Cardiac remodeling in patients with centrifugal left ventricular assist devices assessed by serial echocardiography

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Abstract

Aim: The aim of the study was to characterize the remodeling process in a large cohort of patients supported with a centrifugal left ventricular assist device (cfLVAD) by standardized serial echocardiography.

Methods and Results: From 3/2018 all cfLVAD patients underwent transthoracic echocardiography at 6 and 12 months after implantation using a standardized protocol. A total of 512 echocardiograms were reviewed (216 preoperative, 156 at 6 months, 140 at 12 months). While on cfLVAD support, left ventricular (LV) diameter decreased (p < .001). LV ejection fraction (LVEF) and LV fractional area change improved (p < .001). Potential for cfLVAD explantation (as defined by an LVEF ≥45% and opening of the aortic valve [AV]) was seen in nine patients at 6 and 21 patients at 12 months. The tricuspid annular excursion decreased significantly, while the right ventricular fractional area change did not change. Tricuspid regurgitation (TR) and mitral regurgitation (MR) improved significantly during LVAD support. Opening of the AV was seen in >64% of the patients at 6 months and in 66% at 12 months. Moderate aortic regurgitation (AR) was rare with 3.8% at 6 months but increased with the duration of cfLVAD support (8.5% at 12 months). We found no significant difference in echocardiographic parameters between patients supported with a HeartWare HVAD™ or a HeartMate 3™ device.

Conclusion: LVAD therapy can lead to reverse LV remodeling and improvement of MR and TR. However, right ventricular function does not improve and prevalence of AR progressively increases during mechanical support.

Keywords
echocardiography, LVAD, left ventricular assist device

1 INTRODUCTION

The latest generation of centrifugal left ventricular assist devices (cfLVAD) yields excellent results with regards to outcome, complication profile, functional status, and quality of life.1 Therefore, the use of cfLVADs for the treatment of advanced heart failure has increased significantly in recent years.2 Echocardiography plays an important role in the clinical care of patients under long-term mechanical circulatory support and is used for surveillance, pump speed optimization, troubleshooting, and evaluation of myocardial recovery.3 There are some important publications dealing with echocardiographic results in patients with continuous-flow left ventricular assist devices; however,
the number of patients included is low and most of the data originate from patients supported with axial flow pumps.\(^5\)\(^6\)

The aim of our study was to evaluate the echocardiographic results of a large population of patients supported with the cfLVADs HeartWare HVAD™ or HeartMate 3™ who underwent standardized echocardiography at 6 and 12 months after implantation.

2 | METHODS

2.1 | Study population

Between March 2018 and January 2020, 219 patients without congenital heart disease underwent implantation of a cfLVAD at our center. The patients postoperatively received a standardized echocardiographic assessment every 6 months in the outpatient clinic. The assessment also included an interview, physical examination, laboratory tests, ECG, and a 6-min walk test. Transthoracic echocardiography was performed using a standardized protocol (see below).

All data were captured and analyzed in a RedCap database. The study was reviewed and approved by the ethics committee at Charité University (EA2/229/19). The ethics committee waived the need for informed written consent for publication of the study data.

2.2 | Surgical technique

In the majority of cases, LVAD implantation was performed via median sternotomy. In patients with previous cardiac surgery and a status post sternotomy, LVAD implantation was performed via left lateral thoracotomy. The implantation was carried out primarily using off-pump techniques; however, in case of hemodynamic instability, circulatory support was provided by ECLS. If the patients were already on mechanical circulatory support with ECLS or Impella® preoperatively, the support was continued during the LVAD implantation. If concomitant intra-cardiac procedures (e.g., valve surgery, left ventricular thrombectomy, or closure of patent foramen ovale) were necessary, the implantation was performed employing cardiopulmonary bypass.

2.3 | Device and patient management

The device speed was clinically adjusted to optimize flow and organ perfusion prior to discharge and at every outpatient visit. During the hospital stay and in the later follow-up, echocardiography was performed serially to evaluate the position of the inter-ventricular septum as well as the left ventricular (LV) and right ventricular (RV) size and function. The goals of adjusting the device speed were to avoid suction events and to achieve not only a mid-position of the inter-ventricular septum but also, to the best extent possible, periodic valve opening. Anticoagulation with warfarin plus antiplatelet therapy was administered as recommended by current guidelines.\(^6\)\(^7\) All patients received heart failure medication as recommended by the heart failure guide-lines. Management of blood pressure included a target mean arterial pressure lower than 80 mmHg. Loop diuretics were given in case of fluid overload.

2.4 | Echocardiography

Transthoracic echocardiographic results were obtained up to ten days preoperatively. For the 6- and the 12-month follow-up, echocardiography was performed by seven experienced physicians as per current guideline recommendations and following a standardized protocol (see Supplementary Table S1).\(^3\)\(^8\) The degree of aortic and mitral regurgitation was quantified by measuring 2D vena contracta width (VCW). AR was rated as mild if the VCW was <3 mm or as severe if the VCW was >6 mm. To quantify tricuspid regurgitation, the vena contracta was measured in two planes. A spectral Doppler of the hepatic veins was additionally performed to detect systolic flow reversal. All postoperative echocardiographies were performed using Vivid E9, Vivid S70, or Vivid E95 ultrasound systems (GE Healthcare).

2.5 | Statistical analysis

Continuous data are summarized as mean and standard deviation or, in case of skewed data, as median and interquartile range (IQR). For categorical data, frequencies and percentages are reported. Comparisons prior to surgery versus at 6 months or between 6 and 12 months were performed using a paired t-test or the Wilcoxon signed-rank test. Comparisons between the HeartWare HVAD™ and HeartMate 3™ devices were performed using a t-test or the Wilcoxon signed-rank test. A p-value of less than .05 was considered statistically significant. In the case of multiple testing, the Bonferroni post-hoc test was applied to adjust the p-values. Alluvial plots were used to visualize the development of valvular regurgitation.

Calculations and plotting were performed using R version 4.0.3 software (R Foundation for Statistical Computing, Vienna, Austria).

3 | RESULTS

3.1 | Study population

The patients underwent implantation of a HeartWare HVAD™ (n = 155; 70.8%) or a HeartMate 3™ (n = 64; 29.2%) device. For baseline characteristics of all patients see Table 1.

3.2 | Preoperative status and LVAD implantation

Most of the patients were in Interagency Registry for Mechanically Assisted Circulation (INTERMACS) profile 1 (n = 60; 27.4%), INTERMACS profile 2 (n = 55; 25.1%), INTERMACS profile 3 (n = 48; 21.9%), INTERMACS profile 4 (n = 52; 23.7%), or INTERMACS profile 5 (n = 4; 1.8%). 128 patients (58.4%) received inotropic support and 64 patients
TABLE 1 Preoperative characteristics (n = 219)

| Characteristic                  | Value                  |
|--------------------------------|------------------------|
| Age (years), n = 219           | 57.5 ± 11.5            |
| Male, n = 219                  | 189 (86.3%)            |
| BMI (kg/m²), n = 219           | 27.4 ± 5.59            |
| BSA (m²), n = 219              | 2.05 ± .24             |
| Hypertension, n = 214          | 144 (65.8%)            |
| Diabetes, n = 219              | 82 (37.4%)             |
| COPD, n = 219                  | 51 (23.3%)             |
| Cardiomyopathy, n = 219        | Idiopathic dilated    |
|                               | cardiomyopathy 97      |
|                               | (44.3%)                |
|                               | Inflammatory (positive |
|                               | histology) 5 (2.3%)    |
|                               | Ischemic cardiomyopathy|
|                               | 112 (51.1%)            |
|                               | Others 5 (2.3%)        |
| Previous cardiac surgery, n = 219 | 46 (21.0%)             |
| CIED, n = 210                  | No: 78 (35.6%)         |
|                               | ICD: 80 (36.5%)        |
|                               | CRT: 12 (3.2%)         |
|                               | CRT-D: 45 (24.7%)      |
| History of atrial fibrillation, n = 219 | 112 (51.1%)         |
| GFR (ml/min/1.73 m²), n = 212  | 55.2 ± 27.5            |
| Bilirubin (mg/dl), median [IQR], n = 212 | 1.668–1.725       |
| Hematocrit (%), n = 213        | 33.6 ± 6.8             |

Note: Values are expressed as mean ± standard deviation, median (interquartile range), or n (%).
Abbreviations: BMI, body mass index; BSA, body surface area; COPD, chronic obstructive pulmonary disease; CIED, cardiovascular implantable electronic device; ICD, implantable cardioverter defibrillator; CRT, cardiac resynchronization therapy; CRT-D, cardiac resynchronization therapy®-defibrillator; GFR, glomerular filtration rate.

were on temporary mechanical circulatory support with ECMO (n = 34; 15.5%) or Impella® (n = 30; 13.7%). 20.1% (n = 44) were intubated and ventilated before the implantation.

Twenty patients underwent concomitant valvular surgery (seven AV replacements, 12 tricuspid valve repairs, one tricuspid valve replacement).

Postoperatively, 56 patients (26%) required re-thoracotomy mainly due to bleeding, and 23 patients (10.5%) received temporary right ventricular mechanical circulatory support (RVAD). Only seven patients who underwent RVAD implantation survived and were seen again at 6 months. Only five of them were alive after 12 months.

3.3 | Follow-up

One hundred fifty-six patients presented for the 6-month follow-up (median 187 days [177–210]) and 144 patients at the 12-month follow-up (median 371 days [357–396]). During the above period, 62 patients died, seven underwent transplantation, and ten were lost to follow-up. Most patients were in New York Heart Association Class I or II (78.5% at 6 months, 72.7% at 12 months) with a mean arterial pressure of 81.4 ± 11.5 mmHg and 82.1 ± 11.2 mmHg, respectively. All received intensive medical heart failure treatment. For details and device settings see Table 2.

3.4 | Echocardiography

A total of 512 echocardiograms were reviewed for the study (216 preoperative, 156 at 6 months, and 140 at 12 months). In three patients no preoperative echocardiographic examination was available. All echocardiograms at 6 and 12 months followed the standardized protocol (Supplementary Table S1). There was no significant difference in echocardiographic results between patients supported with a HeartWare HVAD™ or a HeartMate 3™ device (Supplementary Tables S2A,S2B,S2C and S3A,S3B,S3C).

- **Left ventricular size and function**

Preoperatively, there was severe dilation of the left ventricle with a left ventricular end-diastolic diameter (LVEDD) of 66.2 ± 10.9 mm and a left ventricular end-diastolic volume of 251 ± 104 ml. The left ventricular systolic function was severely impaired with a left ventricular ejection fraction of 20% (IQR 15.0–25.0). During circulatory support, the LVEDD and the left ventricular end-diastolic area decreased significantly (p < .001). The end-systolic diameter and the end-systolic area also decreased (p < .001). The systolic function, estimated visually and measured using the fractional area change, showed a significant improvement. The left ventricular ejection fraction improved from 20.0% (IQR 15.0–24.0) to 25.0% (IQR 20.0–35.0) at 6 months and remained stable at 25.0% (IQR 15.0–40.0) at 12 months. At 6 months, nine patients had an ejection fraction ≥45% and an AV opening intermittently or with every heartbeat. At 12 months, 21 patients had an ejection fraction ≥45% and an AV opening intermittently or with every heartbeat. The left ventricular fractional area change (LV-FAC) improved from 13.1% (IQR 8.4–16.3) to 19.9% (13.1–30.7) at 6 months and remained stable at 20.2% (IQR 11.7–40.7) at 12 months. For details see Table 3.

- **Right ventricular size and function**

LVAD implantation led to a significant decrease in tricuspid regurgitation peak gradient. There was no significant change in the proximal right ventricular outflow tract diameter (RVOTprox), the right ventricular end-diastolic area (RV-EDA), and the right ventricular end-systolic area (RV-ESA). Only the basal right ventricular diameter (RVD1) decreased significantly during circulatory support from 45.3 ± 8.48 mm to 41.4 ± 6.84 mm at 6 months and remained stable at 12 months. Postoperatively, the tricuspid annular excursion (TAPSE) decreased significantly while the global parameters of right ventricular
**TABLE 2** Clinical status and pump settings at 6 months and 12 months

|                          | 6 months                  | 12 months                 |
|--------------------------|----------------------------|----------------------------|
| **NYHA class**           | I 67 (43.5%)               | I 47 (32.9%)               |
|                          | II 54 (35.1%)              | II 57 (39.8%)              |
|                          | III 31 (20.1%)             | III 36 (25.2%)             |
|                          | IV 2 (1.3%)                | IV 3 (2.1%)                |
| **Mean arterial pressure (mmHg)** | 81.4 ± 11.5               | 82.1 ± 11.2               |
| **Rhythm**               | Sinus rhythm 103 (67.4%)  | Sinus rhythm 88 (62.0%)    |
|                          | Atrial fibrillation 23 (14.9%) | Atrial fibrillation 16 (11.3%) |
|                          | Pacer rhythm 26 (17.0%)    | Pacer rhythm 35 (24.6%)    |
|                          | Others 1 (0.7%)            | Others 3 (2.1%)            |
| **Heart failure medication** | Beta-blockers 138 (88.5%) | Beta-blockers 124 (86.7%)  |
|                          | ACE 23 (14.8%)             | ACE 17 (11.9%)             |
|                          | ARB 23 (14.7%)             | ARB 21 (14.7%)             |
|                          | ARNI 104 (66.7%)           | ARNI 98 (68.5%)            |
|                          | Aldosterone antagonists 131 (84.0%) | Aldosterone antagonists 111 (52.4%) |

HeartWare

|                          | N = 104                    | N = 92                     |
|--------------------------|----------------------------|----------------------------|
| **Speed (RPM)**          | 2670 ± 304                 | 2680 ± 300                 |
| **Flow (L/min)**         | 4.73 ± .57                 | 4.72 ± .68                 |
| **Power (Watts)**        | 4.15 ± .68                 | 4.17 ± .75                 |

HeartMate 3™

|                          | N = 52                     | N = 52                     |
|--------------------------|----------------------------|----------------------------|
| **Speed (RPM)**          | 5510 ± 245                 | 5490 ± 237                 |
| **Flow (L/min)**         | 4.65 ± .47                 | 4.63 ± .58                 |
| **Power (Watts)**        | 4.22 ± .46                 | 4.20 ± .44                 |

Note: Values are expressed as n (%) or mean ± standard deviation.

Abbreviations: NYHA, New York Heart Association; ACE, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; ARNI, angiotensin receptor-neprilysin inhibitors; RPM, rotations per minute

function, fractional area change, and visually estimated ejection fraction remained stable. For details see Table 4.

**Valvular function**

At 6 months the AV did not open during the cardiac cycle in 35.7% of the patients, in 9.1% the AV opened intermittently, and in 55.2% it opened with every cardiac cycle. At 12 months the rates were comparable, with 34.0%, 8.0%, and 58.0%, respectively. Moderate AR was detected in 3.8% of the patients at 6 months and in 8.5% of the patients at 12 months. None of the patients who underwent AV replacement showed AR at 6 or 12 months.

Mitral regurgitation and tricuspid regurgitation decreased impressively during mechanical circulatory support. Moderate to severe mitral regurgitation was detectable in only 3.9% of the patients at 6 months and in 4.3% at 12 months. Moderate to severe tricuspid regurgitation was detected in 12.2% of the patients at 6 months and in 10.9% at 12 months. Six of the 12 patients who underwent tricuspid repair survived and were seen again at 6 months. Five of them had an excellent result with no or mild TR. For details of all patients see Table 5. For a visualization of the valvular insufficiencies and their changes over time see Figures 1, 2, and 3.

4 | DISCUSSION

To our knowledge, this is the largest study of echocardiographic results in patients with centrifugal, continuous-flow left ventricular assist devices.

Although guidelines provide a general framework for the echocardiographic assessment and management of patients with continuous-flow LVADs, the use of echocardiography and the values assessed still vary widely between centers. Furthermore, the majority of the reported studies were performed in patients on axial-flow LVADs (afLVAD), whereas the majority of LVADs implanted since 2019 were centrifugal-flow devices. Both afLVADs and cfLVADs are continuous-flow pumps that unload the left ventricle during systole and diastole. However, the measurement of device flow and pulsatility, programmed...
**FIGURE 1**  Alluvial flow diagram illustrating the development of aortic regurgitation (AR) over time. 0, no AR; 1, mild AR; 2, mild to moderate AR; 3, moderate AR

**FIGURE 2**  Alluvial flow diagram illustrating the development of mitral regurgitation over time. 0, no or mild mitral regurgitation; 1, mild to moderate or moderate mitral regurgitation; 2, moderate to severe or severe mitral regurgitation
artificial pulsatility, and the optimal speed differs between manufacturers and device types. Furthermore, echocardiography in patients with cfLVADs is even more challenging than in patients with aLVADs. The device itself is located at the apex and is larger than the inflow cannula of axial flow pumps. This often hinders apical 4-chamber, 2-chamber and 3-chamber views without foreshortening. Also, the device causes characteristic Doppler artifacts that may preclude sufficient Doppler interrogation.

We implemented a standard protocol for LVAD surveillance that includes a limited number of measures that are assessable in most patients with cfLVAD (see Supplementary Table S1).

Note: Values are expressed as mean ± standard deviation or median [interquartile range].

Abbreviations: IVS, interventricular septum thickness; LVEDD, left ventricular end-diastolic diameter; LVEDV, left ventricular end-diastolic volume; LVESD, left ventricular end-systolic diameter; FS, fractional shortening; PW, posterior wall thickness; LVEF vis, visually estimated left ventricular ejection fraction; RV-ESA, right ventricular end-systolic area; LVESV, left ventricular end-systolic volume; LVEF (Simpson), left ventricular ejection fraction measured by Simpson’s rule.

### TABLE 3  Echocardiography I, left ventricle

|                         | Pre-OP            | 6 months       | 12 months       | P (a vs. b) | P (b vs. c) |
|-------------------------|-------------------|----------------|-----------------|-------------|-------------|
| IVS (mm)                | 10.2 ± 2.44 (n = 200) | 10.9 ± 2.62 (n = 152) | 10.5 ± 2.47 (n = 134) | .004        | .160        |
| LVEDD (mm)              | 66.2 ± 10.9 (n = 204) | 55.8 ± 12.7 (n = 155) | 57.9 ± 12.0 (n = 139) | <.001       | .001        |
| LVESD (mm)              | 60.4 ± 12.3 (n = 175) | 49.2 ± 13.8 (n = 148) | 50.4 ± 14.3 (n = 131) | <.001       | 1           |
| FS (%)                  | 8 [5–11] (n = 175)   | 10.3 [7–16.7] (n = 147) | 11.0 [6.0–20.0] (n = 131) | .051        | .366        |
| PW (mm)                 | 10.3 ± 2.54 (n = 196) | 10.9 ± 2.22 (n = 151) | 10.5 ± 2.16 (n = 134) | .092        | .545        |
| LV-EDA (cm²)            | 40.0 [32.0–51.3] (n = 108) | 27.0 [19.9–37.0] (n = 99) | 29.0 [20.3–41.8] (n = 12) | <.001       | 1           |
| LV-ESA (cm²)            | 37.0 [28.9–35.5] (n = 108) | 21.0 [14.8–31.0] (n = 99) | 22.0 [11.3–35.8] (n = 86) | <.001       | 1           |
| LV-FAC (%)              | 13.1 [8.4–16.3] (n = 108) | 19.9 [13.1–30.7] (n = 98) | 20.2 [11.7–40.7] (n = 86) | <.001       | 1           |
| LVEF vis (%)            | 20.0 [15.0–25.0] (n = 207) | 25.0 [20.0–35.0] (n = 153) | 25.0 [15.0–40.0] (n = 139) | <.001       | 1           |
| LVEDV                   | 251 ± 104 (n = 166)   | 204 ± 94 (n = 152)    |                  |             |             |
| LVESV (ml)              |                   | 204 ± 94 (n = 152)    |                  |             |             |
| LVEF (Simpson)          | 21 ± 7 (n = 159)     |                  |                  |             |             |

Note: Values are expressed as mean ± standard deviation or median [interquartile range].

Abbreviations: RVOTprox, proximal diameter of right ventricular outflow tract; RVD1, basal right ventricular linear dimension; RV-EDA, right ventricular end-diastolic area; RV-ESA, right ventricular end-systolic area; RV-FAC, right ventricular fractional area change; RV-EF vis, visually estimated right ventricular ejection fraction; RV-EDA, right ventricular end-diastolic area; RV-ESA, right ventricular end-systolic area; RV-FAC, right ventricular fractional area change; RV-EF, right ventricular end-diastolic volume; RVESV, right ventricular end-systolic volume; RV-EF vis, visually estimated right ventricular ejection fraction; TRPG, tricuspid regurgitation peak gradient.

### TABLE 4  Echocardiography II, right ventricle

|                         | Pre-OP           | 6 months       | 12 months       | P (a vs. b) | P (b vs. c) |
|-------------------------|------------------|----------------|-----------------|-------------|-------------|
| RVOTprox (mm)           | 36.4 ± 7.54 (n = 192) | 35.0 ± 6.48 (n = 153) | 34.9 ± 6.24 (n = 131) | .845        | 1           |
| RVD1 (mm)               | 45.3 ± 8.48 (n = 192) | 41.4 ± 6.84 (n = 133) | 41.6 ± 6.89 (n = 106) | .002        | 1           |
| RV-EDA (cm²)            | 28.5 [22.0–33.0] (n = 116) | 23.9 [19.9–30.0] (n = 71) | 25.0 [21.0–28.0] (n = 71) | 1           | 1           |
| RV-ESA (cm²)            | 21.0 [15.5–26.0] (n = 115) | 15.0 [13.1–21.2] (n = 71) | 16.0 [14.00–20.0] (n = 71) | 1           | 1           |
| RV-FAC (%)              | 25.8 [19.0–33.3] (n = 115) | 33.3 [27.3–40.7] (n = 71) | 33.3 [27.6–39.3] (n = 71) | .442        | 1           |
| TAPSE (mm)              | 16.0 ± 4.48 (n = 153) | 14.0 ± 3.60 (n = 128) | 13.4 ± 3.20 (n = 99) | <.001       | 1           |
| RV-EF vis (%)           | 40.0 [37.3–50.0] (n = 196) | 45.0 [40.0–55.0] (n = 151) | 50.0 [45.00–55.0] (n = 128) | .001        | 1           |
| TRPG (mmHg)             | 34.2 ± 11.6 (n = 173) | 21.0 ± 6.35 (n = 70) | 23.6 ± 8.40 (n = 68) | <.001       | 1           |
### TABLE 5  Heart valves

|        | Pre-OP       | 6 months     | 12 months     |
|--------|--------------|--------------|---------------|
| **AR** | None 178 (85.6 %) | None 69 (44.2 %) | None 56 (39.7 %) |
|        | I 20 (9.6 %)  | I 70 (44.9 %) | I 59 (41.8 %)  |
|        | I-II 5 (2.4 %) | I-II 11 (7.1 %) | I-II 14 (9.9 %) |
|        | II 3 (1.4 %)  | II 6 (3.8 %)  | II 12 (8.5 %)  |
|        | II-III 2 (1.0 %) |             |               |

| **AV opening** | 100% | No 55 (35.7 %) | Intermittently 14 (9.1 %) | No 47 (34.0 %) | Every cycle 85 (55.2 %) | Every cycle 80 (58.0 %) |
|----------------|------|----------------|--------------------------|---------------|-------------------------|-------------------------|

| **MR** | None 18 (8.5 %) | None 87 (56.5 %) | None 65 (47.2 %) |
|        | I 48 (22.8 %)   | I 39 (25.3 %)    | I 47 (34.1 %)      |
|        | I-II 27 (12.8 %) | I-II 12 (7.8 %)  | I-II 10 (7.2 %)    |
|        | II 50 (23.7 %)  | II 10 (6.5 %)    | II 10 (7.2 %)      |
|        | II-III 23 (10.9 %) | II-III 4 (2.6 %) | II-III 1 (7 %)     |
|        | III 45 (21.3 %) | III 2 (1.3 %)    | III 5 (3.6 %)      |

| **TR** | None 33 (15.4 %) | None 58 (37.2 %) | None 40 (29.0 %) |
|        | I 54 (25.2 %)   | I 53 (33.9 %)    | I 62 (44.9 %)     |
|        | I-II 29 (13.6 %) | I-II 10 (6.4 %)  | I-II 11 (8.0 %)   |
|        | II 44 (20.6 %)  | II 16 (10.3 %)   | II 10 (7.2 %)     |
|        | II-III 17 (7.9 %) | II-III 5 (3.2 %) | II-III 3 (2.2 %)  |
|        | III 37 (17.3 %) | III 14 (9.0 %)   | III 12 (8.7 %)    |

Values are expressed as n (%). AR, aortic regurgitation; AV open, opening of the aortic valve; MR, mitral regurgitation; TR, tricuspid regurgitation.

**FIGURE 3**  Alluvial flow diagram illustrating the development of tricuspid regurgitation over time. 0, no or mild tricuspid regurgitation; 1, mild to moderate or moderate tricuspid regurgitation; 2, moderate to severe or severe tricuspid regurgitation.
Left ventricular unloading during cLVAD support leads to a significant decrease in left ventricular diameter. This is in line with the results of former studies dealing with axial pumps.\(^4,5,9\) Although the left ventricle is supported by the device, it is important to assess left ventricular systolic function. This is of particular relevance if myocardial recovery is possible and LVAD explantation may be considered as a therapeutic option. However, a decrease in LV size and an improvement in LVEF could be due to LV unloading rather than a reverse remodeling process and requires further assessment.

Left ventricular planimetry in the 4-chamber or the 2-chamber view to measure the volume and calculate the ejection fraction is often not feasible in patients with cLVADs. We therefore focused on left ventricular area measurements in the parasternal short-axis view and calculated the fractional area change as suggested by current guidelines.\(^3\) The left ventricular end-diastolic and the left ventricular end-systolic area decreased significantly. The median left ventricular fractional area change (LV-FAC) showed a mild but significant improvement. This is consistent with the results in patients with aLVAD.\(^4,5\) It is important to consider the afterload when looking at systolic function. A rate of about 65% of patients with intermittent or regular opening of the AV can be considered high when compared with other studies.\(^4,5,9\) Many groups regard an ejection fraction \(\geq 45\%\) with opening of the AV as an important criterion when evaluating the possibility of LVAD explantation.\(^10,11\) This constellation was found in nine patients at 6 months and in 21 patients at 12 months. Consequently, 14.6% of the patients who underwent echocardiography at 12 months showed a significant left ventricular improvement and were subsequently evaluated for potential weaning following a standardized protocol.\(^11\)

LVAD implantation decompresses the pulmonary circulation and subsequently decreases pulmonary artery pressure. This may lead to reverse remodeling of the right ventricle.\(^12,13\) Despite a significant decrease in tricuspid regurgitation peak gradient, we found no relevant decrease in right ventricular dimensions with an unchanged proximal RVOT diameter and a stable right ventricular end-diastolic and end-systolic area. Tricuspid annular excursion (TAPSE) is an established measure of longitudinal right ventricular function. In a study dealing mainly with patients who underwent aLVAD implantation, mechanical circulatory support led to an increase in TAPSE.\(^13\) It has also been shown that cardiac surgery can cause a decrease in longitudinal right ventricular function which may be compensated by increased transversal motion.\(^14,15\) In our study TAPSE significantly decreased after cLVAD implantation but right ventricular fractional area change remained stable, indicating a significant change in the right ventricular contractile pattern.

Preoperative and postoperative tricuspid regurgitation (TR) is associated with poor survival and may be a risk factor for the development of early and late right heart failure.\(^16–18\) Preoperative TR was very common in this study (see Table 4 and Figure 2). Only 13 patients underwent concomitant tricuspid valve repair; one patient underwent tricuspid valve replacement. However, mechanical circulatory support led to an impressive improvement in tricuspid regurgitation. This may be explained by the decrease in right ventricular afterload caused by pulmonary decompression. Interestingly, many patients who had ms-sTR during the follow-up had no relevant TR preoperatively (see Figure 2). One cause could be a leftward shift of the septum during support, leading to dilation of the tricuspid annulus, as is often seen in patients with severe left ventricular unloading.

Mitral regurgitation was common preoperatively. With aggressive heart failure therapy and the above device settings, preoperative mitral regurgitation improved dramatically. Only 3.9% of the patients exhibited moderate to severe or severe mitral regurgitation at 6 months, compared to 4.3% at 12 months.

The development and progression of AR during LVAD support has been demonstrated in many studies.\(^19–21\) It causes retrograde flow from the aorta into the left ventricle resulting in a decreased forward cardiac output and an increased capillary wedge pressure.\(^22\) Moderate or severe AR impacts not only hemodynamics but also hospitalizations and survival in patients on continuous-flow LVAD support.\(^19,23\) In most studies the severity of AR is estimated by eyeballing. In our study the VCW was measured in a focused, parasternal long-axis view. For the quantification, the cut-off values (<3 mm and >6 mm) suggested by current guidelines were applied. With optimized pump speed, AV opening was seen in >64% of the patients at 6 months and in 66% at 12
**VIDEO 1**  Parasternal long axis view. Mild aortic regurgitation early postoperatively

**VIDEO 2**  Parasternal long axis view. Progressive regurgitation of the aortic valve
months. Thanks to these measures, moderate AR was rare, with 3.8% at 6 months, but increased with the duration of left ventricular support (8.5% at 12 months) (Figures 1, 4, Videos 1, 2, 3). The rate of AR is slightly lower than the one mentioned in large registries where the rate of AV opening and details of AR quantification are unknown.19

5 | LIMITATIONS

The limitations of echocardiography in patients with centrifugal LVAD are outlined above. Although all examiners were asked to include only measures that are reliable and reproducible, echocardiography in patients with cfLVAD cannot be compared with echocardiography in patients with other heart diseases. Furthermore, no core lab was involved in our study and inter-observer variability cannot be excluded completely.

Some centers prefer routine ramp protocols for LVAD speed optimization.24 This may be performed before discharge and under surveillance echocardiography. However, ramp protocols are complex and time-consuming, and their impact on the outcome is unknown. Furthermore, ramp protocols are performed under standardized conditions. Exercise, changes in blood pressure, and fluid status may have a significant effect on the results and may change rapidly during the follow-up. In addition, a commonly recognized definition of the optimum speed is still lacking.3,47 Our goals of speed adjustment are mentioned above. Usually, the LVAD speed was adjusted immediately after echocardiography. Ramp tests were performed only in difficult cases, such as in patients with moderate or severe regurgitation.

6 | CONCLUSION

LVAD therapy can lead to reverse left ventricular remodeling and improvement of mitral and tricuspid regurgitation. However, right ventricular function does not improve and prevalence of AV regurgitation progressively increases during mechanical support.

CONFLICT OF INTEREST STATEMENT AND SOURCES OF FUNDING

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher’s website.

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