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# Bridging to transplant with HeartMate 3 left ventricular assist devices in the new heart organ allocation system: An individualized approach

Matan H. Uriel, MD,[a] Kevin J. Clerkin, MD, MSc,[a] Koji Takeda, MD, PhD,[b] Yoshifumi Naka, MD, PhD,[b,c] Gabriel T. Sayer, MD,[a] Nir Uriel, MD, MSc,[a] and Veli K. Topkara, MD, MSc[a]

*From the [a]Division of Cardiology, Department of Medicine, Columbia University Irving Medical Center, New York, New York; [b]Division of Cardiothoracic Surgery, Department of Surgery, Columbia University Irving Medical Center, New York, New York; and the [c]Division of Cardiothoracic Surgery, Department of Surgery, Weill Cornell Medical Center, New York, New York.*

**KEYWORDS:**
heart transplantation;
left ventricular assist device;
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**BACKGROUND:** Following the MOMENTUM 3 trial and the discontinuation of the HeartWare HVAD, the HeartMate 3 LVAD (HM 3) has become the main durable device for bridging to transplantation; however, outcome of this strategy in the new heart allocation system is not well understood.

**METHODS:** The United Network for Organ Sharing (UNOS) registry was queried to include adult patients (≥18 years old) listed for heart transplantation between 2010 and 2020. Trends in durable LVAD utilization and outcomes of patients with HM 3 LVAD were examined in the pre- vs post-heart allocation system.

**RESULTS:** From 2017 to 2020, there was a 28.3% decline in the number of patients waitlisted with an FDA-approved durable LVAD. Overall, 449 patients were waitlisted with HM 3 in the pre-allocation era compared to 1094 patients in the post-allocation. Cumulative incidence of heart transplantation (53.4% vs 50.7%, $p = 0.76$) and death or delisting for worsening status (5.0%, vs 4.2%, $p = 0.43$) at 1-year after listing with HM 3 LVAD was comparable in the pre- vs post-allocation era. Old age (>50), ischemic HF, poor functional status, elevated creatinine (>1.3 mg/dL), pulmonary hypertension (>3 WU), and obesity (body mass index > 33 kg/m$^2$) were predictors of post-transplant graft mortality after bridging with HM 3.

**CONCLUSIONS:** While the utilization of durable devices as BTT have declined under the new heart allocation system, bridging with HM 3 LVAD remains a safe strategy in carefully selected patients. Bridging decision should be individualized based on patient risk factors.

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Subject terms: Mechanical Circulatory Support; Bridge to Transplantation; Heart Failure; Ethics and Policy

Reprint requests: Veli K. Topkara, MD, MSc, Center for Advanced Cardiac Care, Columbia University Medical Center − New York Presbyterian, 622 West 168th St, PH10-203A, New York, NY 10032. Telephone: 212-305-4600. Fax: 212-305-7439.

E-mail addresses: vt2113@cumc.columbia.edu, vktopkara@gmail.com

Left ventricular assist devices (LVADs) have become a mainstay therapy for advanced heart failure patients both as bridge to transplantation (BTT) and destination therapy (DT). In the multicenter MOMENTUM 3 trial, the fully magnetically levitated HeartMate 3 (HM 3) centrifugal-flow LVAD demonstrated superior survival free of disabling stroke or reoperation to replace or remove a malfunctioning

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device.[1] The majority of durable LVAD implants in 2019 were HM 3 as reported in the annual INTERMACS Registry.[2] Moreover, Medtronic announced a decision to stop the distribution and sale of the HeartWare HVAD in June 2021, due to a higher frequency of neurological adverse events and mortality with HVAD system in comparison to other commercially available LVADs.[3] As a result, the HM 3 is the only FDA-approved durable BTT device in 2021.

In addition to the recent changes in the LVAD field, a new heart allocation system was implemented on October 18, 2018, which has had significant implications for patients implanted with durable LVADs who are designated as Status 4 or higher in presence of a LVAD complication.[4-6] A recent analysis from the UNOS registry suggested nearly a 90% decline in the number of patients listed with durable LVADs nationwide from 102 in April 2017 to 12 in April 2020; however, this study did not specify the device types such as HVAD and HM II, which are no longer available for routine clinical use.[7] Another question is whether bridging to transplant becomes too high risk for a subset of patients who are stably doing well on HM 3, as the 2-year survival on HM 3 is approximating to 2-year post-transplant survival. The purpose of this study was[1] to analyze trends in durable LVAD utilization as BTT in the pre- vs post-allocation system in the light of recent changes in the field,[2] to compare waitlist and post-transplant outcome of patients waitlisted with HM 3 in the old vs new heart allocation system, and[3] to determine risk factors associated with high-risk after bridging to transplant with HM 3 LVAD.

## Methods

### Patient population

The United Network for Organ Sharing (UNOS) registry was queried to include adult patients (≥18 years old) listed for heart transplantation. Trends in durable continuous-flow LVAD utilization was investigated in patients who were waitlisted or transplanted between January 2010 and December 2020 with HM II, HVAD, or HM 3. VAD_BRAND1_TCR and VAD_BRAND1_TRR variables were used to identify patients who were listed or transplanted with HM II (code 205), HVAD (code 224), and HM 3 (code 236). Follow-up data were available through June 31, 2021. LVAD brand text field variables (VAD_BRAND1_OSTXT_TCR and VAD_BRAND1_OSTXT_TRR) were also screened to include patients who were waitlisted or transplanted with HM II, HVAD, and HM 3 and were text coded into UNOS. HM 3 patients were then stratified based on the date of transplant listing (before or on/after October 18, 2018) into pre-allocation vs post-allocation system era. Baseline characteristics including demographics, etiology of heart disease, comorbid conditions, tobacco use, presence of ICD, inotrope use, status at listing, hemodynamics, and serum creatinine were compared between the 2 groups. Poor functional status was defined as per functional status variable in the UNOS dataset (Supplementary Table S1). Study endpoints included competing waitlist outcomes of transplantation and death or delisting for worsening status, as well as post-transplant graft survival. Crossover patients who were waitlisted in the pre-allocation system but transplanted in the post-allocation system were excluded from the analysis. However, a sensitivity analysis was performed by including these patients. Recent studies suggest that post-transplant survival estimates in the new allocation system could be biased downwards due to systematic differences in data submission by transplant centers resulting in informative censoring bias.[8,9] Therefore, we performed additional post-transplant survival analysis restricted to HM 3 patients transplanted through December 2019 instead of December 2020. Due to differential length of post-transplant follow-up of HM 3 patients in the pre- vs post-heart allocation system, we also performed an additional survival analysis using administrative censoring at 1 year. The study was submitted to the Institutional Review Board of Columbia University Medical Center and was determined to be exempt from review.

### Statistical analysis

Continuous variables were presented as mean ± standard deviation or median (interquartile range) where appropriate. Categorical variables were expressed as numbers and percentages. Differences between groups were quantified using t-test, Wilcoxon rank sum test, and $\chi^2$ when appropriate. Cochrane-Armitage test was used to assess trends in utilization of LVAD types over time. Cumulative incidence of function was utilized to estimate competing waitlist outcomes of transplantation vs death or delisting for worsening clinical status, along with Gray's test when comparing HM 3 patients listed in the pre- vs post-heart allocation system. Patients who crossed over from pre- to post-allocation were excluded from the waitlist outcome analysis. Kaplan-Meier survival estimates were used to assess post-transplant survival, with log-rank testing used to compare HM 3 patients transplanted in the pre- vs post-heart allocation system. The association of the clinical risk factors with hazard of the waitlist outcomes and post-transplant graft mortality were assessed using univariable and multivariable Cox proportional hazards regression models. Proportional hazards assumption has been checked by testing the relationship between residuals and time. Time-dependent receiver-operating characteristic curves were calculated to determine discriminatory power of continuous predictors (Supplementary Table S2).[10] Optimal cutoff point for each predictor was identified by using maximum value of the Youden index. All $p$ values were reported as 2-sided tests with $p < 0.05$ considered statistically significant. R version 4.2.1 (R Foundation for Statistical Computing, Vienna, Austria) was used to perform statistical analysis.

## Results

### Changing trends in durable continuous-flow LVAD utilization as BTT

Trends in CF-LVAD utilization for transplant waitlisting from 2010 through 2020 has been represented in Figure 1A. Patients waitlisted with an FDA-approved durable LVAD increased steadily from 509 in 2010 to 1,168 in 2017 and declined to 837 in 2020 (Figure 1A). From 2017 to 2020, there was a 28.3% decline in the number of patients waitlisted with durable CF-LVAD. There was also a significant shift in the device types utilized. In 2017, 179 patients (15.3%) were listed with HM 3, followed by 354 patients (30.3%) with HVAD, and 635 patients (54.4%) with HM II. However, in 2020, 538 patients (64.3%) were listed with HM 3, followed by 202 patients (24.1%) with HVAD, and 97 patients (11.6%) with HM II (Supplementary Figure S1A).

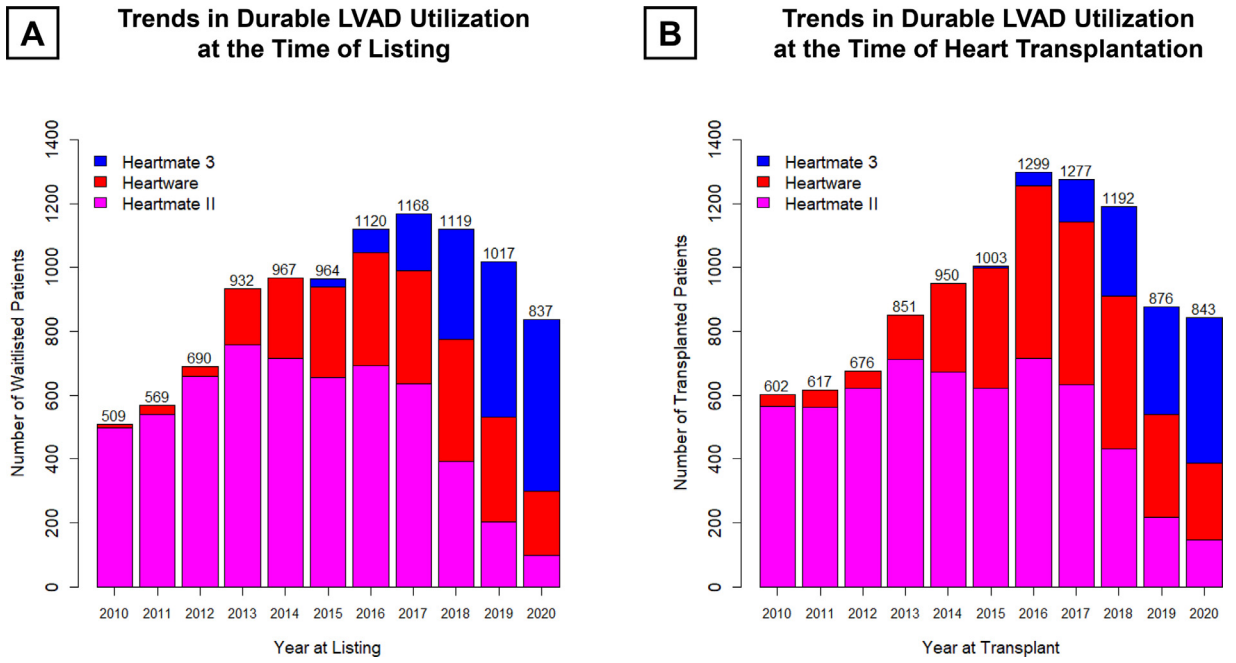


**Figure 1** Trends in durable LVAD utilization for bridging to transplantation. (A) Number of patients waitlisted with durable LVAD by year at listing; (B) Number of patients transplanted with durable LVAD by year at transplantation.

Trends in CF-LVAD utilization at the time of transplant from 2010 through 2020 has been represented in Figure 1B. Similarly, the number of patients transplanted with an FDA-approved durable LVAD increased steadily from 602 in 2010 to 1,299 in 2016 and declined to 843 in 2020 (Figure 1B). Overall, there was a 35.1% decline in the number of patients transplanted with a durable CF-LVAD from 2016 to 2020. In 2016, 44 patients (3.4%) were transplanted with HM 3, followed by 540 patients (41.6%) with HVAD, and 715 patients (55.0%) with HM II. However, in 2020, 455 patients (54.0%) were transplanted with HM 3, followed by 241 patients (28.6%) with HVAD, and 147 patients (17.4%) with HM II (Supplementary Figure S1B). LVAD utilization has declined from 48.6% of all transplanted patients in 2016 to 32.7% of all transplanted patients in 2020 (Supplementary Figure S2).

## Characteristics and outcomes of patients waitlisted with HM 3 LVAD

Overall, 1,543 patients had HM 3 LVAD at the time of transplant listing including 449 in the pre-allocation and 1049 patients in the post-allocation era. HM 3 patients who were waitlisted in the pre- vs post-allocation era were comparable with regards to age at listing, gender, race, HF etiology, renal function, and body mass index (BMI) (Table 1). HM 3 patients who were waitlisted in the post allocation era had significantly lower pulmonary artery pressures. The majority of HM 3 patients (72.6%) were initially listed as Status 4, followed by 18.4% as Status 3, and 3.4% as Status 1.

Transplant waitlist outcomes of patients who were waitlisted with HM 3 LVAD in the pre- vs post-allocation era are shown in Figure 2A. Cumulative incidence of heart transplantation at 1-year after listing with HM 3 LVAD comparable in the pre- vs post-allocation era (53.4% vs 50.7% at 1 year, $p = 0.760$). In multivariable adjusted cox-regression analysis, listing with HM 3 in the post-allocation era was not a significant risk factor for transplantation (hazard ratio 1.02, 95% confidence interval 0.88-1.19, $p = 0.780$). Cumulative incidence of death or delisting for worsening clinical status was comparable in the pre- vs post-allocation era (5.0% vs 4.2% at 1 year, $p = 0.430$). After multivariable adjustment, listing with HM 3 in the post-allocation era was not a significant risk factor for death or delisting for worsening clinical status (hazard ratio 0.84, 95% confidence interval 0.55-1.27, $p = 0.402$).

## Characteristics and outcomes of patients transplanted with HM 3 LVAD

Overall, 998 patients were bridged to transplant with HM 3 LVAD including 406 in the pre-allocation and 592 patients in the post-allocation era. HM 3 patients who were transplanted in the pre- vs post-allocation era were comparable with regards to age at listing, gender, race, HF etiology, renal function, and BMI (Table 2). HM 3 patients who were transplanted in the pre-allocation era were more likely to be blood type O compared to those transplanted in the post-allocation era (41.4% vs 34.1%, $p = 0.024$). Time to transplant was significantly longer in patients bridged with HM 3 in the pre- vs post-allocation era (155 [interquartile range 63-318] vs 81 [interquartile range 21-223] days, $p < 0.001$); however, donor ischemic times were significantly shorter ($3.0 \pm 1.01$ vs $3.5 \pm 1.24$ hours, $p < 0.001$). Utilization of Hep C antibody positive donors was significantly higher in

**Table 1** Clinical Characteristics of Patients Waitlisted with HeartMate 3 LVAD by Allocation System

| Variable | Pre-allocation system (n = 449, 29.1%) | Post-allocation system (n = 1094, 70.9%) | *p*-value |
|---|---|---|---|
| Age at listing (years) | 54.6 ± 11.7 | 53.6 ± 11.6 | 0.137 |
| Gender (female) | 88 (19.6%) | 184 (16.8%) | 0.219 |
| Race/ethnicity | | | 0.071 |
| White | 303 (67.5%) | 649 (59.3%) | |
| AA | 115 (25.6%) | 329 (30.1%) | |
| Hispanic | 22 (4.9%) | 71 (6.5%) | |
| Other | 9 (2.0%) | 45 (4.1%) | |
| Non-ischemic HF | 295 (65.7%) | 735 (67.2%) | 0.616 |
| RCM/HCM | 6 (1.3%) | 12 (1.1%) | 0.891 |
| Congenital | 3 (0.7%) | 3 (0.3%) | 0.365 |
| Myocarditis | 4 (0.9%) | 6 (0.6%) | 0.489 |
| Postpartum | 8 (1.8%) | 17 (1.6%) | 0.920 |
| Retransplant | 1 (0.2%) | 2 (0.2%) | 0.999 |
| Diabetes | 152 (33.9%) | 358 (32.7%) | 0.712 |
| CVA | 26 (5.8%) | 79 (7.2%) | 0.380 |
| Smoking | 247 (55.0%) | 553 (50.5%) | 0.124 |
| AICD at listing | 366 (81.5%) | 810 (74.0%) | **0.006** |
| Blood type O | 218 (48.6%) | 532 (48.6%) | 0.999 |
| Poor functional status | 156 (34.7%) | 397 (36.3%) | 0.606 |
| BMI (kg/m$^2$) | 29.3 ± 4.5 | 29.6 ± 4.6 | 0.277 |
| BSA | 2.10 ± 0.23 | 2.11 ± 0.24 | 0.485 |
| Status at listing | | | **<0.001** |
| 1 | . . . | 11 (1.0%) | |
| 2 | . . . | 37 (3.4%) | |
| 3 | . . . | 201 (18.4%) | |
| 4 | . . . | 794 (72.6%) | |
| 5 | . . . | 0 (0.0%) | |
| 6 | . . . | 29 (2.7%) | |
| 1A | 99 (22.1%) | . . . | |
| 1B | 311 (69.3%) | . . . | |
| 2 | 25 (5.6%) | . . . | |
| Inactive | 14 (3.1%) | 22 (2.0%) | |
| Median waitlist time (days) | 197 [65-645] | 221 [60-437] | **0.014** |
| Hemodynamics | | | |
| PA systolic | 39.0 ± 13.7 | 35.4 ± 11.7 | **<0.001** |
| PA diastolic | 18.3 ± 8.7 | 16.2 ± 8.0 | **<0.001** |
| PA mean | 26.1 ± 10.1 | 23.4 ± 8.9 | **<0.001** |
| PCWP | 16.2 ± 9.1 | 14.0± 7.8 | **<0.001** |
| Cardiac output | 4.66 ± 1.28 | 4.74 ± 1.21 | 0.266 |
| PVR (Woods Units) | 2.29 ± 1.43 | 2.11 ± 1.22 | **0.023** |
| Serum creatinine (mg/dL) | 1.29 ± 1.63 | 1.32 ± 0.69 | 0.704 |
| Dialysis | 5 (1.1%) | 25 (2.3%) | 0.190 |
| Heart-kidney listing | 14 (3.1%) | 76 (7.0%) | **0.005** |
| Heart-liver listing | 0 (0.0%) | 2 (0.2%) | 0.999 |

Abbreviations: AICD, automated internal cardioverter defibrillator; BIVAD, biventricular assist device, BMI, body mass index; BSA, body surface area; CVA, cerebrovascular accident; ECMO, extracorporeal membrane oxygenation, MCSD, mechanical circulatory support device; PA, pulmonary artery; PCWP, pulmonary artery capillary wedge pressure, PVR, pulmonary vascular resistance; RCM/HCM, restrictive/hypertrophic cardiomyopathy.

Continuous data reported as mean ± standard deviation except for waitlist time which was reported as median [interquartile range].

the post-allocation era. HM 3 patients who were transplanted in the post-allocation era have significantly lower pulmonary artery pressures.

With regards to UNOS status at transplant, 276 HM 3 patients (46.6%) were transplanted as Status 3, followed by 214 HM 3 patients (36.1%) as Status 4, 75 HM 3 patients as Status 2 (27.2%), and 27 HM 3 patients (4.6%) as Status 1 in the post-allocation era (Figure 3A). The majority of patients bridged with HM 3 as Status 3 used 30-day discretionary time (73.6%), followed by 15.9% of patients who were upgraded for device infection (Figure 3B). The use of Status 3 for other LVAD complications including right heart failure (2.5%), aortic insufficiency (1.8%), mucosal bleed (1.4%), and device thrombosis (0.4%) were rare in patients bridged with HM 3. The majority of Status 1 and Status 2 upgrades were due to exception (Figure 3B).

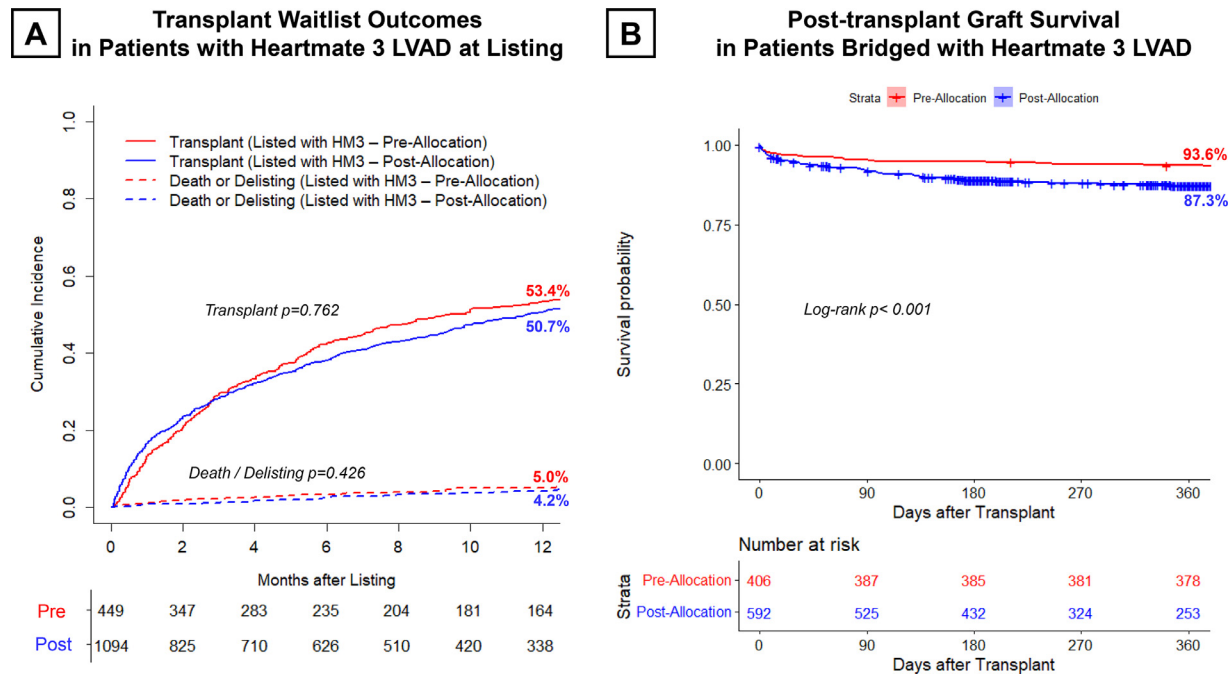


**Figure 2** Waitlist and transplant outcomes of patients bridging with HeartMate 3 LVAD. (A) Competing events of transplantation (line) and death or delisting for worsening clinical status (dotted line) in patients waitlisted with HeartMate 3 LVAD in the pre- (red) vs post- (blue) heart organ allocation system. (B) Post-transplant survival of patients bridged with HeartMate 3 LVAD in the pre- (red) vs post- (blue) heart organ allocation system.

Post-transplant graft survival of patients who were transplanted with HM 3 LVAD in the pre- vs post-allocation era is represented in Figure 2B. One-year post-transplant survival after bridging with HM 3 was significantly higher in the pre- vs post-allocation era (93.6% vs 87.3% log-rank $p < 0.001$). In this analysis, 268 (45.3%) of patients in the post-allocation era were alive but did not complete 1-year follow-up indicating a potential informative bias. Accordingly, we performed an additional survival analysis including HM 3 patients transplanted through December 2019 (instead of December 2020), which resulted in a reduction in the number of patients who did not have complete 1-year follow-up (32, 14.9%). However, 1-year post-transplant graft survival remained significantly higher in the pre- vs post-allocation era (93.6% vs 86.0%, log-rank $p < 0.001$) (Supplementary Figure S3). Including crossover patients (Supplementary Figure S4) or administrative censoring at 365 days (Supplementary Figure S5) did not eliminate significant difference in post-transplant graft survival between pre- vs post allocation era patients. One-year post-transplant graft survival of patients who were bridged with HM 3 LVAD in presence of a device complication was comparable to those who were bridged with HM 3 LVAD without a device complication (Status 4 or Status 3 30-day discretionary time) in the post-allocation era (88.2% vs 86.8%, log-rank $p = 0.910$) (Supplementary Figure S6).

## HM 3 bridge risk score

To determine whether a subset of patients waitlisted with HM 3 is at high risk for bridging to transplantation and to identify the risk factors for poor post-transplant outcome, a cox regression analysis was performed (Table 3). Optimal cut-off points for significant continuous predictor variables were defined by Youden's index (Supplementary Table S2). Multivariable analysis revealed, old recipient age (>50), ischemic etiology of HF, poor functional status, elevated BMI (>33), pulmonary hypertension (>3 WU), and listing in the new allocation system as significant predictors of post-transplant graft mortality. Elevated creatinine (>1.3 mg/dL) and older donor age were borderline significant.

Incorporating the recipient risk factors identified in the regression analysis, we derived a simple 6-point risk score (Figure 4A). One point was assigned to each risk factor to simplify the calculation of the composite risk score in the clinical setting given relatively comparable hazard ratios of each predictor in the multivariable model. Overall, 295 (31.1%) HM 3 patients had low risk score (0 or 1 risk factors), 547 HM 3 (57.6%) patients had medium risk score (2 or 3 risk factors), and 108 (11.4%) HM 3 patients had high risk score (4 or more risk factors) at the time of transplantation. Proportion of patients with low- (32.1% vs 30.3%), medium- (56.3% vs 58.5%), and high-risk patients (11.6% vs 11.2%) were comparable in the pre- vs post-heart allocation system (Figure 4A). HM 3 patients with a high-risk score had significantly lower 1-year post-transplant graft survival (75.2%), compared to those with medium (90.4%) or low risk (95.4%) scores (Figure 4B). Each successive increase in the HM 3 risk score was associated with worse 1-year post-transplant graft survival (Score 0: 97.6%, Score 1: 95.2%, Score 2: 94.8%, Score 3: 86.4%, Score 4: 82.0%, and Score 5: 66.7%, log-rank $p < 0.001$) (Supplementary Figure S7).

**Table 2** Donor and Recipient Characteristics of Patients Bridged to Transplantation With HeartMate 3 LVAD by Allocation System

| Variable | Pre-allocation system (n = 406, 40.7%) | Post-allocation system (n = 592, 59.3%) | *p*-value |
|---|---|---|---|
| Recipient characteristics | | | |
| Age at transplant (years) | 55.5 ± 10.8 | 54.9 ± 11.4 | 0.403 |
| Gender (female) | 84 (20.7%) | 117 (19.8%) | 0.781 |
| Race/ethnicity | | | 0.283 |
| White | 281 (69.2%) | 383 (64.7%) | |
| AA | 80 (19.7%) | 149 (25.2%) | |
| Hispanic | 29 (7.1%) | 40 (6.8%) | |
| Other | 16 (3.9%) | 20 (3.4%) | |
| Non-ischemic HF | 264 (65.0%) | 405 (68.4%) | 0.294 |
| RCM/HCM | 7 (1.7%) | 6 (1.0%) | 0.491 |
| Congenital | 4 (1.0%) | 7 (1.2%) | 0.999 |
| Myocarditis | 2 (0.5%) | 3 (0.5%) | 0.999 |
| Postpartum | 5 (1.2%) | 6 (1.0%) | 0.988 |
| Retransplant | 0 (0.0%) | 0 (0.0%) | . . . |
| Diabetes | 137 (33.7%) | 209 (35.3%) | 0.659 |
| CVA | 21 (5.2%) | 36 (6.1%) | 0.661 |
| Smoking | 215 (53.0%) | 279 (47.1%) | 0.081 |
| AICD at listing | 341 (84.0%) | 458 (77.4%) | **0.023** |
| Blood type O | 168 (41.4%) | 202 (34.1%) | **0.024** |
| Poor functional status | 125 (30.8%) | 205 (34.6%) | 0.231 |
| BMI (kg/m$^2$) | 28.7 ± 4.6 | 29.2 ± 4.7 | 0.149 |
| BSA | 2.06 ± 0.24 | 2.08 ± 0.24 | 0.342 |
| Status at transplant | | | **<0.001** |
| 1 | . . . | 27 (4.6%) | |
| 2 | . . . | 75 (12.7%) | |
| 3 | . . . | 276 (46.6%) | |
| 4 | . . . | 214 (36.1%) | |
| 5 | . . . | 0 (0.0%) | |
| 6 | . . . | 0 (0.0%) | |
| 1A | 280 (69.0%) | . . . | |
| 1B | 126 (31.0%) | . . . | |
| 2 | 0 (0.0%) | . . . | |
| Inactive | 0 (0.0%) | 0 (0.0%) | |
| Median waitlist time (days) | 155 [63-318] | 81 [21-223] | **<0.001** |
| Hemodynamics | | | |
| PA systolic | 36.5 ± 12.0 | 33.8 ± 10.6 | **<0.001** |
| PA diastolic | 16.7 ± 7.2 | 15.4 ± 7.0 | **0.004** |
| PA mean | 24.6 ± 8.5 | 22.3 ± 7.7 | **<0.001** |
| PCWP | 14.9 ± 7.5 | 13.4 ± 7.0 | **0.002** |
| Cardiac output | 4.77 ± 1.20 | 4.85 ± 1.28 | 0.316 |
| PVR (Woods Units) | 2.16 ± 1.28 | 1.95 ± 1.03 | **0.008** |
| Serum creatinine (mg/dL) | 1.25 ± 0.46 | 1.34 ± 0.63 | **0.016** |
| Dialysis | 8 (2.0%) | 18 (3.0%) | 0.396 |
| Heart-kidney transplant | 7 (1.7%) | 32 (5.4%) | **0.005** |
| Heart-liver transplant | 0 (0.0%) | 1 (0.2%) | 0.999 |
| | | | |
| Donor characteristics | | | |
| Donor age | 31.5 ± 10.4 | 33.3 ± 10.5 | **0.009** |
| Donor gender (Female) | 104 (25.6%) | 157 (26.5%) | 0.806 |
| Hypertension | 64 (15.8%) | 100 (16.9%) | 0.673 |
| Diabetes | 13 (3.2%) | 25 (4.2%) | 0.491 |
| CAD | 15 (3.7%) | 28 (4.7%) | 0.992 |
| Hep C Ab positive | 30 (7.4%) | 85 (14.4%) | **0.001** |
| Ischemic time | 2.98 ± 1.01 | 3.49 ± 1.24 | **<0.001** |
| PHM ratio | 1.03 ± 0.15 | 1.01 ± 0.14 | **0.006** |

Abbreviations: AICD, automated internal cardioverter defibrillator; BIVAD, biventricular assist device, BMI, body mass index; BSA, body surface area; CVA, cerebrovascular accident; ECMO, extracorporeal membrane oxygenation, MCSD, mechanical circulatory support device; PA, pulmonary artery; PCWP, pulmonary artery capillary wedge pressure, PHM, predicted heart mass ratio, PVR, pulmonary vascular resistance; RCM/HCM, restrictive/hypertrophic cardiomyopathy.

Continuous data reported as mean ± standard deviation except for waitlist time which was reported as median [interquartile range]. Bold p values indicate < 0.05.

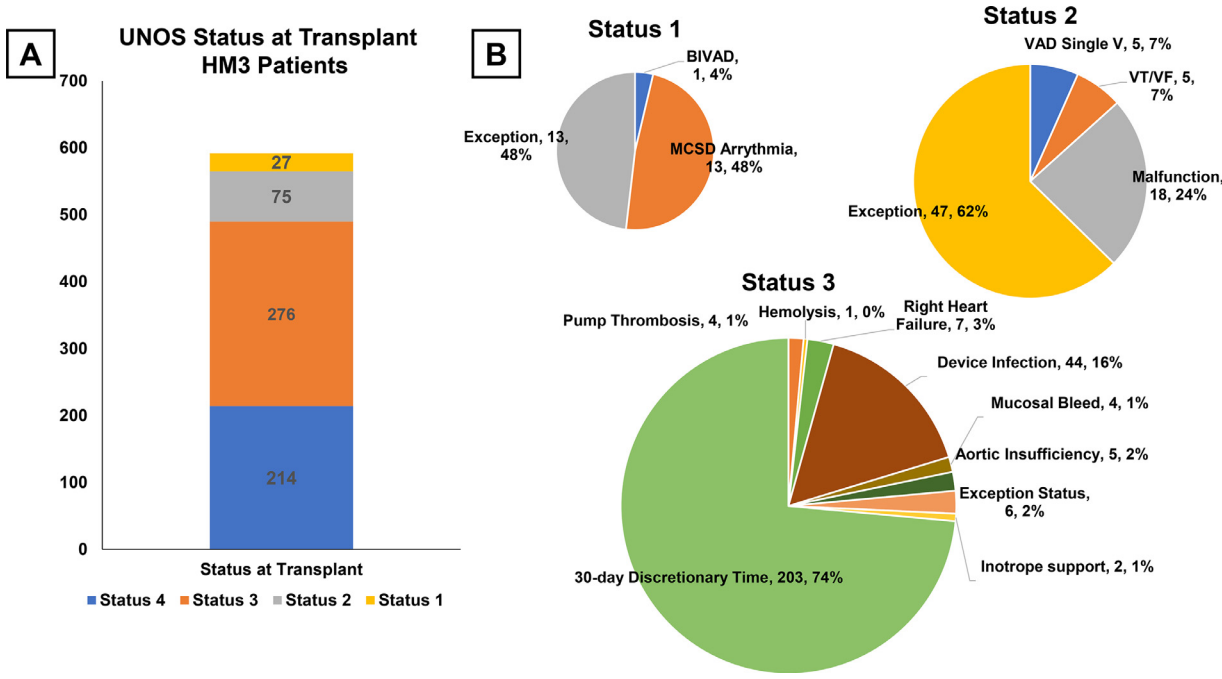


**Figure 3** UNOS status at transplant in patients bridged with HeartMate 3 LVAD. (A) Distribution of UNOS status at transplant in patients bridged with HeartMate 3 LVAD in the post-heart allocation system. (B) Specific indications for UNOS status at transplant in patients bridged with HeartMate 3 LVAD in the new heart allocation system.

## Discussion

The current study examines changing trends in utilization of durable contemporary continuous-flow LVADs. The important findings of the study are as follows: (1) The 2018 heart allocation system change resulted in ~30% decline in utilization of durable LVADs at listing and transplantation; (2) Candidates waitlisted with a HM 3 LVAD have comparable waitlist outcomes including transplantation and death or delisting for worsening clinical status in the pre- vs post-heart allocation system; (3) Post-transplant survival of patients bridged with a HM 3 LVAD remains inferior in the post-allocation era; and (4) Old age, ischemic HF, poor functional status, poor renal function, elevated pulmonary hypertension, and increased BMI are risk factors associated with poor post-transplant survival in patients bridged with HM 3. Taken together, our findings suggest that an individualized approach for patients may improve outcomes of transplant bridging in patients supported with HM 3 LVAD.

The new heart allocation policy promotes a strategy that enables broader geographic sharing and prioritization of the most critically ill patients on the transplant waitlist.[4,11] As such, patients who are supported with temporary mechanical circulatory support, including intra-aortic balloon pump, percutaneous support devices, VA-ECMO, and non-dischargeable LVADs, receive the highest priority status. This shift has resulted in a significant reduction in transplant waitlist time, an increased probability of heart transplantation, and a decrease in waitlist mortality in patients supported with temporary MCS.[12] On the other hand, patients supported with durable LVAD are prioritized as Status 4 in the absence of LVAD complications and have been associated with longer waitlist time, similar waitlist outcomes, and decreased post-transplant survival. The new allocation policy change led to an increase in the utilization of temporary MCS and a decrease in the utilization of durable LVADs for bridging to transplantation. While a recent study reported a nearly 90% reduction in the number of patients listed for transplant with a durable LVAD (from April 2017-April 2020), our analysis focusing on FDA-approved contemporary durable LVADs with longer follow-up (January 2010-December 2020) demonstrate a reduction of 30%.[7] The reduction in the use of durable LVAD among patients listed for transplant is not surprising since a greater proportion of patients are able to go directly to transplant with temporary MCS without the need for durable LVAD placement in the 2018 allocation system. However, a significant number of patients are still being listed with durable LVAD. In addition to reduction in numbers, new heart allocation system has likely changed the clinical profile of LVAD patients bridging to transplantation. For example, cardiogenic shock patients who are dependent on temporary device support could be rapidly transplanted as Status 1 or 2. As such, transplant eligible shock patients meeting hemodynamic criteria rarely use durable LVAD as a bridging strategy in the new allocation system.

Following the MOMENTUM 3 trial and discontinuation of HVAD implants, the HM 3 remains the only durable LVAD option for bridge to transplantation. Our analysis indicates that the new heart allocation system did not negatively impact the incidence of transplantation or waitlist mortality for patients bridging to transplantation with HM 3

**Table 3** Multivariable Hazard Ratio Estimates of Post-Transplant Mortality in Patients Bridged With HeartMate 3 LVAD

| | Univariable analysis | | Multivariable analysis | |
|---|---|---|---|---|
| Variable | HR (95% CI) | *p*-value | HR (95% CI) | *p*-value |
| | Recipient risk factors | | | |
| Age > 50 years | 2.06 (1.28-3.33) | **0.003** | 1.84 (1.11-3.06) | **0.019** |
| Female gender | 1.08 (0.70-1.66) | 0.720 | . . .. | . . . |
| Race/ethnicity (white) | 1.03 (0.97-1.50) | 0.876 | . . .. | . . . |
| Blood type O | 0.78 (0.53-1.13) | 0.187 | . . .. | . . . |
| Diabetes | 1.31 (0.91-1.87) | 0.145 | . . .. | . . . |
| CVA | 0.85 (0.38-1.94) | 0.704 | . . .. | . . . |
| Smoking | 1.27 (0.89-1.82) | 0.178 | . . .. | . . . |
| Body surface area | 1.28 (0.91-1.80) | 0.161 | . . .. | . . . |
| BMI > 33 kg/m$^2$ | 1.84 (1.25-2.68) | **0.002** | 1.92 (1.28-2.88) | **0.002** |
| Ischemic etiology of heart failure | 1.65 (1.16-2.36) | **0.006** | 1.49 (1.02-2.18) | **0.038** |
| Poor functional status | 1.72 (1.20-2.45) | **0.003** | 1.48 (1.02-2.14) | **0.041** |
| Creatinine > 1.3 mg/dL | 1.83 (1.29-2.61) | **<0.001** | 1.46 (1.00-2.14) | 0.053 |
| PVR > 3 Woods Units | 0.93 (0.88-0.98) | **0.008** | 2.00 (1.32-3.10) | **0.002** |
| Cardiac output | 1.03 (0.97-1.10) | 0.326 | . . .. | . . . |
| New heart allocation system | 2.02 (1.33-3.06) | **<0.001** | 2.05 (1.32-3.17) | **0.001** |
| Heart-kidney dual transplant | 2.32 (1.18-4.59) | **0.015** | 1.58 (0.78-3.20) | 0.204 |
| Waitlist time (days) | 0.99 (0.99-1.0) | 0.484 | | |
| | Donor risk factors | | | |
| Donor age > 40 years | 1.51 (1.02-2.23) | **0.041** | 1.45 (0.97-2.16) | 0.071 |
| Female gender | 1.25 (0.85-1.84) | 0.259 | . . .. | . . . |
| Hypertension | 1.15 (0.73-1.83) | 0.122 | . . .. | . . . |
| Diabetes | 1.64 (0.21-2.03) | 0.452 | . . .. | . . . |
| LVEF < 55% | 1.36 (0.43-4.28) | 0.206 | . . .. | . . . |
| Hep C Ab positivity | 1.39 (0.72-0.83) | 0.206 | . . .. | . . . |
| Ischemic time > 4 hours | 1.15 (0.75-1.76) | 0.515 | . . .. | . . . |
| PHM ratio < 0.86 | 1.12 (0.68-1.85) | 0.652 | . . .. | . . . |

Abbreviations: BMI, body mass index; CI, confidence interval; CVA, cerebrovascular accident; HR, hazard ratio; LVEF, left ventricular ejection fraction, PHM, predicted heart mass ratio, PVR, pulmonary vascular resistance. Bold p values indicate < 0.05.

LVAD. However, since temporary MCS provides a potentially more rapid pathway to transplantation in the current heart allocation system, eligible candidates may avoid the additional step of LVAD by bridging with temporary MCS devices and eliminating the need for sternotomy which may further complicate future transplant operation.[13] However, as shown in our analysis, the risk of waitlist mortality is extremely small in patients waitlisted with HM 3 LVAD as opposed to those waitlisted with VA-ECMO (4.2% LVAD vs 16.3% VA-ECMO[14]). As such, the risk of various device strategies must be carefully considered in each transplant candidate.

The majority of HM 3 LVAD patients (70.4%) were bridged to transplantation without a complication as Status 4 or using 30-day discretionary time. Device infection was the most common indication for status upgrade followed by arrythmia, and device malfunction. Other LVAD complications such as RV failure, aortic insufficiency, mucosal bleed, and pump thrombosis were rare indications for status upgrade. These findings are consistent with MOMENTUM 3 trial results and support favorable complication profile of patients supported with HM 3 LVAD. To our surprise, HM 3 patients who had a status upgrade for a device-related complication at the time of transplant did not have increased post-transplant graft mortality. However, current study did not examine other relevant outcomes such as hospitalization for infection, rejection, or allograft dysfunction, risk of which could certainly increase in complicated HM 3 LVAD patients going into heart transplantation.

One of the most important questions is whether it is the safe to transplant a patient who is clinically doing well on HM 3 support and potentially has high risk features for transplant. MOMENTUM 3 trial demonstrates 86.6% survival at 1 year and 79.0% at 2-year follow-up, which is approaching post-transplant survival.[1] However, long-term follow-up data in patients supported with HM 3 LVAD are limited. In this study, we found that a subset of HM 3 patients with several risk factors could be at high risk for bridging. These factors included old age, ischemic etiology, poor renal function, poor functional status, obesity, and pulmonary hypertension. It was evident that patients with at least 4 of these risk factors had worse 1-year post-transplant survival. Transplanting HM 3 patients in the high-risk group should be a shared decision with both the patient and the program well-understanding the risks associated with it. It is also worthwhile to mention that we did not have complete data for HLA allosensitization and

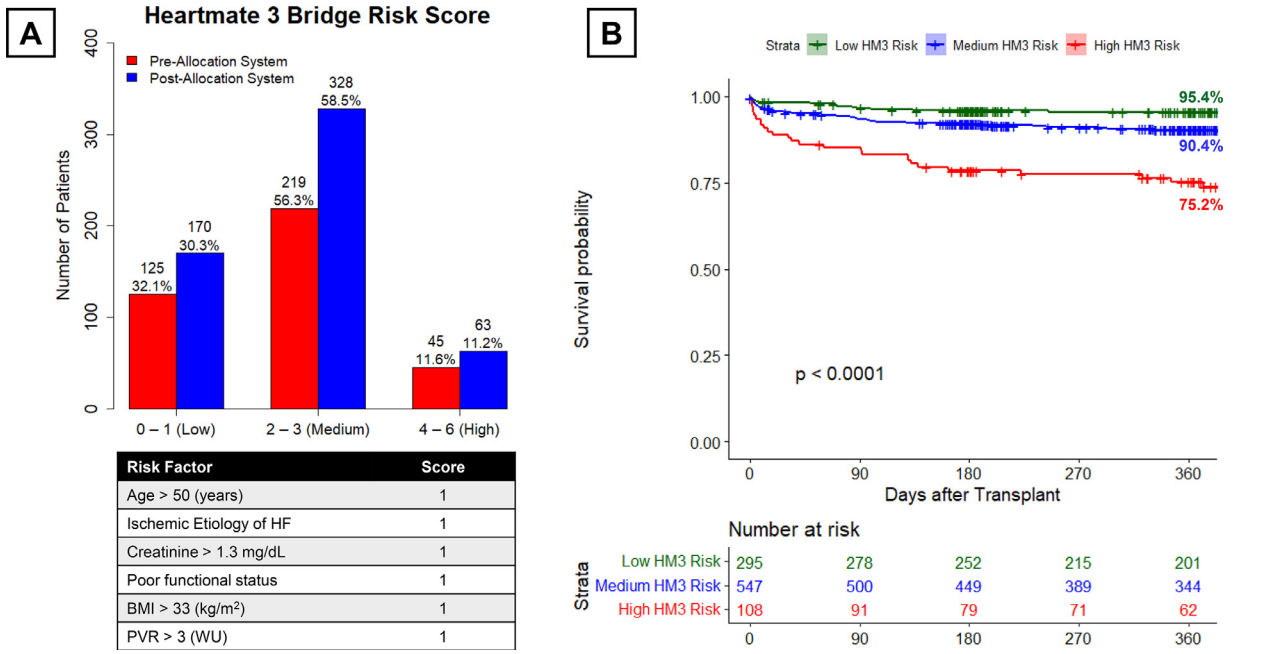


**Figure 4** HeartMate 3 bridge risk score. (A) Distribution of HeartMate 3 bridge risk score resulting in low (score 0-1), medium (score 2-3), and high risk (score 4-6) groups in the pre- vs post-heart allocation system. (B) Post-transplant survival of patients bridged with HeartMate 3 LVAD based on the risk category.

HM 3 patients who are highly sensitized could also be further risk for post-transplant rejection and mortality.[15] In the current study the risk for post-heart transplant mortality was higher between in patients bridged with HM 3 in the post-allocation era, however this comparison is subject to potential bias due to informative censoring.[16] We found longer ischemic times in the new heart allocation system, and as such the risk of primary graft failure in patients bridged with LVAD could potentially be higher.[17] Future studies with higher number of patients and longer follow-up are needed to better characterize HM 3 patients who are at higher risk for bridging to transplant.

The current study has multiple limitations. First, the UNOS registry is subject to missing data and errors in data entry. Second, several LVAD specific information such as pump settings, device optimization was unavailable in the registry. Because risk stratification was performed without a validation cohort, our analysis may overestimate the differences in post-transplant mortality among risk score groups. Lastly, the available data does not take into consideration HM 3 patients who were never listed. Since the current analysis is performed using the UNOS Registry, our findings may not apply to HM 3 LVAD patients in European, Asian, or other international programs with distinct transplant guidelines and policies.

In conclusion, while the utilization of durable devices as BTT has declined in the 2018 heart allocation system, bridging with HM 3 LVAD remains a safe strategy. A subset of HM 3 LVAD patients with multiple comorbid conditions could be at high risk for transplant. Assessment of clinical risk factors and individualizing the bridging decision based on clinical risk profile in patients supported with HM 3 LVAD may improve patient outcomes, organ utilization, as well as post-transplant outcomes. Future research will guide optimal support and bridging strategies in transplant candidates.

## Disclosure statement

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## Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.healun.2022.08.022.

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