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Should Left Ventricular Assist Devices be Implanted in Patients Seventy Years of Age and Older: A Comparative Analysis

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ABSTRACT

Background: We evaluated outcomes in left ventricular assist device (LVAD) recipients aged seventy years and above and compared results to outcomes in LVAD recipients below seventy years of age.

Methods: From March 2006 through June 2012, 130 patients underwent implantation of either a HeartMate II (HM II; Thoratec Corp., Pleasanton, CA) or HeartWare (HeartWare Inc., Framingham, MA) LVAD at our institution. Four patients underwent device exchanges and were excluded. Of the remaining 126 patients, 6 (4.7%) were ≥ 70 years of age. Patients in the age group ≥ 70 years were compared to the group of patients < 70 years for perioperative mortality, long-term survival and incidence of postoperative complications.

Results: Mean age was 72.2 ± 2.3 (70-75) years for the older group and 52.8 ± 11.4 (18-69) years for the younger group ($P < .001$). There was no significant difference in the incidence of diabetes, hypertension, chronic renal insufficiency, dialysis, hepatic function, preoperative ventilation or previous cardiac surgery between the groups (P = NS). There was no significant difference in survival between the groups, with survival at 6 months, 1 year, and 2 years of 100%, 100% and 66.7% respectively for the older groups, versus 88.6%, 81.3% and 76.7% for the younger group ($P = .634$). There was no significant difference in postoperative bleeding requiring re-exploration, driveline infections, strokes, pneumonia, right ventricular failure, gastrointestinal bleeding or readmissions within thirty days (P = NS).

Conclusions: These data demonstrate similar short- and long-term results for the two groups of recipients of LVAD implantation. Results support the use of long-term mechanical circulatory support in carefully selected elderly patients.

INTRODUCTION

The superiority of mechanical circulatory support (MCS) over medical therapy for the treatment of advanced refractory heart failure is widely accepted. [Rose 2001; Dembitsky 2004; Starling 2011]. In addition, survival in these patients has significantly improved and postoperative complication rates have decreased with the use of continuous-flow left ventricular assist devices (CF-LVADs) over pulsatile flow devices [Pagani 2009; Slaughter 2009; Slaughter 2010].

An ageing population and improved treatments for hypertension, coronary artery and valvular disease are factors which contribute to the resulting increment in prevalence of elderly patients with chronic refractory heart failure [Jessup 2003; Lloyd-Jones 2010]. Many LVAD centers consider advanced age a contraindication for long-term MCS due to concerns that elderly patients have increased perioperative mortality, decreased post-implant survival and a higher incidence of postoperative complications. This study compared perioperative mortality, long-term survival and the incidence of postoperative complications in two groups of patients, those ≥ 70 years and patients < 70 years, who underwent LVAD implantation for advanced refractory heart failure, either as a bridge to transplantation (BTT) or as destination therapy (DT).

MATERIALS AND METHODS

This study was approved by our Institutional Review Board. We included all patients who underwent implantation of a CF-LVAD at our institution since the start of our CF-LVAD program in March 2006. From March 2006 through June 2012, 130 patients underwent implantation of a CF-LVAD. Of these, 4 patients had device exchanges and were excluded from the study. Patients received either a HeartMate II (Thoratec Corp., Pleasanton, CA) (n = 113) or Heartware HVAD (HeartWare Inc., Framingham, MA) (n = 13) and were stratified into two age groups, ≥ 70 years and < 70 years, based on age at the time of the LVAD implant.

Patient demographics, history and physical characteristics included age, gender, race, body surface area (BSA), body mass index (BMI), etiology of heart failure, indication for mechanical circulatory support (MCS; BTT or DT); associated co-morbidities, including diabetes mellitus (DM), hypertension (HTN), chronic obstructive pulmonary disease (COPD), chronic renal insufficiency (CRI), dialysis and peripheral vascular disease (PVD); and baseline creatinine and hepatic function tests. Chronic renal insufficiency was defined as GFR < 60 mL/min/m^2. The operative characteristics analyzed were based on the type of device (HeartMate II or Heartware HVAD).

Hemodynamic and echocardiographic data were evaluated pre- and post-LVAD (at 1 month and 6 months) and included central venous pressure (CVP), pulmonary artery (PA) pressure, pulmonary capillary wedge pressure (PCWP),

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cardiac output (CO), cardiac index (CI), left ventricular ejection fraction (LVEF), and left ventricular end diastolic diameter (LVEDD).

Outcome variables included perioperative mortality, postoperative survival at 1 month, 6 months, 1 year, and 2 years, intensive care unit (ICU) and overall hospital length of stay (LOS), postoperative complication rates for bleeding requiring re-exploration, infection, stroke, respiratory failure, renal failure, right ventricular (RV) failure, gastrointestinal bleeding, aortic insufficiency (AI), re-admission rates, and causes of death. RV failure was defined as either the need for inotropic support for more than 14 days, or the need for RVAD support.

Bridge to transplant criteria included the following: NYHA Class IV symptoms, life expectancy less than one year without LVAD implantation, frequent hospital admissions for exacerbation of heart failure, six minute walk of < 300 meters, peak VO2 < 14 cc/kg/min, listed for transplant at the time of LVAD implantation, no severe end organ (renal, hepatic, pulmonary, cerebral) dysfunction or failure, ability to tolerate anticoagulation, appropriate family and social support, appropriate living conditions, no significant cognitive deficits that interfere with ability to manage device, and no active infections.

Destination therapy criteria included the following: not eligible for transplantation due to advanced age, body mass index (BMI), pulmonary vascular resistance (PVR), recent malignancy, HIV, diabetes with severe end organ dysfunction, renal failure with or without hepatic insufficiency. Exclusion criteria for DT-LVAD included irreversible renal or hepatic dysfunction not explained by underlying congestive heart failure, severe COPD defined as FEV-1 < 50%, FVC < 50%, and/or DLCO < 50%, severe end organ dysfunction due to long-standing diabetes mellitus, symptomatic peripheral or cerebrovascular arterial disease, recent malignancy, active infection, presence of other life threatening diseases likely to limit length of life despite successful device implantation, and/or severe cognitive deficits that interfere with ability to appropriately understand and independently manage the device.

STATISTICAL ANALYSIS

Patient demographics and operative characteristics were compared between the two groups. Continuous variables were reported as mean, standard deviation, minimum, and maximum and were compared using two-sided two-sample t-tests. Alternatively, Wilcox rank-sum tests were used if normality

Patient Demographics and Comorbidities

Variable	< 70 (N=120) mean ± sd [min, med, max]	≥70 (N=6) mean ± sd [min, med, max]	*P*
Age	52.8 ± 11.4	72.2 ± 2.3	< .001**
Male	34 (28.3%)	0 (0%)	.190‡
Female	86 (71.7%)	6 (100%)	
African American	48(41.4%)	2 (33.3%)	1.000‡
Caucasian	68 (58.6%)	4 (66.7%)	
ischemic Cardiomyopathy	41 (34.2%)	3 (50.0%)	.420‡
Non-ischemic Dilated Cardiomyopathy	79 (65.8%)	3 (50.0%)	
Body Surface Area	2.0 ± 0.3	2.1 ± 0.2	.382*
Body Mass Index	28.0 ± 5.4	30.1 ± 4.5	.356*
Albumin	3.3 ± 0.5	3.3 ± 0.4	.990*
Bridge to Transplant	74 (61.7%)	0 (0.0%)	.004‡
Destination Therapy	46 (38.3%)	6 (100%)	
Diabetes Mellitus	51 (42.5%)	3 (50.0%)	.866‡
Hypertension	100 (83.3%)	5 (83.3%)	.723‡
Chronic Renal Insufficiency	46 (38.3%)	1 (16.7%)	.167‡
Dialysis	4 (3.3%)	0 (0.0%)	.074‡
Chronic Obstructive Pulmonary Disease	22 (18.3%)	2 (33.3%)	.509‡
Peripheral Vascular Disease	13 (10.8%)	1 (16.7%)	.090‡
Vented	7 (5.8%)	0 (0.0%)	.040‡
Previous Cardiac Surgery	36 (30.0%)	3 (50.0%)	.047‡
Creatinine	1.4 ± 0.5	1.4 ± 0.5	.643**

Variable	< 70 (N=120) mean ± sd [min, med, max]	≥70 (N=6) mean ± sd [min, med, max]	*P*
Aspartate Transaminase	42.4 ± 81.2	69.5 ± 101.3	.355**
Alanine Aminotransferase	44.6 ± 80.6	68.2 ± 110.6	.941**
Pre VAD Central Venous Pressure	11.4 ± 6.1	11.0 ± 4.1	.884
Pre VAD Pulmonary Artery Systolic	51.7 ± 14.6	51.8 ± 9.3	.986
Pre VAD Pulmonary Artery Diastolic	24.3 ± 9.4	22.6 ± 4.2	.687
Pre VAD Pulmonary Artery Mean Pressure	34.8 ± 10.8	33.8 ± 7.2	.846
Pre VAD Pulmonary Capillary Wedge Pressure	23.3 ± 9.7	19.0 ± 5.3	.383
Pre VAD Cardiac Index	1.9 ± 0.5	1.7 ± 0.5	.610
Pre VAD Right Ventricular End Eiastolic Dimension	27.6 ± 11.0	33.3 ± 7.2	.374
Pre VAD Right Ventricular	Mod. decrease: 70.0%	Mod. decrease: 50.0%	.642
Function on Echo	Severe decrease: 14.2%	Severe decrease: 16.7%	.722
INTERMACS Patient Profile			
INTERMACS 1	8 (6.7%)	0	
INTERMACS 2	52 (43.3%)	3 (50.0%)	
INTERMACS 3	28 (23.3%)	2 (33.3%)	
INTERMACS 4	25 (20.8%)	1 (16.7%)	
INTERMACS 5	6 (5.0%)	0	
INTERMACS 6	1 (0.08%)	0	

* Probabilities based on two-sided two-sample t-tests

** Probabilities based on two-sided Wilcoxon rank-sum tests

† Probabilities based on Chi-square tests

‡ Probabilities based on Fisher's exact tests

could not be assumed. Categorical variables were reported as count and percent, and were compared using chi-square tests. Alternatively, Fisher's exact tests were used if expected cell counts were not sufficiently large. These tests were repeated for postoperative outcomes and pre/postoperative hemodynamic variables. Survival at 1 month, 6 months, 1 year, and 2 years were compared using log-rank tests. Finally, preoperative and operative characteristics were placed in a multiple Cox proportional hazards model. Variables were restricted to those that had at least 95% non-missing values. A stepwise selection process was used to restrict each of the models to contain all significant predictors. Adjusted odds ratios and 95% confidence intervals for odds ratios were reported. Tests were considered significant at $P < .05$. An independent statistician from the department of Biostatistics performed the statistical analyses using SAS 9.2 and determined that the study was appropriately powered.

RESULTS

The table outlines the baseline clinical characteristics and demographics of the two groups. There were six (4.8%) patients 70 years and above and 120 (95.2%) patients under 70 years. Mean age was 72.2. ± 2.3 years (range: 70-75 years) in the older cohort and 52.8 ± 11.4 (range: 18-69 years) in the younger cohort ($P < .001$). In the older cohort, 100% of patients were implanted as BTT compared to 38.3% in the younger group ($P = .004$). Patients in both cohorts had a similar incidence of diabetes mellitus, hypertension, chronic renal insufficiency, and chronic obstructive pulmonary disease (P = NS). There was a higher incidence of previous cardiac surgery in the older cohort (50.0% versus 30.0%; $P = .047$). Both groups had similar renal and hepatic function and similar baseline albumin levels. Preoperative central venous pressure (CVP), pulmonary artery pressure (PAP), pulmonary capillary wedge pressure (PCWP), cardiac index (CI), right ventricular (RV) function, and INTERMACS profiles were similar when comparing both groups (P = NS) .

Survival was similar for both groups, with 30-day, 6-month, 1-year, and 2-year survivals of 100%, 100%, 100%, and 66.7% respectively, for patients 70 and older versus 95.0%, 88.6%, 81.3%, and 76.7% respectively, for patients under 70 years ($P = .634$) (Figure 1).

Length of ICU stay was similar for both groups with a median of 5.5 days for the older cohort and 8.1 days for the younger cohort ($P = .086$). Overall hospital stay was also similar: a median of 16.5 days for the older cohort and 16.0 days for the younger cohort ($P = .653$).

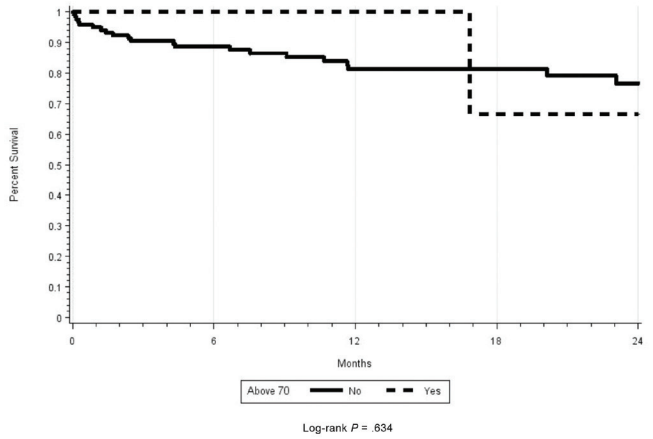

Figure 1. Kaplan-Meier curve comparing survival after LVAD implantation between patients ≥ 70 years versus < 70 years at time of LVAD implantation.

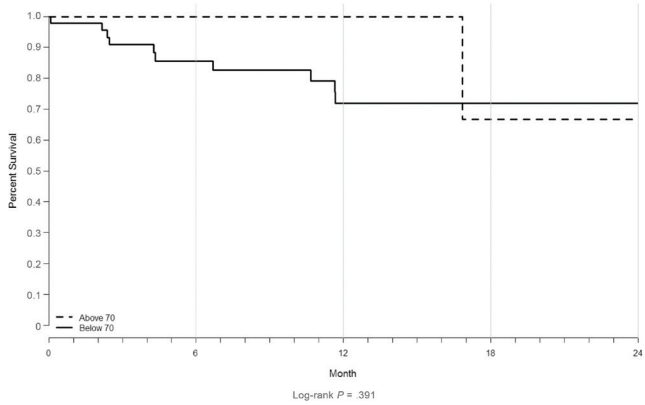

Figure 2. Kaplan-Meier curve comparing survival after LVAD implantation between destination therapy patients ≥ 70 years versus < 70 years at time of LVAD implantation.

There was no significant difference between the two groups in the incidence of bleeding requiring re-exploration (0% in the older cohort versus 11.7% in younger cohort; $P = .683$), drive-line infections (0% in older cohort versus 10.8% in younger cohort; $P = .367$), hemorrhagic strokes (0% in older cohort versus 8.3% in younger cohort; $P = .611$), ischemic strokes (0% in older cohort versus 5.0% in younger cohort; $P = 1.000$), pneumonia (0% in older cohort versus 9.2% in younger cohort; $P = .625$), or renal failure (0% in older cohort versus 28.3% in younger cohort; $P = .126$). There was, however, a significantly higher incidence of right ventricular failure in the younger cohort (13.3% in younger cohort versus 0% in older cohort; $P < .001$), and a significantly higher incidence of gastrointestinal bleeding in the older cohort (33.3% in older cohort versus 23.3% in younger cohort; $P < .001$).

Results of the Cox proportional hazard models, which analyzed the effects of advanced age on survival, showed that advanced age was not an independent predictor of outcome in univariate analysis ($P = .808$). Survival was similar for DT patients below 70 years of age compared to the six DT patients above 70 years, with 30 day, 6 month, 1 year, and 2 year survivals of 100%, 100%, 100%, and 66.7% respectively, for patients 70 and older versus 97.9%, 85.6%, 72.0% and 72.0% respectively, for patients < 70 years (n = 46; $P = .391$) (Figure 2).

DISCUSSION

Left ventricular assist devices have become an accepted therapeutic strategy for both bridge to transplant and destination therapy in patients with refractory end-stage heart failure, and the use of continuous flow pumps has been shown to result in longer survival and a lower incidence of device-related complications. [Frazier 2001; Dang 2005; Park 2005; Kirklin 2012]. However, despite these encouraging results, advanced age is still viewed by many LVAD centers as a relative contraindication for surgery, due to decreased survival and a higher incidence of postoperative adverse events. In this study we reviewed our single institutional experience with patients ≥ 70 years on long-term continuous flow LVAD support and evaluated their perioperative and mid-term survival and incidence of postoperative complications. In our 6 year experience with 126 long-term CF-LVADs, we demonstrated that patients 70 years of age and above had equivalent perioperative mortality and mid-term survival up to two years after LVAD implantation as patients in the younger group. Additionally, the incidence of LVAD related complications was similar. Finally, the ICU and overall hospital length of stay was similar in both groups. The trend toward a shorter median duration of ICU stay for older patients (5.5 versus 8.1 days; $P = .086$) was likely a reflection of the small sample size.

Our study has several limitations. First, it was an observational, non-randomized study and is subject to the limitations inherent in a retrospective study. Second, some statistical tests may have been insufficiently powered due to a relatively small sample size. Third, the duration of follow-up was relatively short and longer term follow-up is necessary. Finally, selection bias may have been introduced due to the fact that the study was done at single institution.

CONCLUSIONS

Patients of advanced age should not be denied a long-term LVAD solely on basis of age. Rather, elderly patients should be evaluated in the same careful, thorough manner in which younger patients are evaluated to assess their candidacy for long-term device therapy. Our results demonstrate that in appropriately selected elderly patients, LVAD implantation can be performed with similar perioperative mortality, hospital stay, incidence of postoperative complications, and long-term survival as with younger patients. Advanced age is not a negative predictor of survival and should not serve as a contraindication for LVAD implantation.

Since one of the goals of LVAD therapy is to increase functional capacity and quality of life, further studies are needed to assess whether there are differences in improvement in quality of life in elderly LVAD recipients compared to younger

recipients. Such studies would further clarify the role of long-term LVAD therapy in the elderly and are currently underway at our institution.

REFERENCES

Dang NC, Topkara VK, Kim BT, et al. 2005. Clinical outcomes in patients with chronic congestive heart failure who undergo left ventricular assist device implantation. J Thorac Cardiovasc Surg 130:1302-9.

Dembitsky WP, Tector AJ, Park S, et al. 2004. Left ventricular assist device performance with long-term circulatory support: lessons from the REMATCH trial. Ann Thorac Surg 78:2123-30.

Frazier OH, Rose EA, Oz MC, et al. 2001. Multicenter clinical evaluation of the HeartMate vented electric left ventricular assist system in patients awaiting heart transplantation. J Thorac Cardiovasc Surg 122:1186–95.

Jessup M, Brozena S. 2003. Heart failure. N Engl J Med 348:2007-18.

Kirklin JK, Naftel DC, Pagani FD, et al. 2012. Long-term mechanical circulatory support (destination therapy): on track to compete with heart transplantation? J Thorac Cardiovasc Surg 144:584-603.

Lloyd-Jones D, Adams RJ, Brown TM, et al. 2010. Heart disease and stroke statistics—2010 update: a report from the American Heart Association. Circulation 121:e46-e215.

Pagani FD, Miller LW, Russell SD, et al. 2009. Extended mechanical circulatory support with a continuous-flow rotary left ventricular assist device. J Am Coll Cardiol 54:312–21.

Park SJ, Tector A, Piccioni W, et al. 2005. Left ventricular assist devices as destination therapy: a new look at survival. J Thorac Cardiovasc Surg 129:9-17.

Rose EA, Gelijns AC, Moskowitz AJ, et al. 2001. Long-term use of a left ventricular assist device for end-stage heart failure. N Engl J Med 345:1435-43.

Slaughter MS, Pagani FD, Rogers JG, et al. 2010. Clinical management of continuous-flow left ventricular assist devices in advanced heart failure. J Heart Lung Transplant 29:S1–39.

Slaughter MS, Rogers JG, Milano CA, et al. 2009. Advanced heart failure treated with continuous-flow left ventricular assist device. N Engl J Med 361:2241–51.

Starling RC, Naka Y, Boyle AJ, et al. 2011. Results of the post-U.S. Food and Drug Administration approval study with a continuous flow left ventricular assist device as a bridge to heart transplantation: a prospective study using the INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support). J Am Coll Cardiol 57:1890-8.