A left ventricular end-diastolic dimension less than 6.0 cm is associated with mortality after implantation of an axial-flow pump

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ABSTRACT

Objective: The effects of having a lower left ventricular end-diastolic dimension before HeartMate II (Thoratec Corp, Pleasanton, Calif) left ventricular assist device implantation remain unclear. We analyzed our single-center data on HeartMate II implantation to determine whether having a lower left ventricular end-diastolic dimension preoperatively was associated with inferior outcomes.

Methods: From November 2003 to March 2016, 393 patients with chronic heart failure underwent primary HeartMate II implantation. We compared the preoperative left ventricular end-diastolic dimension and associated survival outcomes of these patients to determine the left ventricular end-diastolic dimension cutoff for worse overall survival. Then, we compared the preoperative demographics, stroke rate, and mortality of patients with a left ventricular end-diastolic dimension above the cutoff for worse survival with those of patients with a left ventricular end-diastolic dimension below the cutoff.

Results: A Cox multivariate regression model showed that low left ventricular end-diastolic dimension was an independent predictor of mortality (hazard ratio, 1.49; $P = .02$). The Contal and O'Quigley method showed that overall survival postimplantation was decreased in patients with a left ventricular end-diastolic dimension less than 6.0 cm ($n = 91$). Kaplan–Meier analysis confirmed that the left ventricular end-diastolic dimension less than 6.0 cm group had lower overall survival than the left ventricular end-diastolic dimension 6.0 cm or greater group ($P = .04$). Furthermore, a competing-risk analysis showed that postoperative stroke was more common in the left ventricular end-diastolic dimension less than 6.0 cm group than in the left ventricular end-diastolic dimension 6.0 cm or greater group ($P < .01$).

Conclusions: Overall survival was decreased and postoperative stroke was increased in HeartMate II recipients with a preoperative left ventricular end-diastolic dimension less than 6.0 cm. Future research should determine the left ventricular end-diastolic dimension cutoff values for safely implanting other support devices, and device designs should be improved to better accommodate the needs of patients with a limited left ventricle size. (J Thorac Cardiovasc Surg 2019;157:2302-10)

Survival of HM-II (Thoratec Corp, Pleasanton, Calif) recipients with a preoperative LVEDD less than 6.0 cm or an LVEDD 6.0 cm or greater.

Central Message

A preoperative LVEDD less than 6.0 cm is a risk factor for mortality and stroke after HM-II (Thoratec Corp, Pleasanton, Calif) implantation.

Perspective

Current CF-LVAD guidelines do not have implantation recommendations about left ventricular size, so we sought to determine the LVEDD cutoff value for safely implanting the HM-II (Thoratec Corp, Pleasanton, Calif). Future research should determine the LVEDD cutoff values for safely implanting other support devices, and the designs of such devices should be improved to better accommodate the needs of patients with a limited left ventricle size.

See Commentaries on pages 2311 and 2313.

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Implantation of left ventricular assist devices (LVADs) for long-term support has increased exponentially over the past decade.¹⁻³ Continuous-flow LVADs (CF-LVADs) are currently the gold standard therapy for advanced heart

Scanning this QR code will take you to the article title page to access supplementary information.

Abbreviations and Acronyms

CF-LVAD	= continuous-flow left ventricular assist device
CI	= confidence interval
HM-II	= HeartMate II
HR	= hazard ratio
LVAD	= left ventricular assist device
LVEDD	= left ventricular end-diastolic dimension
MR	= mitral regurgitation

failure and are the most widely used mechanical circulatory devices for long-term support.⁴ Nevertheless, it has been suggested that suction events, which can lead to impairment of pump filling, may cause pump dysfunction. This impairment could be from intermittent obstruction of the inflow of the CF-LVAD during the cardiac cycle, which could be particularly problematic in patients with smaller ventricles if the ventricular volume reservoir is compromised.^{4,5} Previous studies have reported that having a low preoperative left ventricular end-diastolic dimension (LVEDD) is a risk factor for mortality after LVAD implantation; however, these studies had several limitations, such as low numbers of CF-LVAD recipients and short follow-up periods.⁵⁻⁷ Thus, the outcomes of CF-LVAD implantation have not been evaluated sufficiently for patients with a lower LVEDD.

In the current study, we compared the LVEDD and associated survival outcomes of patients who underwent HeartMate II (HM-II) implantation to determine the LVEDD cutoff for worse overall survival. Then, using this cutoff to define our study groups, we compared the preoperative demographics, postoperative incidence of stroke, and long-term survival of the patients who had an LVEDD below the calculated cutoff value for worse survival with those of the patients with an LVEDD above the cutoff.

MATERIALS AND METHODS

Study Design

This was a single-center retrospective review of data from 403 patients who underwent primary implantation of an HM-II (Thoratec Corp, Pleasanton, Calif) axial-flow CF-LVAD between November 2003 and March 2016. The primary outcome of interest for this study was the long-term survival of the HM-II recipients who had a lower preoperative LVEDD. Of the 403 patients who received an HM-II device during the study period, 10 had no data about LVEDD before LVAD implantation; therefore, these 10 patients were excluded from the analysis. For the patients included in the study, the LVEDD was determined from a preoperative transthoracic echocardiogram obtained at our center. The LVEDD was measured from the parasternal long-axis view during the end-diastolic phase of the cardiac cycle. The LVEDD measurements were obtained perpendicular to the long axis of the left ventricle at the level of the mitral valve leaflet tips from the leading edge of the septal endocardium to the leading edge of the posterior wall endocardium.⁸

Approval to conduct this review was obtained from our institutional review board, which waived the consent requirement because the study

was retrospective. Patient data collected retrospectively from the Texas Heart Institute/Baylor College of Medicine clinical LVAD database included demographics, preoperative characteristics, postoperative complications, and survival outcomes. Preoperative data and survival/mortality data (including date of death, when applicable) were collected for all patients. Overall survival calculations were made on the basis of the number of deaths that occurred at any time after implantation. The patients who underwent heart transplantation or LVAD explantation due to left ventricular recovery were censored at the time of the event. For 91.6% of the patients, follow-up care was obtained at our institution. Heart disease etiology was classified as ischemic or nonischemic. Stroke was defined as a new neurologic deficit associated with abnormal neuroimaging findings; in each case, a neurologist examined the findings and classified the stroke as ischemic or hemorrhagic.

Statistical Analysis

Most statistical analyses were performed with SAS 9.2 software (SAS Institute Inc, Cary, NC). We used a Cox multivariable regression analysis to identify predictors of overall postoperative mortality (hazard ratios [HRs] and 95% confidence intervals [CIs] were calculated). For this, we first performed a univariate analysis of all the preoperative and operative variables. Then, the variables with a *P* value less than .20 in the univariate Cox analysis were included in our final multivariate model. Because having a lower LVEDD was found to be a predictor of postoperative mortality, we performed a Contal and O'Quigley analysis to statistically determine the LVEDD cutoff for worse overall survival outcomes. This value was used for defining our 2 study groups: (1) patients with an LVEDD above the cutoff for worse overall survival and (2) patients with an LVEDD below the cutoff. These 2 groups were compared in regard to demographics, postoperative incidence of stroke, and long-term survival. Univariate analyses were used to compare the demographic and perioperative characteristics. Continuous variables were reported as mean and standard deviation and were compared by using the 2-sample *t* test. Categorical variables were reported as number and percentage and were compared by using chi-square tests. The Kaplan–Meier method was used to estimate survival on LVAD support for the 2 study groups, and a log-rank test was performed to compare the survival of the groups. The patients who underwent heart transplantation or LVAD explantation were censored from the survival analysis in alive status on the date of the event. The Kaplan–Meier analysis was performed with EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). More precisely, it is a modified version of R commander designed to add statistical functions frequently used in biostatistics.⁹ Competing-risk analyses were performed in which the cumulative incidence and associated CIs were determined for the postoperative incidence of stroke, and death was treated as a competing variable. Logistic regression was used to assess the predictors of early (30-day) postoperative mortality.

RESULTS

Cox Multivariable Regression Analysis of the Predictors of Overall Mortality After HeartMate II Implantation

Preoperative and operative variables were included in a univariate analysis of potential predictors of survival after LVAD implantation (Table E1). All the variables with a *P* value less than .20 in the univariate Cox analysis were included in a multivariate Cox proportional hazards model with overall mortality as the outcome. Stepwise regression analysis showed that having a low LVEDD was a significant predictor of postoperative mortality (HR, 1.49; 95% CI,

TABLE 1. Cox multivariable regression analysis: Predictors of overall mortality

Variable	HR (95% CI)	P value
Age (y)	1.02* (1.01-1.04)	<.01
Female	0.84 (0.56-1.28)	.42
Ischemic cardiomyopathy	1.09 (0.79-1.52)	.57
Low LVEDD	1.49 (1.05-2.14)	.02
LVEDD <6.0 cm	1.79 (1.17-2.72)	<.01
Previous sternotomy	1.00 (0.99-1.00)	.32
Cardiopulmonary bypass time (min)	1.00 (0.99-1.00)	.21
Aortic crossclamp time (min)	1.00 (0.99-1.02)	.71
Operation time (min)	1.00 (0.99-1.00)	.86
Concomitant procedure	0.91 (0.64-1.32)	.64
Intraoperative RVAD use	1.61 (1.16-2.22)	<.01

HR, Hazard ratio; CI, confidence interval; LVEDD, left ventricular end-diastolic dimension; RVAD, right ventricular assist device. *Increased age was a predictor of increased mortality.

1.05-2.14; $P = .02$) (Table 1). LVEDD was also analyzed as a dichotomous variable using the LVEDD cutoff value of 6.0 cm obtained from the Contal and O'Quigley statistical test. LVEDD 6.0 cm or greater was used as a reference. Having an LVEDD less than 6.0 cm was a significant predictor of mortality (HR, 1.79; CI, 1.17-2.72; $P < .01$). Other independent predictors of postoperative mortality were preoperative older age ($P < .01$) and intraoperative use of a right ventricular assist device ($P < .01$). Gender was not an independent risk factor ($P = .42$). The proportional risk assumption was not violated in this Cox multivariable regression.

Left Ventricular End-Diastolic Dimension Cutoff Determination for Worse Overall Survival

Table 2 shows the distribution of patients according to LVEDD, as determined from the preoperative transthoracic echocardiogram. When we ran the Contal and O'Quigley statistical test to determine an LVEDD cutoff value for worse overall survival outcomes, we found that survival was decreased in the patients with an LVEDD less than 6.0 cm. We then used this LVEDD value as the cutoff for defining our 2 study groups: (1) patients with an LVEDD less than 6.0 cm ($n = 91$, 23% of the cohort) and (2) patients with an LVEDD 6.0 cm or greater ($n = 302$, 77% of the cohort). Figure E1 shows a spline graph of the relationship between cumulative survival and LVEDD; the trend seen is a steep decrease in survival in patients with an LVEDD less than 6.0 cm.

Comparison of Demographic and Perioperative Characteristics

An analysis of the demographic and perioperative characteristics of the HM-II recipients showed that the

TABLE 2. Distribution of patients according to preoperative left ventricular end-diastolic dimension

LVEDD (cm)	N (%)
Total	393 (100)
LVEDD <6.0 cm	91 (23.2)
<4.0	4 (1.0)
4.0-4.5	3 (0.8)
4.5-5.0	8 (2.0)
5.0-5.5	18 (4.6)
5.5-6.0	58 (14.8)
LVEDD ≥6.0 cm	302 (76.8)
6.0-6.5	81 (20.6)
6.5-7.0	83 (21.1)
7.0-7.5	57 (14.5)
7.5-8.0	30 (7.6)
8.0-8.5	29 (7.4)
8.5-9.0	13 (3.3)
>9.0	9 (2.3)

LVEDD, Left ventricular end-diastolic dimension.

group with an LVEDD less than 6.0 cm had more female patients and a higher prevalence of ischemic cardiomyopathy and diabetes mellitus than the group with an LVEDD 6.0 cm or greater (Table 3). In addition, the group with an LVEDD less than 6.0 cm had a higher left ventricular ejection fraction, cardiac index, and pulmonary artery pressure; a longer operative time; and a higher rate of right ventricular assist device use. In contrast, in the group with an LVEDD 6.0 cm or greater, severe tricuspid regurgitation and mitral regurgitation (MR) were more prevalent, and the pulmonary capillary wedge pressure was higher. As for the laboratory values, the hemoglobin and albumin concentrations were higher in the group with an LVEDD 6.0 cm or greater than in the group with an LVEDD less than 6.0 cm. A concomitant mitral valve procedure was performed in 1 (25.0%) of the patients with severe preoperative MR and an LVEDD less than 6.0 cm and in 25 (33.8%) of the patients with severe preoperative MR and an LVEDD 6.0 cm or greater ($P = .71$). A concomitant tricuspid valve procedure was performed in 1 (25.0%) of the patients with severe preoperative tricuspid regurgitation and an LVEDD less than 6.0 cm and in 10 (27.0%) of the patients with severe preoperative MR and an LVEDD 6.0 cm or greater ($P = .93$).

Comparison of Postoperative Survival and Stroke Rate

When compared with patients with an LVEDD 6.0 cm or greater, those with an LVEDD less than 6.0 cm were found to have significantly lower overall survival ($P = .04$, Figure 1). The median survival duration for the nonsurvivors with a preoperative LVEDD less than 6.0 cm was 359 days, whereas that for the nonsurvivors with a

TABLE 3. Demographic and perioperative characteristics of the HeartMate II recipients

Variable	Overall (n = 393)	LVEDD <6.0 cm (n = 91)	LVEDD ≥6.0 cm (n = 302)	P value
Age (y)	54.8 ± 13.5	57.0 ± 12.9	54.2 ± 13.5	.07
Female	76 (19.3)	21 (23.1)	55 (18.2)	<.01
BMI (kg/m ²)	28.6 ± 6.73	27.9 ± 7.1	28.8 ± 6.6	.25
BSA (m ²)	2.0 ± 0.2	2.0 ± 0.2	2.0 ± 0.2	.24
Bridge to transplantation	173 (44.0)	36 (39.6)	137 (45.4)	.33
Ischemic cardiomyopathy	177 (45.0)	51 (56.0)	126 (41.7)	.01
Hypertension	237 (60.3)	52 (57.1)	185 (61.3)	.48
Diabetes mellitus	173 (44.0)	52 (57.1)	121 (40.0)	<.001
Smoking history	160 (40.7)	42 (46.1)	118 (39.1)	.22
Atrial fibrillation	164 (41.7)	40 (44.0)	124 (41.0)	.62
Chronic obstructive pulmonary disease	50 (12.7)	13 (14.3)	37 (12.3)	.69
Previous cardiac surgery	131 (33.3)	38 (41.8)	93 (30.8)	.06
Preoperative short-term MCS	211 (53.7)	52 (57.1)	159 (52.6)	.45
Laboratory results				
Hemoglobin (g/dL)	11.5 ± 2.0	11.0 ± 1.9	11.7 ± 2.0	<.01
WBCs (1000/mm ³)	9.2 ± 4.1	9.6 ± 4.7	9.0 ± 4.0	.25
Platelets (1000/mm ³)	209.1 ± 93.7	204.2 ± 94.7	210.0 ± 93.3	.56
Sodium (mEq/L)	135.1 ± 4.6	135.7 ± 4.8	134.9 ± 4.5	.19
Creatinine (mg/dL)	1.4 ± 0.7	1.4 ± 0.6	1.4 ± 0.7	.93
BUN (mg/dL)	31.1 ± 18.7	30.2 ± 19.2	31.4 ± 18.5	.61
AST (U/L)	75.0 ± 158.4	96.2 ± 259.7	68.7 ± 110.0	.14
ALT (U/L)	87.5 ± 185.2	83.7 ± 139.0	88.7 ± 197.0	.82
Total bilirubin (mg/dL)	1.7 ± 2.8	1.8 ± 2.5	1.7 ± 2.9	.93
Albumin (g/dL)	3.5 ± 0.6	3.3 ± 0.7	3.5 ± 0.6	<.01
INR	1.2 ± 0.4	1.2 ± 0.5	1.2 ± 0.4	.75
Preoperative echocardiogram results				
LVEF (%)	21.7 ± 3.1	23.1 ± 4.3	21.3 ± 2.6	<.001
LVEDD (cm)	6.6 ± 1.0	5.4 ± 0.5	7.0 ± 0.8	<.001
Severe TR	41 (10.4)	4 (4.4)	37 (12.3)	.03
Severe MR	78 (19.8)	4 (4.4)	74 (24.5)	.03
Severe AR	4 (1.0)	0 (0)	4 (1.3)	.26
Right heart catheterization results				
CI (L/min/m ²)	1.8 ± 0.5	2.0 ± 0.7	1.8 ± 0.5	.01
CVP (mm Hg)	12.1 ± 7.3	11.7 ± 6.9	12.2 ± 7.5	.63
PAP (mm Hg)	36.5 ± 11.3	33.7 ± 10.7	26.4 ± 10.3	.02
PCWP (mm Hg)	25.3 ± 10.5	21.7 ± 10.3	26.4 ± 10.3	<.01
PVR (Wood units)	3.3 ± 3.4	3.5 ± 2.7	3.2 ± 2.4	.85
Operative variables				
CPB use	382 (97.2)	86 (94.5)	296 (98.0)	.07
CPB time (min)	91.9 ± 49.7	92.0 ± 60.8	91.8 ± 45.8	.98
Crossclamp use	42 (10.7)	9 (9.9)	33 (10.9)	.77
Crossclamp time (min)	5.1 ± 20.1	6.6 ± 28.5	4.6 ± 16.8	.40
Operative time (min)	281 ± 102	286 ± 108	240 ± 101	<.001
Intraoperative RVAD use	32 (8.1)	12 (13.2)	20 (6.6)	.04

Continuous data are shown as mean ± standard deviation. Categorical data are presented as No. (%). LVEDD, Left ventricular end-diastolic diameter; BMI, body mass index; BSA, body surface area; MCS, mechanical circulatory support; WBC, white blood cell; BUN, blood urea nitrogen; AST, aspartate aminotransferase; ALT, alanine aminotransferase; INR, international normalized ratio; LVEF, left ventricular ejection fraction; TR, tricuspid regurgitation; MR, mitral regurgitation; AR, aortic valve regurgitation; CI, cardiac index; CVP, central venous pressure; PAP, pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure; PVR, pulmonary vascular resistance; CPB, cardiopulmonary bypass; RVAD, right ventricular assist device.

preoperative LVEDD 6.0 cm or greater was 572 days ($P = .03$). Within 3 months of CF-LVAD implantation, 27.2% of the deaths in the LVEDD less than 6.0 cm group had occurred, compared with 21.7% of the deaths in the LVEDD 6.0 cm or greater group. For both groups, the highest risk of mortality was within the first 30 days after CF-LVAD implantation (Figure E2).

When the postoperative stroke rates were compared, the patients with an LVEDD less than 6.0 cm were found to have a higher incidence of stroke than those with an LVEDD 6.0 cm or greater ($P < .01$, Figure 2). An analysis of the patients who had a stroke indicated that the group with an LVEDD less than 6.0 cm had a higher incidence of ischemic stroke than the group with an LVEDD 6.0 cm or greater ($P < .01$, Figure 3, A). Hemorrhagic stroke was also more common in the group with an LVEDD less than 6.0 cm than in the group with an LVEDD 6.0 cm or greater, but the difference was not statistically significant ($P = .06$, Figure 3, B).

Logistic Regression Analysis of the Predictors of 30-Day Mortality

All the variables shown in Table 4 were placed in a logistic regression analysis with 30-day mortality as the outcome. Higher age ($P < .01$) and intraoperative right ventricular assist device use ($P = .03$) were predictors of

30-day mortality, but no association was found between LVEDD and 30-day mortality ($P = .22$).

Patients Who Underwent Heart Transplantation or Left Ventricular Assist Device Explanation

Table E2 shows the details regarding the patients who underwent heart transplantation or LVAD explantation. Of the 393 patients in our total cohort, 173 were bridge-to-transplant recipients. When the heart transplant recipients with an LVEDD less than 6.0 cm were compared with those with an LVEDD 6.0 cm or greater, no difference was found in the number of days on LVAD support before heart transplantation (mean $\pm$ standard deviation, 615 ± 713 days vs 460 ± 590 days; $P = .43$) or in survival times after heart transplantation (mean $\pm$ standard deviation, 434 ± 1329 days vs 1193 ± 1387 days; $P = .20$). In our cohort, 20 patients underwent LVAD explantation because of left ventricular recovery; 7 had an LVEDD less than 6.0 cm, and 13 had an LVEDD 6.0 cm or greater.

The 2 groups showed no difference in the number of days on LVAD support before LVAD explantation (mean $\pm$ standard deviation, 583 ± 1066 days vs 366 ± 925 days; $P = .73$).

Overall Outcomes Regarding Gender

The total cohort consisted of 317 male and 76 female patients; the LVEDD for the female patients was significantly

FIGURE 1. Kaplan-Meier plot showing a significant decrease in overall survival after HM-II (Thoratec Corp, Pleasanton, Calif) implantation for patients with an LVEDD less than 6.0 cm compared with those with an LVEDD 6.0 cm or greater. LVEDD, Left ventricular end-diastolic dimension.

FIGURE 2. Graph showing the postoperative incidence of stroke in patients with an LVEDD less than 6.0 cm and in those with an LVEDD 6.0 cm or greater. LVEDD, Left ventricular end-diastolic dimension.

smaller than that for the male patients (6.3 ± 0.9 cm vs 6.8 ± 1.1 cm; $P < .01$). The group with an LVEDD less than 6.0 cm consisted of 70 male and 21 female patients; the male and female patients in this group showed no significant difference in LVEDD (5.4 ± 0.5 cm vs 5.3 ± 0.8 cm; $P = .23$). We performed the Contal and O'Quigley analysis for male and female patients separately and found that the respective LVEDD cutoff values were 6.0 and 6.1. We also included gender in the Cox multivariate regression analysis and found that it was not a predictor of overall mortality ($P = .42$).

Comparison of Patients With Left Ventricular End-Diastolic Dimension 5.5 to 6.0 Centimeters Versus 6.0 to 6.5 Centimeters

Figure E3 shows the Kaplan–Meier curves comparing survival on LVAD support for the patients with an LVEDD 5.5 to 6.0 cm ($n = 58$, 14.8% of full cohort, 63.7% of LVEDD <6.0 cm group) and those with an LVEDD 6.0 to 6.5 cm ($n = 81$, 20.1% of full cohort, 26.8% of LVEDD ≥ 6 cm group). Although the difference in survival on LVAD support was not statistically significant, the LVEDD 6.0 to 6.5 cm group showed a trend of better survival in the postoperative period for a few years before the number at risk decreased in both groups. The number at risk on days 1000, 1500, and 2000 decreased to 12, 7, and 2, respectively, in the LVEDD 6.0 to 6.5 cm group and to 21, 8, and 4, respectively, in the LVEDD 5.5 to 6.0 cm group.

DISCUSSION

This study is one of the largest single-center studies to assess the correlations between preoperative LVEDD and postoperative mortality and stroke rates after primary HM-II implantation. We found that having an LVEDD less than 6.0 cm before HM-II implantation was significantly associated with a higher mortality rate and a higher incidence of postoperative stroke (Video 1).

Implantation of a CF-LVAD is the standard of care for patients with end-stage heart failure who require long-term mechanical circulatory support.^{2,10} However, the effects of having a low preoperative LVEDD on CF-LVAD implantation outcomes have not been well established. A previous study reported that having a low preoperative LVEDD was a risk factor for mortality after LVAD implantation; however, the effect of using a CF-LVAD remained unclear because more than 80% of the patients in the study received an extracorporeal pulsatile LVAD.⁶ Another study reported that having a low preoperative LVEDD increased the 30-day morbidity and mortality rates after HM-II implantation, but the study had a small sample size ($n = 83$) and a short follow-up period (30 days).¹⁰ One analysis of a large INTERMACS dataset assessed whether device flow configuration (axial vs centrifugal), left ventricular dimension, or the interaction of these variables affect postoperative mortality.¹¹ The study found that the interaction between LVEDD and device flow configuration had no effect on survival, but it did show a linear increase in

FIGURE 3. Subgroup analysis of the patients who had a stroke. Graphs show the incidence of ischemic stroke (A) and hemorrhagic stroke (B) in patients with an LVEDD less than 6.0 cm and in those with an LVEDD 6.0 cm or greater. *LVEDD*, Left ventricular end-diastolic dimension.

TABLE 4. Logistic regression analysis of predictors of 30-day mortality

Variable	HR (95% CI)	P value
Age (y)	1.05* (1.02-1.09)	<.01
Female	0.98 (0.92-1.70)	.98
Ischemic cardiomyopathy	1.2 (0.60-1.06)	.11
Low LVEDD	0.58 (0.24-1.38)	.22
Previous sternotomy	0.98 (0.73-1.32)	.91
Cardiopulmonary bypass time (min)	1.00 (0.99-1.09)	.98
Aortic crossclamp time (min)	0.99 (0.97-1.02)	.64
Concomitant procedure	0.87 (0.69-1.18)	.36
Intraoperative RVAD use	2.48 (1.15-6.24)	.03

HR, Hazard ratio; CI, confidence interval; LVEDD, left ventricular end-diastolic dimension; RVAD, right ventricular assist device. *Increased age was a predictor of 30-day mortality.

survival with increasing LVEDD. Our study analyzed only 1 type of LVAD, the HM-II, but it also identified small LVEDD as an independent predictor of mortality. In our study, the patients with a preoperative LVEDD less than 6.0 cm had a significantly lower long-term survival rate after HM-II implantation than the patients with an LVEDD 6.0 cm or greater (Table 1). However, there was no significant association between LVEDD and 30-day mortality (Table 4), but this may have been due to the increased mortality in all patients, regardless of LVEDD, in the weeks immediately after LVAD implantation. If a patient with an LVEDD below this 6.0-cm cutoff needs to undergo HM-II implantation, the pump inlet position and the inlet angle of the HM-II device should be carefully considered to ensure that they are optimal because it is thought that malpositioning of the inflow could occur more easily in these patients than in those with an LVEDD 6.0 cm or greater. Malpositioning of the device could lead to impaired pump filling and ventricular sucking events, which may lead to secondary pump malfunction.

In our analysis, patients with a preoperative LVEDD less than 6.0 cm had a significantly higher incidence of stroke after HM-II implantation than the patients with an LVEDD 6.0 cm or greater. Specifically, a subanalysis showed that the group with an LVEDD less than 6.0 cm had a higher incidence of ischemic stroke. We think that impaired pump filling and ventricular sucking events in the patients with an LVEDD less than 6.0 cm could have caused low flow through the LVAD and may have played a role in the postoperative embolic events and ischemic stroke seen in these patients. Because of the suction event detection algorithm in the HM-II axial pump, suction events are typically detected after they occur. Therefore, it may be difficult to prevent a suction event in an HM-II device before it happens. Thus, it is critically important to carefully position the inflow when implanting an HM-II device. Preoperative

VIDEO 1. The main message of this article is explained. Low LVEDD is an independent predictor of mortality after HM-II (Thoratec Corp, Pleasanton, Calif) primary implantation. The LVEDD cutoff value for worse survival outcomes was 6.0 cm. These findings should be considered when deciding whether to implant an HM-II device in patients with a small left ventricle. Video available at: [https://www.jtcvs.org/article/S0022-5223\(19\)30067-4/fulltext](https://www.jtcvs.org/article/S0022-5223(19)30067-4/fulltext).

atrial fibrillation is a known risk factor for morbidity and mortality after cardiac operations.^{12,13} In our study, the patients with an LVEDD less than 6.0 cm and those with an LVEDD 6.0 cm or greater showed no significant difference in the preoperative prevalence of atrial fibrillation (44.0% vs 41.0%, $P = .62$), suggesting that the higher postoperative incidence of stroke in the patients with an LVEDD less than 6.0 cm was not due to preoperative atrial fibrillation.

The International Society for Heart and Lung Transplantation guidelines for anticoagulation after LVAD implantation recommend an international normalized ratio target of 2.0 to 3.0 or 2.5 to 3.5 with the use of antiplatelet therapy.¹⁴ In our study, the group with an LVEDD less than 6.0 cm had a higher incidence

of stroke. If this complication was caused by thromboembolic events, one solution might be to use a higher international normalized ratio target for patients with an LVEDD less than 6.0 cm, although further study is needed to confirm our hypothesis. However, the therapy should be individualized and based on the patient's risk of stroke and bleeding. In our retrospective study, it was difficult to determine how many of the mortalities were due to pump malfunction/thrombus or thromboembolism because we did not have autopsy data for all the patients and because many of the patients who died had multiple postoperative complications, such as multiple organ failure. However, a future prospective study could reveal more about the complications and mortalities specifically due to pump malfunction or related events in patients with a low LVEDD.

Study Limitations

Our study had some limitations. First, our study was not a prospective, randomized trial and therefore was subject to the limitations inherent to any retrospective study. Because the data were analyzed retrospectively, we were unable to determine whether the mortalities that occurred were related to pump malfunction or not. In addition, the retrospective nature of this study prevented us from being able to determine the occurrence of complications such as pump or left ventricular thrombosis, ventricular sucking events, and ventricular tachycardia. Furthermore, detailed echocardiography data, including measures of preoperative and postoperative right heart function and septal thickness and assessments of the inflow cannula position within the left ventricle, were not consistently collected over the 13-year period of this study. Additionally, our study specifically analyzed the outcomes of HM-II recipients. Although our data may apply, to some extent, to other CF-LVADs, it cannot be extrapolated completely to others because of differences in LVAD physiology.¹⁵ Finally, this was a single-center study, so selection bias may have been present.

CONCLUSIONS

Our single-center retrospective study showed that having an LVEDD less than 6.0 cm adversely affected patient outcomes after HM-II implantation. Specifically, having a preoperative LVEDD less than 6.0 cm was found to be an independent predictor of overall mortality after HM-II implantation and was associated with an increased risk of postoperative stroke. Future research should determine the LVEDD cutoff values for safely implanting other support devices, and device designs should be improved to better accommodate the needs of patients with a limited left ventricle size.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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