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The Journal of Heart and Lung Transplantation
http://www.jhltonline.org

Uncorrected pre-operative mitral valve regurgitation is not associated with adverse outcomes after continuous-flow left ventricular assist device implantation

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KEYWORDS:
ventricular assist device;
cardiomyopathy;
mitral valve regurgitation;
mechanical support;
heart failure

BACKGROUND: Mitral valve regurgitation (MR) is prevalent in patients with heart failure. Because very few data exist examining the influence of significant pre-operative MR on outcomes after left ventricular assist device (LVAD) implantation, we evaluate our experience.

METHODS: Between October 1996 and August 2013, 756 patients underwent primary LVAD implantation at our institutions. Of these, 508 patients received a continuous-flow LVAD and represent the contemporary cohort for this analysis. Devices implanted included the HeartMate II in 410 patients (81%) and HeartWare HVAD in 98 patients (19%). Based on availability of pre-operative echocardiography, 491 patients were divided into 2 study groups according to degree of pre-operative MR; 189 patients (39%) had moderate to severe or greater MR (MR group), and 302 (61%) had less than moderate to severe MR (less MR group). Median age at operation (60 years in MR group vs 58 years in less MR group, $p = 0.19$), male sex (78% in MR group vs 81% in less MR group, $p = 0.42$), and ischemic etiology (46% in MR group vs 51% in less MR group, $p = 0.35$) were similar between groups.

RESULTS: There were 40 early deaths (7.9%), and follow-up was available in all 468 early survivors for 641 patient-years of support. Patients in the MR group had higher late survival (2 years, 75%; 4 years, 65%) compared with patients in the less MR group (2 years, 66%; 4 years, 48%; $p < 0.04$). Cox proportional hazards model confirmed the independent interaction between MR and late survival (hazard ratio 0.62, $p = 0.04$).

CONCLUSIONS: There was improved survival in patients with severe pre-operative MR after continuous-flow LVAD implantation in our cohort. These findings may lend insight into the possible lack of value of addressing significant MR at the time of LVAD implantation.

J Heart Lung Transplant 2015;34:718–723

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The mechanism of mitral valve regurgitation (MR) in most patients undergoing implantation of a continuous-flow left ventricular assist device (LVAD) is functional, and the

1053-2498/$ - see front matter
http://dx.doi.org/10.1016/j.healun.2014.11.023

resultant left ventricular (LV) unloading after device support is initiated has been shown to result in significantly decreased MR post-implant.[1] A combination of reduction in LV dimension, mitral valve tenting area, and mitral valve annular diameter is hypothesized to account for these findings.[2] Although correcting significant tricuspid valve regurgitation (TR) and aortic valve regurgitation has been shown to impart long-term benefit, some authors advocate addressing significant MR at the time of LVAD implantation. Because this enthusiasm is tempered by more recent reports documenting increased early mortality during LVAD implantation when additional valvular surgery is undertaken and a trend toward lower survival when LVAD implantation is combined with mitral valve surgery alone,[3] the optimal approach to this situation is uncertain.

Because there are no data specifically examining the effect of uncorrected significant pre-operative MR in patients undergoing LVAD implantation, we sought to delineate its effect on LVAD-related complications and late survival. In addition, we examined the interaction of MR and TR on late outcomes.

Methods

Study population

The data collection process and analysis was performed following receipt of informed patient consent and approval by the University of Michigan, Mayo Clinic College of Medicine, and Vanderbilt Heart and Vascular Institute institutional review boards. Between October 1996 and August 2013, 756 patients underwent primary LVAD implantation at the centers that make up the Mechanical Circulatory Support Research Network (University of Michigan Health System, Mayo Clinic [Rochester, MN], and Vanderbilt Heart and Vascular Institute). Between May 2007 and August 2013, 508 patients received a continuous-flow LVAD, and these patients represent the contemporary cohort for this analysis. Devices implanted included the HeartMate II (Thoratec Corporation) in 410 patients (81%) and HeartWare HVAD (HeartWare, Inc) in 98 patients (19%).

Based on availability of pre-operative echocardiography, 491 patients were divided into 2 study groups according to degree of pre-operative MR; 189 patients (39%) had moderate to severe or greater MR (MR group), and 302 patients (61%) had less than moderate to severe MR (less MR group). The TR cohort included patients with TR that was at least moderate to severe (TR group; $n = 153$) and TR that was less than moderate to severe (less TR group; $n = 334$). The combination of valve lesion severity is shown in Table 1. Concomitant tricuspid valve surgery was performed in most patients with significant TR regardless of the degree of MR—56 patients (92%) in the moderate to severe or greater TR and less than moderate to severe MR group and 86 patients (94%) in the moderate to severe or greater TR group and moderate to severe or greater MR group. Conversely, the minority of patients with lesser degrees of TR underwent tricuspid valve surgery regardless of degrees of MR—9 patients (4%) underwent tricuspid valve surgery in the less than moderate to severe TR group and less than moderate to severe MR group and 5 patients (5%) in the moderate to severe or greater TR group and moderate to severe or greater MR group. Severity of LV chamber dilation was stratified according to LV end-diastolic dimension (in millimeters) based on echocardiographic chamber assessment guidelines.[4]

Table 1 Presence of MR and TR in the Study Cohort

	MR < moderate-severe	MR ≥ moderate-severe
TR < moderate-severe	228 (48%)	95 (20%)
TR ≥ moderate-severe	61 (13%)	92 (19%)

MR, mitral valve regurgitation; TR, tricuspid valve regurgitation.

Pre-operative clinical characteristics of the study cohorts are presented in Table 2. Data for LVAD-related complications, including hemolysis, suspected or confirmed pump thrombus, stroke, and gastrointestinal bleeding were analyzed for possible interaction with MR.

Statistical analysis

Demographic and other patient-related data were obtained from the University of Michigan, Mayo Clinic College of Medicine, and Vanderbilt Heart and Vascular Institute medical records and our prospectively collected clinical databases. Follow-up data were obtained from subsequent clinic visits and written correspondence from local physicians. Data were expressed either as mean ± SEM for normally distributed data or as median with interquartile range for non-normally distributed data. Normality of continuous variables was assessed using the Shapiro-Wilk test. The Mann-Whitney-Wilcoxon rank sum test was used to compare significantly skewed ($p < 0.05$) continuous data. Two-sample test for equality of proportions was used to compare proportions between the MR and less MR groups. Data between 2 groups were compared using chi-square test for continuous and dichotomous variables. A backward stepwise Cox regression analysis was used to identify peri-operative variables independently affecting survival. Kaplan-Meier survival analysis was used to evaluate the interaction of MR and MR/TR with survival and produce survival plots, which were subsequently compared by the log-rank test. Statistical significance was considered at $p < 0.05$. Early operative mortality was defined as death occurring within 30 days of operation or at any time during the index hospitalization. R software version 3.0.1 (R Foundation for Statistical Computing, Vienna, Austria) was used for statistical analysis and data visualization.

Results

There were 40 early deaths (7.9%) with 35 occurring in patients with pre-operative echocardiography and known MR status—11 in the severe MR group (2.2%) and 24 in the less MR group (4.9%) ($p = 0.026$). Follow-up data (median 13 months, maximum 5.6 years) were available in all 468 early survivors for 641 patient-years of support. When stratified by study group, median follow-up time in the MR group was 1.1 years (interquartile range 161 days to 2.1 years) and 0.9 years in the less MR group (interquartile range 122 days to 1.8 years) ($p < 0.05$). Early non-fatal morbidity that differed between groups included a higher need for temporary right ventricular (RV) assist device in the MR group ($n = 19$; 10%) compared with the less MR group ($n = 13$; 4%) ($p = 0.01$). During the follow-up period, there were no significant