVADs is known to result in device-specific long-term complications, such as aortic insufficiency (AI),[2–11] which is thought to be at least partially due to changes in shear forces across the aortic valve after CF-LVAD implantation.[12] As the number of CF-LVAD recipients continues to rise, it has become

increasingly important to evaluate these long-term complications, particularly as the duration of CF-LVAD support for many DT patients continues to lengthen.

Although a number of studies have identified AI as a significant complication of CF-LVADs, none have demonstrated an association between AI development and decreased survival.[2,4,9] Risk factors reported to be associated with the development of AI include older age at time of implant, female gender, low body mass index (BMI), longer duration of CF-LVAD support, a continuously closed aortic valve after implantation, and an increased aortic sinus diameter after implantation.[2–5,8,9]

The development of AI is likely multifactorial, but appears to be related to a higher-than-normal transvalvular pressure gradient across the aortic valve, resulting in fusion of commissures and stenosis of the valve, which leads to subsequent regurgitation.[7,12] In addition, AI is often progressive, leading to a closed circulatory loop that results in ineffective CF-LVAD output, poor end-organ perfusion and greater biomechanical work for an already failing heart.

We sought to evaluate the incidence of long-term (>3 years) AI in HeartMate II recipients and the risk factors associated with long-term AI development. We also aimed to determine the impact of AI on long-term mortality.

Methods

Cohort

In this retrospective study, we identified 237 recipients of a HeartMate II CF-LVAD (Thoratec Corp., Pleasanton, CA) at our institution between June 2005 and June 2013. Excluded from our study group were 27 recipients who underwent concomitant aortic valve surgery at the time of implantation, those who had pre-existing moderate AI identified on echocardiogram before implantation, and those who had undergone previous prosthetic aortic valve surgery. Patients were managed post-operatively by a multidisciplinary team, which included the cardiothoracic surgery service and the heart failure cardiology service. Our database and study were approved by the institutional review board at the University of Minnesota, which waived the need for individual patient consent.

Patient care and device management

As per our local practice at the University of Minnesota, HeartMate II speed was adjusted to provide adequate cardiac output and achieve optimal left ventricular decompression, while maintaining a pulsatility index of >3.5 to 4.0. When possible, the speed of the HeartMate II was also adjusted to allow for the aortic valve to open at least 1 out of every 3 beats. Using the aforementioned parameters as well as hemodynamic and echocardiographic variables, fixed-rate speed was optimized at the time of implantation in the operating room, during the post-operative period before discharge, and whenever clinical events (new symptoms or suction events) warranted further adjustment.

Development of AI

To evaluate the development of AI, we compared echocardiogram reports before implantation, after implantation before discharge and annually thereafter (until either death or a transplant). When echocardiogram findings did not clearly indicate the presence or

degree of AI, a cardiologist reanalyzed them in a non-blinded fashion. AI was defined according to the American Society of Echocardiography report,[13] and graded visually using the following scale: 0 = no AI; 0.5 = trace AI; 1 = mild AI; 2 = moderate AI; and 3 = severe AI. Only moderate and severe categories of AI were considered clinically significant. Recipients who developed clinically significant (i.e., moderate or severe) AI were defined as the "AI group"; those in the other 3 categories (i.e., none, trace, or mild) were defined as the "non-AI group."

Aortic valve opening status was evaluated visually, using 2-dimensional and M-mode imaging on echocardiograms between 1 and 6 months post-operatively, according to the following interval scale: 0 = closed; 1 = intermittent opening; and 2 = fully open with each beat.

Data collection

Baseline demographic (e.g., age at time of implantation, gender, BMI and smoking status), and clinical (e.g., etiology of heart failure, laboratory values, Interagency Registry for Mechanically Assisted Circulatory Support [INTERMACS] profile and medication use) characteristics, as well as outcomes data, were analyzed to determine risk factors for the development of AI. In addition, collected variables included duration of device support, echocardiographic data, mean arterial pressure and pump speed. We calculated overall survival and heart transplant rates for both the AI group and the non-AI group.

Statistical analysis

All analyses were performed using STATA statistical software, release 13 (StataCorp, College Station, TX). For all statistical testing, we used a 2-sided significance level of 0.05, and for between-group comparisons we used a 2-sample *t*-test (for continuous variables) or a chi-square test (for categorical variables). Survival analysis and transplantation rates were assessed using the Kaplan-Meier method and log-rank test to compare unadjusted all-cause mortality for patients who developed AI and those who did not.

Results

Patients' characteristics

For the 210 HeartMate II recipients in our final study group, the mean age at implantation was 56 ± 14 years (mean ± SD); 165 (78.6%) of them were male. Etiology of heart failure was ischemic in 117 (55.7%) patients and non-ischemic (including postpartum cardiomyopathy, myocarditis, congenital heart disease, post-cardiotomy shock and idiopathic) in 93 (44.3%). Treatment strategy was BTT in 167 (79.5%) recipients. The overall median duration of HeartMate II support was 582 days (interquartile range [IQR] 242 to 1,069 days). During the total LVAD follow-up time of 377 patient-years, 17 (8%) of the HeartMate II recipients underwent device exchanges, none for AI-related reasons; 67 (32%) underwent heart transplantation.