Survival After Orthotopic Heart Transplantation in Patients Undergoing Bridge to Transplantation With the HeartWare HVAD Versus the Heartmate II

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Background. **Our objective was to determine whether the choice of a HeartWare HVAD as opposed to a Heartmate II left ventricular assist device (HMII LVAD), impacts survival after heart transplantation after controlling for patient, donor, and center characteristics.**

Methods. **We queried the United Network for Organ Sharing (UNOS) database, which has recently made pretransplantation device duration available, for all adult patients undergoing bridge to transplantation (BTT) between January 2011 and March 2016. Recipient, donor, and transplant-specific characteristics were compared between patients receiving either device. Unadjusted survival was estimated with the Kaplan-Meier method. Risk-adjusted Cox proportional hazard models were constructed to determine the independent impact of device selection on mortality.**

Results. **Three thousand three hundred fifty-six patients who received the HMII and 1,051 patients who received the HVAD met inclusion criteria. Patients who received the HMII had a longer mean duration of VAD support (HMII, 429 days versus HVAD, 314 days; $p < 0.001$) but spent shorter periods on the waiting list (median, 190 days versus 232 days; $p < 0.001$). Patients who received the HMII had worse pre-LVAD renal function than did those who received the HVAD (glomerular filtration rate [GFR], 57 mL/min versus 62 mL/min, respectively; $p = 0.001$), but there was no difference in postoperative new-onset dialysis after transplantation (11.6% versus 10.5%, respectively; $p = 0.14$). There was no difference in unadjusted posttransplantation 30-day (95.5% versus 96.7%, respectively; log-rank $p = 0.09$), 6-month (91.8% versus 92.6%, respectively; $p = 0.35$), or 1-year (89.7% versus 90.9%, respectively; $p = 0.22$) survival between the 2 groups. After risk adjustment with Cox modeling, device selection did not predict mortality at any time point.**

Conclusions. **Among patients who received a BTT LVAD and then received a heart transplant, no survival differences were seen between patients initially implanted with an HVAD versus an HMII.**

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Continuous-flow left ventricular assist devices (LVADs) have become a cornerstone of therapy for patients with advanced heart failure to improve quality of life and functional capacity [1]. The devices have been used both as a bridge to orthotopic heart transplantation (OHT) and as destination therapy [2]. Excellent posttransplantation survival has been demonstrated for patients who receive bridge to transplantation (BTT) [3]. A number of continuous-flow devices are available for this indication, including the Heartmate II (HMII; Thoratec, Pleasanton, CA), and the HeartWare HVAD (HVAD; HeartWare International, Inc, Framingham, MA). The former is an axial-flow LVAD, whereas the later uses centrifugal technology.

To date, studies comparing survival among patients who receive BTT have principally been restricted to relatively small, often single-center, series [4–9]. Moreover, larger studies are unable to control for important confounders such as duration of the bridge period. To date, conflicting evidence exists about whether or not the duration of LVAD therapy before transplantation impacts posttransplantation survival [10–15]. With the recent

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Abbreviations and Acronyms

BMI = body mass index
BTT = bridge-to-transplantation
CI = confidence interval
GFR = glomerular filtration rate
HMII = HeartMate II
HW HVAD = HeartWare HVAD
HR = hazard ratio
LVAD = left ventricular assist device
MELD-XI = Model for End-Stage Liver Disease Excluding International Normalized Ratio
OHT = orthotopic heart transplantation
UNOS = United Network for Organ Sharing

publication of a large database of patients receiving mechanical circulation that captures the duration of LVAD therapy, we sought to assess differences in post-transplantation survival among patients who receive BTT with the HMII versus the HVAD.

Patients and Methods

Patient Population

After obtaining appropriate institutional review board approval, we reviewed the records of all patients in the United Network for Organ Sharing (UNOS) thoracic transplantation database who underwent OHT between January 2011 and March 2016. To be included in the study, patients had to have had only a single LVAD (either an HMII or an HVAD) implanted and to have subsequently undergone OHT. Although inclusion was conditional on OHT being performed, patients were not required to survive for any particular duration after undergoing transplantation to be included in this study. Patients who did not undergo OHT were excluded from the analysis, as were patients bridged to OHT with any device other than the HMII or the HVAD or those who were bridged with multiple devices (eg, a right ventricular assist device). Records with missing data (1.9%) were excluded from the final analysis.

Data Definitions and Primary Outcomes

We analyzed all available covariates captured in the UNOS data, including age, preoperative comorbidities and data, intensive care unit and operative status, operative techniques, donor-related comorbidities, and the duration of LVAD therapy before transplantation. Variable definitions have been previously described [16, 17]. The primary outcome of our study was survival after OHT as measured at 30 days, 6 months, and 1 year after transplantation. Secondary outcomes included the need for new-onset hemodialysis, pacemaker insertion, or stroke before discharge after transplantation, as well as treatment for acute rejection within a year of discharge. The latter secondary outcome, acute rejection, could not be analyzed in a time-to-event analysis because no dates of diagnosis or treatment were available for this outcome in the UNOS database.

Statistical Analysis

All statistical analysis was performed using Stata, version 12.0 (StataCorp LP, College Station, TX). Continuous variables were analyzed using the Student t test or rank-sum test according to distribution, whereas categorical variables were analyzed with the χ^2 test. All p values are 2 sided, with statistical significance defined as a p value less than 0.05. Unadjusted survival analysis was analyzed using the method of Kaplan and Meier along with log-rank tests. To control for confounding covariates in the analysis of survival between the 2 LVAD types, we constructed multivariable risk-adjusted Cox proportional hazards models for each of our 3 survival time points. All available covariates were first analyzed in univariable analyses against the outcome of survival, and those with a p value less than 0.20 were then entered manually forward into a multivariable model. Model strength was assessed at the addition of each covariate using the Akaike information criterion and likelihood ratio tests to construct the most parsimonious model possible.

Results

A total of 4,407 patients were included in the study: 3,356 patients who received the HMII (76.2%) and 1,051 patients who received the HVAD (23.8%). Patients receiving either device were generally similar, although patients implanted with an HMII tended to be men (81.7% versus 74.3%; $p < 0.001$), have a lower glomerular filtration rate (GFR) (57 mL/min versus 62 mL/min; $p = 0.001$), and spent less time listed for transplantation (median, 190 days versus 232 days; $p < 0.001$) (Table 1). The mean duration of LVAD support was longer in patients who received an HMII compared with patients who received an HVAD (429 days versus 314 days; $p < 0.001$). Karnofsky performance status score at listing for transplantation tended to be better in patients who received the HMII (35.9% versus 47.2% with scores $\leq$40; $p = 0.001$), although this difference did not persist until the time of transplantation. A lower number of patients who received the HMII required a balloon pump (3.0% versus 8.4%; $p < 0.001$). There was also a lower proportion of patients who received the HMII undergoing transplantation at higher-volume centers (transplantation at center performing at least 12 OHTs/y, 89.0% versus 91.6%; $p < 0.001$).

Donor and transplant operative characteristics were similar between both patient cohorts (Table 2). Donor age did not differ between patients who received an HMII and patients who received an HVAD (mean, 32 years versus 32 years; $p = 0.85$). A majority of patients in both groups underwent OHT through a bicaval technique (79.5% versus 82.3%; $p = 0.009$). A greater proportion of patients who received the HMII had public insurance as their primary payer (50.7% versus 46.8%; $p = 0.03$).

The median follow-up time was 720 days (interquartile range, 317.5–1109 days) for patients who received the