The Development of Aortic Insufficiency in Continuous-Flow Left Ventricular Assist Device–Supported Patients

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Background. **Significant aortic insufficiency (AI) after left ventricular assist device (LVAD) placement affects device performance and end-organ perfusion. This study examined the development and progression of AI after implantation of continuous-flow LVAD.**

Methods. **Seventy-nine patients undergoing Heart Mate II (Thoratec Corp, Pleasanton, CA) LVAD implantation for predominantly destination therapy (n = 69 [87%]) were examined. Preoperative and postoperative echocardiograms for all patients were reviewed at the intervals of 0 to 3, 3 to 6, 6 to 12, 12 to 18, and 18 to 24 months. AI was graded on an interval scale of 0, none; 0.5, trivial; 1, mild; 1.5, mild to moderate; 2, moderate; 2.5, moderate to severe; and 3, severe. Development and progression of AI were analyzed.**

Results. **The incidence of significant AI (mild or greater) was 52% (n = 41). Median time to AI development was 187 days. The median duration of VAD support was 761 days. Mild AI developed in 41 patients (52%). No severe AI developed. In the Cox regression model (hazard ratio [95% confidence interval]), aortic valve closure (2.51 [1.06 to 5.89]; $p = 0.03$), and age (1.04 [1.008 to 1.08]; $p = 0.01$) were independent predictors of AI development. There was no difference in mortality rates in the two groups ($p = 0.40$ by log-rank test). A mixed-model linear regression analysis showed a significant overall progression of AI over time ($\beta \pm$ standard error, 0.06 ± 0.02; $p = 0.006$).**

Conclusions. **AI develops over time in a significant number of Heart Mate II LVAD patients. AI is more common in patients with closed aortic valves and in the older age group. As more patients require long-term VAD support, the development of AI will need careful attention and monitoring.**

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Heart failure currently affects 5.8 million Americans, with 670,000 new cases diagnosed annually and an average of 280,000 deaths per year [1]. The lifetime risk of developing heart failure has reached the epidemic proportion of 1 in 5 for both men and women by age 40 years [1]. When medical therapy fails to alleviate advanced end-stage heart failure, surgical alternatives, such as heart transplantation and mechanical circulatory support (MCS) devices, are viable options. Heart transplantation has been the preferred choice, but due to constraints, such as donor availability and strict eligibility criteria, this is a limited treatment option [2]. MCS devices for acute or chronic heart failure are used as a bridge to transplantation (BTT) or as long-term use as destination therapy (DT). The use of MCS has been growing due to enhanced survival and quality of life ratings.

A potential obstacle that has arisen for successful long-term left ventricular assist device (LVAD) support is the native heart's ability to withstand the hemodynamic and ultrastructural fluctuations that are induced by prolonged MCS. One such unanticipated complication is the development of de novo aortic valve (AoV) lesions, which can lead to commissural fusion, stenosis, and aortic insufficiency (AI) [3, 4]. Significant AI can lead to ineffective LVAD output and end-organ malperfusion due to reduced effective forward flow.

Studies have looked at the long-term incidence and the factors that possibly help us predict and prognosticate the future development of AI in patients on LVADs. However, these studies have mostly included patients with LVADs implanted as BTT [5, 6]. With limited donor availability and better LVAD technologies, more patients will be implanted with LVADs as DT. Longer durations of device support might lead to increased severity of AI with hemodynamic consequences that might affect long-term survival.

This study examined the temporal trend of AI after

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Abbreviations and Acronyms

AI = aortic insufficiency
AoV = aortic valve
BTT = bridge to transplantation
CI = confidence interval
DT = destination therapy
HM II = Heart Mate II
HR = hazards ratio
IABP = intraaortic balloon pump
LV = left ventricle
LVAD = left ventricular assist device
LVEDD = left ventricular end diastolic diameter
LVEF = left ventricular ejection fraction
LVESD = left ventricular end systolic diameter
MAP = mean arterial pressure
MCS = mechanical circulatory support
OR = odds ratio
RPM = rotations per minute
SD = standard deviation
SE = standard error
VAD = ventricular assist device

implantation of continuous-flow LVAD devices in patients implanted predominantly under the DT strategy to identify correlates of AI development and progression.

Material and Methods

This study was approved by the hospital Institutional Review Board and individual patient consent was waived.

Patients

We identified 154 patients who were implanted with Heart Mate II (HM II) LVADs (Thoratec Corp, Pleasanton, CA) between January 2005 and January 2011. The study excluded 75 patients: 48 with mild or greater AI before LVAD implant, 3 with previous AoV replacement, and 24 with a follow-up of less than 6 months. The final study population included 79 patients with continuous-flow HM II devices; of these, 74 (93.6%) had no AI and 5 (6.3%) had trivial AI on preoperative echocardiograms.

Transthoracic echocardiograms from the 79 patients with an HM II LVAD implanted between January 2005 and March 2011 were retrospectively reviewed. Studies performed within 2 months preceding device placement were deemed baseline. Subsequent studies were categorized in the postoperative time intervals of 0 to 3, 3 to 6, 6 to 12, 12 to 18, and 18 to 24 months.

AI Assessment

Echocardiograms were performed according to American Society of Echocardiography guidelines and were reviewed by a single reader in a nonblinded manner. Three-beat image capture was used. AI was evaluated visually in the parasternal short-axis and long-axis views and was graded on an interval scale of absence of AI, 0; trivial, 0.5; trivial to mild, 0.75; mild, 1.0; mild to moderate, 1.5; moderate, 2.0; moderate to severe, 2.5; and severe, 3.0. The presence of AoV opening was evaluated visually and with M-mode imaging at each follow-up and was graded as full opening, intermittent opening (defined as 1 to 2 openings in 3 systoles), or full closure during 3 LV systoles. The AoV opening was timed with the onset of QRS complex signifying the onset of ventricular systole.

Statistical Analysis

Statistical analysis was performed using SPSS 19 software (SPSS Inc, Chicago, IL). Continuous variables are expressed as mean and standard deviation and were compared using the Student t test. The Wilcoxon rank sum test was used to determine differences in nonnormally distributed data. Categoric variables, expressed as number of patients and percentage, were compared using the χ^2 test or the Fisher exact test. Values of p less than 0.05 were considered significant. Univariate and Cox proportional hazards regression models were performed to identify risk factors for AI at any given time point. Kaplan-Meier survival curves were plotted for freedom from the development of AI and LVAD support.

The effect of baseline clinical characteristics and baseline echocardiogram measurements on AI progression after LVAD implantation was evaluated using a mixed-effect linear regression model with restricted maximum likelihood estimates and compound symmetry covariance structure. In this model, time was treated as a continuous variable; an estimate of time $\times$ variable interaction term was used to evaluate the change in AI severity over time after LVAD implantation for the presence or absence of a categoric variable or per unit measure of a continuous variable [5].

Results

Entire Patient Population

The analysis included 79 patients with HMII devices. Of these, 69 (87%) received the device for DT and 10 (13%) for BTT. The cohort was a mean age of 63.2 $\pm$ 11.8 years with a median duration of LVAD support of 761 days (range, 145 to 2434 days). Most patients were men (68 [85%]) and had ischemic cardiomyopathy (47 [59%]). The mean LV ejection fraction was 0.19 $\pm$ 0.08. Mild or greater AI developed in 41 of the 79 patients (52%) at a median of 187 days after LVAD implantation. Of these 41 patients, 5 (12%) progressed to mild to moderate AI and 4 (10%) progressed to moderate AI. No severe AI developed.

AI vs No AI

Table 1 lists the baseline characteristics comparing the patients with and without AI. The two groups were similar with respect to the demographic characteristics (sex, race, body mass index, and body surface area), except the age; patients with AI tended more often to be significantly older than those without AI (67.67 $\pm$ 8.5 vs