Outcomes and Predictors of Early Mortality After Continuous-Flow Left Ventricular Assist Device Implantation as a Bridge to Transplantation

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Left ventricular assist devices (LVADs) are fast becoming standard of care for patients with advanced heart failure. However, despite continuous improvement in VAD technology, there remains a significant early postoperative morbidity and mortality in this extreme patient group. The aim of the current study was to explore the short-term outcomes and predictors for 90 day mortality in the patients after implantation of continuous-flow LVAD. Perioperative clinical, echocardiographic, hemodynamic, and laboratory data of 90 day survivors and nonsurvivors were collected and compared retrospectively. Multivariate logistic regression analysis was performed on univariate predictors for 90 day mortality with an entry criterion of \( p < 0.1 \). Between July 2006 and May 2012, 117 patients underwent implantation of a continuous-flow LVAD as a bridge to transplantation: 71 (60.7%) HeartMate II (Thoratec Corp, Pleasanton, CA) and 46 (39.3%) HVAD (HeartWare International, Framingham, MA). All-cause 90 day mortality was 17.1%. Multivariate analysis revealed higher preoperative central venous pressure (odds ratio \([OR]\), 1.18; 95% confidence interval \([CI]\), 1.01–1.38; \( p = 0.033 \)) and higher age (OR, 1.14; 95% CI, 1.01–1.38; \( p = 0.045 \)) as the only independent predictors for 90 day mortality. Optimization of preoperative volume status, preload, and right heart function as well as age-based selection of candidates for LVAD support are the critical factors influencing early outcome after continuous-flow LVAD implantation. ASAIO Journal 2014; 60:162–169.

Key Words: ventricular assist device, HeartWare, HVAD, HeartMate II

Left ventricular assist devices (LVADs) have become efficient treatment for a large number of patients with advanced heart failure either as a bridge to transplant, bridge to recovery, or as destination therapy.1–8 Technological development and increasing clinical implementation have significantly improved the survival in patients supported with continuous-flow (CF) LVADs and are associated with decreased incidence of adverse events and a better quality of life compared to pulsatile devices.3 However, despite continuous improvement in the LVAD technology and results, the patients on mechanical support still experience a significant mortality, particularly in the early postoperative phase.2,9,10 Also, because the number of cardiac transplantations has been significantly restricted due to donor organ shortage, the LVADs have been increasingly used particularly as a bridge to transplantation. Despite decreased mortality and morbidity, the hazard of LVAD-related complications which is highest in the early phase after listing for transplant can dramatically worsen the survival on the waiting list.11

The aim of this study was to present outcomes and to evaluate the risk factors for early (90 day) mortality after CF-LVAD implantation as a bridge to transplantation in patients with advanced heart failure in view of optimizing the patient selection and the operative strategy in this extreme patient group.

Methods

All 117 consecutive patients who received a CF-LVAD for end-stage heart failure at our institution from July 2006 up to May 2012 were included in this retrospective observation. All the patients were eligible for heart transplantation and LVADs were implanted as a bridge to transplantation. The patients on preoperative temporary mechanical circulatory support including intraaortic balloon pump (IABP), extracorporeal membrane oxygenation (ECMO), as well as short- and long-term VADs were also included in the study. The primary end point was overall survival to 90 days after LVAD implantation (survival on LVAD support, after heart transplant or after explantation for myocardial recovery). The secondary end points were perioperative clinical characteristics and adverse events that could have an impact on early postoperative mortality. All the patients completed a follow-up period of at least 90 days and were divided into two groups depending on the 90 day survival. The demographic and perioperative variables of the 90 day survivors and nonsurvivors were compared to identify the predictors of 90 day overall mortality.

The analysis was performed using a prospectively maintained institutional patient database. The variables evaluated included
the following: baseline characteristics (patient's demographics: sex, age, height, weight, body mass index, human leukocyte antigen, and cytomegalovirus infection status, cause of heart failure, as well as additional disorders); preoperative laboratory parameters (white blood cell count, C-reactive protein, total bilirubin, alanine aminotransferase, blood urea nitrogen [BUN], and creatinine); baseline hemodynamic characteristics (heart rate, heart rhythm, mean arterial pressure, mean pulmonary artery pressure, central venous pressure [CVP], pulmonary capillary wedge pressure [PCWP], cardiac output, central venous saturation, and echocardiographic data [ejection fraction, left ventricular diastolic (LVDD) and systolic (LVSD) diameters]) as well as further preoperative clinical data (preoperative length of stay [LOS], use of an IABP, ECMO, or short- or long-term VAD, ventilator or inotropic support, presence of an implantable cardioverter defibrillator [ICD], body temperature, blood culture status, presence of major infection, and condition after sternotomy or noncardiac surgery); intraoperative data (on/off-pump approach, use of aortic cross-clamp, theater time, conventional/double-tunnel driveline placement technique); and postoperative variables (inotropic or ventilator support > 7 days, right ventricular failure [RVF] requiring short- or long-term mechanical support, acute renal failure [ARF] requiring renal replacement therapy, respiratory insufficiency, tracheostomy, ECMO, early postoperative infections, bleeding and transfusion requirements, postoperative intensive care unit, and total LOS).

Statistical Analysis

All data were presented as continuous or categorical variables. The continuous data were evaluated for normality using one-sample Kolmogorov–Smirnov test. Univariate analysis was performed using either Student's t-test or Mann–Whitney U test for normal and nonnormal continuous variables, respectively. Pearson's χ² or Fisher exact tests were used for categorical data dependent on the minimum expected count in each cross tab.

Kaplan–Meier actuarial survival estimate was generated to analyze post-LVAD survival of the entire cohort. All data were analyzed using Statistical Package for Social Sciences, version 20.0 (SPSS Inc., Chicago, IL) and are expressed as the mean ± standard deviation in case of normal distributed or median (interquartile range) in case of nonnormal distributed continuous variables. The categorical data are expressed as total numbers and percentages. Multivariate logistic regression analysis was performed on univariate predictors for 90 day mortality with an entry criterion of p < 0.1.

Results

Perioperative Outcome

A total of 117 patients with severe end-stage heart failure (mean age of 44±13 years; male/female ratio, 97/20) underwent implantation with the HeartMate II (Thoratec Corp, Pleasanton, CA) (n = 71, 60.7%) or HVAD (HeartWare International, Framingham, MA) (n = 46, 39.3%) CF-LVAD at our institution between July 2006 and May 2012. The cause of the heart failure was dilated cardiomyopathy (n = 99, 84.6%), ischemic cardiomyopathy (n = 14, 12%), postpartum dilated cardiomyopathy (n = 2, 1.7%), and hypertrophic obstructive cardiomyopathy (n = 2, 1.7%).

The mean preoperative LOS in hospital was 23.5 ± 19.1 days. Nine patients (7.7%) required preoperative mechanical ventilation, 88 (75.2%) inotropic support, 24 (20.5%) IABP, 7 (6.0%) ECMO, 13 (11.1%) short-term VAD, and 11 (9.4%) long-term VAD in the form of isolated LVAD (n = 9, 7.7%) or biventricular assist device support (n = 12, 10.3%). Eleven patients (11.3%) had preoperative cardiac arrhythmias with hemodynamic compromise, 31 (26.5%) had a previous sternotomy, and 54 (46.2%) had an ICD. A preoperative major infection was present in seven (6.0%) patients out of whom four (3.4%) were presented with positive blood cultures. Preoperative mean body temperature accounted for 37.1°C ± 0.7°C. There were no patients with previous cardiac transplantation in this cohort.

Majority of the LVAD implantations were performed through a median sternotomy (n = 113, 96.6%) on cardiopulmonary bypass without cross-clamping the aorta (n = 96, 82.1%). Four patients, who received HVAD, underwent minimally invasive LVAD implantation through bilateral anterior minithoracotomy. In 25 patients (21.4%), a modified C-shaped double tunnel technique was used for the placement of subcutaneous driveline.

The overall 90 day mortality was 17.1% (Figure 1) and mean LVAD support duration was 434.3 ± 410.5 days. Of the patients who died within 90 days (n = 20, 17.1%) of LVAD implantation, 18 (90%) died on primary LVAD support and 2 (10%) underwent the device exchange in the meantime. In the 90 day survival group (n = 97, 82.9%), 18 patients (18.6%) died on support after 90 days, 9 (9.3%) underwent LVAD exchange and were alive at the study cut off, 39 (40.2%) were on ongoing VAD support, 19 (19.6%) underwent device explantation for myocardial recovery, and 12 (12.4%) were transplanted during the follow-up period. The perioperative bleeding requiring reexploration and operative hemostasis occurred in 32 (27.8%) patients whereas the mean transfusion rate was 8.7 ± 9.9, 5.4 ± 7.3, and 2.1 ± 3.2 units for red blood cells (RBCs), fresh frozen plasma, and platelets, respectively. Thirty-five (32.4%) patients required prolonged (>7 days) postoperative inotropic support and 19 (17.8%) required prolonged mechanical ventilation. Two (1.7%) patients required postoperative venoaerial ECMO support due to device failure. Twenty-nine (24.8%) patients suffered post-LVAD RVF requiring temporary mechanical right ventricular support with CentriMag (Levitronix, Zurich, Switzerland) short-term VAD and two of them were subsequently upgraded to a long-term right ventricular assist device (RVAD) with Jarvik 2000 (Jarvik Heart Inc, New York, NY). Additional postoperative complications included ARF requiring renal replacement therapy (n = 33, 28.7%), respiratory insufficiency requiring reintubation for mechanical ventilation (n = 24, 21.1%), or surgical tracheostomy (n = 13, 11.6%) and infections (n = 63, 53.8%). Percutaneous side infections (PSIs) with the need for at least intravenous antibiotic therapy occurred in 33 (28.2%) cases whereas 10 among them (8.5%) required additional surgical treatment, such as wound debridement, drainage, or vacuum-assisted closure therapy. The median infection-free survival was 219.0 ± 182.8 days, and the most frequent organisms isolated in the patients with postoperative PSI were Staphylococcus aureus and Enterobacter and Collitorm species.

Univariate Analysis

A subgroup analysis of the 90 day survivors and nonsurvivors is presented in Tables 1–6. The survivors were significantly younger (43.0 ± 13.3 vs. 49.9 ± 9.2, p = 0.008) with the trend toward less frequent peripheral vascular disease.
(1.0% vs. 10.0%, p = 0.075) (Table 1). The preoperative laboratory parameters (Table 2) and intraoperative variables (Table 5) were comparable between both groups. The evaluation of preoperative hemodynamic and echocardiographic parameters revealed a significantly higher CVP (19.5 ± 8.6 vs. 13.6 ± 7.6, p = 0.011) as well as significantly lower LVDD and LVSD in the 90 day nonsurvivor group compared to the 90 day survivor group (Table 3). Moreover, there was a trend toward higher rate of preoperative long-term mechanical support resulting in the LVAD exchange compared to primary LVAD implantation in the 90 day nonsurvival group (20% vs. 7.2%, p = 0.093). This group was also associated with the higher perioperative transfusion rate with RBCs (13 [4, 19] vs. 5 [2, 11], p = 0.014) and platelets (3 [1, 6] vs. 1 [0, 2], p = 0.003). Finally, the nonsurvivors were more pre-disposed to prolonged (>7 days) postoperative mechanical ventilation (42.9% vs. 14%, p = 0.017) and inotropic support (53.3% vs. 29.0%, p = 0.078) and had a significantly higher rate of postoperative ARF requiring hemofiltration (66.7% vs. 21.6%, p < 0.001).

Figure 1. Kaplan–Meier survival curve for patients undergoing continuous-flow left ventricular assist device implantation. The patients were censored when they underwent cardiac transplantation, device exchange, or device explantation for myocardial recovery.

| Table 1. Patient’s Baseline Preoperative Demographics |
|---------------------------------|-----------------|-----------------|---|
|                                | 90 Day Survivors | 90 Day Nonsurvivors | p  |
|------|------------------|-------------------|---|
| Age (years) | 43.0 ± 13.3 | 49.9 ± 9.2 | **0.008** |
| Female | 14 (14.4%) | 6 (30.0%) | 0.108 |
| BMI | 25.7 ± 4.1 | 25.5 ± 5.9 | 0.927 |
| Mean INTERMACS class | 2.5 ± 1.1 | 2.13 ± 0.83 | 0.199 |
| INTERMACS class 1 | 12 (12.1%) | 4 (23.5%) | 0.250 |
| Primary diagnosis | | | |
| DCM | 83 (85.6%) | 16 (80.0%) | 0.508 |
| ICM | 11 (11.3%) | 3 (15.0%) | 0.705 |
| PPDCM | 2 (2.1%) | 0 | 1.000 |
| HOCM | 1 (1.0%) | 1 (5.0%) | 0.314 |
| CHD | 0 | 0 | |
| Comorbidities | | | |
| COPD | 2 (2.1%) | 0 | 1.000 |
| Diabetes mellitus | 12 (12.4%) | 5 (25.0%) | 0.166 |
| PVD | 1 (1.0%) | 2 (10.0%) | **0.075** |

Boldface indicates p < 0.100.

BMI, body mass index; CHD, congenital heart defect; COPD, chronic obstructive pulmonary disease; DCM, dilated cardiomyopathy; HOCM, hypertrophic obstructive cardiomyopathy; ICM, ischemic cardiomyopathy; PPDCM, postpartum dilated cardiomyopathy; PVD, peripheral vascular disease.
Independent Predictors of 90 Day Mortality

The predictors of the 90 day mortality obtained by multivariate regression analysis were a higher preoperative CVP (odds ratio, 1.18; 95% confidence interval [CI], 1.014–1.378; \( p = 0.033 \)) and a higher age (odds ratio, 1.14; 95% CI, 1.01–1.38; \( p = 0.045 \)). To provide a cutoff point for age and CVP, both continuous variables were converted into categorical variables and multiple serial \( \chi^2 \) testing was performed with stepwise threshold progression to determine maximal divergence between survivors and nonsurvivors. This approach established cutoff points for age and CVP and identified age > 45 years (\( p = 0.024 \)) and CVP > 18 mm Hg (\( p = 0.042 \)) as the most significant predictors of the 90 day mortality after LVAD implantation (Figure 2). Other univariate predictors did not reach the statistical significance in the multivariate analysis.

**Discussion**

The current report represents a single-center experience with the two CF-LVADs (HeartMate II and HVAD) that have increasingly been used in our institution in the recent years. The two devices have some similarities and divergences. The HeartMate II is an axially configured pump with the rotor being parallel to the direction of flow. The HVAD uses a centrifugal blood pump that provides flow using hydrodynamic and centrifugal forces. The devices contain only one electromagnetically suspended moving part resulting in great durability and can generate a flow of up to 10 L/min. Because of its smaller size and weight, the HVAD is usually implanted intrapericardially without a need for additional pump pocket formation or can be implanted using minimal invasive access.\(^9,12\) By contrast, the HeartMate II is usually placed in a preperitoneal location requiring LVAD pocket.\(^5\) Nevertheless, the type of device used did not appear to be a predictor for early mortality in our analysis: 15.7% of patients on HeartMate II and 19.1% of patients on HeartWare died within the first 90 days postoperatively (\( p = 0.629 \)).

We presented perioperative morbidity and mortality after CF-LVAD implantation which in general are comparable to those of other series.\(^4,6,9\) However, unlike the other series, the patients who had been on ECMO, short- and even long-term mechanical circulatory support preoperatively were not excluded from this study for the purpose of evaluating the influence of previous mechanical support and the impact of the second surgery as possible risk factors on early mortality. Significantly, higher risk of bleeding and higher morbidity and mortality associated with the VAD exchange has been described previously.\(^5\) This outcome was partially reflected in our results with higher percentage of patients who had been on long-term VAD support preoperatively (Table 4) with significantly higher transfusion requirements with RBCs and platelets (Table 6) in 90 day nonsurvivor group. Even though, the difference in preoperative support with the long-term VAD did not reach statistical significance (\( p = 0.093 \)), the trend toward higher mortality in this subgroup has an obvious clinical relevance. The postoperative complications which usually occur after 90 days of LVAD implantation were logically excluded from this observation.

Risk factors for long-term mortality in patients undergoing LVAD implantation have been reported in previous research.
It was shown that age and RVF requiring RVAD were significant risk factors for long-term mortality in such patients.\textsuperscript{14} However, due to limited device selection, a pulsatile extracorporeal LVAD which was primarily designed for short-term support was used in the majority of cases. Furthermore, it is interesting to note that in contrast to that and to our study, Adamson et al.\textsuperscript{15} did not find significant differences in outcome after CF-LVAD implantation in patients ≥70 years of age and <70 years of age indicating that age should not be an absolute contraindication for LVAD implantation in elderly patients. The outcome of the entire population in that study was similar to our results.

In another study about the risk factors for early mortality in INTERMACS level 1 patients after LVAD implantation, higher preoperative creatinine was found to be the only independent predictor of 90 day mortality in a critical subpopulation of 41 patients.\textsuperscript{10} The degree of preoperative renal dysfunction with high creatinine levels (1.63±0.98 mg/dl) and BUN levels (36.9±21.8 mg/dl) in that patient group could have led to increased perioperative requirement for hemodialysis and further complications resulting from this condition influencing early mortality. Furthermore, most patients in this subpopulation underwent implantation of a pulsatile extracorporeal LVAD questioning comparability of the results. The incidence of postoperative ARF after CF-LVAD implantation reported previously ranges between 8.7% and 13%\textsuperscript{4,6,16} and seems to be considerably lower in our study. The reason for this discrepancy might be the fact that the patients who were at high risk for postoperative complications, such as the patients on ECMO or other mechanical circulatory support, were not excluded in our study. The rate of postoperative ARF requiring renal replacement therapy in our population in the univariate analysis was significantly higher in the 90 day non-survival group (p < 0.001). This finding corroborates the results of Borgi et al.\textsuperscript{17} which suggested an association between the postoperative ARF and a higher mortality at 30, 180, and 360 days after LVAD implantation. Moreover, similar to our results, Sandner et al.\textsuperscript{18} demonstrated that the patients with post-LVAD ARF had significantly lower survival regardless of pre-LVAD renal function. Nevertheless, this variable did not reach statistical significance in the logistic regression analysis (odds ratio, 1.71; 95% CI, 1.15–19.12; p = 0.061) and was not found to be an independent predictor of early mortality in our study.

Another variable which was significantly higher in the 90 day non-survival group in our study was the dependency on mechanical ventilation for >7 days (p = 0.017). Interestingly, other clinical signs of respiratory failure, such as a need for reintubation or a surgical tracheostomy, were similarly distributed between the two groups. This controversy can be explained by high mortality in 90 day nonsurvivors within the first 2 weeks of LVAD implantation which also corroborates the previous research.\textsuperscript{2,9,10} Due to this a number of patients with respiratory failure who were ventilated >7 days deceased before they would receive a surgical tracheostomy leading to a lower number of surgical tracheostomies in the patients with respiratory failure.

The need for the reintubation usually occurs during first few postoperative days due to atelectasis, pleural effusions, and general postoperative weakness. After quick improvement, the majority of them can be weaned off ventilator within the first postoperative week. This explains why the reintubation and

### Table 4. Preoperative Clinical Status

|                  | 90 Day Survivors | 90 Day Nonsurvivors | p       |
|------------------|------------------|---------------------|---------|
| LOS (days)       | 24.0±19.1        | 20.7±19.4           | 0.481   |
| Temperature (°C) | 37.1±0.7         | 37.0±0.5            | 0.761   |
| Arrhythmia       | 9 (11%)          | 2 (13.3%)           | 0.677   |
| Positive blood culture | 4 (4.1%) | 0                  | 1.000   |
| Major infection  | 5 (5.2%)         | 2 (10%)             | 0.342   |
| Previous sternotomy | 23 (23.7%)  | 8 (40.0%)           | 0.133   |
| Noncardiac surgery | 1 (1.0%)    | 0                  | 1.000   |
| ICD              | 44 (45.4%)       | 10 (50%)            | 0.705   |
| Mechanical ventilation | 7 (7.2%) | 2 (10.0%)           | 0.650   |
| Aspirin          | 7 (7.2%)         | 3 (15%)             | 0.372   |
| Inotropic support | 72 (74.2%)    | 16 (80%)            | 0.778   |
| IABP             | 19 (19.6%)       | 5 (25.0%)           | 0.556   |
| ECMO             | 6 (6.2%)         | 1 (5.0%)            | 1.000   |
| STMS             | 9 (9.3%)         | 4 (20%)             | 0.233   |
| LTMS             | 7 (7.2%)         | 4 (20%)             | 0.093   |
| Any MS           | 15 (15.5%)       | 6 (30%)             | 0.196   |

Boldface indicates p < 0.100.

ECMO, extracorporeal membrane oxygenation; IABP, intraaortic balloon pump; ICD, implantable cardioverter defibrillator; LOS, length of stay; LTMS, long-term mechanical support; MS, mechanical support; STMS, short-term mechanical support.

### Table 5. Intraoperative Variables

|                   | 90 Day Survivors | 90 Day Nonsurvivors | p       |
|-------------------|------------------|---------------------|---------|
| Cross-clamping    | 15 (15.5%)       | 6 (30.0%)           | 0.196   |
| On-pump           | 82 (84.5%)       | 14 (70%)            | 0.196   |
| Theater time (minutes) | 300 (250, 435) | 330 (300, 420)     | 0.331   |
| Device implanted  |                  |                     | 0.629   |
| HeartMate II      | 59 (64.3%)       | 11 (15.7%)          |         |
| HeartWare         | 38 (90.8%)       | 9 (19.1%)           |         |
tracheostomy did not have direct clinical relevance on the 90 day mortality in our study. By contrast, the postoperative requirement for prolonged mechanical ventilation appeared to be more optimal for considering respiratory failure as a risk factor for 90 day mortality. Nevertheless, although this parameter was significantly higher in the 90 day nonsurvivor group in the univariate analysis, it did not reach statistical significance in the logistic regression analysis and was not shown to be an independent predictor of the 90 day mortality.

In accordance with the results from Yoshioka et al., the preoperative serum bilirubin level in our study was not found to be a risk factor for early mortality in univariate and logistic regression analysis. However, this finding disagrees with those of several research studies. The reason for this inconsistency seems to be more aggressive temporary RVAD support protecting from congestive hepatic dysfunction in both studies. Moreover, early and ungrudging implantation of RVAD may be responsible for perioperative biventricular support, which has

| Table 6. Early Postoperative Characteristics |
|---------------------------------------------|
|                                      | 90 Day Survivors | 90 Day Nonsurvivors | p    |
| Inotropic support > 7 days                | 27 (29.0%)       | 8 (53.3%)           | 0.078|
| Ventilation > 7 days                      | 13 (14.0%)       | 6 (42.9%)           | 0.017|
| RVAD                                       | 22 (22.7%)       | 7 (35%)             | 0.263|
| ECMO                                       | 1 (1.0%)         | 1 (5.0%)            | 0.314|
| Hemofiltration                             | 21 (21.6%)       | 12 (66.7%)          | <0.001|
| Reintubation                               | 22 (22.9%)       | 2 (11.1%)           | 0.355|
| Tracheostomy                               | 12 (12.8%)       | 1 (5.6%)            | 0.689|
| Transfusions                               |                 |                    |      |
| RBC (units)                                | 5 (2, 11)        | 13 (4, 19)          | 0.014|
| Platelets (units)                          | 1 (0, 2)         | 3 (1, 6)            | 0.003|
| FFP (units)                                | 3 (0, 6)         | 5 (2, 14)           | 0.107|
| Infections                                 |                 |                    |      |
| Sepsis                                     | 13 (13.4%)       | 0                   | 0.121|
| Bronchopulmonary                           | 17 (17.5%)       | 4 (20%)             | 0.756|
| CVP line                                   | 6 (6.2%)         | 0                   | 0.588|
| Urine tract                                | 5 (5.2%)         | 0                   | 0.586|
| Other                                      | 9 (9.3%)         | 3 (15%)             | 0.429|

Boldface indicates p < 0.100.
CVP, central venous pressure; ECMO, extracorporeal membrane oxygenation; FFP, fresh frozen plasma; RBC, red blood cells; RVAD, right ventricular assist device.
been previously associated with poorer outcome\textsuperscript{21} not to be a predictor of early mortality in our study.

The 90 day mortality in patients with INTERMACS class 1 in our study was 23.5% which is comparable to previous research.\textsuperscript{10} The mean INTERMACS class was lower in the 90 day nonsurvivor group compared to the 90 day survivor group (2.13 ± 0.83 vs. 2.5 ± 0.11), not reaching a statistical significance ($p = 0.199$). This could be due to the inclusion of the patients who underwent LVAD exchange and were stable at the time of redo LVAD implantation. However, it cannot be ignored that these patients incurred higher perioperative mortality risk due to redo procedure, described previously.\textsuperscript{2} Also in our study, preoperative long-term LVAD support was one of the univariate risk factors for 90 day mortality, and one fifth of the patients who died within 90 days were on previous long-term LVAD support.

The only influenceable independent risk factor predictive of the 90 day mortality in our cohort was the preoperative CVP. The data from several sources have identified the role of CVP as a critical hemodynamic parameter in the LVAD patients. Shiga \textit{et al.}\textsuperscript{21} found that the CVP/PCWP ratio was predictive of the need for perioperative biventricular support which was associated with a significantly poorer survival. The preoperative CVP has also been shown to be significantly higher in patients who developed ARF after LVAD implantation which also had a negative effect on postoperative outcome.\textsuperscript{17} Dang \textit{et al.}\textsuperscript{22} found elevated intraoperative CVP as only independent predictor of post-LVAD RVF among all pre- and intraoperative hemodynamic parameters. This is partially consistent with our results. Being an independent predictor for 90 day mortality, an elevated preoperative CVP caused by suboptimal right ventricular function, fluid overloading, or significant pulmonary hypertension may have led to development of serious perioperative complications causing early post-LVAD mortality. Such complications were postoperative ARF requiring hemodialysis, prolonged mechanical ventilation, and extended perioperative bleeding requiring massive transfusion. However, incidence of postoperative RVAD use was not significantly different in both groups apparently due to relatively early and aggressive use. Nevertheless, a clear clinical trend toward higher rate of prolonged inotropic support in the nonsurvivor group which is usually associated with RVF pleads for an increased likelihood of RVF in this group. Additionally, preoperative LVSD and LVDD which were significantly smaller in the nonsurvivor group in our study were also significantly smaller in patients who developed RVF in the study by Drakos \textit{et al.}\textsuperscript{23} and may emphasize the role of RVF as a pathophysiological mechanism influencing early mortality in our study.

The multivariate logistic regression analysis revealed patient's age as an independent factor for 90 day mortality in our study. This finding is in agreement with Shiga \textit{et al.}\textsuperscript{21} who showed age as an independent risk factor for death after pulsatile extracorporeal LVAD implantation. Additionally, patients 60 years and older were shown to have significantly poorer survival after the heart transplantation at 30 days and 1 year when previously bridged by the CF-LVAD compared to those bridged by inotropic support or transplanted directly.\textsuperscript{24} Therefore, patient's age seems to play a crucial role in predicting early post-LVAD mortality suggesting appropriate selection of the patients for LVAD implantation as a bridge to transplantation. On the contrary, Adamson \textit{et al.}\textsuperscript{15} found no difference in the outcome of advanced heart failure patients receiving a Heart Mate II LVAD grouped as younger and older than 70 years of age and concluded that the age should not be an independent contraindication and LVAD therapy is suitable for destination therapy in elderly patients.

In conclusion, our analysis based on long-term experience with implantation of CF-LVADs allows us to suggest that optimization of the preoperative volume status, preload, and the right ventricular function using CVP as an important hemodynamic indicator is of vital importance for improving the early postoperative outcome. Furthermore, patient's age should be considered as an important factor by selecting the candidates for CF-LVAD support, particularly as bridge to transplantation.

\textbf{Study Limitations}

The main limitations of this study are its retrospective non-randomized design and analysis of limited number of patients from a single institution. Furthermore, the data collection was restricted to the variables which were available in electronic or written patient notes and flowcharts. Also, the patients who underwent LVAD implantation with concomitant surgical procedures were not included in the present observation.

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