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The Impact of Obesity on Patients Bridged to Transplantation With Continuous-Flow Left Ventricular Assist Devices

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ABSTRACT

OBJECTIVES This study sought to determine if obese patients had worse post–left ventricular assist device (LVAD) implantation outcomes and if the implantation of an LVAD allowed for weight loss.

BACKGROUND Obesity is a risk factor for cardiovascular disease including heart failure. Obese heart failure patients have better outcomes than those with normal weight; however, obese patients have worse outcomes after heart transplantation.

METHODS Patients were identified in the United Network for Organ Sharing (UNOS) database that underwent LVAD implantation as bridge to transplantation from May 2004 and April 2014, with follow-up through June 2014. Patients were grouped according to body mass index (BMI) based on the World Health Organization classification.

RESULTS Among 3,856 patients, the risk of death or delisting was not significantly different between BMI groups ($p = 0.347$). There was no increased risk of death ($p = 0.234$) or delisting ($p = 0.918$). The risk of complication requiring UNOS status upgrade was increased for those with class II obesity or greater (hazard ratio: 1.48; $p = 0.004$), driven by increased infection and thromboembolism. Obese patients had worse post-transplantation outcomes. Weight loss substantial enough to decrease BMI group was achieved by a small proportion of patients listed with class I obesity or greater (9.6% to 15.5%).

CONCLUSIONS Patients with obesity had similar freedom from death or delisting while on LVAD support. However, class II obese or greater patients had an increased risk of complications requiring UNOS status upgrade compared with those with normal BMI during LVAD support and decreased post-transplantation survival. Weight loss on device therapy was possible, but uncommon. Careful consideration is needed when a bridge to weight loss strategy is proposed. (J Am Coll Cardiol HF 2016;■:■–■) © 2016 by the American College of Cardiology Foundation.

Obesity is a worldwide epidemic with more than one-third of adults in the United States obese (body mass index [BMI] >30 kg/m^2). Obesity is a risk factor for heart failure and, despite the "obesity paradox" where obese patients with heart failure have better outcomes than those with a "normal" BMI (1), many proceed to stage D heart failure. Morbid obesity (BMI >35 kg/m^2) is a barrier to candidacy for heart transplantation (HT) (2) and those who are obese and undergo transplantation have worse outcomes after HT (3). For these patients, options include destination continuous-flow left ventricular assist device (CF-LVAD), palliative care, weight loss, or a bridge to decision (weight loss) LVAD.

Less is known about the outcomes of obese patients after implantation of an LVAD. Studies have suggested increased device-thrombosis (4) and

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ABBREVIATIONS AND ACRONYMS

BMI = body mass index

CF-LVAD = continuous-flow left ventricular assist device

UNOS = United Network for Organ Sharing

infections (5,6), but the data on mortality for LVAD is limited. One registry and a number of small, single-center studies have not shown a statistically significant difference in post-implantation survival (5-9), although there has been up to a 12% difference in survival between groups, raising the possibility that the studies were underpowered to show a true difference. This study sought to determine if obese patients had worse post-LVAD implantation outcomes and if the implantation of an LVAD allowed for weight loss.

METHODS

The United Network for Organ Sharing (UNOS) database was analyzed for patients bridged to transplantation with a CF-LVAD between May 2004 and April 2014. Follow-up data were collected through June 2014. This study included adult candidates (age ≥18 years) registered for single-organ, primary HT who received a United States Food and Drug Administration approved CF-LVAD. Devices were limited to the Heartmate II (Thoratec/St. Jude, Pleasanton, California) and Heartware HVAD (Heartware, Framingham, Massachusetts) which are contemporary durable devices. Patients who required temporary left-sided mechanical circulatory support, biventricular assist device, or total artificial heart were excluded from the analysis. The primary endpoint was freedom from death or delisting while on device support. Secondary endpoints included death on LVAD support, delisting on LVAD support, complications (thromboembolism, device infection, device malfunction, or life-threatening ventricular arrhythmia) requiring UNOS listing status upgrade, change in BMI group while on device support, and post-transplantation survival. By nature of the UNOS database, bridge to transplantation was the ultimate strategy for all patients. Patients were grouped according to BMI based on the World Health Organization classification: underweight (BMI <18.5 kg/m^2), normal (BMI 18.5 to 24.99 kg/m^2), overweight (BMI25 to 29.99 kg/m^2), obese class I (BMI 30 to 34.99 kg/m^2), and obese class II or greater (BMI >35 kg/m^2). Individual patient weight data were recorded at the time of listing for transplantation and at the time of waiting list removal. There were missing data for patients in this study: up to 15% for hemodynamic parameters, although no other variable had more than 1% missing. Imputation was not used for missing data. The study was submitted to the Institutional Review Board of Columbia University Medical Center and was determined to be exempt from review.

STATISTICAL ANALYSIS. Demographic and clinical variables were summarized with standard descriptive statistics and expressed as median (with interquartile range) for skewed continuous variables and count (with percentage) for categorical variables. Group comparisons were made with the chi-square test and the Kruskal-Wallis test where appropriate. Kaplan-Meier survival analysis with Dunnett's test applied for pairwise comparisons, univariate, and multivariable Cox proportional-hazards regression were performed to determine survival statistics. Cause-specific hazard models were created and cumulative incidence functions were calculated with death and delisting alternating as a competing event. A 2-tailed p value of <0.05 was considered significant. Analyses were performed using SAS version 9.4 (SAS Institute, Inc., Cary, North Carolina).

RESULTS

During the study period, 3,856 patients met inclusion criteria, 3,245 (84.2%) with a Heartmate II and 611 (15.8%) with an HVAD. The distribution of BMI at time of listing was 2.2% underweight, 25.5% normal, 35.5% overweight, 26.6% class I obese, and 10.2% class II obese or greater. Baseline characteristics were similar for all BMI groups except underweight, which was more female, had fewer ischemic cardiomyopathies, increased HVAD use, higher glomerular filtration rate, less implantable cardiac defibrillator use, a higher baseline pulmonary vascular resistance, and fewer were former smokers (**Table 1**).

Freedom from death or delisting was analyzed based on BMI group. Between BMI groups there was no statistically significant difference in event-free survival while on LVAD support (**Figure 1**). An unadjusted Cox-proportional hazards model similarly showed that when compared to those with a normal BMI, there was no significant difference between risk of death or delisting between BMI groups. There was a trend towards an increased risk of event for patients with class II obesity or greater compared with patients with a normal BMI (hazard ratio [HR]: 1.265, $p = 0.054$), but this did not reach statistical significance. A competing risk analysis again did not show a difference between BMI groups for risk of delisting while on LVAD support (**Figure 2A**) ($p = 0.918$) or death (**Figure 2B**) ($p = 0.234$). Analysis of BMI as a continuous variable found no association between BMI and the combined endpoint of death or delisting on unadjusted (HR: 1.01, $p = 0.14$) or multivariable analysis (HR: 1.011, $p = 0.11$).

Adverse events were categorized as those that necessitated UNOS listing status upgrade while on