

Retrospective Study

## Short and long term outcomes of 200 patients supported by continuous-flow left ventricular assist devices

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### Abstract

**AIM:** To study the institutional experience over 8 years with 200 continuous-flow (CF) - left ventricular assist devices (LVAD).

**METHODS:** We evaluated our institution's LVAD database and analyzed all patients who received a CF LVAD as a bridge to transplant (BTT) or destination therapy from March 2006 until June 2014. We identified 200 patients, of which 179 were implanted with a HeartMate II device (Thoratec Corp., Pleasanton, CA) and 21 received a Heartware HVAD (HeartWare Inc., Framingham, MA).

**RESULTS:** The mean age of our LVAD recipients was 59.3 years (range 17-81), 76% (152/200) were males, and 49% were implanted for the indication of BTT. The survival rate for our LVAD patients at 30 d, 6 mo, 12 mo, 2 years, 3 years, and 4 years was 94%, 86%, 78%, 71%, 62% and 45% respectively. The mean duration of LVAD support was 581 d (range 2-2595 d). Gastrointestinal bleeding (was the most common adverse event (43/200, 21%), followed by right ventricular failure (38/200, 19%), stroke (31/200, 15%), re exploration for bleeding (31/200, 15%),

ventilator dependent respiratory failure (19/200, 9%) and pneumonia (15/200, 7%). Our driveline infection rate was 7%. Pump thrombosis occurred in 6% of patients. Device exchanged was needed in 6% of patients. On multivariate analysis, preoperative liver dysfunction, ventilator dependent respiratory failure, tracheostomy and right ventricular failure requiring right ventricular assist device support were significant predictors of post LVAD survival.

**CONCLUSION:** Short and long term survival for patients on LVAD support are excellent, although outcomes still remain inferior compared to heart transplantation. The incidence of driveline infections, pump thrombosis and pump exchange have declined significantly in recent years.

**Key words:** Left ventricular assist device; Outcomes; Heart failure; Continuous-flow

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**Core tip:** In this paper, we report our experience over the last 8 years with implanting continuous-flow left ventricular assist devices (LVADs). The aim of this analysis is to identify common occurring complications after LVAD implantation and identify areas for potential improvement in both patient management and selection. This is the largest single institutional LVAD experience that has been published, to the best of our knowledge.

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## INTRODUCTION

Continuous-flow left ventricular assist devices (CF LVADs) are now the standard treatment for patients with end stage heart failure refractory to medical management<sup>[1-3]</sup>. The shortage of heart donors and the overall minimal therapeutic impact of heart transplantation on advanced heart failure have certainly accelerated the recent advances made in LVAD technology. In 2001, the landmark REMATCH trial demonstrated superiority of the pulsatile-flow HeartMate XVE vs best medical management, although these devices were still limited by their large size, reduced durability, significant and frequent postoperative complications<sup>[4]</sup>. Newer generation CF LVAD has by and large overcome most of the limitations of the pulsatile devices. Following the HeartMate II (HM II) trial<sup>[1]</sup>, continuous flow devices

were approved by the FDA, initially for bridge to transplantation (BTT) and subsequently for destination therapy (DT). Increasing clinical implementation and a multidisciplinary approach between cardiac surgeons and cardiologists to postoperative LVAD therapy have in recent years further improved LVAD outcomes. Despite these significant advances, LVAD implantations are still associated with significant morbidity, especially in the early postoperative period<sup>[5,6]</sup>. Improvements are still required if LVADs are to become a plausible alternative to heart transplantation or a therapeutic option for less sick patients in earlier stages of heart failure. The aim of our study was to investigate our institution's 8-year experience with CF LVADs and to analyze short and long term results with a goal to identify areas of improvement.

## MATERIALS AND METHODS

This retrospective study was approved by our health system's Institutional Review Board. We reviewed our institution's LVAD dataset and analyzed all patients who received a CF LVAD as a BTT or DT from March 2006 until June 2014. We identified 200 patients, of which 179 were implanted with a HeartMate II device (Thoratec Corp., Pleasanton, CA) and 21 received a Heartware HVAD (HeartWare Inc., Framingham, MA).

### Patient data

Multiple patient comorbidities from our LVAD database were analyzed. Pre and postoperative hemodynamic measurements were also evaluated. Finally we examined post LVAD related complications. We defined ventilator dependent respiratory failure (VDRF) as inability to extubate after 7 d right ventricular (RV) failure was considered for patients who needed a RVAD or who required inotropes in excess of two weeks in order to support the RV. Defining acute renal failure, was based on the RIFLE criteria (two fold increase in creatinine or a decline in glomerular filtration rate by half).

### Statistical analysis

Patient data were compared between patients who received LVAD as DT or BTT using chi-squared tests for nominal data and Wilcoxon two-sample tests for continuous variables. Nominal data were reported as count and percent whereas as mean and standard deviations were calculated for continuous variables. For counts that were not large, the fisher exact tests were utilized. Kaplan Meier curves were used to generate estimates of survival and Cox proportional hazards models were used to assess the various covariates effect on survival. A backward stepwise routine was used to generate the most parsimonious model where all variables included were significant. Statistical significance was considered  $P < 0.05$ . SAS 9.2 was utilized for our analysis.

**Table 1 Patient demographics and comorbidities**

| Variable                            | Total (n = 200) | BTT (n = 98)  | DT (n = 102)   | P value |
|-------------------------------------|-----------------|---------------|----------------|---------|
| Age (yr)                            | 54.3 ± 12.5     | 50.1 ± 12.8   | 58.4 ± 10.7    | 0.001   |
| Gender                              |                 |               |                |         |
| Female                              | 24% (48/200)    | 25.5% (25/98) | 22.8% (23/102) | 0.652   |
| Male                                | 76% (151/200)   | 74.5% (73/98) | 76.5% (78/102) |         |
| Race                                |                 |               |                |         |
| AA                                  | 46% (92/200)    | 39.8% (39/98) | 52% (53/102)   | 0.375   |
| Caucasian                           | 54% (108/200)   | 54.1% (53/98) | 42.4% (47/102) |         |
| Etiology of heart failure           |                 |               |                |         |
| ICM                                 | 52% (104/200)   | 29% (28/98)   | 74.5% (76/102) | 0.001   |
| NIDCM                               | 48% (96/200)    | 51% (50/98)   | 45.1% (46/102) |         |
| BSA                                 | 1.97 ± 0.27     | 1.96 ± 0.27   | 1.98 ± 0.28    | 0.667   |
| BMI                                 | 28.3 ± 5.5      | 28.1 ± 4.3    | 28.5 ± 6.5     | 0.763   |
| Albumin (g/dL)                      | 4.14 ± 10.03    | 3.19 ± 0.51   | 5.06 ± 14.05   | 0.015   |
| DM                                  | 46% (92/200)    | 38.8% (38/98) | 52.9% (54/102) | 0.038   |
| HTN                                 | 83% (166/200)   | 79.6% (78/98) | 86.2% (88/102) | 0.153   |
| CRI                                 | 40% (81/200)    | 29.6% (29/98) | 51% (52/102)   | 0.002   |
| Dialysis                            | 2.5% (5/200)    | 3.1% (3/98)   | 1.8% (2/102)   | 0.680   |
| COPD                                | 15.5% (31/200)  | 15.3% (15/98) | 15.7% (16/102) | 0.917   |
| PVD                                 | 12% (23/200)    | 7.1% (7/98)   | 15.7% (16/102) | 0.055   |
| Vented                              | 12% (25/200)    | 9.2% (9/98)   | 15.7% (16/102) | 0.134   |
| Previous cardiac surgery            | 32% (63/200)    | 20.4% (20/98) | 42% (43/102)   | 0.001   |
| Creatinine (mg/dL)                  | 1.42 ± 0.62     | 1.43 ± 0.58   | 1.42 ± 0.65    | 0.869   |
| AST (U/L)                           | 48.3 ± 82.8     | 58.0 ± 106.8  | 38.9 ± 45.7    | 0.212   |
| ALT (U/L)                           | 46.5 ± 78.5     | 59.8 ± 99.4   | 33.5 ± 47.3    | 0.002   |
| CPB time (min)                      | 113.5 ± 46.1    | 109.5 ± 46.0  | 117.8 ± 46.1   | 0.178   |
| XCL time (min)                      | 71 ± 30.6       | 85.2 ± 33.7   | 51.7 ± 26.0    | 0.054   |
| MCS at time of VAD                  | 18% (36/200)    | 24% (23/98)   | 13% (13/102)   | 0.051   |
| On inotropes at time of VAD         | 75% (150/200)   | 81% (80/98)   | 69% (70/102)   | 0.036   |
| Pre VAD CVP (mmHg)                  | 11.8 ± 6.4      | 11.6 ± 6.4    | 12.0 ± 6.4     | 0.653   |
| Pre VAD PAPs (mmHg)                 | 51.4 ± 14.2     | 50.5 ± 14.5   | 52.3 ± 13.8    | 0.412   |
| Pre VAD PAPd (mmHg)                 | 24.5 ± 9.2      | 24.4 ± 9.8    | 24.7 ± 8.5     | 0.682   |
| Pre VAD CI (L/min per square metre) | 1.85 ± 0.51     | 1.87 ± 0.54   | 1.83 ± 0.47    | 0.961   |
| Pre VAD PCWP (mmHg)                 | 23.0 ± 9.6      | 22.7 ± 9.8    | 23.4 ± 9.4     | 0.463   |
| Blood transfusions                  | 23% (46/200)    | 18% (18/98)   | 27% (28/102)   | 0.250   |
| Concomitant cardiac procedure       | 19% (39/200)    | 23% (23/98)   | 15% (16/102)   | 0.137   |

BTT: Bridge to transplant; DT: Destination therapy; ICM: Ischemic cardiomyopathy; NIDCM: Non ischemic dilated cardiomyopathy; BSA: Body surface area; BMI: Body mass index; DM: Diabetes mellitus; HTN: Hypertension; CRI: Chronic renal insufficiency; COPD: Chronic obstructive pulmonary disease; PVD: Peripheral vascular disease; AST: Aspartate transaminase; ALT: Alanine aminotransferase; CPB: Cardiopulmonary bypass; XCI: Cross clamp; MCS: Mechanical circulatory support; VAD: Ventricular assist device; CVP: Central venous pressure; PAP: Pulmonary artery systolic pressure; PAPd: Pulmonary artery diastolic pressure; CI: Cardiac index; PCWP: Pulmonary capillary wedge pressure.

## RESULTS

### **Preoperative patient demographics and operative characteristics**

The mean age of our LVAD recipients was 59.3 years (range 17–81), 76% (152/200) were males and 24% females (48/200). BTT was the indication for LVAD implantation in 49% of patients (98/200) and DT in 51% (102/200) of patients. Additional patient demographics and comorbidities are presented in Table 1. In terms of operative characteristics, 31% of patients had undergone previous median sternotomy, the average cardiopulmonary bypass time was 113 min, cross clamp time (when used) was 71 min, and 19% of patients underwent a concomitant procedure at the time of LVAD implantation. In our cohort, 18% were on some type of mechanical circulatory support (MCS) at the time of LVAD insertion. Types of pre CF LVAD MCS included intraortic balloon pumps (23/36, 63%), pulsatile flow HeartMate XVE (5/36, 15%),

CentriMag devices (5/36, 15%), Impella (2/26, 8%) and AbioMed support (1/36, 3%). BTT patients were significantly younger, had worse pre LVAD liver function and albumin, whereas DT patients were more likely to be diabetic, to have PVD, CRI and to have undergone previous cardiac surgery. Pre-LVAD inotropic support or MCS was more likely in the BTT patients (Table 1).

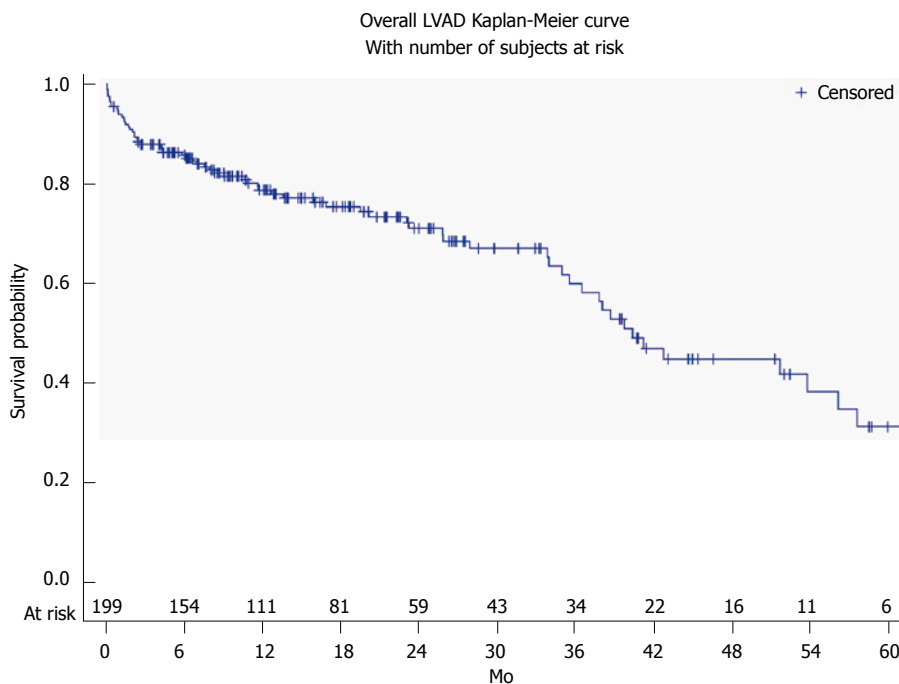
### **Duration of support, heart transplant and survival rates**

The mean duration of LVAD support was 581 d (range 2–2595 d) (Table 2). A 56-year-old male, who received a CF LVAD for DT, is our longest survivor having been on LVAD therapy for just over 7 years. Overall, 27% of LVAD recipients and 46% of the BTT patient underwent heart transplantation (Table 2). At 2 years, the survival rate for our heart transplant recipients was 95% (52/55) which was significantly superior to the 2 year 71% survival rate for DT patients ( $P = 0.02$ ). The survival rate at 30 d, 6 mo, 12 mo, 2 years, 3 years and 4 years was 94%, 86%, 78%, 71%, 62% and 45%

**Table 2 Postoperative outcomes**

| Variable                       | Total (n = 200) | BTT (n = 98)   | DT (n = 102)    | P value |
|--------------------------------|-----------------|----------------|-----------------|---------|
| Postoperative ICU stay (d)     | 195 10.7 ± 10.4 | 95 10.2 ± 7.7  | 100 11.2 ± 12.5 | 0.833   |
| Overall length of stay (d)     | 198 21.4 ± 14.3 | 98 20.8 ± 12.9 | 100 22.1 ± 15.6 | 0.517   |
| Readmitted within 30 d         | 26.5% (53/200)  | 26.0 (25/96)   | 27% (28/102)    | 0.725   |
| Reexploration for bleeding     | 15% (31/200)    | 10% (10/98)    | 5% (6/102)      | 0.040   |
| DL infection                   | 7% (15/200)     | 9% (9/98)      | 5% (6/102)      | 0.386   |
| Pocket infection               | 1% (2/200)      | 1% (1/98)      | 1% (1/102)      | 0.493   |
| Pneumonia                      | 7% (15/200)     | 9% (9/98)      | 5% (6/102)      | 0.375   |
| Hemorrhagic stroke             | 10% (21/200)    | 9% (9/98)      | 11% (12/102)    | 0.432   |
| Emboli stroke                  | 5% (10/200)     | 6% (6/98)      | 3% (4/102)      | 0.493   |
| VDRF                           | 9% (19/200)     | 10% (10/98)    | 8% (9/102)      | 0.774   |
| Tracheostomy                   | 2% (5/200)      | 1% (1/98)      | 3% (4/102)      | 0.369   |
| Dialysis                       | 2% (5/200)      | 3% (3/98)      | 1% (2/102)      | 0.680   |
| GIB                            | 21% (43/200)    | 17% (17/98)    | 25% (26/102)    | 0.289   |
| Reoperation for AI             | 2% (4/200)      | 4% (4/98)      | 0% (0/102)      | 0.058   |
| RV failure                     | 19% (38/200)    | 15% (15/98)    | 22% (23/102)    | 0.192   |
| RV failure requiring milrinone | 13% (26/200)    | 9% (9/98)      | 16% (17/102)    | 0.103   |
| RV failure requiring RVAD      | 6% (12/200)     | 6% (6/98)      | 5% (6/102)      | 0.803   |
| Heart transplant               | 27% (55/200)    | 45% (45/98)    | 10% (10/102)    | 0.001   |
| Duration of support (d)        | 581.0 ± 517.9   | 554.8 ± 535.0  | 606.4 ± 502.1   | 0.253   |

ICU: Intensive care unit; DL: Driveline; VDRF: Ventilator dependent respiratory failure; GIB: Gastrointestinal bleeding; AI: Aortic insufficiency; RV: Right ventricular; RVAD: Right ventricular assist device.



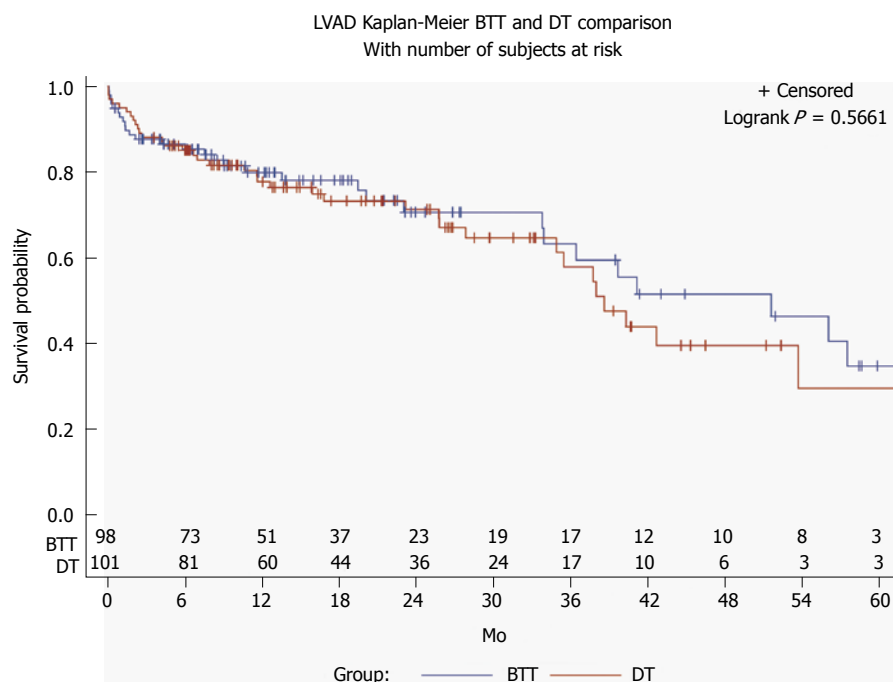
**Figure 1** Kaplan-Meier survival curve for all patients receiving continuous-flow left ventricular assist devices. LVAD: Left ventricular assist device.

respectively (Figure 1). Survival rates were similar for BTT and DT patients ( $P = 0.566$ ). Survival at 1 mo, 6 mo, 1 year, 2 years, 3 years and 4 years for the BTT patients was 93%, 87%, 70%, 70%, 63% and 52% respectively whereas for the DT group survival was 95%, 85%, 78%, 71%, 58% and 40% respectively (Figure 2). Competing outcomes of BTT vs DT patients is demonstrated in Table 3.

### Causes of death

Since implanting our first CF LVAD in 2006, a total

of 63 patients have died. Causes of death included: stroke (20/63, 32% of which 15 /63, 24% were hemorrhagic and 5/63, 8% were ischemic, range 2-654 d postoperatively, median 35 d), sepsis (17/63, 27%, range 5-320 d postoperatively, median 47 d), multi-organ failure (15/63, 24%, range 4-211 d median 35 d), right ventricular failure (6/63, range 2-139 d, median 10 d), refractory arrhythmia (2/63, 3%, at 64 and 128 d after LVAD implantation), bowel perforation (1/63, 1.5%, on postoperative day-11 and day-13), disconnection from the power source (1/63, 1.5%, 14



**Figure 2** Comparison of Kaplan-Meier survival between bridge to transplan and destination therapy patients. LVAD: Left ventricular assist device; BTT: Bridge to transplan; DT: Destination therapy.

**Table 3** Outcomes for bridge to transplan and destination therapy patients

|     | Variable   | Patients (%)  |
|-----|------------|---------------|
| BTT | Died       | 28.6 (28/98)  |
|     | Ongoing    | 25.5 (25/98)  |
|     | Transplant | 45.9 (45/98)  |
| DT  | Died       | 34.3 (35/102) |
|     | Ongoing    | 54.8 (56/102) |
|     | Transplant | 9.8 (10/102)  |

mo after implantation), and pump thrombosis (1/63, 1.5%, 18 mo after implantation).

### Postoperative LVAD complications

Post LVAD complications are listed in Table 2. GIB was the most common adverse event (43/200, 21%), followed by RV failure (38/200, 19%), stroke (31/200, 15%), re exploration for bleeding (31/200, 15%), VDRF (19/200, 9%) and pneumonia (15/200, 7%). Our driveline infection rate was 7%. Pump thrombosis occurred in 6% of patients. Device exchanged was needed in 6% of patients, of which 77% (10/13) were for pump thrombosis and 13% (3/13) for severe driveline and pocket infections. No differences were noted between BTT and DT patients in terms of adverse events.

### Length of ICU and hospital stay, and early readmissions

The average length of hospital stay (LOS) for our LVAD patients was 21 d, of which 11 d were spent in the intensive care unit (ICU). Readmissions within 30 d of index hospitalization discharge occurred in 27% of patients. No differences were observed between the

BTT and DT patients in terms of LOS, ICU stay and readmission (Table 2). The most common cause of 30 d readmission were cardiac related (chest pain, SOB/heart failure, arrhythmia), gastrointestinal bleeding (GIB) (25%), infections 12% (pneumonia, wound/driveline infections, UTI) and stroke 8%.

### Hemodynamic measurements pre LVAD and post LVAD at 6 mo

Hemodynamic measurements prior to LVAD implantation and after 6 mo of LVAD therapy are demonstrated in Table 4. Significant improvement was noted for all indices and measurements, which confirmed adequate LV decompression and improvement in RV function.

### Predictors of survival

Univariate analysis showed that pre-LVAD renal (HR = 1.56; 95%CI: 1.11-2.21,  $P = 0.012$ ) and hepatic function (HR = 1.03; 95%CI: 1.01-1.05,  $P = 0.004$ ), length of ICU stay (HR = 1.34; 95%CI: 1.12-1.61,  $P = 0.001$ ), the occurrence of VDRF (HR = 4.66; 95%CI: 2.51-8.67,  $P = 0.001$ ), the need for tracheostomy (HR = 15.18; 95%CI: 5.56-41.4,  $P = 0.001$ ) and the occurrence of post LVAD RV failure that required RVAD support (HR = 5.81; 95%CI: 2.84-11.9,  $P = 0.001$ ) were significant predictors of survival. Variables with a  $P < 0.25$  were included in a cox regression model. On multivariate analysis, pre LVAD liver function, VDRF, tracheostomy and implantation of a RVAD for RV failure still predicted survival (Table 5).

## DISCUSSION

Continuous flow LVADs have now become an efficient



**Table 4 Hemodynamic measurements pre and post left ventricular assist device at 6 mo**

| Variables                   | Pre VAD       | Post VAD      | P value |
|-----------------------------|---------------|---------------|---------|
| CVP (mmHg)                  | 12 ± 6        | 8 ± 4.5       | 0.001   |
| PAPs (mmHg)                 | 53.52 ± 13.76 | 36.03 ± 11.85 | 0.001   |
| PAPd (mmHg)                 | 26.15 ± 9.50  | 16.11 ± 6.24  | 0.001   |
| CI (L/min per square meter) | 1.78 ± 0.39   | 2.52 ± 0.60   | 0.001   |
| PCWP (mmHg)                 | 25.09 ± 10.05 | 11.93 ± 7.84  | 0.001   |
| LVEDD (mm)                  | 71.70 ± 13.61 | 57.45 ± 15.3  | 0.001   |
| LVEF (%)                    | 16 ± 7.90     | 21 ± 9.00     | 0.017   |

VAD: Ventricular assist device; CVP: Central venous pressure; PAP: Pulmonary artery systolic pressure; PAPd: Pulmonary artery diastolic pressure; CI: Cardiac index; PCWP: Pulmonary capillary wedge pressure; LVEDD: Left ventricular end diastolic diameter; LVEF: Left ventricular ejection fraction.

treatment for patients with end stage heart failure for the indication of BTT or DT, with excellent short and long term survival, as demonstrated in this study. Our analysis showed that after CF LVAD implantation, survival at 30 d was 94%, at 1 year 78%, at 2 year 71%, and at 4 years 45%. Our longest survivor has been on LVAD therapy for over 7 years. Although these results by far surpass outcomes of patients with advanced heart failure on medical therapy, they are still inferior to heart transplantation which remains the gold standard for treating ESHF<sup>[7]</sup>. At 2 years the survival rate for our heart transplant recipients was 95% (52/55), which was superior to the 2 year 71% survival rate for DT patients ( $P = 0.02$ ). Apart from improvement in survival, LVAD patients benefit from improved peripheral perfusion which certainly enhances quality of life. As demonstrated in our hemodynamic and ECHO measurements, 6 mo of LV therapy is associated with adequate LV decompression, significant improvement in RV function and in end organ perfusion. This is achieved with close postoperative surveillance and by obtaining regular echocardiograms to assess for aortic ejection, LV decompression, positions of the interventricular septum, right ventricular function, and for residual mitral and tricuspid regurgitation<sup>[5]</sup>. We aim to maintain a flow index (CI) > 2.2 L/min per square metre. We also regularly adjust revolutions per minute (rpm) speed to achieve adequate flow, LV decompression, peripheral perfusion, and end organ function.

Our multivariate analysis demonstrated that preoperative liver dysfunction, and postoperative VDRF, tracheostomy, and RV failure requiring RVAD support were significant predictors of post LVAD mortality. These variables have previously been reported as potential risk factors for early post LVAD death in several published series<sup>[8-10]</sup>. High preoperative LFTs are an indication of poor end organ perfusion and RV dysfunction, which are certainly expected to increase postoperative mortality. These patients are coagulopathic, which cause postoperative bleeding, tamponade, and makes fluid management more challenging, especially with RV dysfunction which frequently co-exists with abnormal

**Table 5 Multiple cox proportional hazard models**

| Variable                  | HR 95%CI           | P value | Backwards stepwise model |
|---------------------------|--------------------|---------|--------------------------|
| Albumin                   | 0.64 (0.27, 1.52)  | 0.310   |                          |
| Length of stay            | 0.85 (0.62, 1.17)  | 0.319   |                          |
| CPB time                  | 1.05 (0.98, 1.14)  | 0.175   |                          |
| CRI                       | 1.13 (0.44, 2.91)  | 0.804   |                          |
| PVD                       | 0.95 (0.30, 3.03)  | 0.931   |                          |
| Vented                    | 0.93 (0.17, 4.97)  | 0.929   |                          |
| Creatinine                | 0.77 (0.37, 1.63)  | 0.495   |                          |
| PreVAD AST                | 1.03 (1.00, 1.07)  | 0.072   | 1.03 (1.01, 1.05) 0.01   |
| PreVAD ALT                | 1.02 (1.00, 1.05)  | 0.064   | 1.02 (1.01, 1.04) 0.02   |
| Blood transfusion         | 1.19 (0.45, 3.14)  | 0.732   |                          |
| ICU stay                  | 0.80 (0.52, 1.24)  | 0.320   |                          |
| Reexploration             | 1.70 (0.50, 5.79)  | 0.794   |                          |
| VDRF                      | 4.92 (1.62, 14.93) | 0.005   | 3.05 (1.41, 6.59) 0.005  |
| Tracheostomy              | 5.53 (0.65, 46.78) | 0.116   | 4.54 (1.35, 15.32) 0.015 |
| RV failure                | 0.45 (0.09, 2.26)  | 0.330   |                          |
| RVAD                      | 8.90 (1.30, 61.06) | 0.066   | 3.64 (1.59, 8.36) 0.002  |
| Age                       | 1.02 (0.95, 1.12)  | 0.176   |                          |
| Gender                    | 0.75 (0.66, 1.56)  | 0.321   |                          |
| Resternotomy              | 1.31 (0.83, 4.55)  | 0.673   |                          |
| Etiology of heart failure | 1.23 (0.59, 4.08)  | 0.512   |                          |

CPB: Cardiopulmonary bypass; CRI: Chronic renal insufficiency; PVD: Peripheral vascular disease; AST: Aspartate transaminase; ALT: Alanine aminotransferase; ICU: Intensive care unit; VDRF: Ventilator dependent respiratory failure; RV: Right ventricular; RVAD: Right ventricular assist device.

liver function. VDRF and tracheostomy both indicate critical illness and prolonged ICU support which are also expected to be predictors of poor outcome.

Several major centers around the world have also reported excellent survival outcomes, analogous to those reported in our study. A multi-institutional analysis from the United Kingdom and Germany<sup>[11]</sup> published survival rates of 89% at 30 d, 76% at 1 year and 66% at 2 years, from 139 CF LVAD implantations over a 6-year period. The average duration of support in this study was 514 d. No differences were identified between HeartMate II and HeartWare devices in terms of survival, although there was a trend towards more transfusions in the HeartMate group. These findings match our results when comparing the two types of devices. John *et al*<sup>[12]</sup> from the University of Minnesota published their single institutional experience with 130 CF LVADs. Overall, 30 d, 6 mo, and 1 year survival was 95.1%, 83.5%, and 78.8%, respectively. Driveline infections (25%), GIB 18% and stroke were the most common adverse events.

Possibly the most common and hazardous adverse events of the old generation pulsatile flow LVADs were resistant pocket/driveline infections and pump thrombosis<sup>[4,13,14]</sup>. Both these complications resulted in frequent device exchanges. Newer generation devices are more reliable and durable and fortunately these events are less frequent with CF LVADs<sup>[15-17]</sup>, as clearly demonstrated in our study. Device exchange was performed in 6% of our patients, of which 77% (10/13) were for pump thrombosis and 13% (3/13)

for severe driveline and pocket infections. Our overall pump thrombosis rate was 6% (12/200), with 10/12 (83%) of these incidence occurring between 2006-2012 and only two cases of pump thrombosis over the past 3 years. Based on initial reports that suggested that anticoagulation could be less aggressive for Heartmate II devices, we followed a less aggressive anticoagulation policy, which may explain the higher frequency of pump thrombosis during the first six years of our CF-LVAD program. Since 2012, all patients receiving CF LVADs are postoperatively started on Aspirin 81 mg and Warfarin with an INR target of 2.0-2.5. In addition we have recently been creating a larger sized pump pockets which reduces the effect of diaphragmatic excursion on the angle of the inflow cannula, thus reducing the incidence of pump thrombosis. Our driveline infection rate was only 7% which is significantly lower than the reported incidence of 20%<sup>[15]</sup>. It has been over 3 years since we have had a driveline infection. We feel that our success in preventing this challenging complication is linked with a new antibiotic and dressing protocol which was initiated at the end of 2011. The night before surgery patients are given 1.5 g of IV vancomycin, 2 g of IV cefepime, 400 mg IV Fluconazole and 600 mg of IV Rifampin. In penicillin or cephalosporin allergic patients, cefepime is substituted with 2 g of IV Aztreonam. Postoperatively, 4 doses of IV Vancomycin (15 mg/kg) every 12 h, 4 doses of IV Cefepime (2 g) every 12 h (or 2 daily doses of IV Aztreonam) and 2 daily doses of IV Fluconazole (400 mg) and IV Rifampin (600 mg) are administered. In the operating room, the drivelines are covered with Acticoat 3 Flex, which is a silver coated antimicrobial barrier that lasts for 3 d, followed by application of a tegaderm. Chlorhexidine and sterile water is used every 3 d to clean the driveline area, after which a new acticoat dressing is applied<sup>[5]</sup>.

In our series, GIB was the most common adverse event (43/200, 21%), followed by RV failure (38/200, 19%) and stroke (31/200, 15%) rates which are similar to previously published data<sup>[1,17-22]</sup>. The occurrence of GI bleeding makes postoperative LVAD management more challenging, as temporary discontinuation of anticoagulation is required, which may increase the risk of pump thrombosis and stroke. GI bleeding is also a common cause for early postoperative readmission<sup>[23]</sup>. The frequent association of GIB with CF LAVDs is presumed to be from the lack of pulsatility which causes AV malformations and angiodysplasia. A similar mechanism, known as Heyde's syndrome<sup>[24]</sup>, has been described in severe aortic stenosis, which also causes AV malformations and GIB. In addition, acquired von Willebrand syndrome has been reported as a potential cause for the development of GIB<sup>[25]</sup>. This frequent complication can be minimized through close INR monitoring, although recent studies have suggested that prophylactic administration of Octreotide may reduce the incidence of GIB<sup>[26,27]</sup>. RV failure is also a common LVAD related complication with a complex underlying mechanism. LV decompression

causes a leftward shift of the interventricular septum, which reduces its contractility thus impairing RV function<sup>[28]</sup>. It is also challenging for the RV to keep up with the sudden increase in LV output which further decreases RV function. In addition, subtle changes in the pulmonary microcirculation before and after LVAD implantation also add to RV dysfunction<sup>[19,23]</sup>. We have previously published the patients who develop post LVAD RV failure and only require inotropic support with Milrinone, have equivalent outcomes to patients without RV failure<sup>[29]</sup>. It is only when RVAD support is required, does the morbidity and mortality increase, which is clearly demonstrated in our current study. Although certain risk factors predicting RV failure and RVAD support after LVAD implantation have been described, such as renal and liver failure, leucocytosis, high CVP/PCWP ratio, high CVP and decreased right ventricular stroke work index, predicting severe RV failure still remains a challenge<sup>[29-31]</sup>.

Two types of LVADs have been implanted at our institution, HMII and HVAD. Of the 200 LVADs, 179 were HMII and 21 were HVADs. These devices have similarities and divergences. The HMII is an axial flow pump with an electromagnetically suspended rotor. The larger HMII device requires an additional pump pocket formation in the upper abdominal preperitoneal space<sup>[32]</sup>. The HVAD is a centrifugal flow pump, characterized by a smaller size, which allows for its placement within the pericardial cavity<sup>[33]</sup>. Although the number of HVADs we implanted was insufficient to generate results for meaningful conclusions, so far we haven't identified a significant difference in the overall mortality rate (32% for HMII vs 23% for HVADs,  $P = 0.301$ ) or other complications. There only appeared to be a higher rate of blood transfusions with the HMII (20% vs 9%), which possibly corresponds to the need to form a pump pocket. Nevertheless, the higher transfusion rate did not correspond with higher incidences of re-exploration for bleeding and had no significant impact on survival.

An area of controversy and discussion amongst LVAD centers is patient's age as exclusion criteria for LVAD implantation. Several studies<sup>[8,10]</sup> have shown worse outcomes in older LVAD patients, although this was not observed in our analysis. In our 200 patient cohort, 14 patients were above the age of 70. Our oldest patient was 81 years. Survival at 2 years for patients above 70 was 62%. In addition, age was not found to be an independent predictor of survival. Other reports agree with our findings<sup>[34,35]</sup>. We feel that in appropriately selected patients, age should not be a contraindication to implantation<sup>[36]</sup>.

Our study was not without limitations. Considering that this was not a prospective, randomized trial, it was subject to limitations inherent to any retrospective analysis. In addition statistical power was limited. Selection bias may also be present, since this is a single institution study. Finally, data on functional status and quality of life were not collected, which is an important target of LVAD therapy.

In conclusion, our single institutional analysis demonstrates superb short and long term outcomes, up to 4 year, with CF LAVDs. Compared to old generation devices, major adverse events such as pump thrombosis and driveline infections and frequent device exchanges, are now less frequent. Nevertheless, certain LVAD-related complications, such as GIB, stroke and RV failure do continue to occur. In addition to identifying new means of power transmission, new LVAD technology aims at reducing these adverse events. Preoperative hepatic and RV dysfunction appear to be predictors of post LVAD survival, which should certainly be taken into account in the patient selection process, whereas other significant variables, such as age, sex, etiology of heart failure, other comorbidities and reoperative cardiac surgery, do not appear to influence short and long term survival.

## COMMENTS

### Background

As the availability of left ventricular assist device (LVAD) therapy expands, there are still concerns regarding the relatively frequent occurrence of postoperative LVAD complications. Improvements are still required if LVADs are to become a plausible alternative to heart transplantation or a therapeutic option for patients in earlier stages of heart failure. The aim of this study was to review the authors' institutional experience over 8 years with 200 continuous-flow (CF) LVADs.

### Research frontiers

To our knowledge this is the largest single institutional CF LVAD report.

### Innovations and breakthroughs

Their single institutional analysis demonstrates excellent short and long term outcomes, up to 4 years, with CF LAVDs. Compared to old generation devices, major adverse events such as pump thrombosis and driveline infections and frequent device exchanges, are now less frequent. Nevertheless, certain LVAD-related complications, such as gastrointestinal bleeding, stroke and right ventricular failure do continue to occur.

### Applications

Post-operative management of LVADs and appropriate patient selection.

### Terminology

CF LVADs: Continuous-flow left ventricular assist device. They are centrifugal or axial flow pumps that replace the function of the failing heart.

### Peer-review

The authors present an interesting review of experience with LVAD and analytical results about postoperative prognosis.

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