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Clinical Investigation

Preoperative Determinants of Quality of Life and Functional Capacity Response to Left Ventricular Assist Device Therapy

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ABSTRACT

Background: Left ventricular assist devices (LVADs) improve survival, quality of life (QOL), and functional capacity (FC) among patients with end-stage heart failure. Few data are available regarding characteristics associated with QOL and FC response.

Methods and Results: Patients enrolled in the Heartmate II clinical trials that were alive with ongoing LVAD support at 6 months were included. QOL response criteria included scoring above the lowest quartile on either the Minnesota Living With Heart Failure Questionnaire or the Kansas City Cardiomyopathy Questionnaire. FC responder criteria included improvement in 6-minute walk distance (6MWD) >70 meters from baseline, a 6MWD >220 meters at 6 months, or New York Heart Association functional class I or II. Independent variables associated with QOL nonresponse included history of diabetes (odds ratio [OR] 1.82, 95% confidence interval [CI] 1.20–2.78), lower mean pulmonary arterial pressure (OR 0.97, 95% CI 0.95–0.99), or a Heartmate II right ventricular risk score >2 (OR 1.77, 95% CI 1.00–3.12). Variables associated with FC nonresponse included history of COPD (OR 1.92, 95% CI 1.22–3.03) or diabetes (OR 1.52, 95% CI 1.01–2.27). Compared with responders, QOL and FC nonresponders had reduced long-term survival.

Conclusions: Preoperative comorbidities, including diabetes, COPD, and right heart failure, may limit the QOL and FC response to LVAD therapy and should be considered during the shared decision-making process. (*J Cardiac Fail 2016;*■■*:*■■–■■)

Key Words: Left ventricular assist device, heart failure, quality of life, functional capacity, exercise tolerance, predictors, survival.

Left ventricular assist devices (LVADs) improve survival among patients with refractory heart failure (HF).[1] Importantly, quality of life (QOL) and functional capacity (FC) also improve after LVAD implantation.[2–5] Nearly all patients undergoing LVAD implantation have baseline New York Heart Association (NYHA) functional class IV symptoms,[6–8] and by 6 months >80% of patients improve to NYHA functional class I or II.[4] However, despite LVAD therapy ~1 in 5 patients continue to suffer from moderate to severe HF symptoms.

Many HF patients express a desire for improvements in QOL and functionality even if at the expense of longevity.[9,10] Given continued improvements in long-term survival, the potential for the expanding use of LVADs, particularly as destination therapy, will likely depend largely on their ability to improve QOL. Although a great deal of attention has been given to evaluating baseline predictors of postoperative survival, few data are available to assist in patient selection as

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it relates to QOL outcomes. In the present study, we sought to identify baseline variables associated with higher QOL and FC response to LVAD therapy at 6 months.

Methods

Study Subjects

Data in this analysis are from the Heartmate II bridge to transplant (BTT) and destination therapy (DT) clinical trials conducted at 38 U.S. centers. Detailed inclusion criteria for the Heartmate II clinical trials have been previously reported.[6,7] Patients who were alive with ongoing LVAD support at 6 months were included in the present analyses.

Variable Selection

Baseline covariates evaluated included preoperative demographic, clinical, laboratory, and hemodynamic variables. Also included were echocardiographic data regarding the qualitative degree of tricuspid regurgitation and whether concomitant tricuspid valve repair was performed. A previously defined model of right heart failure (RHF) was examined.[11] From this model a Heartmate II right ventricular (RV) risk score was created: right atrial (RA) pressure/pulmonary capillary wedge pressure (PCWP) >0.63: 2 points; blood urea nitrogen level >39 mg/dL: 2 points; and preoperative mechanical ventilation: 6 points. This was evaluated as a dichotomous variable with a score >2 points indicating high risk and ≤2 points low risk.

During the Heartmate II trials, LVAD parameters including speed, power, flow, and pulsatility index (PI) were recorded every day for up to 7 days after implantation, weekly through discharge, and then every month during follow-up for up to 6 months for BTT subjects and 24 months for DT subjects. Pulsatility index is a measure of flow pulse through the pump; it is proportional to the degree of native left ventricular (LV) contractility and inversely related to pump speed.[12] The average of these parameters from implantation through 6 months was determined.

Baseline and Postimplantation Assessments

QOL and FC assessments were evaluated at baseline and at 6 months after implantation.[6,7] NYHA functional classification at each time period was assessed by an independent assessor. Submaximal exercise performance was measured by means of the 6-minute walk distance (6MWD).

HF-related QOL was assessed by means of the Minnesota Living With Heart Failure Questionnaire (MLHFQ)[13] and the Kansas City Cardiomyopathy Questionnaire (KCCQ).[14] These are disease-specific health status measures that assess the impact of heart failure on physical and emotional symptoms, social functioning, and QOL from the perspective of the patient. An overall summary score (OSS) is derived for the KCCQ by combining the individual domain scores. Higher QOL is represented by a lower score on the MLHFQ and a higher score on the KCCQ-OSS.

Outcomes

Quality of Life. Patients were classified as QOL responders or nonresponders. Criteria for a QOL nonresponse included either a KCCQ-OSS ≤50 points or an MLHFQ score ≥52 points. These scores represent the lower quartiles for each questionnaire in the study cohort. Subjects who did not meet these criteria were classified as QOL responders.

Functional Capacity. The 6MWD is a validated measure of FC in patients with HF.[15] Patients were classified as FC responders or FC nonresponders based on NYHA functional classification and 6MWD performance. Criteria for an FC response at 6 months included meeting any of the following: improvement in 6MWD of >70 m from baseline, 6MWD >220 m at 6 months, or NYHA I/II functional classification. The distance of 70 m represents 0.5× the standard deviation of baseline 6MWD in the DT clinical trial[7] and was chosen to reflect a clinically significant change.[16] The distance of >220 m at 6 months represents the cutoff for the lowest quartile. Subjects who did not meet any of these criteria were classified as FC nonresponders.

Evaluation of Functional Capacity Criteria. To evaluate how well the FC criteria captured the intended outcome, 6MWD and NYHA functional classification were compared with reported activity levels. Activity levels were assessed with the use of metabolic equivalent task scores (METs) for which patients described their highest activity level during the reporting period. Scores ranged from very low (<1 MET: bedbound, nonambulatory), through moderate (2–4 METs: light house work), to very high (>6 METs: dancing).[14] Activity level and NYHA functional classification were dichotomized to ≥3 METs versus <3 METs and NYHA I/II versus III/IV.

Survival. The associations between QOL and FC response and long-term survival among patients alive with ongoing LVAD support at 6 months were evaluated. We compared differences in survival between QOL and FC response groups. Patients were censored at the time of transplantation. BTT patients were followed for a minimum of 6 months and DT patients were followed for ≥2 years after implantation.[6,7]

Statistical Analysis

Laboratory and hemodynamic data were evaluated as continuous variables. Continuous data were evaluated for normality and between-group comparisons of baseline characteristics were performed with the use of either Student t or Mann-Whitney U test for normal and nonnormal data, respectively. Categoric data were compared with the use of Fischer exact test. Given the nonnormal distribution of the data, QOL and FC were not maintained as continuous variables for analysis with linear regression, but were dichotomized into variables of response versus nonresponse as defined above. Stepwise forward multivariable logistic regression analyses were performed on univariable predictors of QOL and FC responders (entry criterion $P < .05$). Kaplan-Meier survival curves were created to evaluate survival (defined as continued LVAD support at the time of last follow-up, LVAD explantation due to recovery, or