Persistent mitral regurgitation after left ventricular assist device: a clinical conundrum

Jose B. Cruz Rodriguez1,2, Arka Chatterjee1, Salpy V. Pamboukian1, Jose A. Tallaj1, Joanna Joly1, Andrew Lenneman1, Sudeep Aryal1, Charles W. Hoopes3, Deepak Acharya4 and Indranee Rajapreyar1*

1Division of Cardiovascular Diseases, University of Alabama at Birmingham, 1900 University Boulevard, Tinsley Harrison Tower 311, Birmingham, AL 35223, USA; 2Division of Cardiovascular Diseases, Texas Tech University Health Science Center El Paso, El Paso, TX, USA; 3Department of Surgery, University of Alabama at Birmingham, Birmingham, AL, USA; 4Division of Cardiovascular Diseases, University of Arizona, Tucson, AZ, USA

Abstract

Aims Persistent mitral valve regurgitation (MR) after continuous flow left ventricular assist device implantation (cflVAD) is associated with pulmonary hypertension and right ventricular failure with variable effects on survival across published studies. The aim of this study is to determine the incidence and predictors of persistent MR at 6-month follow-up after cflVAD implantation and its impact on survival, haemodynamics, right ventricular function, and morbidity.

Methods and results We performed a retrospective review of all adult cflVAD recipients from January 2012 to June 2017 at a single tertiary university hospital with follow-up until April 2019. Primary outcome was to compare survival between patients with no-to-mild compared with persistent moderate-to-severe MR at 6 months. Secondary outcomes included right heart failure (RHF), length of stay, re-hospitalizations, and composite of death, transplant, and pump exchange during the length of follow-up. Final analytic sample was 111 patients. The incidence of persistent moderate or severe MR at 6 months was 26%. Significant predictors of persistent MR at 6 months were left atrium dimension and volume. The group with persistent moderate-to-severe MR at 6 months had higher incidence of RHF at 6 months (45% vs. 25%, P = 0.04). There was no difference in survival at 1 year between the groups (no-to-mild MR 85.5%, moderate-to-severe MR 87.9%, Wilcoxon P-value = 0.63). There was no difference in re-hospitalizations, length of stay, composite of death, transplant, or pump exchange during the length of follow-up between the comparison groups.

Conclusions Persistent moderate-to-severe MR after cflVAD implantation is present in one fourth of patients and is associated with increased incidence of RHF, higher mean pulmonary pressure, and pulmonary capillary wedge pressure with no effect on 1 year survival. Increased left atrium size was associated with persistent moderate-to-severe MR at 6 months.

Keywords Mitral regurgitation; Continuous flow ventricular assist device

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*Correspondence to: Indranee Rajapreyar, Division of Cardiovascular Diseases, University of Alabama at Birmingham, 1900 University Boulevard, Tinsley Harrison Tower 311 Birmingham, AL 35223, USA.
Email: irajapreyar@uabmc.edu

Introduction

Continuous flow left ventricular assist devices (cflVAD) are being increasingly used to support end-stage systolic heart failure patients as bridge to transplant, recovery, or destination therapy. The annual data summary of the Society of Thoracic Surgeons Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) database reports increased use of cflVAD as destination therapy.1 The increasing number of patients in the wait list for orthotopic heart transplantation and change in the organ allocation system may result in increased support duration with cflVAD, irrespective of implant strategy.

Haemodynamic optimization after cflVAD implantation to prevent late right heart failure (RHF) is pivotal for long-term survival. The mechanisms for worsening RHF include inter-ventricular shift, increased preload to the right ventricle (RV), or persistent pulmonary hypertension (increased afterload). Persistent pulmonary hypertension can result from elevated left atrium (LA) pressure due to inadequate...
ventricular unloading, persistent mitral valve regurgitation (MR), or coexistent pulmonary diseases.²

Functional mitral regurgitation (FMR) due to ischaemic or non-ischaemic dilated cardiomyopathy results from displacement of papillary muscles or annular dilation due to left ventricular (LV) or LA dilation leading to defective coaptation of mitral leaflets.³ The prevalence of functional MR in systolic heart failure ranges from 60% in patients admitted for decompensation to 100% in patients referred for cardiac transplantation.⁴,⁵ The prevalence of moderate-to-severe MR in the Society of Thoracic Surgeons INTERMACS database before cfLVAD implantation was 57%.³

Majority of patients have improvement in FMR after LV unloading and positive effects of LV remodelling with long-term cfLVAD support. Retrospective, single-centre studies have shown that the incidence of persistent MR after cfLVAD implantation varies from 2.4% to 20% at 6 month follow-up.⁶–⁸ Recent reports have emerged challenging the conventional belief of ignoring MR at time of cfLVAD implantation. Persistent MR after cfLVAD implantation has been associated with persistent pulmonary hypertension, worsening RV function, shorter time to death, and first hospitalization.⁶,⁹ Concomitant mitral valve procedures for moderate-to-severe MR at time of cfLVAD implantation has been associated with reduced incidence of RHF and hospital re-admissions for heart failure without survival benefit.¹⁰–¹² Surgical correction of MR remains a clinical conundrum and will remain so, until the identification of a FMR phenotype that is unresponsive solely to LV unloading.

The aim of our study is to determine the incidence and predictors of persistent MR at 6 month follow-up after cfLVAD implantation and its impact on survival, haemodynamics, RV function, and morbidity.

Methods

We performed a retrospective review of all adult patients with cfLVAD implantation from January 2012 to June 2017 at a single tertiary LVAD/transplant centre with follow-up until April 2019. All patients with cfLVAD were identified by a master list kept by the mechanical support team, and the variables were obtained by review of the medical records. Patients receiving only continuous flow axial (HeartMate II®) and centrifugal (HeartWare®) devices were included. Heartmate III was not available for commercial use during the study period. We excluded patients who had concurrent planned or rescue right VAD placement, transferred care to another institution, re-implantation, mortality in the index hospitalization, or incomplete echocardiogram/right heart catheterization data at 6 months.

Each chart was abstracted by one investigator, and the primary exposure and outcomes were validated by a second investigator. Co-morbidities, demographics, and baseline catheterization and echocardiographic data were collected from the last assessment before cfLVAD implantation.

Left ventricular assist device parameters at baseline (discharge from index hospitalization) and 6 month follow-up were collected from the medical records. All patients had an echocardiographic-guided ramp study before hospital discharge to optimize LVAD parameters. High speed was defined as ≥9200 rpm for axial pumps and ≥2600 for centrifugal pumps.

Echocardiogram measurements were reviewed manually by the two authors and validated against the original study interpretation. LV, LA, and RV dimensions and volumes were measured from standard views as recommended by American Society of Echocardiography guidelines.¹³ Mitral and tricuspid regurgitation were graded qualitatively as none, mild, moderate, or severe. Patients were then dichotomized into two groups based on MR severity at 6 months: no-to-mild MR (n = 82) and moderate-to-severe MR (n = 29).

Invasive haemodynamic data were used to define RHF as right atrial pressure ≥14, cardiac index <2.2 L/min/m² or need for inotropic support at 6 months.

The primary outcome was to compare cfLVAD survival (time to death, transplant, or end of follow-up) between the groups with no-to-mild and persistent moderate-to-severe MR at 6 month follow-up. Secondary outcomes included comparison of RVF, length of stay (LOS), re-hospitalization, and composite of death, transplant, and pump exchange between the groups until the end of follow-up.

We present data as either mean ± standard deviation or as median with interquartile range, based on the distribution of the data. Demographic, clinical, echocardiographic, laboratory, and haemodynamic data were compared using unpaired t-tests for normal continuous data, χ² tests for categorical data, and Wilcoxon rank-sum test for non-normal data. Kaplan–Meier method was used to evaluate time to death, which was subsequently compared between groups by Wilcoxon log-rank test. Based on the existing literature and clinical experience, variables that were considered confounders were included a priori in a multivariable logistic regression model to evaluate risk factors for moderate-to-severe MR at 6 months.

We utilized available case method for handling of missing data, assuming missing at random. All statistical analyses were performed using Stata 14.2 (Stata Corporation, College Station, TX, USA). The local institutional review board approved this project.

Results

We identified 128 implants in the specified timeframe, with a final analytic sample of 111 patients (Figure 1). Moderate-to-
severe MR at 6 month follow-up was present in 29 (26.1%) patients. Median time to follow-up until death, censoring (transplant), or end of the study was 1.93 years. Invasive haemodynamic and echocardiographic assessment was available post-LVAD implantation in all but one patient, performed an average of 143 days after implantation.

We only had two patients with concomitant mitral valve repair at the time of LVAD implantation (1.8% of the sample).

Table 1 Baseline demographics and characteristics stratified by MR severity at 6 months

| Variablea | No-to-mild MR (n = 82) | Moderate-to-severe MR (n = 29) | P-valueb |
|-----------|------------------------|-------------------------------|----------|
| Age at implant (years) | 55.5 (46.3, 63.4) | 54.0 (42.9, 57.8) | 0.32 |
| Male | 63 (77%) | 24 (83%) | 0.50 |
| Race | | | |
| White | 53 (65%) | 18 (62%) | 0.79 |
| Black/otherc | 28 (34%) | 11 (38%) |
| Body mass index | 28.9 (5.7) | 27.7 (5.2) | 0.34 |
| Diabetes mellitus | 29 (35%) | 9 (31%) | 0.67 |
| Hypertension | 46 (56%) | 15 (52%) | 0.68 |
| Atrial fibrillation | 16 (20%) | 10 (34%) | 0.10 |
| Ischaemic cardiomyopathy | 31 (38%) | 10 (34%) | 0.75 |
| Concomitant mitral valve repair | 2 (2.4%) | 0 (0%) | 0.39 |
| LVAD type | | | |
| Centrifugal flow | 40 (49%) | 9 (31%) | 0.10 |
| Axial flow | 42 (51%) | 20 (69%) |
| Destination therapy | 24 (29%) | 8 (28%) | 0.86 |
| INTERMACS class | | | |
| 1 | 43 (52%) | 15 (52%) | 0.76 |
| 2 | 28 (34%) | 11 (38%) |
| 3 | 8 (10%) | 3 (10%) |
| 4 | 3 (4%) | 0 (0%) |
| Pre-implant use of inotropes | 74 (90%) | 26 (90%) | 0.93 |
| Pre-implant mechanical support | | | |
| None | 27 (35%) | 12 (43%) | 0.85 |
| IABP | 40 (52%) | 14 (50%) |
| VA ECMO | 3 (4%) | 1 (4%) |
| Othersd | 7 (9%) | 1 (4%) |

BMI, body mass index; IABP, intra-aortic balloon pump; MR, mitral regurgitation; LVAD, left ventricular assist device; VA ECMO, venoarterial extracorporeal membrane oxygenation.

aAll continuous variables presented as median (25th–75th percentile) or mean (SD).
bWilcoxon rank-sum test for non-normal distributed variables, t-test for normal variables, and χ² test for categorical variables.
cOnly one Hispanic patient in the no-to-mild MR group.
dOther include VA ECMO + IABP and Abiomed.
Table 2  LVAD parameters, echocardiographic, and haemodynamic data

| LVAD parametersb | No-to-mild MR (n = 82) | Moderate-to-severe MR (n = 29) | P-valuea |
|------------------|------------------------|-------------------------------|---------|
| **Baseline**     |                        |                               |         |
| Flow (L/min)     | 5.6 (1.0)              | 5.5 (1.2)                     | 0.49    |
| Speed centrifugal pump (rpm) | 2740 (147.6)            | 2800 (174.4)                  | 0.45    |
| Speed axial pump (rpm)  | 9400 (323.4)            | 9400 (253.9)                  | 0.41    |
| High speed categoryd | 65 (76%)                   | 26 (90%)                     | 0.13    |
| Power (watts)    | 5.2 (1.4)              | 5.1 (1.3)                     | 0.65    |
| **6 months**     |                        |                               |         |
| Flow (L/min)     | 5.2 (1.3)              | 5.0 (1.1)                     | 0.5     |
| Speed centrifugal pump (rpm) | 2760 (143.1)            | 2850 (172.2)                  | 0.81    |
| Speed axial pump (rpm)  | 9400 (297.4)            | 9400 (253.9)                  | 0.58    |
| High speed categoryd | 67 (79%)                   | 26 (90%)                     | 0.19    |
| Power (watts)    | 5.2 (1.2)              | 5.2 (1.1)                     | 0.83    |
| **Haemodynamic datad** |                      |                               |         |
| RA pressure      | 13 (9, 17)             | 14 (10, 18)                   | 0.52    |
| Systolic PAP     | 53 (45, 62)            | 54 (48, 68)                   | 0.3     |
| Diastolic PAP    | 27.6 (8.6)             | 29.8 (7.5)                    | 0.23    |
| Mean PAP         | 38.7 (9.8)             | 41.1 (10.7)                   | 0.27    |
| PCWP             | 26.3 (7.6)             | 30.6 (7.9)                    | 0.01    |
| Cardiac output by Fick (L/min) | 4.0 (3.3, 4.88)       | 3.8 (3.3, 4.5)                | 0.50    |
| Cardiac index by Fick (L/min/m²) | 1.9 (1.6, 2.5)       | 1.9 (1.7, 2.1)                | 0.39    |
| SVR (Wood units) | 17.5 (5.7)             | 18.0 (6.4)                    | 0.74    |
| PVR (Wood units) | 2.8 (2.0, 4.5)         | 2.5 (2.1, 3.2)                | 0.32    |
| PVR ≥ 3 Wood units | 37 (47%)               | 7 (25%)                      | 0.04    |
| Transpulmonary gradient | 12 (9, 15)          | 9 (8, 12)                     | 0.01    |
| **6 months**     |                        |                               |         |
| RA pressure      | 9.3 (4.9)              | 11.1 (5.4)                    | 0.17    |
| Mean PAP         | 23.3 (7.0)             | 27.4 (9.4)                    | 0.04    |
| PCWP             | 12.8 (6.2)             | 16.5 (7.8)                    | 0.03    |
| Cardiac output by Fick (L/min) | 5.4 (1.1)            | 5.2 (1.5)                     | 0.52    |
| Cardiac index by Fick (L/min/m²) | 2.6 (0.3)             | 2.5 (0.6)                     | 0.2     |
| SVR (Wood units) | 14.8 (4.4)             | 15.3 (4.9)                    | 0.7     |
| PVR (Wood units) | 1.8 (1.5, 2.5)         | 2.4 (1.3, 3.1)                | 0.45    |
| PVR ≥ 3 Wood units | 8 (16%)               | 7 (32%)                      | 0.14    |
| Transpulmonary gradient | 10 (8, 12)         | 11 (7, 13)                    | 0.88    |
| **Echo parameters** |                      |                               |         |
| Mitral regurgitation |                      |                               |         |
| No               | 1 (1%)                 | 0 (0%)                        | 0.17    |
| Mild             | 14 (17%)               | 2 (7%)                        |         |
| Moderate         | 32 (39%)               | 8 (28%)                       |         |
| Severe           | 35 (43%)               | 19 (66%)                      |         |
| Tricuspid regurgitation |                |                               |         |
| No               | 5 (5%)                 | 0 (0%)                        | 0.32    |
| Mild             | 27 (34%)               | 7 (24%)                       |         |
| Moderate         | 33 (41%)               | 14 (48%)                      |         |
| Severe           | 15 (19%)               | 8 (28%)                       |         |
| LVEDV (cc³)      | 233.95 (187.2, 308.1)   | 289.7 (206.6, 373.8)          | 0.08    |
| LVEDV indexed (cc³/m²) | 115.98 (89.6, 154.7)  | 141.8 (110.2, 173.8)          | 0.09    |
| LA volume (cc³)  | 102.96 (33.8)          | 122.39 (42.6)                 | 0.02    |
| LA volume indexed (cc³/m²) | 50.53 (16.0)         | 59.6 (20.5)                   | 0.02    |
| LVIDd (cm)       | 6.9 (1.1)              | 7.3 (1.0)                     | 0.18    |
| RVId (cm)        | 4.0 (0.8)              | 4.2 (1.0)                     | 0.44    |
| LA dimension (cm) | 4.56 (0.7)            | 5.01 (0.7)                    | <0.01   |
| **6 months**     |                        |                               |         |
| No-to-mild AR    | 69 (96%)               | 26 (90%)                      | 0.08    |
| Moderate AR      | 3 (4%)                 | 3 (10%)                       |         |
| Aortic valve opening | 40 (56%)           | 13 (45%)                      | 0.33    |
| Improvement of TR | 41 (50%)              | 14 (48%)                      | 0.87    |
| Worsening of TR  | 7 (9%)                 | 4 (14%)                       | 0.42    |

(Continues)
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Table 2 (continued)

|                      | No-to-mild MR (n = 82) | Moderate-to-severe MR (n = 29) | P-valuea |
|----------------------|------------------------|-------------------------------|----------|
| LVIDd (cm)           | 5.9 (4.8, 6.4)         | 6.7 (6.2, 7.6)                | <0.01    |
| RVIDd (cm)           | 4.1 (0.8)              | 4.0 (0.9)                     | 0.5      |
| LA dimension (cm)    | 3.9 (0.9)              | 4.7 (0.8)                     | <0.01    |

AR, aortic regurgitation; MR, mitral regurgitation; LA, left atrium; LVAD, left ventricular assist device; LVEDV, left ventricular end diastolic volume; LVEF, left ventricle ejection fraction; LVIDd, left ventricular internal diameter in diastole; PAP, pulmonary artery systolic pressure; PCWP, pulmonary capillary wedge pressure; PVR, pulmonary vascular resistance; RA, right atrium; RV, right ventricle; RVIDd, right ventricular internal diameter in diastole; SVR, systemic vascular resistance.

Wilcoxon rank-sum test for non-normal distributed variables, t-test for normal variables, and χ² test for categorical variables.

Table 3 Multivariable logistic regression for persistent moderate-to-severe MR at 6 months

| Variable                | Odds ratio | 95% CI   | P-valueb |
|-------------------------|------------|----------|----------|
| Baseline PCWP           | 0.97       | 0.89–1.05| 0.46     |
| Baseline LA dimension   | 2.86       | 1.10–7.26| 0.03     |
| Baseline LVIDd          | 0.99       | 0.51–1.76| 0.97     |
| High speed category at baseline | 0.60 | 0.16–3.07| 0.50     |
| PVR ≥ 3 Wood units      | 0.84       | 0.17–6.11| 0.32     |

LVIDd, left ventricular internal diameter in diastole; MR, mitral regurgitation; PCWP, pulmonary capillary wedge pressure; PVR, pulmonary vascular resistance.

Echocardiogram

The incidence of persistent moderate-to-severe MR at 6 months was 26% in our cohort (Figure 2). LA dimension (4.5 cm vs. 5 cm, P = 0.005) and LA volume, both crude and indexed (indexed LA volume 116 cc vs. 142 cc, P = 0.02) were

Haemodynamics

At baseline, persistent moderate-to-severe MR group had significantly elevated pulmonary capillary wedge pressure (30.6 mmHg vs. 26.3 mmHg, P = 0.01) and lower transpulmonary gradient (9 mmHg vs. 12 mmHg, P = 0.01). There was no difference in baseline RA pressures, mean pulmonary artery pressures, and Fick cardiac index between the two groups.

At 6 month follow-up, patients with persistent moderate-to-severe MR had a non-significant trend towards higher RA pressure (9 mmHg vs. 11 mmHg, P = 0.19), significantly higher mean pulmonary artery pressures (mean difference 3.2 mmHg, P = 0.034) and pulmonary capillary wedge pressure (PCWP, P = 0.033). There was a non-significant trend towards higher pulmonary vascular resistance (2.4 WU vs. 1.8 WU, P = 0.42) and higher proportion of patients with pulmonary vascular resistance > 3 WU in the group with persistent moderate-to-severe MR compared with no-to-mild MR.
the only significant echocardiographic parameter between two groups at baseline. LV volumes (crude and indexed) at baseline were higher in the group with persistent moderate-to-severe MR group, albeit statistically non-significant. The moderate-to-severe MR group had significantly higher LA (4.7 cm vs. 3.9 cm, \( P < 0.001 \)) and LV internal dimension in diastole at 6 month follow-up (Table 2).

There was no significant difference at 6 months of the severity of aortic regurgitation, with only three patients in each group in the moderate range, none with severe. There was also no difference in the rate of aortic valve opening at 6 months between the evaluated groups.

We did not have any tricuspid annuloplasty or repair in our cohort. Nonetheless, we observed that 49.5% of patients showed improvement in tricuspid regurgitation at 6 months (Table 2).

As shown in Table 3, in multivariate analysis, the only significant baseline predictors of persistent moderate-to-severe MR at 6 month was baseline LA dimension.

### Survival

We found no statistical difference in the survival curves of patients with respect to their MR severity at 6 months, 1 year, or during full follow-up (1 year survival; no-to-mild MR 85.5%, moderate-to-severe MR 87.9%, Wilcoxon \( P \)-value = 0.63, Figure 3). We found no statistical difference in the reasons for death between the patients with moderate-to-severe MR at 6 months compared with those without MR. Overall, 25% of the deaths were due to infectious processes, 35% due to intracerebral haemorrhage, 32% due to pump thrombosis, and 7% due to other reasons (lithium overdose and VT arrest). There was no difference in secondary outcome measures like LOS, hospitalizations, and composite of death, transplant, and pump exchange (Table 4). The incidence of RVF in the persistent moderate-to-severe MR group was significantly higher compared with those who had no-to-mild MR at 6 month follow-up (45% vs. 25%, \( P = 0.04 \)).

### Discussion

Our study evaluating the incidence, predictors, and significance of persistent moderate-to-severe MR corroborates findings from studies of persistent MR after cFLVAD implantation. The incidence of persistent moderate or severe MR in our cohort was 26% which is slightly higher\(^4\) than reported in the literature (6–20%). All patients had an echocardiographic-guided ramp study before discharge, and the haemodynamic improvement after cFLVAD implantation was noted regardless of MR severity. However, mean pulmonary artery pressures and PCWP were significantly higher (4.2 and 3.7 mmHg, respectively) in the persistent moderate-to-severe MR group compared with no-to-mild MR at 6 months.

Our overall incidence of RHF at 6 months was 30.6%, which is comparable to randomized clinical trials\(^4\) and national reports on the subject.\(^15,16\) We had higher proportion of patients in INTERMACS profile I, reflecting the severity of illness of the patients we encounter, likely secondary to the referral pattern of our region. It has been reported that
patients with residual MR had significantly larger post-operative RV dimensions and worse RV function.\(^6^{,8,17}\) In our study, the incidence of RHF at 6 months was significantly higher in persistent moderate-to-severe MR group by haemodynamic definition (45% compared with 25% \(P = 0.04\)). We found no difference in the RV dimensions between the groups. Contrary to other studies, we did not find an association between RVF and lower survival, which is likely because our study was underpowered to establish this association. The mechanisms of RHF in our study is likely a result of persistent pulmonary hypertension due to MR or progression of underlying cardiomyopathy. At our centre, haemodynamic and echocardiographic optimization is performed during index hospitalization for cfLVAD implantation before discharge from the hospital and at 6 month follow-up or earlier if persistent heart failure symptoms.

Patients with persistent moderate-to-severe MR at 6 months had significantly larger LA size and volumes and higher incidence of atrial fibrillation at baseline compared with patients with resolution of MR. The explanation of the findings could be due to long-standing history of heart failure with chronic moderate-to-severe MR and MR secondary to atrial fibrillation-induced LA enlargement. The proposed mechanisms of atrial fibrillation and LA enlargement-induced MR include posterior annular displacement causing impaired posteromedial leaflet coaptation, mitral leaflet remodelling, leaflet tethering due to enlarged LA, and decreased mitral annular descent.\(^18\) Patients with persistent moderate-to-severe MR had significantly larger LA and LV dimensions at 6 months. Concordantly, patients with improvement or resolution of MR had decrease in LA size (0.65 cm difference at 6 months, \(P < 0.01\)) whereas no significant difference was seen in patients with moderate-to-severe MR (0.33 cm, \(P = 0.10\)). These findings suggest that LA size decreases with improvement in MR. The underlying mechanism for persistent LA enlargement could be ineffective unloading by cfLVAD, severity and duration of MR, chronicity of LA enlargement, or combination of all.

The clinical implications of persistent moderate-to-severe MR have been mostly reported in single-centre studies. However, the prognostic significance of persistent moderate-to-severe MR in terms of survival and HF hospitalizations is not consistent across studies.\(^6^{,8}\) In the randomized MOMENTUM 3 trial, patients with HeartMate 3 were less likely to have residual MR at 1 month compared with those with HeartMate II but that residual MR did not impact 2 year mortality.\(^19\) Hence, we can only speculate that the increased use of axial flow pump in our study may have contributed to higher incidence of persistent moderate-to-severe MR. In our study, moderate-to-severe MR at 6 months was not statistically associated to survival or other endpoints like hospitalizations, LOS, or composite of death, transplant, or pump exchange.

The data on concomitant mitral valve procedures at time cfLVAD implantation are limited by retrospective and non-randomized study design. Analysis of the INTERMACS database showed decreased hospital re-admission and improved quality of life but no survival benefit with mitral valve procedures.\(^11\) Kawabori et al. reported no differences in survival, re-admissions, or post-operative RVF with concomitant MV procedures for severe MR.\(^20\) Fukuwara et al. reported less late RVF after concomitant MV procedures.\(^10\) A recent study by Imamura et al. reported increase in pulmonary pressure with concomitant MV surgeries, despite having higher CO and better response of CO at incremental LVAD speed.\(^21\) With the current evidence, it is still unclear whether mitral valve correction for severe MR should be performed at time of cfLVAD implantation.

To date, there is only a single-centre study that showed that residual MR after cfLVAD implantation might be predicted by posterior displacement of mitral leaflet coaptation on pre-operative echocardiograms.\(^22\) In our cohort, the strongest baseline predictor for persistence moderate-to-severe MR was the LA dimension at baseline. LA enlargement or remodelling due to atrial fibrillation or long-standing HF contributes to severity of MR due to factors mentioned earlier and may not reverse with unloading after cfLVAD implantation or mitral valve procedures.

Our study is not free of the limitations of the single-centre retrospective design; hence, prognostic significance of persistent MR needs to be confirmed in a prospective randomized multicentre study. We used qualitative measures to estimate MR as used in other studies. Quantitative measurements of MR may have strengthened the associations found, but some quantitative measurements of MR post-cfLVAD may be challenging due to artefacts.\(^23\) Echocardiographic parameters of RV systolic function like tricuspid annular plane systolic excursion and RV fractional area change were not consistently available. However, we reported invasive haemodynamic data, which are more sensitive than echocardiographic estimation of RV systolic function. Long-term prospective study regarding factors responsible for persistent MR, prognostic significance in terms of survival, RVF, re-hospitalizations, recovery, optimal LV unloading without compromising RV function, and quality of life in these patients are needed before decision making regarding mitral valve corrective procedures can be made. Finally, given the retrospective nature of this study, interventions (surgically, medically, or with different LVAD parameters) to improve MR were not evaluated.

In conclusion, LVAD implantation effectively improves MR severity in end-stage heart failure patients. Persistent moderate-to-severe MR was associated with significantly higher mean pulmonary pressure, PCWP, and RV failure in our study. There was no effect on long-term survival with persistent MR during follow-up.
Conflict of interest

None declared.

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