# Hemodynamic Effects of Concomitant Mitral Valve Surgery and Left Ventricular Assist Device Implantation

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**There are conflicting data regarding whether concomitant mitral valve surgery (MVS) at left ventricular assist device (LVAD) implantation is beneficial. This study aimed to assess the hemodynamic effects of concomitant MVS. Of all 73 enrolled patients, 44 patients had undergone concomitant MVS and 29 patients had not. Before LVAD implantation, MVS group had higher pulmonary capillary wedge pressure ($p = 0.04$). After LVAD implantation, MVS group had higher mean pulmonary artery pressure and cardiac output (CO). During the hemodynamic ramp study, MVS group had steeper CO slopes (0.18 [0.13 0.28] *vs.* 0.15 [0.08, 0.20] L/min/step; $p = 0.04$) at incremental LVAD speed and achieved a higher CO at the optimized set speed (5.5 [4.7, 6.9] *vs.* 4.9 [4.0, 5.7] L/min; $p = 0.03$). One-year freedom from death or heart failure readmission was statistically comparable between the two groups (61% *vs.* 80%, $p = 0.20$). Thus far, after LVAD implantation and concomitant MVS, patients had increased pulmonary hypertension, despite having higher CO and a better response of CO at incremental LVAD speed. The implication of hemodynamic features after concomitant MVS on clinical outcomes warrants further investigation. *ASAIO Journal* XXX; XX:00–00.**

**Key Words: mitral valve regurgitation, ramp, HeartMate**

Continuous-flow left ventricular assist devices (LVADs) are increasingly becoming a standard therapy in patients with end-stage heart failure (HF).[1,2] Advanced HF often has valvular diseases, which may impact LVAD performance if not addressed at the time of the surgery. For example, preoperative aortic valve regurgitation can deteriorate after LVAD implantation and concomitant aortic valve procedures are established strategy to avoid this complication.[3–5] However, there are conflicting data regarding the benefit of mitral valve (MV) procedures concomitant to LVAD implantation for patients with preoperative significant mitral regurgitation (MR).

Mitral regurgitation in advanced HF is typically functional, resulting from tethering of the MV leaflets secondary to the remodeling of the left ventricle (LV).[6,7] Theoretically, decompression of the LV cavity by LVAD therapy (*i.e.*, reverse remodeling) reduces mitral annular size and decreases the severity of MR. Because of the proposed mechanism of MR progression, several investigators have argued against concomitant MV surgery (MVS; including repair or replacement) at the time of LVAD implant.[8,9] In contrast, others have reported that moderate-to-severe MR can persist even after LVAD implantation in more than 30% of patients and they recommended that this degree of MR should be addressed at the time of LVAD implantation.[10] Also, other group showed that residual MR was associated with shorter times to rehospitalization or death in LVAD patients.[11]

Recently, the INTERMACS registry failed to demonstrate a survival benefit in LVAD patients receiving concomitant MVS.[12] Does concomitant MVS really have no clinical benefit? In this study, we focused on hemodynamic profile and reconsidered the implication of concomitant MVS at LVAD implantation.

## Methods

### *Patient Selection*

Clinically stable outpatients with the HVAD LVAD (Medtronic, Minneapolis, MN) or the HeartMate II LVAD (Abbott, Abbott Park, IL) underwent the previously described hemodynamic ramp study according to our institutional protocol between April 2014 and February 2017.[13] Patients were stratified into two groups based on a history of concomitant MVS at LVAD implantation (MVS group and non-MVS group). No patient had a history of MVS before LVAD implantation. In principal, the indication and operative procedures of concomitant MVS were determined by the attending surgeons. Mitral regurgitations with moderate or greater, which were determined within 1 week before the surgery, were considered concomitant MVS at LVAD implantation. The operative procedures of MVS were determined considering the best way to terminate the regurgitation of MV. Written informed consent was obtained from all participants before the ramp test, and the study protocol was approved by The University of Chicago Institutional Review Board. Grading of the valve regurgitation was performed by

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**Table 1. Baseline Characteristics**

| | Total (N = 73) | MVS (n = 44) | Non-MVS (n = 29) | *p* Value |
|---|---|---|---|---|
| Age (years) | 61 (53, 67) | 61 (55, 69) | 60 (50, 66) | 0.29 |
| Body mass index | 28.1 (23.1, 33.3) | 28.4 (23.4, 34.5) | 28.1 (23.0, 32.4) | 0.55 |
| Gender (male) | 47 (64.4%) | 29 (65.9%) | 18 (62.1%) | 0.74 |
| Race (Caucasian) | 41 (56.2%) | 23 (52.3%) | 18 (62.1%) | 0.41 |
| Device: HVAD | 24 (32.9%) | 12 (27.3%) | 12 (41.4%) | 0.21 |
| Device: HeartMate II | 49 (67.1%) | 32 (72.7%) | 17 (58.6%) | 0.21 |
| Ischemic cardiomyopathy | 29 (39.7%) | 17 (38.6%) | 12 (41.4%) | 0.82 |
| Destination therapy | 58 (79.5%) | 37 (84.1%) | 21 (72.4%) | 0.23 |
| Diabetes mellitus | 28 (38.4%) | 13 (29.5%) | 15 (51.7%) | 0.06 |
| Hypertension | 39 (53.4%) | 23 (52.3%) | 16 (55.2%) | 0.81 |
| Peripheral artery disease | 3 (4.11%) | 3 (6.82%) | 0 (0.0%) | 0.15 |
| Atrial fibrillation | 27 (37.0%) | 18 (40.9%) | 9 (31.0%) | 0.40 |
| Chronic obstructive pulmonary disease | 14 (19.2%) | 6 (13.6%) | 8 (27.6%) | 0.14 |

Variables were compared using the Mann–Whitney *U* test or the Fischer's exact test.
MVS, mitral valve surgery.

one consistent reviewer using the PISA method in accordance with the guidelines of American Society of Echocardiography.[14]

### *Hemodynamic Ramp Study Protocol*

The protocol was previously detailed.[15] In brief, a right heart catheterization was performed at the patients' baseline LVAD speed with the complete assessment of hemodynamics. Next, the LVAD speed was lowered to 2,300 rpm (HVAD) or 8,000 rpm (HeartMate II). Speeds were incrementally raised by 100 rpm (HVAD) or 400 rpm (HeartMate II) until a maximum speed of 3,200 rpm (HVAD) or 12,000 rpm (HeartMate II).

Repeat hemodynamic assessments were performed at each step, and finally, the appropriate LVAD speed ("set" speed) was chosen to optimize hemodynamics: right atrial pressure (RAP) < 12 mm Hg, pulmonary capillary wedge pressure (PCWP) < 18 mm Hg, and cardiac index (CI) > 2.2 L/min/m$^2$. Speed-dependent changes in hemodynamic parameters were expressed as "slopes," defined as the change/step over the entire range of LVAD speeds.[16] We can obtain hemodynamic parameters in each step of LVAD speed. Next, a "regression line" can be created. A slope can be calculated as a gradient of the regression line, *i.e.*, change in hemodynamic parameters per step. Transthoracic echocardiography was also performed at each LVAD speed, and LV end-diastolic diameter and the degree of MR were recorded.

### *Statistical Methods*

Continuous variables are reported as median and interquartile. Categorical variables are expressed as frequencies and percentage. Comparisons between continuous variables were performed using the Mann–Whitney *U* test. Categorical variables were compared using the Fischer's exact test. Continuous variables before and after LVAD implantation were compared using the Wilcoxon signed-rank test. Categorical variables before and after LVAD implantation were compared using the McNemar test.

Time-to-event analysis was performed by Kaplan–Meier analyses and log-rank test. All patients were followed for 1 year after the ramp study, and the incidence of death or admissions for HF was recorded. All statistical analyses were performed using the SPSS Statistics 22 (SPSS Inc, Chicago, IL).

## Results

### *Baseline Characteristics*

Preoperative baseline characteristics are shown in **Table 1**. The age was 61 (53, 67) years, the majority of patients were male (64%) and implanted for destination therapy (80%). There were 44 (60%) patients who underwent concomitant MVS. No significant differences in baseline characteristics were identified between MVS and non-MVS groups. Perioperative parameters are shown in Appendix Table 1, Supplemental Digital Content, http://links.lww.com/ASAIO/A413. Cardiopulmonary bypass time and cross clump time were significantly longer in the MVS group compared with the non-MVS group. Other parameters including perioperative complications and blood product uses were statistically comparable between two groups.

### *Preoperative Grades of Mitral Regurgitation*

Moderate or greater MR was present in 55 (75%) patients before LVAD implantation (**Table 2**). Only one of the 10 patients with moderate MR received MV repair, whereas the remaining nine patients with moderate MR did not receive any valve surgery. Of two patients with moderate-to-severe MR, one patient received MV repair and the other patient did not have valve surgery. Among the 43 patients with severe MR, 34 patients received MV repair, eight patients received MV replacement, and only one patient received no valve surgery.

**Table 2. Preoperative Grades of MR and Types of Concomitant MVS at LVAD Implantation**

| | Total (N = 55) | Moderate MR (n = 10) | Moderate-to-Severe MR (n = 2) | Severe MR (n = 43) | *p* Value |
|---|---|---|---|---|---|
| No MVS | 11 | 9 | 1 | 1 | <0.001* |
| MV repair | 36 | 1 | 1 | 34 | <0.001* |
| MV replacement | 8 | 0 | 0 | 8 | <0.001* |

Only those with moderate or greater MR are shown.
*$p < 0.05$ by Fischer's exact test.
LVAD, left ventricular assist device MR, mitral regurgitation; MVS, mitral valve surgery.

**Table 3. Pre- and Post-LVAD Hemodynamic Comparison Between Two Groups**

| | Total (N = 73) | MVS (n = 44) | Non-MVS (n = 29) | *p* Value |
|---|---|---|---|---|
| Pre-LVAD hemodynamics | | | | |
| RAP (mm Hg) | 10 (7, 17) | 10 (8, 17) | 10 (5, 16) | 0.21 |
| Mean PAP (mm Hg) | 40 (30, 45) | 40 (34, 45) | 37 (21, 50) | 0.20 |
| PCWP (mm Hg) | 24 (17, 30) | 27 (20, 30) | 18 (16, 28) | 0.04* |
| PVR (woods units) | 2.8 (2.1, 4.4) | 3.4 (2.5, 4.4) | 2.7 (1.4, 5.9) | 0.35 |
| Fick CO (L/min) | 3.8 (3.0, 4.6) | 3.9 (3.0, 5.0) | 3.7 (2.9, 4.4) | 0.55 |
| Fick CI (L/min/m$^2$) | 1.9 (1.4, 2.3) | 1.9 (1.4, 2.3) | 1.9 (1.3, 2.3) | 0.75 |
| PAPi | 2.7 (1.7, 4.0) | 2.4 (1.7, 3.1) | 3.0 (1.9, 5.5) | 0.08 |
| MAP (mm Hg) | 82 (75, 89) | 82 (76, 89) | 80 (75, 93) | 0.86 |
| dPAP–PCWP > 5 mm Hg | 15 (20.5%) | 9 (20.5%) | 6 (20.7%) | 0.98 |
| Post-LVAD hemodynamics (baseline LVAD speed) | | | | |
| RAP (mm Hg) | 8 (5, 14) | 10 (6, 14) | 6 (3, 14) | 0.06 |
| Mean PAP (mm Hg) | 25 (19, 31) | 26 (21, 31) | 20 (16, 28) | 0.04* |
| PCWP (mm Hg) | 14 (10, 18) | 15 (11, 19) | 14 (8, 15) | 0.35 |
| PVR (woods units) | 1.9 (1.1, 2.6) | 2.1 (1.5, 2.7) | 1.8 (0.8, 2.5) | 0.36 |
| Fick CO (L/min) | 5.2 (4.5, 6.2) | 5.5 (4.8, 6.2) | 4.9 (4.0, 6.0) | 0.03* |
| Fick CI (L/min/m$^2$) | 2.7 (2.3, 3.0) | 2.9 (2.5, 3.1) | 2.4 (2.3, 2.9) | 0.02* |
| PAPi | 2.1 (1.5, 4.1) | 2.0 (1.3, 2.8) | 2.4 (1.5, 5.0) | 0.12 |
| Doppler BP (mm Hg) | 90 (82, 97) | 86 (80, 92) | 92 (85, 100) | 0.03* |
| LVEDD (cm) | 6.0 (5.3, 6.8) | 6.1 (5.5, 7.0) | 5.6 (5.0, 6.3) | 0.06 |
| Flow (L/min) | 4.8 (4.3, 5.4) | 4.7 (4.3, 5.2) | 5.0 (4.2, 5.5) | 0.82 |
| dPAP–PCWP > 5 mm Hg | 30 (41.1%) | 20 (45.5%) | 10 (34.5%) | 0.35 |

*$p < 0.05$. Continuous variables were compared using the Mann–Whitney *U* test.

CI, cardiac index; CO, cardiac output; dPAP, diastolic pulmonary artery pressure; LVAD, left ventricular assist device; LVEDD, left ventricular end-diastolic diameter; MAP, mean arterial pressure; MVS, mitral valve surgery; PAP, pulmonary artery pressure; PAPi, pulmonary artery pulsatility index; PCWP, pulmonary capillary wedge pressure; PVR, pulmonary vascular resistance; RAP, right atrial pressure.

Overall, 44 (80%) of 55 patients with moderate or greater MR received valve procedures. Of all MV interventions, there were 36 valve repairs and eight valve replacements.

### *Hemodynamics Before Left Ventricular Assist Device Implant*

Hemodynamics before LVAD implantation stratified by MVS are shown in **Table 3**. Pulmonary capillary wedge pressure was higher in the MVS group ($p = 0.04$). Mean pulmonary artery pressure (PAP) tended to be higher, and pulmonary arterial pulsatility index (PAPi) was numerically lower in the MVS group.

### *Hemodynamics During Ramp Testing*

The ramp tests were performed at a median of 246 (100, 634) days after LVAD implantation. Nobody had any HF readmissions before testings. Also, all patients had no or trace MR at the time of ramp test. At baseline LVAD speed, the MVS group had a higher mean PAP and cardiac output (CO) and a lower Doppler blood pressure ($p < 0.05$ for all; **Table 3**).

After LVAD implantation, RAP, PAP, PCWP, and pulmonary vascular resistance decreased and CO increased significantly in both MVS group and non-MVS group ($p < 0.05$ for all; **Table 4**). Prevalence of inappropriate decoupling between diastolic PAP and PCWP increased in the MVS group and remained unchanged in the non-MVS group.

The results of the ramp study are shown in **Table 5**. All patients had no or trace MR at any LVAD speed settings during ramp tests (including at minimum LVAD speed), irrespective of concomitant MVS. During the ramp study, PCWP, mean PAP, and RAP decreased with incremental LVAD speed at a statistically comparable rate in both groups ($p > 0.05$ for all). However, only the CO slope was significantly higher in the

**Table 4. Changes in Hemodynamics Before and After LVAD Implantation**

| | MVS (n = 44) | | | Non-MVS (n = 29) | | |
|---|---|---|---|---|---|---|
| | Trend | Absolute Change | *p* Value | Trend | Absolute Change | *p* Value |
| RAP (mm Hg) | Decrease | –2 (–9, 1) | 0.04* | Decrease | –3 (–7, 1) | 0.002* |
| Mean PAP (mm Hg) | Decrease | –14 (–20, –8) | <0.001* | Decrease | –14 (–22, –6) | <0.001* |
| PCWP (mm Hg) | Decrease | –11 (–19, –6) | <0.001* | Decrease | –9 (–16, –2) | <0.001* |
| PVR (woods units) | Decrease | –0.9 (–2.3, –0.2) | <0.001* | Decrease | –1.0 (–1.8, 0.2) | <0.001* |
| Fick CO (L/min) | Increase | 1.55 (0.45, 2.60) | <0.001* | Increase | 0.95 (0.20, 1.95) | <0.001* |
| Fick CI (L/min/m$^2$) | Increase | 0.81 (0.34, 1.34) | <0.001* | Increase | 0.47 (0.11, 1.22) | <0.001* |
| PAPi | – | –0.29 (–1.12, 0.59) | 0.17 | – | –0.25 (–1.63, 1.23) | 0.72 |
| MAP (mm Hg) | – | 3 (–3, 17) | 0.06 | – | 15 (2, 35) | 0.06 |
| dPAP–PCWP > 5 | Increase | – | <0.001* | – | – | 0.06 |

*$p < 0.05$. Variables were compared using the Wilcoxon signed-rank test or the McNemar test as appropriate.

CI, cardiac index; CO, cardiac output; dPAP, diastolic pulmonary artery pressure; LVAD, left ventricular assist device; MAP, mean arterial pressure; MVS, mitral valve surgery; PAP, pulmonary artery pressure; PAPi, pulmonary artery pulsatility index; PCWP, pulmonary capillary wedge pressure; PVR, pulmonary vascular resistance; RAP, right atrial pressure.

**Table 5. Hemodynamic Data During Ramp Test**

| | MVS (n = 44) | Non-MVS (n = 29) | *p* Value |
|---|---|---|---|
| Slopes of variables | | | |
| RAP slope (mm Hg/step) | −0.26 (−0.38, −0.11) | −0.20 (−0.47, 0.00) | 0.58 |
| Mean PAP slope (mm Hg/step) | −0.95 (−1.33, −0.50) | −0.71 (−1.05, −0.42) | 0.52 |
| PCWP slope (mm Hg/step) | −1.09 (−1.39, −0.75) | −1.10 (−1.69, −0.71) | 0.41 |
| Fick CO slope (L/min/step) | 0.18 (0.13, 0.28) | 0.15 (0.08, 0.20) | 0.04† |
| Fick CI slope (L/min/m²/step) | 0.09 (0.06, 0.15) | 0.07 (0.04, 0.11) | 0.04† |
| Doppler BP slope (mm Hg/step) | 0.97 (0.00, 2.44) | 0.99 (0.22. 2.10) | 0.99 |
| LVEDD slope (cm/step) | −0.16 (−0.22, −0.08) | −0.14 (−0.25, −0.10) | 0.77 |
| Post-LVAD speed optimization | | | |
| RAP (mm Hg) | 10 (6, 14) | 7 (4, 11) | 0.10 |
| Mean PAP (mm Hg) | 26 (21, 31) | 23 (16, 28) | 0.05† |
| PCWP (mm Hg) | 14 (9, 17) | 12 (8, 16) | 0.47 |
| PVR (woods units) | 2.2 (1.4, 2.9) | 2.0 (1.3, 2.9) | 0.50 |
| Fick CO (L/min) | 5.5 (4.7, 6.9) | 4.9 (4.0, 5.7) | 0.03† |
| Fick CI (L/min/m²) | 2.7 (2.3, 3.2) | 2.5 (2.3, 2.8) | 0.04† |
| PAPi | 2.0 (1.4, 3.4) | 2.5 (1.3, 6.3) | 0.22 |
| Doppler BP (mm Hg) | 88 (77, 97) | 89 (82, 102) | 0.54 |
| LVEDD (cm) | 6.1 (5.4, 6.7) | 5.7 (5.0, 6.4) | 0.27 |
| Flow (L/min) | 4.8 (4.3, 5.2) | 4.7 (3.7, 5.5) | 0.48 |
| Optimized HVAD speed (n = 24) | 2,800 (2,625, 2,885) | 2,660 (2,500, 2,840) | 0.34 |
| Optimized HMII speed (n = 49) | 9,385 (9,000, 9,600) | 9,600 (8,800, 9,700) | 0.42 |
| Optimized hemodynamics* | 31 (70.5%) | 16 (55.2%) | 0.19 |
| dPAP–PCWP > 5 mm Hg | 24 (54.5%) | 10 (34.5%) | 0.09 |

*Optimized hemodynamics is defined as satisfying all three criteria: CVP < 12 mm Hg, PCWP < 18 mm Hg, and CI > 2.2 L/min/m².

†$p < 0.05$. Continuous variables were compared using the Mann–Whitney *U* test. Categorical variables were compared using the Fischer's exact test.

CI, cardiac index; CO, cardiac output; dPAP, diastolic pulmonary artery pressure; LVAD, left ventricular assist device; LVEDD, left ventricular end-diastolic diameter; MVS, mitral valve surgery; PAP, pulmonary artery pressure; PAPi, pulmonary artery pulsatility index; PCWP, pulmonary capillary wedge pressure; PVR, pulmonary vascular resistance; RAP, right atrial pressure.

MVS group: 0.18 (0.13, 0.28) *vs.* 0.15 (0.08, 0.20) L/min/step ($p = 0.04$; **Figure 1**).

At the set LVAD speed, CO was higher in the MVS group than in the non-MVS group (5.5 [4.7, 6.9] *vs.* 4.9 [4.0, 5.7] L/min, $p = 0.03$; **Figure 2**), despite statistically comparable LVAD speeds and blood pressure between groups. The MVS group also had a higher mean PAP ($p = 0.05$). Furthermore, more patients in the MVS group exhibited inappropriate decoupling between diastolic PAP and PCWP. All other hemodynamic data including the prevalence of optimized hemodynamics were statistically comparable between both groups.

Among the MVS group (n = 44), slope parameters and hemodynamics at set LVAD speed were statistically comparable between those with MV repair (n = 36/44) and those with MV replacement (n = 8/44) and between those with HeartMate II (n = 32/44) and those with HVAD (n = 12/44) ($p > 0.05$ for all).

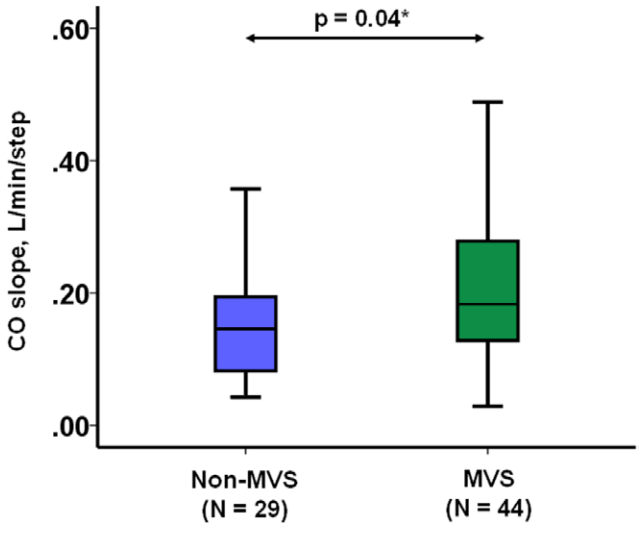


**Figure 1.** Comparison of cardiac output slope between the MVS group and the non-MVS group. *$p < 0.05$ by Mann–Whitney *U* test. MVS, mitral valve surgery.

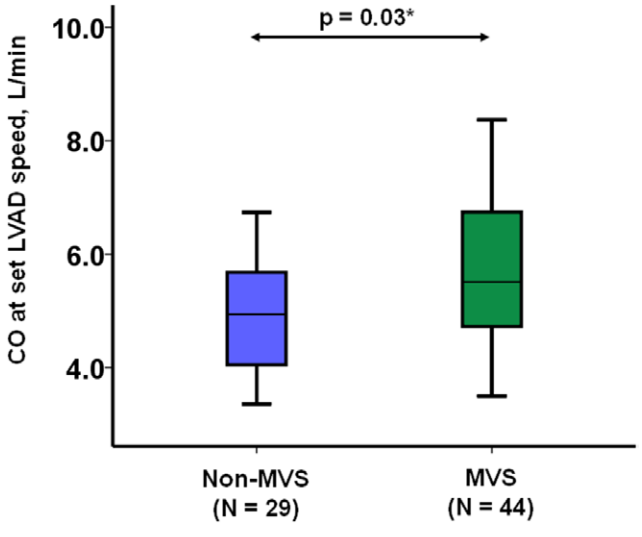


**Figure 2.** Comparison of cardiac output at set LVAD speed between the MVS group and the non-MVS group. *$p < 0.05$ by Mann–Whitney *U* test. LVAD, left ventricular assist device; MVS, mitral valve surgery.

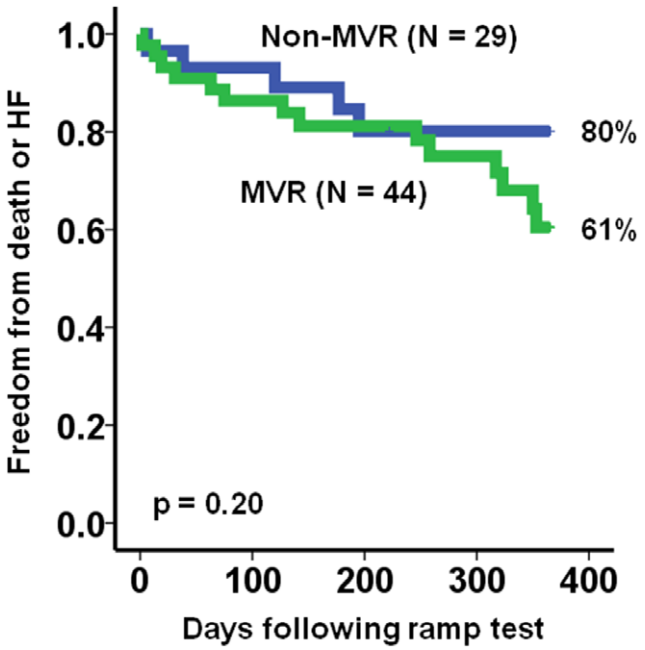


**Figure 3.** Freedom from death or HF readmission stratified by concomitant MVS. Both curves were compared using the log-rank test. HF, heart failure; MVS, mitral valve surgery.

*Clinical Outcomes After Ramp Testing*

One-year freedom from death or HF readmissions was numerically lower in the MVS group than in the non-MVS group (61% *vs.* 80%, $p = 0.20$; **Figure 3**), although the difference did not reach statistical significance.

*Subanalyses Among Those With Pre-Left Ventricular Assist Device Moderate or Greater Mitral Regurgitation*

Among those with pre-LVAD moderate or greater MR (N = 55), 44 patients received MVS and 11 patients did not. During the ramp test, CO slope was significantly higher in the MVS group ($p = 0.03$). At set LVAD speed, CO was higher in the MVS group than in the non-MVS group ($p = 0.02$). One-year survivals free from HF readmission were statistically comparable between two groups (72% *vs.* 60%, $p = 0.81$).

## Discussion

This study investigated the implication of concomitant MVS at the time of LVAD implantation on subsequent hemodynamics during LVAD support. Our primary findings were as follows: 1) patients with concomitant MVS had higher PCWP before LVAD implantation; 2) after LVAD implantation, patients in the MVS group had elevated mean PAP that remained high even after LVAD speed optimization; and 3) patients who had concomitant MVS during LVAD implantation had a higher CO and a better response of CO to LVAD speed changes during a hemodynamic ramp study.

*Current Perspectives on Concomitant Mitral Valve Surgery During Left Ventricular Assist Device Implantation*

Whether to intervene on the MV at the time of LVAD implant has been a source of significant controversy. Proponents of MVS have argued that residual MR after LVAD implantation may lead to persistent pulmonary hypertension and RV dysfunction.[11] Concomitant MVS has been shown to confer greater reductions in pulmonary vascular resistance.[17] Our team showed that the concomitant MVS had an advantage in preventing the recurrence of MR after LVAD implantation.[18]

In contrast, others emphasize that concomitant MR is unnecessary. Significant LV unloading after LVAD implantation reduces the size of LV cavity and minimizes the degree of MR without concomitant MVS.[8,9] Goodwin *et al.*[19] demonstrated that significant resolution of MR occurred after LVAD implantation without concomitant MVS, irrespective of the severity of pre-LVAD MR, and 97.6% of patients were free from MR recurrence at 180 days. Concomitant valve procedures increase the length of cardiopulmonary bypass time, which may have adverse consequences on RV function and may increase the length of stay.[5,20] Recently, it was demonstrated using the INTERMACS database that concomitant MVS was not associated with increased survival.[12] The current ISHLT guidelines recommend avoiding MV interventions during LVAD implantation unless there is a significant structural abnormality such as a ruptured chordae tendineae.[21]

*Implication of Concomitant Mitral Valve Surgery on Hemodynamics*

Most of the prior analyses of concomitant MV intervention have used large databases and focused on survival. To our knowledge, this is the first study to address the impact of concomitant MVS on hemodynamics and LVAD performance. As has been shown in other studies,[22] the overall hemodynamics of our population improved significantly after LVAD implantation and this improvement was almost comparable regardless of concomitant MVS, except for two important hemodynamics findings, although we should state that there were several differences in baseline parameters because of the indication of MVS in our institute:

1. The MVS group had worse pulmonary hypertension; even though the PCWP was reduced to the same degree in both the groups after LVAD implantation, the mean PAP remained higher in the patients receiving concomitant MVS. This lack of normalization of PAP raises concern that the pulmonary vasculature was more damaged before LVAD implantation and cannot reverse remodel despite reductions in the PCWP. Furthermore, decoupling, which is defined as an increased difference between diastolic PAP and PCWP and suggests pulmonary vasculature damage,[23] seems to be similar before LVAD implantation and tended to be higher in the MVS group after LVAD implantation. These findings raise concerns that despite significant LV unloading after LVAD implantation and concomitant MVS, postcapillary pulmonary vasculature damage may still persist probably with a higher mortality, as we previously hypothesized.[23] Randomized control trial among those with comparable baseline hemodynamics is warranted to more accurately investigate the effect of MVS on postcapillary pulmonary hypertension.
2. Pulmonary arterial pulsatility index tended to be lower before LVAD implantation and after LVAD implantation in the MVS group, indicating worse RV function. One possibility is that patients with higher degree of pre-LVAD

MR are likely to have suffered more pulmonary vascular damage (as proposed previously) and subsequent RV dysfunction. Longer pulmonary bypass time in the MVS group may also affect negatively on post-LVAD RV function. Whether the concomitant MVS and normalization of MR would overcome postcapillary pulmonary hypertension and prevent RV dysfunction after LVAD implantation remains a next concern.

3. Patients in the MVS group had higher CO and a better CO response to LVAD speed changes, which may suggest that the MV intervention enhances the function of the LVAD. In other words, it may be easier for the LVAD to unload LV, reverse remodel, and augment CO because it does not need to overcome MR from just after LVAD implantation in patients who have received MVS. Left ventricular assist device implantation alone may be sufficient to normalize MR. However, concomitant MVS may be helpful not only for the normalization of MR but also for improving cardiac reserve. We modified the sentence to more clarify our state.

### *Clinical Implication of Concomitant Mitral Valve Surgery*

There has been a renewed interest in the importance of hemodynamic optimization in HF patients during the last decade. Denardo *et al*.[24] reported in a subanalysis of the ESCAPE trial that HF patients with lower PCWP and higher CI had improved survival. The dramatic reduction in HF readmission in patients implanted with an implantable PAP monitor emphasizes the importance of hemodynamic management.[25,26] Among LVAD patients, 6 minute walk distance improved when patients' hemodynamics were normalized by invasive hemodynamic ramp tests.[13,27] Our team also demonstrated that optimized hemodynamics was associated with reduced HF readmissions in LVAD patients.[28]

The improvement in CO in the MVS group did not translate into an improvement in survival free of HF readmissions. As noted previously, pulmonary vasculature damage remained after LVAD implantation and concomitant MVS and the negative impact of this comorbidity may have balanced out benefits that would have been seen because of MVS.

Concomitant MVS may have a beneficial impact on exercise capacity by enhanced LVAD function, probably improving cardiac reserve. In a study by Jung *et al.*,[29] increased CO changes per change in LVAD RPM, which is quite similar concept with "slope" that we use, was correlated with improvements in the quality of life. However, persistent pulmonary vasculature damage after concomitant MVS may negatively impact these outcomes in our cohort. Considering the overall hemodynamic effects, the impact of concomitant MVS on exercise capacity remains still uncertain.

### *Study Limitations*

Our study is a single-center, nonrandomized study with a moderate sample size. Although we performed a subanalyses among those with pre-LVAD moderate or greater MR, there was a potential selection bias between two groups in the main analyses particularly in the severity of MR. A randomized approach to moderate or greater MR at the time of LVAD implantation may be needed to better address the potential benefits and disadvantages of concomitant MVS. Nevertheless, we believe that this is the best study investigating the detailed hemodynamics during the ramp test under the current indication of MVS for moderate or greater MR.

A further limitation of our study is that the hemodynamic measurements were obtained at varying durations of time after LVAD implantation and we do not have longitudinal data on hemodynamic changes over time. We assessed RV function using PAPi,[30] but other parameters including echocardiography tests would give us more detailed findings. Our cohort includes HeartMate II and HVAD patients, and our findings may not simply be adopted in other devices including HeartMate 3. Also, we enrolled only those who underwent the ramp tests and those who died or transplanted before the tests were not analyzed. We note that there were no HF readmissions before the ramp tests and all participants received ramp tests at clinically stable condition. Most importantly, we did not analyze the impact of MVS on clinical outcomes such as quality of life and exercise capacity. Although we could not directly answer the question whether concomitant MVS should be performed at LVAD implantation, we believe that a unique hemodynamic profile after concomitant MVS and LVAD implantation that we demonstrated in this study would lead to the clue of the final answer in the next future studies.

## Conclusion

Left ventricular assist device patients receiving concomitant MVS at LVAD implantation for moderate or greater degree of MR have worse pulmonary hypertension, despite having higher CO and a better response of CO to LVAD speed changes. The clinical implications of this hemodynamics impact warrant further investigation.

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