Aortic Insufficiency in Patients With Sustained Left Ventricular Systolic Dysfunction After Axial Flow Assist Device Implantation

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Background: Predicting the occurrence of aortic insufficiency (AI) during left ventricular assist device (LVAD) support has remained unsolved.

Methods and Results: We enrolled 52 patients who had received continuous flow LVAD (14 axial and 38 centrifugal pumps) and who had been followed for ≥6 months between Jun 2006 and Dec 2013. Native aortic valve (AV) opening was observed in 18 patients (35%) with improved LV systolic function, and none of them had AI. On multivariate logistic regression analysis preoperative shorter heart failure duration was the only independent predictor of postoperative native AV opening (P=0.042; odds ratio [OR], 0.999). Of the remaining 34 patients (65%) with closed AV, 11 had AI with enlargement of the aortic root and narrow pulse pressure. Among those with closed AV, axial pump use (n=13) was the only significant predictor of the development of AI (P=0.042; OR, 4.950). Patients with AI had lower exercise capacity and a higher readmission rate than those without AI during 2-year LVAD support (55% vs. 8%; P<0.001).

Conclusions: Native AV opening during LVAD support is profoundly associated with reversal of LV systolic function, especially in patients with preoperative shorter heart failure duration. Among those in whom the native AV remains closed, low pulsatility of axial flow pump may facilitate aortic root remodeling and post-LVAD AI development that results in worse clinical outcome. (Circ J 2015; 79: 104–111)

Key Words: Centrifugal; EVAHEART; HeartMate II; Ventricular assist device

Although the outcome of left ventricular assist device (LVAD) treatment has been improving thanks to the development of the continuous flow (CF) pump, patient selection, and perioperative management,1–5 aortic insufficiency (AI) remains an unsolved problem during LVAD support.6 AI leads to reduced forward cardiac output and end-organ hypoperfusion,7 which eventually results in poor outcome.8,9

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There have been no established treatments for AI thus far. Although some authors recently reported successful replacement or plasty of aortic valve (AV) for progressed AI, such procedures are invasive and still have various fatal complications.10 Preoperative risk stratification and successful prevention of AI is an inevitable concern for successful long-term LVAD treatment.

AI is a multifactorial phenomenon, but continuous closure of native AV would be a key for the development of AI.10 Although several studies proposed higher age, usage of CF pump, or preoperative lower left ventricular ejection fraction (LVEF) as risk factors for AI,9,11–13 the precise mechanism has remained unknown. Therefore, the aim of the present study was to identify the perioperative factors affecting AI during CF LVAD support.

Methods

Patients
We retrospectively enrolled 52 patients with stage D heart failure (HF) who had received CF LVAD (14 axial pumps: HeartMate II, n=11; Jarvik 2000, n=3; 38 centrifugal pumps: EVAHEART, n=24; DuraHeart, n=14) as a bridge to heart transplantation and who had been followed at the University of Tokyo.
of Tokyo Hospital for at least 6 months between 2006 and 2013. Those with concomitant AV replacement were excluded. No patients had received concomitant right VAD implantation.

All patients were treated preoperatively with guideline-directed medical therapy consisting of β-blocker, angiotensin-converting enzyme inhibitor, and aldosterone antagonist unless contraindicated and doses of these drugs were titrated considering patient hemodynamics.

The rotation speed of LVAD was optimized as low as possible considering patient hemodynamics and interventricular septum shift observed in regular echocardiography. Written informed consent was obtained before LVAD implantation from all patients. The study protocol was approved by the Ethics Committee of the Graduate School of Medicine, University of Tokyo [application number 779 (1)].

Preoperative Variables
Preoperative baseline data including patient demographics and laboratory parameters were obtained within 24 h before surgery. Hemodynamic and echocardiographic parameters were obtained within 1 week before operation or before initiation of intraaortic balloon pump. LVEF was calculated using the biplane Simpson method. Valvular regurgitation was classified into 5 grades: 0, none; 1, trace; 2, mild; 3, moderate; 4, severe. Valsalva sinus and aortic root diameters were measured in all patients on long axis view. HF duration was defined as the time between HF diagnosis and LVAD implantation.

Postoperative Variables
Hemodynamic examination was carried out in all patients at 5 weeks after operation. VAD flow was estimated using algorithms of each device. Transthoracic echocardiography was performed regularly, and AI was defined as aortic regurgitation ≥grade 2 at 6 months. To determine the frequency of the native AV opening, we counted the number of native AV openings per native heart rate over at least 1 min. We defined native AV opening for <30% of the native heart rate as “remaining closed”. Computed tomography was done in all patients, and the height from native AV to the VAD outflow graft anastomosed at the ascending aorta was measured. Peak oxygen consumption during cardiopulmonary exercise test and 6-min walk distance were measured at 6 months after operation. Readmission due to cardiovascular events was counted during 2 years after the first discharge.

Statistical Analysis
All statistical analysis was done using PASW Statistics 18 (SPSS, Chicago, IL, USA). All hypothesis tests were 2-tailed, and used P<0.05 as significant. All data are expressed as mean±SD unless otherwise specified. Continuous variables were compared using unpaired t-test or Mann-Whitney U-test as appropriate. Categorical variables were compared using chi-squared test or Fisher’s exact test as appropriate. Logistic regression analysis was used to calculate significant predictors for AI or native AV opening. Kaplan-Meier analysis was performed to compare readmission-free rate among those with/without AI. Variables significant on univariate analysis at P<0.05 were used in multivariate analysis.

Results
AI and Native AV Opening During LVAD Support
All 18 patients (35%) who had achieved native AV opening, did not have AI (group X; Table 1). Among those with continuous AV closure, 23 patients (44%) had no AI (group Y), whereas 11 (21%) did have AI (group Z).

Preoperative Predictors for Postoperative Native AV Opening
The mean age was 41±13 years, and 43 patients (83%) were male (Table 2). All patients were dependent on continuous inotrope infusion and received elective LVAD implantation. No patients had AI preoperatively. On multivariate logistic regression preoperative shorter HF duration was the only significant predictor for native AV opening (Table 2).

Postoperative Characterization of Native AV Opening
Compared with those whose native AV remained closed, wider pulse pressure and higher systolic blood pressure were observed in patients with native AV opening (Table 3). Improved LVEF with smaller Valsalva sinus or aortic root was also associated with native AV opening (Table 3). Postoperative medical treatment was similar among all patients.

Predictors for Development of AI in Continuous AV Closure
In patients with continuous AV closure (n=34), univariate logistic regression analyses indicated that use of axial pump was the only significant predictor for AI (P=0.042; odds ratio, 4.950; Table 4). There were no significant statistical differences in patient background except for gender and Valsalva sinus diameter between the axial and centrifugal pumps (Table S1). Notably, larger Valsalva sinus diameter was observed in patients with centrifugal pump.

Postoperative Characterization of AI
Among postoperative variables, narrow pulse pressure along with enlargement of Valsalva sinus and aortic root were associated with the development of AI during LVAD support (P<0.05 in all; Table 5). Patients with centrifugal LVAD had significantly wider pulse pressure than those with axial LVAD (Table S2). There were no significant differences in estimated VAD flow between axial and centrifugal pumps. Patients with axial pump experienced more enlargement in Valsalva sinus and aortic root during LVAD support (Table S2).

Clinical Course vs. Presence of AI
Patients with AI had lower peak oxygen consumption during cardiopulmonary exercise test compared to those without AI (Figure A; 11.0±3.3 vs. 14.4±3.5 ml/min⁻¹·kg⁻¹, P=0.004) and shorter 6-min walk distance (Figure B; 328±84 vs. 407±66m, P=0.001) at 6 months after LVAD implantation. Patients with AI had a higher readmission rate due to cardiovascular events than those without AI during the 2-year LVAD support period (Figure C; 55% vs. 8%, P<0.001). There was no difference in 2-year survival under LVAD support regardless of AI (Figure D; P=0.856). The prevalence of AI was 6% at 1 month (3/52), 13% at 3 months (7/52), 21% at 6 months (11/52), and 18% at 1 year (7/40). No significant AI newly developed after the first 6 months. LVAD was explanted in 2 patients (4%), and 7 pa-

| Table 1. AV Opening vs. AI |
|---------------------------|
| AV opening (+) | AV opening (−) |
| AI (+) | 0 (0) | 11 (21) (Z) |
| AI (−) | 18 (35) (X) | 23 (44) (Y) |

Data given as n (%). *P<0.02 (chi-squared test). Al, aortic insufficiency; AV, aortic valve; X, native AV opening; Y, no AI during continuous AV closure; Z, AI during continuous AV closure.
Table 2. Preoperative Predictors for Postoperative Native AV Opening

| Preoperative parameters | Total (n=52) | AV opening (+) (n=18) | AV opening (−) (n=34) | Univariate analysis | Multivariate analysis |
|-------------------------|--------------|-----------------------|-----------------------|--------------------|----------------------|
|                         | Group X      | Group Y+Z             |                       |                     |                      |
|                         | Total        | AV opening (+)        | AV opening (−)        | P-value | OR | 95% CI | P-value | OR | 95% CI |
| Demographic parameters  |              |                       |                       |                     |                      |
| Age (years)             | 41±13        | 40±11                 | 42±13                 | 0.584              | 0.987 | 0.941–1.035 |
| Male                    | 43 (83)      | 17 (94)               | 26 (76)               | 0.068              | 0.128 | 0.045–1.020 |
| Ischemic etiology       | 5 (10)       | 4 (22)                | 1 (3)                 | 0.054              | 9.429 | 0.966–92.06 |
| Body surface area (m²)  | 1.7±0.2      | 1.72±0.11             | 1.65±0.17             | 0.141              | 20.13 | 0.370–1094 |
| HF duration (days)      | 2,138±1,721  | 1,122±1,650           | 2,677±1,522           | 0.024*             | 0.999 | 0.999–1.000 |
| Device selection and valve plasty |          |                       |                       |                     |                      |
| Axial pump              | 14 (27)      | 1 (6)                 | 13 (38)               | 0.030*             | 0.095 | 0.011–1.010 |
| Centrifugal pump        | 38 (73)      | 17 (94)               | 21 (62)               | –                  | –     | –          |
| Mitral valve plasty     | 20 (38)      | 7 (39)                | 13 (38)               | 0.963              | 0.973 | 0.301–3.144 |
| Tricuspid annuloplasty  | 22 (42)      | 10 (56)               | 12 (4)                | 0.163              | 0.436 | 0.136–1.400 |
| Hemodynamic parameters  |              |                       |                       |                     |                      |
| SBP (mmHg)              | 85±13        | 86±12                 | 85±14                 | 0.885              | 1.003 | 0.961–1.048 |
| DBP (mmHg)              | 56±12        | 54±12                 | 57±11                 | 0.382              | 0.977 | 0.927–1.030 |
| Heart rate (beats/min)  | 87±15        | 85±14                 | 89±14                 | 0.264              | 1.025 | 0.981–1.072 |
| mPAP (mmHg)             | 32±8         | 35±10                 | 31±10                 | 0.140              | 1.046 | 0.985–1.111 |
| PCWP (mmHg)             | 23±8         | 26±6                  | 22±9                  | 0.181              | 1.055 | 0.975–1.142 |
| Cardiac index (L·min⁻¹·m⁻²) | 2.0±0.4       | 2.0±0.5               | 2.0±0.4               | 0.655              | 0.738 | 0.187–2.917 |
| mRAP (mmHg)             | 10±5         | 12±4                  | 8±5                   | 0.014*             | 1.192 | 1.037–1.372 |
| RVSWI (g/m²)            | 7.2±3.4      | 6.8±3.3               | 7.4±3.6               | 0.538              | 0.946 | 0.795–1.127 |
| Echocardiographic parameters |          |                       |                       |                     |                      |
| LVDD (mm)               | 75±15        | 75±16                 | 75±14                 | 0.984              | 1.000 | 0.962–1.040 |
| LVEF (%)                | 19±8         | 22±6                  | 19±9                  | 0.259              | 1.042 | 0.970–1.118 |
| AR (grade)              | 0.4±0.6      | 0.2±0.4               | 0.5±0.7               | 0.058              | 0.289 | 0.072–1.010 |
| MR (grade)              | 2.3±1.0      | 2.2±1.0               | 2.4±1.1               | 0.669              | 0.888 | 0.515–1.532 |
| TR (grade)              | 1.5±0.7      | 1.6±0.6               | 1.5±0.8               | 0.686              | 1.177 | 0.534–2.592 |
| Valsalva sinus diameter (mm) | 29±3         | 30±4                  | 29±3                  | 0.136              | 1.145 | 0.958–1.368 |
| AV ring diameter (mm)   | 20±2         | 20±1                  | 19±2                  | 0.088              | 1.365 | 0.955–1.951 |
| Laboratory parameters   |              |                       |                       |                     |                      |
| Hemoglobin (g/dl)       | 11.5±2.0     | 11.4±1.5              | 11.6±2.3              | 0.682              | 0.940 | 0.699–1.264 |
| Platelets (×10⁹/μl)    | 21.1±7.1     | 20.6±8.5              | 20.3±8.8              | 0.898              | 1.005 | 0.928–1.088 |
| Serum albumin (g/dl)    | 3.5±0.6      | 3.4±0.5               | 3.6±0.7               | 0.178              | 0.530 | 0.201–1.346 |
| Serum sodium (mEq/L)    | 134±5        | 132±7                 | 134±4                 | 0.234              | 0.937 | 0.842–1.043 |
| Serum creatinine (mg/dl) | 1.1±0.5      | 1.0±0.3               | 1.2±0.6               | 0.249              | 0.451 | 0.116–1.746 |
| Serum total bilirubin (mg/dl) | 1.6±1.3 | 2.1±1.6               | 1.4±1.0               | 0.065              | 1.611 | 0.971–2.673 |
| Plasma BNP (pg/ml)      | 877±667      | 872±630               | 880±695               | 0.968              | 1.000 | 0.999–1.001 |

Data given as mean±SD or n (%). *P<0.05 (logistic regression). ACEI, angiotensin-converting enzyme inhibitor; AR, aortic valve regurgitation; AV, aortic valve; BNP, B-type natriuretic peptide; CI, confidence interval; DBP, diastolic blood pressure; HF, heart failure; LVDD, left ventricular (LV) diastolic diameter; LVEF, LV ejection fraction; mPAP, mean pulmonary artery pressure; MR, mitral valve regurgitation; mRAP, mean right atrial pressure; OR, odds ratio; PCWP, pulmonary capillary wedge pressure; RVSWI, right ventricular stroke work index; SBP, systolic blood pressure; TR, tricuspid valve regurgitation.
Risk Analyses for AI During LVAD Support

We evaluated AI at 6 months after LVAD implantation, which was relatively earlier than the observation periods used in other studies.\(^8,11,12,14\) We chose 6 months for evaluation of endpoints because death or explantation of LVAD occurred in some patients soon after 6 months. Moreover, no significant AI was newly developed after the first 6 months of LVAD implantation in the present study. Although AI is a progressive phenomenon, its onset may be determined within the first 6 months after LVAD implantation with closed native AV.

Prevalence of AI and Optimization of Rotation Speed

Although the prevalence of AI varied in each report, probably because of variation in definition, timing of evaluation, device type, patient background, or perioperative management, most authors reported an AI prevalence of 20–50% within the first year.\(^8,9,11,12,14\) Jorde et al argued that optimization of rotation speed as low as possible so as to accomplish native AV opening eventually repressed development of AI.\(^8\) We here defined native AV opening at <30% of the native heart rate as “remaining closed”, because Slaughter et al noted that AV opening at least once per 3 native heart beats may be sufficient to avoid development of AI.\(^15\) We carried out such optimization in all patients during scheduled hemodynamic examination and serial transthoracic echocardiography, but still observed a prevalence of AI of 33% within 6 months. Lowering rotation speed down to the level of native AV opening sometimes limited maintenance of sufficient cardiac output. Because there has

tients (13%) underwent heart transplant during the study period.

AV condition and clinical course during the study period among the 4 devices (EVAHEART, DuraHeart, HeartMate II, and Jarvik 2000) are summarized in Table 6.

Discussion

All patients who achieved native AV opening were free from AI development during 6 months of CF LVAD support. On logistic regression analysis preoperative shorter HF duration was associated with AV opening accompanied by improved LVEF during LVAD support. Among those with continuous AV closure, more patients with axial LVAD had AI along with less pulsatility, and aortic root remodeling. Patients with AI had worse clinical course than those without AI.

Definition of AI During LVAD Support

We considered that AI \(\geq 2\) was hemodynamically significant, because AI after LVAD implantation was typically continuous throughout the cardiac cycle and the regurgitant fraction was approximately twice as much as that in the patients without VAD support.\(^12\) Patients with preoperative AI \(\geq 2\) received concomitant AV replacement at the time of LVAD implantation, and such patients were excluded from this study. As a result, all AI during LVAD support were de novo. Considering that all AI accompanied continuous AV closure in the present study (Table 1), AI was analyzed in a stepwise manner, that is, continuous AV closure at first, and then the development of AI.

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### Table 3. Postoperative Characterization of Native AV Opening During LVAD Support

| Parameters                      | AV opening (+) (n=18) | AV opening (−) (n=34) | P-value |
|---------------------------------|-----------------------|-----------------------|---------|
| **Postoperative hemodynamics**  |                       |                       |         |
| Heart rate (beats/min)          | 84±9                  | 82±10                 | 0.587   |
| mPAP (mmHg)                     | 18±7                  | 16±5                  | 0.364   |
| PCWP (mmHg)                     | 9±6                   | 8±4                   | 0.695   |
| Cardiac index (L·min⁻¹·m⁻²)     | 2.5±0.6               | 2.6±0.6               | 0.694   |
| mRAP (mmHg)                     | 9±6                   | 7±4                   | 0.458   |
| RVSWI (g/m²)                    | 4.1±2.1               | 3.9±1.9               | 0.738   |
| Pulse pressure (mmHg)           | 24±8                  | 15±7                  | 0.003*  |
| SBP (mmHg)                      | 93±6                  | 89±6                  | 0.042*  |
| DBP (mmHg)                      | 69±7                  | 73±9                  | 0.078   |
| Estimated VAD flow (L/min)      | 4.1±1.3               | 3.5±0.8               | 0.097   |
| Height of outflow cannula (cm)  | 2.2±0.3               | 2.3±0.3               | 0.395   |
| Carvedilol at 6 months (mg/day) | 14.2±5.5              | 15.6±13.7             | 0.600   |
| Enalapril at 6 months (mg/day)  | 2.1±2.0               | 1.6±1.8               | 0.323   |
| **Postoperative echocardiography** |                       |                       |         |
| LVDD (mm)                       | 67±13                 | 63±16                 | 0.378   |
| %change in LVDD (%)             | −11±12                | −15±17                | 0.303   |
| LVEF (%)                        | 28±14                 | 17±7                  | 0.012*  |
| %change in LVEF (%)             | 34±83                 | 2±47                  | 0.139   |
| MR (grade)                      | 0.6±0.7               | 0.6±0.9               | 0.984   |
| TR (grade)                      | 0.6±0.6               | 1.1±0.9               | 0.067   |
| Valsalva sinus diameter (mm)    | 29±3                  | 31±4                  | 0.253   |
| %change in Valsalva sinus diameter (%) | −1±3                 | 8±7                   | 0.001*  |
| AV ring diameter (mm)           | 20±2                  | 21±2                  | 0.225   |
| %change in AV ring diameter (%) | −2±5                  | 6±9                   | 0.002*  |

Data given as mean±SD. *P<0.05 (unpaired t-test or Mann-Whitney test). LVAD, LV assist device; VAD, ventricular assist device. Other abbreviations as in Table 2.
Continuous AV Closure as a Premise for AI

On early histological examination, continuous AV closure was associated with commissural fusion of native AV,\textsuperscript{16} which resulted in the development of AI.\textsuperscript{17} AI developed consistently only in patients with continuous AV closure (groups Y+Z; Table 1). Therefore, the first step to prevent AI would be to open native AV during LVAD support.

Opening of native AV is determined by the pressure gradient between the LV and aortic root during the systolic phase.\textsuperscript{18} Elevated pressure in the aortic root due to VAD outflow causes the native AV to remain closed, especially under decreased LV systolic function. Therefore, recovery of LV systolic function is essential for the opening of native AV, especially under already optimized VAD flow with lower rotation speed. After LVAD implantation, those with native AV opening had higher pulse pressure. Such a pressure gradient would be largely dependent on improved LVEF due to the aforementioned LV reverse remodeling under LVAD support.

Considering the early studies, patients with non-ischemic etiology, less fibrosis in myocardium, less dilated LV cavity with shorter HF duration indicating less remodeling, can expect LV reverse remodeling under LVAD support.\textsuperscript{19–21}

Preoperative shorter HF duration was consistently a significant predictor of AI.\textsuperscript{19–21}
Risk Analyses for AI During LVAD Support

Toda et al noted worse survival in patients with AI during mainly extracorporeal LVAD support.9 AI may contribute to poor survival during extracorporeal VAD support, because AI impairs systemic perfusion and worsens congestion, probably due to the low flow nature of extracorporeal VAD. In contrast, in early studies using mainly CF LVAD,11,28 there were no differences in 2-year survival regardless of AI, as observed in the present study. Systemic perfusion may not be decreased even if AI occurs in CF LVAD support. Consistently, we did not observe any differences in hemodynamic parameters be-

Table 5. Postoperative Characterization of AI During LVAD Support

| Parameters                                      | Continuous AV closure (n=34) |                  |                  | P-value |
|-------------------------------------------------|-----------------------------|------------------|------------------|---------|
|                                                  | AI (+) (n=11)               | AI (−) (n=23)    |                  |         |
| Heart rate (beats/min)                          | 82±10                       | 82±10            | 0.934            |         |
| mPAP (mmHg)                                     | 18±4                        | 16±6             | 0.419            |         |
| PCWP (mmHg)                                     | 9±4                         | 8±4              | 0.317            |         |
| Cardiac index (L·min⁻¹·m⁻²)                     | 2.5±0.7                     | 2.7±0.6          | 0.382            |         |
| mRAP (mmHg)                                     | 8±5                         | 7±4              | 0.714            |         |
| RVSWI (g/m²)                                    | 4.0±1.6                     | 3.9±2.1          | 0.924            |         |
| Pulse pressure (mmHg)                           | 10±7                        | 18±7             | 0.042*           |         |
| SBP (mmHg)                                      | 87±6                        | 89±6             | 0.389            |         |
| DBP (mmHg)                                      | 76±8                        | 73±9             | 0.314            |         |
| Estimated VAD flow (L/min)                      | 3.3±0.6                     | 3.6±0.9          | 0.271            |         |
| Carvedilol at 6 months (mg/day)                 | 16.4±14.3                   | 15.2±13.8        | 0.824            |         |
| Enalapril at 6 months (mg/day)                  | 1.2±1.5                     | 1.6±1.6          | 0.157            |         |

Data given as mean±SD. *P<0.05 (unpaired t-test or Mann-Whitney test). Abbreviations as in Tables 1,2.
Study Limitations

First, data were analyzed in a retrospective manner at a single center, and the sample size was small. The present results should be tested in a prospective manner by randomizing device type in a larger subject group. Second, LVAD were selected by the attending physicians, and selection bias existed. There was no statistical difference, however, in patient background between axial and centrifugal LVAD except for gender and Valsalva sinus diameter. Third, optimization of rotation speed and pre/postoperative sufficient titration of \(\beta\)-blocker treatment were carried out in all patients. The present results would not apply between patients with and without AI (Table 5).

Patients with AI, however, had decreased exercise capacity compared to those without AI. Although hemodynamics were not different with regard to AI at rest condition, AI may be worsened during exercise with increased afterload. Patients with AI had higher readmission rate due to cardiovascular events such as cerebral thrombosis, ventricular tachyarrhythmia, or congestive HF. Turbulence in ascending aorta due to AI along with continuous AV closure may increase unstable thrombus formation. Increased workload on the LV due to trans-aortic regurgitation may trigger ventricular tachyarrhythmia.

Table 6. AV Condition and Clinical Course vs. Device Type

| Aortic valve | Centrifugal pump (n=38) | Axial pump (n=14) |
|--------------|--------------------------|-------------------|
|              | EVAHEART (n=24)          | DuraHeart (n=14)  | HeartMate II (n=11) | Jarvik 2000 (n=3) |
| Aortic valve |                         |                   |                   |                   |
| AV opening   | 11 (46)                  | 6 (43)            | 1 (9)             | 0 (0)             |
| AI           | 3 (13)                   | 3 (21)            | 5 (45)            | 2 (67)            |
| Clinical course |                   |                   |                   |                   |
| PVO\(_2\) (ml·min\(^{-1}\)·kg\(^{-1}\)) | 14.3±3.6               | 13.1±3.0          | 13.0±4.6          | 9.9±2.0          |
| 6MWD (m)     | 404±78                   | 388±46            | 361±104           | 314±44           |
| Re-admission rate (%) | 4 (17)                  | 1 (7)             | 4(36)             | 2 (67)           |

Data given as mean±SD or n (%). PVO\(_2\), peak oxygen consumption; 6MWD, 6-min walk distance. Other abbreviations as in Table 1.

Figure. (A) Peak oxygen consumption (PVO\(_2\)) and (B) 6-min walk distance (6MWD) at 6 months after left ventricular assist device (LVAD) implantation, and (C) readmission-free rate and (D) survival during 2-year LVAD support among those with/without aortic insufficiency (AI). *P<0.05 (unpaired t-test).
in situations in which these procedures were not carried out. And fourth, we did not perform AV plasty or replacement to manage developed AI after LVAD implantation. Whether such procedures improve prognosis is a subject for future study.

Conclusions
Native AV opening during LVAD support is profoundly associated with reversal of LV systolic function, especially in patients with preoperative shorter HF duration. Among those in whom the native AV remains closed, the low pulsatility nature of axial flow pump may facilitate aortic root remodeling and post-LVAD AI development, resulting in poor quality of life.

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Supplementary Files
Table S1. Preoperative parameters vs. device type
Table S2. Postoperative hemodynamics and echocardiographic parameters vs. device type
Please find supplementary file(s);
http://dx.doi.org/10.1253/circj.CJ-14-0944