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Role of ventricular assist therapy for patients with heart failure and restrictive physiology: Improving outcomes for a lethal disease

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BACKGROUND: Restrictive cardiomyopathy (RCM) patients have poor prognosis due to progressive heart failure characterized by impaired ventricular filling of either or both ventricles. The goal of this study was to evaluate the outcome of end-stage RCM patients after left ventricular assist device (LVAD) implantation and to determine factors that may be associated with improved survival.

METHODS: This investigation is a retrospective study of prospectively collected data that include 28 consecutive patients with end-stage RCM who received continuous-flow LVADs at the Mayo Clinic, Rochester, Minnesota. Outcome was assessed by survival with LVAD support until heart transplantation or all-cause mortality.

RESULTS: The mean follow-up time post-LVAD implantation was 448 ± 425 days. The mean hospitalization time was 29 ± 19 days and was complicated mainly by post-operative right ventricular (RV) failure requiring short-term medical support. The short-term in-hospital mortality was 14%. Ten patients underwent heart transplantation with 100% survival post-transplant during the follow-up period. One-year survival for patients with LVADs without transplantation was 64%, and was not significantly different between amyloidosis and non-amyloidosis patients. Larger left ventricle (LV) end-diastolic and end-systolic dimensions were significantly associated with improved survival rates (RR = 0.94 and 0.95, $p < 0.05$, respectively), and left ventricular end-diastolic diameter (LVEDD) ≤46 mm was associated with increased mortality post-LVAD implantation.

CONCLUSIONS: LVAD is a feasible, life-saving therapy for end-stage heart failure related to RCM, especially as a bridge to transplant and in patients with larger LV dimensions.

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Restrictive cardiomyopathy (RCM) constitutes a heterogeneous group of diseases with a common physiology, characterized by impaired ventricular filling, with normal or decreased diastolic volume of either or both ventricles. Regardless of etiology, the overall prognosis is poor and is associated with progression to heart failure and increased mortality.[1–4]

The continuous-flow left ventricular assist device (LVAD) has become a standard therapeutic option to improve survival and quality of life in dilated cardiomyopathy

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patients with advanced heart failure, whether they are awaiting transplantation or as destination therapy (DT).[5,6] However, there are almost no data describing the impact of LVAD therapy on patients with end-stage RCM.

At our center, we have used LVAD therapy in selected RCM patients whose outcome would otherwise be very poor, or those we thought could be bridged to transplant (BTT). We previously described our experience with small numbers of patients and showed that LVAD implantation may be feasible with improved survival compared with medical therapy.[7]

Thus, the goal of this study was to present our extended experience with a larger and more heterogeneous cohort, and to look for factors that may predict better outcome after LVAD implantation for end-stage RCM patients.

Methods

Patient population

We identified all consecutive patients with end-stage heart failure and restrictive physiology (including all 8 patients presented in our previous report[7]) who received a continuous-flow LVAD (either a HeartMate II [Thoratec, Pleasanton, CA] or an HVAD [HeartWare, Inc., Framingham, MA]) for either DT or BTT between January 2008 and August 2013 at the Mayo Clinic, Rochester, Minnesota. Restrictive heart diseases included hypertrophic cardiomyopathy, infiltrative heart disease or chemotherapy/radiation-induced cardiomyopathy. Infiltrative heart disease and hypertrophic cardiomyopathy were defined based on endomyocardial biopsy findings and by the presence of echocardiographic characteristics of restrictive physiology. Chemotherapy/radiation-induced cardiomyopathy patients were included only if they had echocardiographic findings of smaller left ventricular (LV) dimensions and significant (Grade 3-4/4) diastolic dysfunction.

Clinical, demographic and hemodynamic data

Each patient's pre-operative data (demographic, clinical, echocardiographic, hemodynamic and laboratory data) were abstracted from the medical records. Echocardiographic examinations were performed at 19 (range 1 to 101) days and hemodynamic catheterizations were performed at 14 (range 1 to 168) days before surgery. Echocardiographic parameters recorded included: LV ejection fraction (EF, calculated using the modified Simpson's formula); LV end-diastolic diameter (LVEDD); LV end-systolic diameter (LVESD, measured with M-mode or 2-dimensional echocardiography); tricuspid valve regurgitation grade (based on jet characteristics and/or the proximal isovelocity surface area method); and right ventricle (RV) function evaluation (quantitative grading scale = normal, mild, mild–moderate, moderate, moderate–severe, severe dysfunction). Data concerning short-term post-operative adverse events (RV failure, inotropic support, renal failure, length of hospital stay and in-hospital mortality) and long-term LVAD-related complications (thrombotic events, hemolysis, bleeding and infection) were obtained by reviewing the medical records. The primary outcome was defined as all-cause mortality or heart transplantation. Survival information was obtained from the electronic medical records. The study protocol was reviewed and approved by institutional review board at the Mayo Clinic, Rochester, Minnesota.

Statistical analysis

Baseline data are presented as percent or mean (standard deviation). Comparisons of baseline characteristics between patients with and without amyloidosis were done by chi-square test for categorical variables and *t*-test for continuous variables. Survival, overall and by selected subgroups, was assessed using the Kaplan–Meier method and compared (when applicable) using the log-rank test. The bivariate association between selected baseline characteristics and subsequent outcome (i.e., death or transplantation) was evaluated using Cox proportional hazards modeling. Due to the small sample size and high correlation between variables, no multivariable models were fitted. Analyses were performed using SAS version 9.3 (SAS Institute, Inc., Cary, NC) and IBM SPSS version 19 (IBM SPSS, Inc., Chicago, IL).

Results

Baseline characteristics

The study cohort consisted of 28 patients (71% males) with end-stage RCM who underwent LVAD implantation (26 [93%] patients with a HeartMate II and 2 [7%] with an HVAD), either as BTT (61%) or DT (39%). The mean age at the time of implant was 57 ± 13 years. The etiology of restrictive cardiomyopathy was amyloidosis (36%), hypertrophic cardiomyopathy (28.5%), sarcoidosis (18%), chemotherapy/radiation-induced cardiomyopathy (14%) and Fabry disease (3.5%). All patients were severely symptomatic and classified as Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) Profile 1 (25%), 2 (68%) or 3 (7%) (Table 1).

Baseline echocardiographic examination showed the following mean values: LVEF 27 ± 16%; LVEDD 53.7 ± 11.4 mm; and LVESD 46.8 ± 12.3 mm. Most patients were considered to have at least moderate RV dysfunction and greater-than-mild tricuspid valve regurgitation (81% and 61%, respectively). Hemodynamic data showed right atrial pressure, capillary wedge pressure and mean pulmonary pressure to be elevated in most patients.

Short-term post-operative outcomes

The mean hospitalization time was 24 ± 18 days. The most common post-operative complication was RV failure (11 patients, 39%), presented as volume overload, renal failure, liver congestion and elevated right heart and pulmonary pressures. All these patients required inotropic support of the RV (isoproterenol or milrinone), and the mean duration of inotropic support post-surgery was 17 days. Two patients were discharged from the hospital with a continuous intravenous milrinone pump and were able to wean of inotropic support at 6 weeks post-implant. Four patients were treated with oral phosphodiesterase-5 inhibitor medications to lower pulmonary pressure during the hospitalization