De Novo Aortic Regurgitation After Continuous-Flow Left Ventricular Assist Device Implantation

Nikhil Prakash Patil, MRCS, MCh, Anton Sabashnikov, MD, Prashant N. Mohite, MRCS, MCh, Diana Garcia, MD, Alexander Weymann, MD, Bartlomiej Zych, MD, Christopher T. Bowles, PhD, Rachel Hards, RGN, Michael Hedger, RGN, Aron F. Popov, MD, Fabio De Robertis, MD, Ajay Moza, MD, Toufan Bahrami, MD, Mohamed Amrani, MD, PhD, Shelley Rahman-Haley, MD, Nicholas R. Banner, FRCP, FESC, and André Rüdiger Simon, MD, PhD

Departments of Cardiothoracic Transplantation and Mechanical Circulatory Support, Cardiology, and Heart Failure and Transplant Medicine, Harefield Hospital, Royal Brompton and Harefield NHS Foundation Trust, London, United Kingdom

Background. **Significant aortic regurgitation (AR) after continuous-flow left ventricular assist device (cf-LVAD) placement affects device performance and patient outcomes. This study examined the development of AR and long-term results after implantation of cf-LVADs.**

Methods. **The study included all patients with no or less than mild AR who underwent HeartMate II (58 [62%]; Thoratec Corp, Pleasanton, CA) or HeartWare (35 [38%]; HeartWare International, Framingham, MA) implantation at our institute from July 2006 to July 2012. Serial echocardiograms were obtained preoperatively, at 1, 3 and 6 months postoperatively, and then at a minimum of 4-month intervals in patients with longer-term support. Kaplan-Meier estimates for freedom from moderate or greater AR were generated. Logistic regression analysis was used to define independent predictors of AR after cf-LVAD implantation.**

Results. **Median duration of LVAD support was 527 days (25^{th}, 75^{th}: 289, 907; range, 60 to 2,433 days). Mild AR developed in 48 patients (51.6%) over a median duration of 126 days, with progression to moderate AR in 13 (14%) over 493 days and to severe AR in 2 (2.1%) over 1,231 days. The incidence of mild or greater AR was 43.1% in HeartMate II vs 65.7% in HeartWare recipients ($p = 0.035$). Overall freedom from moderate or greater AR was 94.7% ± 2.6% at 1 year, 86.9% ± 4.5% at 2 years, 82.8% ± 5.9% at 3 years, and 31% ± 16.9% at 4 years. Independent predictors of AR were duration of support (odds ratio, 1.002; 95% confidence interval, 1.000 to 1.004; $p = 0.017$) and a persistently closed aortic valve (odds ratio, 0.193; 95% confidence interval, 0.097 to 0.382; $p < 0.001$).**

Conclusions. **AR is associated with longer cf-LVAD support duration and persistent aortic valve closure. Incidence of moderate or greater AR after cf-LVAD implantation increases significantly after 3 years. The clinical implications of these data may warrant consideration of prophylactic aortic valve replacement at the time of cf-LVAD implantation, particularly with expected longer duration of support and in patients with preexisting AR that is more than mild.**

(Ann Thorac Surg 2014;98:850–7)

Mechanical circulatory support, primarily with a left ventricular assist device (LVAD), is increasingly used to treat end-stage heart failure. Recent data from the Interagency Registry for Mechanically Assisted Circulatory Support database [1] show that of more than 6,500 LVADs implanted from June 2006 to June 2012, more than 5,500 were continuous-flow LVADs (cf-LVADs). However, with varying degrees of remaining biological pump function, especially in severely diseased ventricles, the ability of the native heart to cope with the physiologic consequences of continuous flow may be a limiting factor to long-term cf-LVAD support. In this context, aortic regurgitation (AR) increases after LVAD implantation, probably because a continuously closed aortic valve (AoV) is exposed to a different transvalvular pressure gradient-time function generated by the interaction of the device with the failing heart compared with a physiologically normal situation [2].

Significant AR can lead to a closed circulatory loop where blood is returned directly to the device inflow through the incompetent valve, with ineffective biomechanical output and resulting end-organ malperfusion. Although an increase in device output may provide temporary compensation for reduced effective biomechanical output,

Accepted for publication May 5, 2014.

Presented at the Fiftieth Annual Meeting of The Society of Thoracic Surgeons, Orlando, FL, Jan 25–29, 2014.

Address correspondence to Dr Patil, Department of Cardiothoracic Transplantation and Mechanical Circulatory Support, Harefield Hospital, London UB9 6JH, United Kingdom; e-mail: n.patil@rbht.nhs.uk.

Dr Simon discloses financial relationships with Thoratec and HeartWare.

0003-4975/$36.00
http://dx.doi.org/10.1016/j.athoracsur.2014.05.030

Abbreviations and Acronyms

ALT	= alanine aminotransferase
AoV	= aortic valve
AR	= aortic regurgitation
BUN	= blood urea nitrogen
cf-LVAD	= continuous-flow left ventricular assist device
COPD	= chronic obstructive pulmonary disease
CPB	= cardiopulmonary bypass
CRP	= C-reactive protein
CVP	= central venous pressure
ECMO	= extracorporeal membrane oxygenation
FFP	= fresh frozen plasma
HeartWare HVAD	= HeartWare Ventricular Assist Device
HM-II	= HeartMate II
IABP	= intraaortic balloon pump
ICD	= internal cardioverter defibrillator
LVAD	= left ventricular assist device
LVEDD	= left ventricular end diastolic dimension
LVESD	= left ventricular end systolic dimension
MAP	= mean arterial pressure
MCS	= mechanical circulatory support
MPAP	= mean pulmonary artery pressure
MR	= mitral regurgitation
NS	= not significant
RBC	= red blood cells
RVAD	= right ventricular assist device
SD	= standard deviation
Svo_2	= central venous oxygen saturation
TTE	= transthoracic echocardiogram
VAD	= ventricular assist device
WCC	= white cell count

increased device demand may lead to a reduction in LVAD durability [3]. Furthermore, increased wall stress in the non-unloaded ventricle may lead to ventricular distension, mitral regurgitation, and other complications, thereby significantly affecting patient quality of life and survival.

True long-term results in patients with AR after cf-LVAD implantation remain to be ascertained, and whether the development and progression of AR varies with preoperative or postoperative characteristics in these patients is unknown. The aims of this study were to examine the long-term temporal trend of AR after cf-LVAD implantation and to identify correlates of AR development and progression.

Material and Methods

The Institutional Review Board at our center approved this study and waived the need for individual patient consent.

Study Design

This study was a retrospective review of prospectively collected data of 119 patients who underwent cf-LVAD implantation with HeartMate-II (HM-II; Thoratec Corp, Pleasanton, CA) of HeartWare LVAD (HVAD; HeartWare Inc, Framingham, MA) devices at our center from July 2006 to July 2012. The study excluded 20 patients with follow-up of less than 60 days and 6 patients with mild or greater AR at implantation. The final study-population comprised 93 patients: 58 (62%) with an HM-II and 35 (38%) with an HVAD. June 1, 2013, was chosen as the common cutoff date for the end of the observation period for all ongoing patients.

Patients were divided into two groups according to the development and grade of AR during the follow-up: the non-AR group comprising 45 patients with no AR or less than mild AR, and AR group comprising 48 patients with mild or greater AR. The demographic and perioperative characteristics of both groups were compared to define factors associated with development of significant AR and the independent predictors of AR after cf-LVAD implantation.

AR Assessment

Serial transthoracic echocardiogram (TTE) assessments were performed in all patients according to institutional protocol. The baseline TTE was done in the week before LVAD implantation. Routine postoperative TTE assessments were performed at 1, 3, and 6 months, and then at a minimum of 4-month intervals, apart from additional studies when indicated clinically. Three-beat image capture was used. For echocardiographic assessment of AR, several 2-dimensional and Doppler variables were integrated to provide an overall severity grade, including AR jet-width/left ventricular outflow tract-width ratio, AR jet pressure half-time, and diastolic flow reversal in descending aorta. AR 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.

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 the QRS complex signifying the onset of ventricular systole.

For the present analysis, a core group (N.P.P., A.S., and S.R.H.) reviewed more than 900 TTE assessments in a nonblinded manner.

Data Analysis

Statistical analysis was performed using IBM-SPSS 21 software (IBM Corp, Armonk, NY). Continuous variables were evaluated for normality using the 1-sample Kolmogorov-Smirnov test and compared with the Student *t* test for normally distributed data (expressed as mean ± standard deviation) or the Mann-Whitney test for skewed data (expressed as median and the 25^{th}, 75^{th} percentile). Categoric data were compared with the