# Natural history and clinical effect of aortic valve regurgitation after left ventricular assist device implantation

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**Objectives:** Aortic valve regurgitation reduces left ventricular assist device mechanical efficiency. Evidence has also suggested that left ventricular assist device implantation can induce or exacerbate aortic valve regurgitation. However, this has not been compared with aortic valve regurgitation progression in a nonsurgical end-stage heart failure population. Furthermore, its clinical effect is unclear. We sought to characterize the development and progression of aortic valve regurgitation in left ventricular assist device recipients and to identify its clinical effect.

**Methods:** A review of all consecutive patients who received an intracorporeal left ventricular assist device at Duke University Medical Center from January 2004 to January 2011 was conducted. Cases of previous or concomitant aortic valve surgery were excluded. Data from the remaining implants (n = 184) and a control group of contemporaneous nonsurgical patients with end-stage heart failure (n = 132) were analyzed. Serial transthoracic echocardiography was used to characterize aortic valve regurgitation as a function of time.

**Results:** Left ventricular assist device implantation was associated with worsening aortic valve regurgitation, defined as an increase in aortic valve regurgitation grade, relative to the nonsurgical patients with end-stage heart failure ($P < .0001$). The recipients of continuous flow left ventricular assist devices were more likely than recipients of pulsatile left ventricular assist devices to develop worsening aortic valve regurgitation ($P = .0348$). Moderate or severe aortic valve regurgitation developed in 21 left ventricular assist device recipients; this was unrelated to the type of device implanted (continuous vs pulsatile; $P = .754$) or aortic valve regurgitation grade before left ventricular assist device implantation ($P = .42$). Five patients developed severe aortic valve regurgitation; all of whom underwent aortic valve procedures.

**Conclusions:** Native aortic valve regurgitation developed and/or progressed after left ventricular assist device implantation, with this effect being more pronounced in continuous flow left ventricular assist device recipients. However, the preoperative aortic valve regurgitation grade failed to correlate with the development of substantial aortic valve regurgitation after left ventricular assist device implantation. After left ventricular assist device implantation, aortic valve regurgitation had a small, but discernible, clinical effect, with some patients developing severe aortic valve regurgitation and requiring aortic valve procedures. These data have implications for the long-term management of left ventricular assist device recipients, in particular as the durability of implantable continuous flow left ventricular assist device therapy improves. (J Thorac Cardiovasc Surg 2013;145:1373-9)

End-stage heart failure (ESHF) refractory to maximal pharmacologic therapies is an increasingly prevalent problem in the United States and worldwide. ESHF treatment is largely surgical and generally by cardiac transplantation (CT) and implantation of left ventricular (LV) assist devices (LVADs), as either bridging or destination therapy. Because of the limitations in the donor organ supply, a small fraction of all patients with ESHF undergo CT. Thus, with the current technology level, chronic implantable LVAD therapy likely represents the most widely applicable ESHF treatment strategy. Consistent with this, in the United States, the annual number of LVAD implants is approaching the annual number of CTs.[1]

Despite its obvious benefits, LVAD therapy has several limitations. Of these, progression of aortic valve (AV) regurgitation (AR) might substantially effect the physiology and clinical outcomes of LVAD recipients. It is widely recognized that substantial AR recognized at LVAD implantation should be addressed surgically to prevent the loss of LVAD mechanical efficiency that AR would otherwise cause.[2,3] AR results in a requirement for an excessive total left-sided output to maintain the constancy of a normal net antegrade left-sided output, with the difference between the 2 equaling the regurgitant flow rate. In the LVAD

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**Abbreviations and Acronyms**

AR = aortic valve regurgitation
AVR = AV replacement
AV = aortic valve
cfLVAD = continuous flow LVAD
CT = cardiac transplantation
ESHF = end-stage heart failure
HF = heart failure
LV = left ventricular
LVAD = left ventricular assist device
LVIDd = LV diastolic dimensions
NS-ESHF = nonsurgical ESHF
pfLVAD = pulsatile flow LVAD
TTE = transthoracic echocardiography

recipient, this generally results in greater device work and flow rate for the systemic output to be normal.

A range of treatment strategies, including AV repair using various techniques,[4] AV replacement (AVR) with biologic prostheses,[5] AV closure, or left ventricular outflow tract patching,[6,7] and percutaneous transcatheter techniques,[8,9] have been successfully implemented. In addition, it is now increasingly appreciated that LVAD therapy can cause AV damage as a function of time,[10,11] resulting in de novo and/or progressive AR, which, in turn, could adversely affect the mechanical efficiency of the LVAD. Two recent studies[12,13] have echocardiographically characterized the development and progression of post-LVAD implantation AR. These 2 studies suggested that patients with a continuous flow LVAD (cfLVAD) had more rapid progression of AR relative to patients supported with pulsatile flow LVADs (pfLVAD). In addition, greater pump speeds and larger aortic root dimensions were associated with greater progression of AR. In addition, a recent study has reviewed a large series of LVAD recipients who required either concomitant or delayed AV procedures because of AR, with 8 patients having undergone post-LVAD implantation AV procedures at concomitant LVAD exchange.[6] However, the echocardiographic and invasive hemodynamic characteristics of AR in these patients were not reported, and whether AR was a predominant contributor to heart failure (HF) in these patients is not clear. Therefore, we sought to characterize the development and progression of post-LVAD implantation AR relative to a nonsurgical HF control group and to examine its clinical effect.

## METHODS

### Patients and Surgical Procedures

The study groups were composed of patients treated at Duke University Medical Center from January 2004 to January 2011. The LVAD recipient group (n = 184) included pfLVAD (n = 36) and cfLVAD (n = 148) recipients. Patients in the pfLVAD group underwent implantation of the Thoratec HeartMate XVE device (n = 33; Thoratec, Pleasanton, Calif) or the Novacor LVAD (n = 3; Novacor, Oakland, Calif). Patients in the cfLVAD group underwent implantation with the Thoratec HeartMate II (n = 139), HeartWare HVAD (n = 6), or Ventracor VentrAssist (n = 3) device. In patients treated with more than 1 LVAD, the attribution of AR was made to the device in place when AR progressed. Patients who underwent concomitant or previous AV surgery were excluded from the study. The nonsurgical ESHF (NS-ESHF) group (n = 132) included contemporaneous patients who did not undergo LVAD implantation. The NS-ESHF group all underwent evaluation at the advanced HF clinic at Duke University Medical Center from 2005 to 2010. The diagnostic evaluation to assess ESHF included transthoracic echocardiography (TTE), right-sided cardiac catheterization, and cardiopulmonary exercise testing. In both LVAD and NS-ESHF groups, the patients who underwent CT were censored at CT.

### Assessment of AR

Serial TTE assessments were performed in both patient groups. Baseline studies were performed before LVAD implantation. Postimplantation assessments were performed as clinically indicated, rather than at scheduled intervals. AR was graded using standard American Society of Echocardiography criteria[14] translated into a specific grade: none or trivial (grade 0), mild (grade 1), moderate (grade 2), moderate-to-severe (grade 3), and severe (grade 4). Progression was defined as an increase in AR grade of 1 grade or more. Our protocol for determining LVAD speed settings during the study period was to achieve optimal LV unloading, with characteristic TTE findings of normal LV dimensions, neutral septal position, and typically persistent AV closure. Greater pump speeds that resulted in leftward septal distortion and LV collapse were avoided. This strategy was consistent with the study by Amin and colleagues,[15] who first demonstrated that septal distortion and LV collapse occurred at even greater cfLVAD speeds than those required to induce persistent AV closure.

### Data Collection and Statistical Analysis

The institutional review board approved the study, and individual patient consent was waived. Data were collected in a post hoc fashion from a review of the clinically generated patient care documentation. Data were analyzed using R, version 2.15.0 GUI 1.51 Leopard build 64-bit (6148; R Foundation for Statistical Computing, Vienna, Austria).[16] Continuous covariates are reported as the median and interquartile range. Categorical variables are reported as proportions. Continuous covariates were compared using the Wilcoxon rank sum test or Kruskal-Wallis test, as appropriate. Categorical covariates were compared using the Fisher exact test or chi-square test, as appropriate. Survival and failure curves were generated using the Kaplan-Meier method.[16,17] The survival and failure curves were compared using the log-rank test.

## RESULTS

### Patient Characteristics

The characteristics of the NS-ESHF and LVAD recipient groups are listed in Table 1. The LVAD recipients had more severe LV systolic dysfunction, as assessed by the LV ejection fraction. In addition, a greater percentage of LVAD recipients had an ischemic/postmyocardial infarction etiology relative to the NS-ESHF group. Finally, the LVAD recipients were older than their NS-ESHF counterparts. The median duration of LVAD support, total LVAD patient years for the cfLVAD and pfLVAD groups, median interval to echocardiographic follow-up for all 3 groups, and total echocardiographic follow-up in patient years for both groups are also listed in Table 1. As anticipated, the duration of support and the interval to the follow-up echocardiogram were