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

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Background—Aortic insufficiency (AI) following left ventricular assist device (LVAD) placement can affect device performance. The aim of this study was to examine AI development following LVAD implantation.

Methods and Results—Echocardiograms (n=315) from 78 subjects undergoing HeartMate-XVE (n=25 [32%]) or HeartMate-II (n=53 [68%]) implantations from 2004 to 2008 were reviewed. Studies were obtained preoperatively and at 1, 3, 6, 12, 18, and 24 months after surgery. AI was graded on an interval scale (0=none, 0.5=trivial, 1=mild, 1.5=mild-moderate, 2=moderate, 2.5=moderate-severe, 3=severe), and the change in AI at follow-up was analyzed with significance tests. Kaplan–Meier estimates for freedom from moderate or worse AI at follow-up were generated. Mixed-model linear regression was used to identify correlates of AI progression during LVAD support. The median (25th, 75th percentile) duration of LVAD support was 239 (112, 455) days, and preoperative AI grade was 0.0 (0.0, 0.0). At 6 months, 89±4% of subjects (n=49 at risk) were free from moderate or worse AI, but this was reduced to 74±7% (n=29 at risk) and 49±13% (n=13 at risk) by 12 and 18 months, respectively. Correlates (slope±SE) of AI progression included female sex (0.002±0.001; P=0.01), smaller body surface area (−0.003±0.001 per m²; P=0.0017), and HeartMate-II model type (0.002±0.001; P=0.039). Correlates (β±SE) of progressive AI on postoperative echocardiogram included increasing aortic sinus diameter (0.04±0.01 per mm; P=0.001), an aortic valve that remained closed (0.42±0.06; P<0.001) or only intermittently opened (0.34±0.09; P<0.001), and lower left ventricular diastolic (−0.002±0.0004 per cm³; P<0.001) and systolic (−0.002±0.0004 per cm³; P<0.001) volumes.

Conclusions—AI progresses over time in LVAD-supported patients. As we move toward an era of long-term cardiac support, more studies are needed to determine the clinical significance of these findings. (Circ Heart Fail. 2010;3:668-674.)

Key Words: heart-assist devices ■ heart failure ■ valves ■ risk factors

Left ventricular assist device (LVAD) support has offered many individuals with end-stage heart failure an improved quality of life and enhanced survival.1,2 Although published trials to date encompass limited durations of device support (median support durations in the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure and the HeartMate-II [HM-II] trials, 408 and 126 days, respectively),1,2 specialists caring for patients with advanced heart failure have begun looking forward to a future of long-term mechanical cardiac support, hoping to supplant the need for cardiac transplantation in many. Current estimates of the number of people in the United States who could benefit from permanent mechanical cardiac support, hoping to supplant the need for cardiac transplantation in many. Current estimates of the number of people in the United States who could benefit from permanent LVAD support range between 30 000 and 100 000. This number can be expected to increase as long-term outcomes surpass that of current transplantation morbidity and mortality.

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A potential obstacle to the success of long-term LVAD support is the ability of the native heart to withstand the hemodynamic and ultrastructural changes induced by prolonged mechanical assistance. One such unanticipated complication has been the development of de novo aortic valve lesions leading to commissural fusion, stenosis, and aortic insufficiency (AI).3–6 In patients with preexisting AI, the severity of insufficiency often progresses.3–5,7 Significant AI can lead to ineffective LVAD output and end-organ malperfusion due to the recycling of regurgitant blood from the outflow graft in the proximal aorta back into the left ventricular (LV) inflow cannula. Although an increase in device output may provide temporary compensation for reduced effective output, increases in device demand might lead to a reduction in LVAD durability. Similarly, the development of hemodynamically significant aortic valve disease in LVAD-supported patients—an increase in afterload from acquired aortic stenosis and an increase in preload from regurgitation—may impede the success of recovery attempts.

A thorough characterization of the development and progression of AI in a large sample of LVAD-supported subjects...
has not been undertaken. It is unknown whether the progression of AI varies by LVAD model or pump hemodynamics (axial or centrifugal flow versus volume displacement) or whether patient preoperative or postoperative characteristics affect postoperative AI trends. The aims of this study were to examine the temporal trend of AI following LVAD implantation and to identify correlates of AI development and progression.

Methods

Transesophageal echocardiograms from consecutive HeartMate-XVE (HM-XVE) and HM-II (Thoratec Corporation; Pleasanton, Calif) LVADs implanted at the University of Michigan Health System (UMHS) between May 2004 and May 2008 were retrospectively reviewed. Echocardiograms were performed preoperatively within 30 days of LVAD implantation and (according to UMHS LVAD protocol) at approximate intervals of 1, 3, 6, 12, 18, and 24 months postoperatively or until LVAD explantation for any cause. 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- and long-axis views and was graded on an interval scale in 0.5 increments (absence of AI=0, mild=1.0, mild-moderate=1.5, moderate=2.0, moderate-severe=2.5, severe=3.0). The presence of aortic valve 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. Subjects were excluded from the analysis if they did not have a preoperative echocardiogram plus at least 1 echocardiogram within 1 year of device placement from which AI could be accurately assessed.

The UMHS mechanical circulatory support database was then retrospectively reviewed to identify correlates of AI. This prospectively collected LVAD data repository contains preoperative patient demographics and clinical characteristics (including preoperative extracorporeal mechanical support defined as percutaneous [TandemHeart, extracorporeal membrane oxygenation] or surgically placed [Abiomed right ventricular assist device or LVAD] temporary devices) and intraoperative and postoperative information. The study was approved by the UMHS Institutional Review Board.

Institutional Intraoperative and Postoperative Management

Based on prior data, all subjects at UMHS with preoperative AI of moderate or worse severity undergo intraoperative aortic valve repair, bioprosthetic valve replacement, or patch closure of the aortic valve. These subjects (n=8) were excluded from the analysis. Postoperatively, subjects undergoing HM-XVE implantation were generally supported with the device in the automatic mode configuration. In HM-II-supported subjects, pump speeds were set in the early postoperative period to optimize septal positioning to reduce right ventricular failure risks while simultaneously optimizing systemic perfusion. Generally, HM-II speeds were infrequently changed following implantation.

Data Analysis

SAS version 9.1 was used for all data analyses. Data for the entire LVAD cohort were evaluated in total and then analyzed by LVAD model group (HM-XVE and HM-II). Continuous variables were evaluated for normality and then compared with either Student t test (for paired and independent data) or nonparametric testing (Wilcoxon signed rank test for paired data or Mann–Whitney test for independent samples) as appropriate, with data expressed as mean±SEM or median (25th, 75th percentile), respectively, unless otherwise indicated. Categorical data were compared with Fisher exact test.

The within-subject change in AI from baseline was calculated at each echo follow-up, and differences were compared across the entire sample using Student t test. At each follow-up, AI severity was then dichotomized into less-than-moderate AI or moderate or worse AI. Freedom from the development of moderate or worse AI was calculated using Kaplan–Meier estimates.

The impact of baseline clinical characteristics and baseline echocardiogram measurements on AI development after LVAD implantation was evaluated using mixed-model linear regression and random effects modeling. In this model, the slope represents the change in AI severity per day of LVAD support for the presence or absence of a categorical variable or per unit measure of a continuous variable. The slope is obtained through a time×variable interaction term created in the mixed model. For the serial echocardiogram measures obtained after LVAD, mixed modeling for repeated measures (using restricted maximum likelihood and compound symmetry) was used. Time was treated as a continuous variable. β represents the change in AI given the change in each postoperative echocardiogram variable at echo follow-up.

Results

Baseline demographics and clinical characteristics for the cohort (n=78) and by device type are shown in Table 1. Baseline characteristics were similar for the 2 LVAD groups. Eighty-eight percent (n=69) of subjects received a device as a bridge to transplantation, with similar durations of support for those receiving HM-XVE and HM-II LVADs (169 [104, 387] versus 239 [144, 461] days, respectively; P=0.48). Mean LVAD flow for the HM-XVE subjects was 5.3±0.11 L/min. Mean LVAD flow, speed, and pulsatility index for HM-II subjects was 5.4±0.07 L/min, 9465±26 rpm, and 5.4±0.07, respectively.

AI in LVAD-Supported Subjects

Over the period of study, 315 echocardiograms were reviewed for 78 subjects. Figure 1 shows the mean AI grade preoperatively and following LVAD implantation. Preoperatively, median AI in the LVAD cohort was graded as absent (0.0 [0.0, 0.0]). The distribution of AI grade for the cohort increased significantly at each postoperative follow-up (Table 2) and was 2 full grades greater than baseline (n=13 at risk) by 18 months. The within-subject change in AI from baseline also increased significantly through 18 months of follow-up.

Table 1. Baseline Characteristics and Demographics of the Total Cohort and by LVAD Model Type

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total Cohort (n=78)</th>
<th>HM-XVE (n=25)</th>
<th>HM-II (n=53)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>54±13</td>
<td>52±13</td>
<td>54±13</td>
<td>0.60</td>
</tr>
<tr>
<td>Male sex</td>
<td>68 (87%)</td>
<td>24 (96%)</td>
<td>44 (83%)</td>
<td>0.16</td>
</tr>
<tr>
<td>White race</td>
<td>57 (73%)</td>
<td>17 (68%)</td>
<td>40 (75%)</td>
<td>0.41</td>
</tr>
<tr>
<td>BSA, m²</td>
<td>2.0±0.3</td>
<td>2.1±0.2</td>
<td>2.0±0.3</td>
<td>0.36</td>
</tr>
<tr>
<td>Diabetes</td>
<td>28 (36%)</td>
<td>10 (40%)</td>
<td>18 (34%)</td>
<td>0.62</td>
</tr>
<tr>
<td>Hypertension</td>
<td>34 (44%)</td>
<td>10 (40%)</td>
<td>24 (45%)</td>
<td>0.81</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>52 (67%)</td>
<td>15 (60%)</td>
<td>37 (70%)</td>
<td>0.45</td>
</tr>
<tr>
<td>Nonischemic heart failure</td>
<td>39 (50%)</td>
<td>16 (64%)</td>
<td>23 (43%)</td>
<td>0.14</td>
</tr>
<tr>
<td>Preoperative IABP</td>
<td>30 (38%)</td>
<td>11 (44%)</td>
<td>19 (36%)</td>
<td>0.62</td>
</tr>
<tr>
<td>Bridge to transplant</td>
<td>69 (88%)</td>
<td>21 (84%)</td>
<td>54 (90%)</td>
<td>0.46</td>
</tr>
</tbody>
</table>

*For between-group comparison of HM-XVE and HM-II. Student t test was used for age and BSA comparisons, all others were compared with Fisher exact test.

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(Table 2). At 6 months, 89±4% (n=49) of subjects at risk were free from moderate or worse AI, but this was reduced to 74±7% (n=29) and 49±13% (n=13) by 12 and 18 months, respectively. Figure 2 shows an example of AI progression in an HM-II-supported subject.

**AI Trends by LVAD Model**

In the HM-XVE (n=25) and HM-II (n=53) groups, median baseline AI severity was 0.0 (0.0, 0.0) and 0.0 (0.0, 0.5), respectively (P=0.32). Figure 3 shows a profile plot of AI for each subject with the overall AI trend shown for the HM-II and HM-XVE groups. The plot demonstrates an overall increase in AI with the duration of LVAD support, with an increase in AI that appears greater in HM-II-supported subjects. Although AI was similar between the baseline groups at the distribution of AI grade was significantly greater in the HM-II group than in the HM-XVE group at 1, 3, and 6 months of follow-up (Table 3). Likewise, although AI increased in both groups, the overall within-subject change in AI was also greater in HM-II than in the HM-XVE group (Table 3), reaching statistical significance through 6 months of follow-up. In the HM-XVE group, 100±0% (n=12), 80±13% (n=10), and 80±13% (n=5) of subjects at risk were free from moderate or worse AI at 6, 12, and 18 months, respectively. In the HM-II group, 86±5% (n=37) of subjects at risk were free from moderate or worse AI at 6 months, but this was reduced to 72±9% (n=19) and 36±15% (n=8) by 12 and 18 months, respectively (P=0.17 for HM-XVE versus HM-II comparison).

**Correlates of AI Development After LVAD Implantation**

Correlates of worsening AI are shown in Table 4. Smaller patient body surface area (BSA) at implantation and female sex were associated with progressive AI over the duration of LVAD support. No preoperative echocardiography measure (including preoperative AI severity, LV dimensions, and aortic sinus diameter) was associated with worsening AI after LVAD implantation (all P>0.2) (data not shown). Correlates of worsening AI on serial echocardiogram following LVAD implantation included lower postoperative LV volumes, diastolic filling abnormalities, increasing aortic sinus diameter, and an aortic valve that failed to open completely during LVAD support. Finally, subjects receiving an HM-II device were more likely to have progressive AI than those with an HM-XVE, as were subjects with higher LVAD flows. Mean arterial pressure, HM-II speed, and pulsatility index at baseline or at follow-up were not associated with AI (P>0.05).

**Device Replacement and AI**

There were 8 (10%) device malfunctions in the entire cohort, with 6 leading to reoperation. Of these, 2 subjects had moderate or worse AI at the time of device replacement. Both had HM-XVE devices, and the replacement indication was “bearing wear.” Of the 15 subjects with moderate or worse AI on at least 1 follow-up echocardiogram, 4 required hospital admission for management of a heart failure exacerbation, and 3 others were admitted due to intractable arrhythmias. No
subject in the cohort underwent device replacement solely due to AI.

**Discussion**

Given the morbidities associated with cardiac transplantation, the promise of long-term LV mechanical support is enticing. With advances in medical engineering, LVAD durability is approaching 1 decade in animals. As such, studies examining the ability of the native heart to withstand the hemodynamic and physiological changes evoked by long-term LVAD support are warranted.

In this cohort, we demonstrated that AI of the native valve progresses with the duration of LVAD support. AI increased by 0.7 grades by 6 months and 1.1 grades by 18 months, with only 49% of subjects undergoing LVAD support free of moderate or worse AI at 18 months. Because AI progression is likely multifactorial, a definitive explanation of the pathophysiology behind AI development and progression is not possible based on the results of this single analysis. However, using data from other studies and the correlates identified in this analysis, we herein provide hypotheses for mechanisms behind AI development following LVAD implantation.

**Aorta Contribution to AI Development After LVAD**

Changes in aortic blood flow dynamics following LVAD support are likely the primary etiology for AI development and progression. Because the aortic outflow conduit is smaller than the aorta, velocities needed to maintain device flows are higher in LVAD-supported subjects than normally present in the human aorta. Computational fluid modeling and animal studies of LVAD support have demonstrated significant alterations in aortic blood flow dynamics and kinetics. The greatest abnormalities in flow seem to occur when the LVAD is functioning in series with the heart (flow through the aortic valve is minimal) and in the setting of proximal aortic outflow cannulation, which is the standard configuration used in humans.

Changes to the aortic wall due to shear stress and high diastolic luminal pressures also likely play roles in postim-
plantation AI. In this analysis, progressive aortic sinus dilatation led to small, but significant increases in AI during LVAD support. Westaby et al.13 examined the aorta of 7 individuals undergoing Jarvik 2000 LVAD support. After 90 days of support, aortic wall atrophy was evidenced by a decrease in medial aortic thickness, medial smooth muscle cell number, and elastin content. Although aortic root dilatation may not be large in magnitude, small amounts of dilatation with concomitant changes in wall elasticity and chronically high diastolic aortic pressures may promote valve malcoaptation and AI development. Similarly, in women and other patients with smaller BSAs, radial shear stress is likely higher because of smaller aortic roots. Settings for LVAD device flows were devised in average-sized men, and it is possible that smaller individuals subjected to high indexed LVAD outputs may (with resultant smaller LV volumes) be more prone to develop AI due to pressure-induced valvular and aortic wall damage.

### Table 4. Correlates of Worsening AI in LVAD-Supported Subjects

<table>
<thead>
<tr>
<th>Preoperative characteristics</th>
<th>ΔAI Slope ± SE†</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, per 10 y</td>
<td>0.0004 ± 0.0002</td>
<td>0.069</td>
</tr>
<tr>
<td>Female sex</td>
<td>0.002 ± 0.001</td>
<td>0.010</td>
</tr>
<tr>
<td>BSA, m²</td>
<td>−0.003 ± 0.001</td>
<td>0.0017</td>
</tr>
<tr>
<td>Ischemic cardiomyopathy</td>
<td>0.001 ± 0.001</td>
<td>0.27</td>
</tr>
<tr>
<td>Prior sternotomy</td>
<td>−0.001 ± 0.001</td>
<td>0.32</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.001 ± 0.001</td>
<td>0.40</td>
</tr>
<tr>
<td>Preoperative MCS</td>
<td>−0.001 ± 0.001</td>
<td>0.37</td>
</tr>
<tr>
<td>Preoperative IABP</td>
<td>0.001 ± 0.001</td>
<td>0.34</td>
</tr>
</tbody>
</table>

### Device model

| HM-II LVAD (vs XVE)         | 0.002 ± 0.001    | 0.039   |
| LVAD flow, L/min           | 0.090 ± 0.044    | 0.044   |

### Follow-up postoperative echocardiogram

| LVDV, cm³                   | −0.002 ± 0.0004  | <0.001  |
| LSV, cm³                    | −0.002 ± 0.0004  | <0.001  |

### Aortic valve opening

| None (closed)‡             | 0.42 ± 0.06       | <0.001  |
| Intermittent‡              | 0.34 ± 0.09       | <0.001  |
| Aorta sinus, mm            | 0.04 ± 0.01       | 0.0011  |
| Mitral E-wave, cm/s        | −0.004 ± 0.002    | 0.009   |
| Mitral E-wave deceleration time, ms | 0.003 ± 0.001 | <0.001  |
| Mitral A-wave, cm/s        | 0.003 ± 0.002    | 0.12    |
| Mitral E/A                 | −0.09 ± 0.04     | 0.04    |

IABP indicates intraaortic balloon pump; LSV, left ventricular systolic volume; MCS, extracorporeal mechanical circulatory support.

*Comparison of overall AI grade between HM-XVE and HM-II groups using Mann-Whitney test.
†Mann-Whitney test for comparison of the within-subject difference in AI from baseline in the HM-XVE versus HM-II groups.

### The Role of Intermittent Valve Opening in AI Progression

Alterations in blood flow dynamics and aortic pressure also likely contribute directly to the development of aortic valve pathology. In the present analysis, subjects with aortic valves that did not open regularly had greater progression of AI with device support than those with aortic valves that opened on every beat. We hypothesize that failure to open the aortic valve with each LV contraction may play 2 roles in AI development. First, patients who require large amounts of LVAD support are unable to generate the LV systolic pressures required to open the aortic valve. As such, the aortic valve remains closed during systole and is subjected to unaccommodated high systolic pressures with large volumes of blood retrogradely contacting the valve root surface.7,10 Animal studies have demonstrated that LVAD support with proximal aorta outflow cannula anastomoses leads to very high-velocity retrograde flow contacting the root side of the aortic valve.10 Commissural fusion of the aortic valve following LVAD support in humans is well-known. On microscopic examination of the fused areas, Samuels et al.7 noted the presence of myxomatous granulation tissue that was restricted to the root aspect of the coronary cusps. As such, they attributed valve degeneration following LVAD implantation to systemic pressure-related changes induced by turbulent blood backflow from the outflow cannula onto a closed valve.

Second, intermittent opening of the aortic valve also may independently promote valve thickening, leading to reduced valve pliability and fusion with subsequent degeneration.3–5,14 To date, 50 aortic valve specimens explanted from patients supported by HeartMate first generation (n=41) and HM-II...
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Furthermore, the outflow cannula for the HM-II is more-blunted blood flow delivery devices, such as the volumetric ventricular assist devices delivering large blood pulsatility. Studies comparing aortic flow patterns in animals device that delivers continuous flow to the aorta with less provided by the native ventricle. The HM-II is an axial flow asynchronous with the cardiac cycle, still results in systolic and diastolic aortic flow relatively more similar to that provoked by the native ventricle. The HM-II is an axial flow device that delivers continuous flow to the aorta with less pulsatility. Studies comparing aortic flow patterns in animals supported with pulsatile and continuous flow devices demonstrated marked differences in blood flow patterns with pulsatile ventricular assist devices delivering large blood volumes with diastolic rest periods compared with continuous, more-blunted blood flow delivery devices, such as the HM-II.11 Furthermore, the outflow cannula for the HM-II is smaller than that of the HM-XVE, creating even greater flow disturbances and, potentially, even higher areas of aortic root and valve shear stress that may promote root atrophy and valvular insufficiency. Testing of these hypotheses in another sample using other continuous and pulsatile devices is warranted.

Influence of Device Type on AI
Although AI developed in subjects supported with either LVAD model, subjects with an HM-II LVAD appeared to develop more AI than those with an HM-XVE LVAD. Although differences in AI development may be partially explained by longer durations of device support in HM-II subjects, a more important contributor may lie in the differences in aorta fluid dynamics.11 The HM-XVE is a volume displacement device providing pulsatile flow that, while asynchronous with the cardiac cycle, still results in systolic and diastolic aortic flow relatively more similar to that provided by the native ventricle. The HM-II is an axial flow device that delivers continuous flow to the aorta with less pulsatility. Studies comparing aortic flow patterns in animals supported with pulsatile and continuous flow devices demonstrated marked differences in blood flow patterns with pulsatile ventricular assist devices delivering large blood volumes with diastolic rest periods compared with continuous, more-blunted blood flow delivery devices, such as the HM-II.11 Furthermore, the outflow cannula for the HM-II is smaller than that of the HM-XVE, creating even greater flow disturbances and, potentially, even higher areas of aortic root and valve shear stress that may promote root atrophy and valvular insufficiency. Testing of these hypotheses in another sample using other continuous and pulsatile devices is warranted.

Clinical Implications for Aortic Valve Disease Progression During LVAD Support
The clinical implications for progressive AI in patients undergoing long-term LVAD support have yet to be determined. In this analysis, no subject developed severe AI or required device replacement due to progressive AI. However, in this mostly bridge-to-transplantation cohort, the median duration of LVAD support was <1 year. Yet, almost half of the supported subjects at 18 months had moderate or worse AI, and half the subjects with moderate or worse AI required hospital readmission for heart failure or an arrhythmia. With longer durations of device support, it is possible that these small, but linear increases in AI may have a real clinical impact on long-term mechanical support.

Thus, further studies of mechanical support should be designed to monitor the long-term impact of AI on clinical outcomes (hospital readmissions for heart failure, New York Heart Association class, renal function) and the impact of changes in surgical technique, device design, and device management on AI progression. Perhaps patients for whom destination therapy is selected may benefit from intraoperative aortic valve oversew regardless of preoperative AI grade. Reengineering of device outflow cannulas or angulation may alter fluid dynamics such that ultrastructural changes in the aortic wall and valve are reduced. Individuals with a small BSA may benefit from reduced device flows or device flows indexed for body size to prevent pressure-related changes on the root side of aortic valve. The impact of LVAD speed adjustments to promote aortic valve opening also should be examined.

Limitations
Because this investigation was an unblinded study of LVAD implantations at a single medical center, we cannot exclude bias and confounding in terms of patient selection, echocardiography image acquisition and interpretation, and LVAD management that may have affected AI development or assessment. However, the results are in line with those of others.3 We did not have aortic valve specimens available following device explantation to allow for a pathological examination of subjects with progressive AI; thus, we cannot rule out the occurrence of undiagnosed valve pathologies not related to LVAD support. We were not able to evaluate the potential impact of manipulating device speeds or flows on the development of AI because device adjustments rarely are made in the postoperative setting at UMHS. As with most single-center LVAD analyses, study power was limited. However, to our knowledge, this study is the largest analysis of AI trends in LVAD-supported subjects to date and the largest cohort supported on an HM-II, the device most likely to be used for destination therapy in the United States over the next few years. Nonetheless, because several pre- and postoperative variables were evaluated, unadjusted P values should be viewed in the context of risk for type I errors. In this small sample aimed at an exploratory analysis of an understudied topic, Bonferroni P value adjustment was not performed given the risks of dismissing potentially clinically relevant (albeit not statistically significant) results (type II error).15

Conclusions
AI tends to progress with the duration of LVAD support. Postoperative progression of AI is likely multifactorial. As we move into a future in which most devices will be used for the long term, further studies will be needed to determine the clinical significance of AI progression in LVAD-supported patients.

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Disclosures
Dr Cowger has received payment (<$5000) in the past for speaking for the Thoratec and Terumo Corporations. Drs Pagani and Aaronson have received grant support from Terumo and HeartWare that are not directly related to this study. Dr Pagani is a Principal Investigator.
and Dr Aaronson is a Co-investigator on Thoratec-sponsored studies. Dr Aaronson has consulting relationships with the Thoratec and Terumo Corporations. Drs Haft, Romano, and Kolias have no disclosures pertinent to this study.

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CLINICAL PERSPECTIVE
Severe aortic insufficiency (AI) following left ventricular assist device (LVAD) implantation can lead to ineffective cardiac output and heart failure symptomatology. In this analysis, echocardiograms (n=315) from 78 subjects supported with a HeartMate-XVE (n=25) or HeartMate-II (n=53) LVAD were reviewed, and AI severity was quantified at baseline and postoperatively. AI was noted to progress with the duration of LVAD support. Correlates of worsening AI post-LVAD were female sex, smaller body surface area, and HeartMate-II model. AI also was worse in subjects with increasing aortic sinus diameters postoperatively or an aortic valve that did not fully open on systole. Further studies are needed to determine whether progressive AI has a clinical impact on long-term LVAD support and whether interventions may be undertaken to retard its development.
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