Accuracy of Seattle Heart Failure Model and HeartMate II Risk Score in Non–Inotrope-Dependent Advanced Heart Failure Patients

Insights From the ROADMAP Study (Risk Assessment and Comparative Effectiveness of Left Ventricular Assist Device and Medical Management in Ambulatory Heart Failure Patients)

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Background—Timing of left ventricular assist device (LVAD) implantation in advanced heart failure patients not on inotropes is unclear. Relevant prediction models exist (SHFM [Seattle Heart Failure Model] and HMRS [HeartMate II Risk Score]), but use in this group is not established.

Methods and Results—ROADMAP (Risk Assessment and Comparative Effectiveness of Left Ventricular Assist Device and Medical Management in Ambulatory Heart Failure Patients) is a prospective, multicenter, nonrandomized study of 200 advanced heart failure patients not on inotropes who met indications for LVAD implantation, comparing the effectiveness of HeartMate II support versus optimal medical management. We compared SHFM-predicted versus observed survival (overall survival and LVAD-free survival) in the optimal medical management arm (n=103) and HMRS-predicted versus observed survival in all LVAD patients (n=111) using Cox modeling, receiver–operator characteristic (ROC) curves, and calibration plots. In the optimal medical management cohort, the SHFM was a significant predictor of survival (hazard ratio=2.98; P<0.001; ROC area under the curve=0.71; P<0.001) but not LVAD-free survival (hazard ratio=1.41; P=0.097; ROC area under the curve=0.56; P=0.314). SHFM showed adequate calibration for survival but overestimated LVAD-free survival. In the LVAD cohort, the HMRS had marginal discrimination at 3 (Cox P=0.23; ROC area under the curve=0.71; P=0.026) and 12 months (Cox P=0.036; ROC area under the curve=0.62; P=0.122), but calibration was poor, underestimating survival across time and risk subgroups.

Conclusions—In non–inotrope-dependent advanced heart failure patients receiving optimal medical management, the SHFM was predictive of overall survival but underestimated the risk of clinical worsening and LVAD implantation. Among LVAD patients, the HMRS had marginal discrimination and underestimated survival post–LVAD implantation.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT01452802.

Key Words: area under the curve ■ death ■ heart failure ■ survival analysis

The use of continuous-flow left ventricular assist devices (LVADs) as therapy for patients with end-stage heart failure (HF) is growing rapidly, and overall outcomes are improving.1–4 This has prompted consideration of LVAD implantation slightly earlier in the clinical course of HF, in patients who have evidence of advanced disease but have not yet had obvious hemodynamic decompensation requiring inotropic therapy, in the hopes of reducing perioperative risks and improving overall outcomes.5–7 However, in these patients, making an informed clinical choice between LVAD and medical therapy can be challenging for patients and providers. The risk of HF progression may not be obvious, whereas the risks/benefits of LVAD therapy have not been well established because they represented only a small minority of subjects in pivotal LVAD trials.8,9

See Clinical Perspective

Multivariable clinical risk modeling in HF and LVAD may assist in making this difficult decision, but key data are still lacking. There are many validated risk models for HF.
Methods

Parent Study and Patients

The design11 and primary results6 of the ROADMAP study have been previously published. All participating patients provided written informed consent before enrollment. To summarize, ROADMAP is a prospective, nonrandomized, observational study that enrolled 200 patients between October 2011 and July 2013 at 41 US centers and comparing LVAD support versus OMM. The study was sponsored by Thoratec Corporation (Pleasanton, CA; now St. Jude Medical). Subjects were required to have advanced HF (New York Heart Association functional class IIIb/IV and 1 HF hospitalization or 2 unscheduled visits in the previous year and a 6-minute walk distance of <300 m), (2) not receive intravenous inotropic support for 30 days before enrollment, and (3) meet US Food and Drug Administration–approved indications for HMII LVAD as destination therapy, including an ejection fraction ≤25% and maximal treatment with guideline-based OMM for at least 60 days. The OMM cohort includes the patients who met inclusion criteria but chose to remain on OMM as initial therapy on the basis of patient or physician choice, whereas the LVAD cohort consists of patients who underwent LVAD placement as initial therapy. The focus of the present analysis is the performance of established predictive models (SHFM and HMRS) in these patients.

The SHFM performance was assessed in the original OMM cohort (n=103). The HMRS analysis was performed in an enlarged LVAD cohort (n=111) that included 90 patients from the original LVAD cohort (excluding 4 patients with missing data and 3 withdrawn patients) plus 21 patients from the original OMM cohort who underwent delayed LVAD implantation (excluding 1 patient with missing data and 1 withdrawn patient). Of the 21 delayed LVAD patients, 16 were implanted in the first year and 5 in the second year post-enrollment. For the delayed LVAD patients, the index date was the date of implantation, and the HMRS was calculated using data available within 2 weeks of implantation.

Statistical Analysis

To assess SHFM performance, we calculated baseline SHFM-predicted survival and compared it to the observed survival during the first year using 2 different approaches. First, we assessed the predictive value of SHFM for 1-year survival using receiver–operator curves (ROC), and we report the area under the curve (AUC), P values, and 95% confidence intervals (CIs). The trapezoidal method was used to estimate C statistics. We then also constructed univariable Cox proportional hazards models to test the association of SHFM score (as a continuous variable) with survival time (through 1 year). For both analyses, we analyzed 2 different end points. The first was all-cause death regardless of therapy (ie, intention-to-treat survival). However, because placement of an LVAD is an important clinical event that often indicates failure of medical therapy and these patients had the option of LVAD as a bailout strategy should their HF worsen, we also analyzed time to death or LVAD implantation (ie, LVAD-free survival). We assessed model calibration by comparing the average predicted and observed 1-year survival for low- (SHFM score <1.5, <16.5% annual mortality), medium- (1.5 <SHFM score <2.5), and high-risk (SHFM score ≥2.5, >39% annual mortality) groups.12 The SHFM calibration assessment was supplemented with parallel analysis separating the cohort into tertiles, because some of the original risk categories contained few subjects. Error bars on all calibration plots indicate standard error (SEM).

Similarly, to assess HMRS performance in the LVAD group, we used both ROC analysis (reporting the AUC, P values, and 95% CI) and also constructed Cox models of survival post–LVAD implantation, with the HMRS entered as the only variable. Because the HMRS was originally designed to predict 3-month survival and ROADMAP’s primary end point was at 1 year, we examined survival at both 3 months and 1 year. HMRS calibration was assessed by comparing the observed ROADMAP patient survival for low- (HMRS <1.58), medium- (1.58 ≤HMRS <2.48), and high-risk (HMRS ≥2.48) groups to HMRS expected survival. HMRS expected survival was defined as the survival of patients enrolled in the HMII clinical trials for the corresponding low-, medium-, and high-risk groups.13

Continuous variables are reported as median and quartiles (Q1–Q3), and categorical data are reported as percentages. Paired changes in risk scores were compared in patients receiving delayed LVADs from time of enrollment to implant with Wilcoxon signed-rank test. All Cox proportional hazards models were evaluated to ensure that they met the proportional hazards assumption. Time-dependent covariates of the risk scores were added to the models and found to be nonsignificant. Hazard ratios (HRs) are presented for a unit increase in the SHFM score or HMRS. Statistical analysis was performed in SAS version 9.3 (SAS Institute, Cary, NC), and P values <0.05 were considered statistically significant.

Results

Baseline characteristics of the OMM and expanded LVAD groups are shown in Table. Overall rates of death in the OMM group (n=103) at 3 months and at 12 months post-enrollment were 3% (3 deaths) and 17% (18 deaths), respectively. No deaths occurred in OMM patients receiving a delayed LVAD during this time period. For the LVAD cohort (n=111), the 3- and 12-month death rates were 5% and 15%, respectively. Histograms displaying the distribution of SHFM-predicted mortality and ultimate outcome for each patient in the OMM group are shown in Figure 1 (top), first overall and then separated by INTERMACS profile (Interagency Registry for Mechanically Assisted Circulatory Support). Similarly, the baseline HMRS along with patient outcomes, both overall and by INTERMACS category, is shown in the Figure 1 (bottom). The median SHFM score and HMRS did not vary across INTERMACS categories (P=0.21 and P=0.59, respectively). INTERMACS profile was not associated with overall survival or LVAD-free survival or survival post–LVAD implantation (all P>0.05; Figure I in the Data Supplement). For patients receiving delayed LVADs (n=21), the 1-year SHFM-predicted survival decreased from 85±12% at initial study enrollment to 60±32% just before implantation (P=0.001). The comparable HMRS (available in n=19) did not change significantly (2.18±1.29 versus 1.69±0.97; P=0.49).
Figure 2. Depicted are the raw survival (left) and LV AD-free survival (right) where there is no difference in observed risk across SHFM tertiles.

Table. Baseline Characteristics in the OMM (n=103) and LVAD (n=111) Cohorts

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>OMM (n=103)</th>
<th>LVAD (n=111)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enrollment age, y</td>
<td>66 (54–74)</td>
<td>64 (54–70)</td>
</tr>
<tr>
<td>Male sex, %</td>
<td>71 (69)</td>
<td>84 (76)</td>
</tr>
<tr>
<td>NYHA, %</td>
<td></td>
<td></td>
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<tr>
<td>Class III/IIIB</td>
<td>77 (75)</td>
<td>49 (45)</td>
</tr>
<tr>
<td>Class IV</td>
<td>26 (25)</td>
<td>61 (55)</td>
</tr>
<tr>
<td>INTERMACS, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Profile 2–3</td>
<td>0 (0)</td>
<td>9 (8)</td>
</tr>
<tr>
<td>Profile 4</td>
<td>35 (34)</td>
<td>67 (62)</td>
</tr>
<tr>
<td>Profile 5–7</td>
<td>66 (66)</td>
<td>32 (30)</td>
</tr>
<tr>
<td>6-min walk distance, m</td>
<td></td>
<td></td>
</tr>
<tr>
<td>V̇O₂ max, mL kg⁻¹ min⁻¹</td>
<td>9.7 (8.5–12.3; n=61)</td>
<td>10.3 (8.8–11.5; n=69)</td>
</tr>
<tr>
<td>V̇O₂ max RER≥1.1, mL kg⁻¹ min⁻¹</td>
<td>10.9 (9.6–12.7; n=23)</td>
<td>10.2 (8.8–11.3; n=27)</td>
</tr>
<tr>
<td>EQSD VAS</td>
<td>55 (45–75; n=99)</td>
<td>45 (30–50; n=101)</td>
</tr>
<tr>
<td>PHG-9</td>
<td>7 (3–10; n=101)</td>
<td>10 (6–15; n=106)</td>
</tr>
<tr>
<td>Mean SHFM-predicted 1-y survival, %</td>
<td>80</td>
<td>71</td>
</tr>
<tr>
<td>Preimplant HRMRS</td>
<td>1.16 (0.57–1.94)</td>
<td>1.55 (1.06–2.18)</td>
</tr>
<tr>
<td>Expired at 3 mo, %</td>
<td>3 (3)</td>
<td>5 (5)</td>
</tr>
<tr>
<td>Expired at 12 mo, %</td>
<td>18 (17)</td>
<td>17 (15)</td>
</tr>
</tbody>
</table>

EQSD VAS indicates EuroQol Visual Analog Scale; HRMRS, HeartMate II Risk Score; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; LVAD, left ventricular assist device; NYHA, New York Heart Association; OMM, optimal medical management; PHG-9, Patient Health Questionnaire-9; RER, respiratory exchange ratio; SHFM, Seattle Heart Failure Model; and V̇O₂, peak oxygen consumption.

SHFM Discrimination in LVAD-Eligible Noninotrope HF Patients

The survival curves according to original SHFM risk groups (low, medium, and high) and SHFM tertiles are shown in Figure 2. Depicted are the raw survival (left) and LVAD-free survival (right). The performance of the SHFM depended greatly on which of these 2 end points were being considered. As can be seen in the survival curves, the discrimination between groups was much better for overall survival, reaching statistical significance in the Cox model (HR=2.98; 95% CI, 1.65–5.37; P<0.001). As an exploratory analysis, because crossover to LVAD therapy could be handled several ways, we also tested the SHFM for predicting survival with patients censored at that time of LVAD implantation (Figure II in the Data Supplement). This revealed similar performance with HR=2.71 (95% CI, 1.50–4.92) and was again statistically significant (P=0.001). In contrast, when considering LVAD-free survival, the curves are largely overlapping and in Cox model indicates that SHFM was not a significant predictor of the time to LVAD or death (HR=1.41; 95% CI, 0.94–2.10; P=0.097).

We also performed ROC analysis of 1-year outcomes for the same 2 end points (death and death or LVAD implantation), which largely agreed with the Cox model results. The ROC analysis for overall survival to 1 year revealed fair discrimination with an AUC of 0.71 (95% CI, 0.59–0.83; P<0.001). On the contrary, when trying to predict LVAD-free survival to 1 year, SHFM was not statistically significant and showed poor discrimination (AUC=0.56; 95% CI, 0.44–0.68; P=0.31).

Seattle Heart Failure Model Calibration in LVAD-Eligible Non–Inotrope-Dependent HF Patients

In the OMM cohort, the SHFM was well calibrated for overall survival but not LVAD-free survival. The SHFM-predicted 1-year survival of 80% closely reflected the actual OMM survival of 81% but not the LVAD-free survival of 63%. We also assessed calibration by comparing observed versus predicted event rates for both survival and LVAD-free survival separated by baseline SHFM risk groups (high, medium, and low). As can be seen in the figure, the SHFM was well calibrated for 1-year survival (black lines) across the spectrum of risk, not deviating significantly from the line of unity. Calibration was also similar for SHFM-predicted survival with patients censored at that time of delayed LVAD implantation (Figure III in the Data Supplement). In contrast, when considering delayed LVADs as treatment failures (red lines), SHFM overestimated LVAD-free survival. Much of this is actually because of the poor overall discrimination of the SHFM for the end point LVAD-free survival, visualized most clearly in the calibration plot separated by tertiles of baseline SHFM (Figure 3, right) where there is no difference in observed risk across SHFM tertiles.

Heartmate II Risk Score Discrimination in Non–Inotrope-Dependent HF Patients Undergoing LVAD Implantation

The survival curves of the LVAD analysis cohort according to HRMRS baseline risk group (low, medium, and high) are shown in Figure 4 (left). There was not much separation in survival between the risk groups at 3 months (indicated by dashed vertical line). This is in part because few deaths occurred this early in this relatively lower risk cohort. In Cox modeling of survival during 3 months (ie, time to death through the first 3 months post–LVAD implantation), there was no significant association of HRMRS with survival (HR=1.52; 95% CI, 0.77–3.0; P=0.23). However, when analyzing the survival data out to 12-month differences between the HRMRS risk categories did reach significance (HR=1.50; 95% CI, 1.03–2.19; P=0.036). In particular, the highest risk group stood out with only 71% surviving to 1 year. On the contrary, the ROC analyses contrasted somewhat with this result. At 3 months, there was statistically significant, fair discrimination (AUC=0.71; 95% CI, 0.52–0.90; P=0.026), whereas at 1 year, the ROC analysis revealed only marginal, nonsignificant discrimination (AUC=0.62; 95% CI, 0.47–0.76; P=0.12). The inconsistency of result between the 2 analytic methods may be in part explained by the small number of events at 3 months, which should be interpreted with some caution. However, taken all together, these results seem to indicate overall...
marginal discrimination of HMRS in non–inotrope-dependent advanced HF patients undergoing LVAD implantation.

Heartmate II Risk Score Calibration in Non–Inotrope-Dependent HF Patients Undergoing LVAD Implantation

The calibration plot depicting the observed versus expected survival at both 3 and 12 months is shown in Figure 4 (right). The HMRS underestimated survival in all subgroups and at both time points. Because the HMRS was originally defined in higher risk patients enrolled in the HMII clinical trial, we compared the survival by HMRS category in ROADMAP patients to those in the HMII trial cohort (Figure IV in the Data Supplement). The ROADMAP cohort survival curve lies nearly on top of the lowest risk subgroup of HMII trial, yet the median HMRS was actually higher in ROADMAP patients (1.03 in HMII trial versus 1.55 in ROADMAP). This again demonstrates the error in calibration where HMRS

Figure 1. Distribution of Seattle Heart Failure Model (SHFM)–predicted survival and HeartMate II Risk Score (HMRS) in each cohort (optimal medical management [OMM] in top and left ventricular assist device [LVAD] in bottom) overall and divided by INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support) profile. HTx indicates heart transplantation.
overestimates risk of death post–LVAD implantation in non–inotrope-dependent patients.

**Discussion**

Accurate risk modeling is a critical need in advanced HF patients who have not yet had obvious end-stage deterioration requiring inotropes (or temporary mechanical support) in whom the optimal timing of LVAD implantation remains uncertain. In this study, we examined the performance of established risk models in non–inotrope-dependent advanced HF patients enrolled in the ROADMAP study. We found that these models have important limitations in this challenging group of patients. Specifically, we found that the SHFM was predictive of overall survival but was not able to forecast the ≈20% of patients who moved on to LVAD implantation in less than a year. Among the patients receiving an LVAD, the HMRS had marginal discrimination but poor calibration. Although it generally overestimated risk of death post–LVAD implantation, it was still able to identify a relatively small but high-risk subset that had worse survival at 1 year (≈70%), whereas the remainder of the cohort had a more favorable ≈87% survival. We feel that our results indicate that clinicians should be aware that the use, accuracy, and use of the risk scores are likely different in non–inotrope-dependent patients compared with the typical patient being considered for LVAD implantation.

This is the first study to our knowledge to examine the performance of SHFM and HMRS in non–inotrope-dependent advanced HF patients, who are eligible for LVAD implantation but in whom clinical guidelines for implantation are not established. In terms of the risk of continuing OMM alone, the SHFM showed fair discrimination and good calibration in predicting overall survival in this patient population. This is consistent with other studies validating SHFM performance in various settings. At the same time, it is important to note the unique features of the population we studied in ROADMAP,
particularly that by design these patients had ready access to bailout LVAD. Thus, the results might differ in patients with less ready access to LVAD implantation.

With regard to predicting the risk of worsening HF and delayed LVAD implantation, the SHFM did not perform as well. Patients who underwent delayed LVAD implantation in ROADMAP clearly worsened, as evidenced by the mean SHFM-predicted survival dropping from 85% to 60%, declines in 6-minute walk distances, and almost half of these patients starting on inotropes. Although worsening HF leading to LVAD placement is not equivalent to death, it is certainly an important outcome that clinicians would like to be able to anticipate. Our result is consistent with some previous reports suggesting that SHFM may underestimate risk in patients referred to advanced HF programs, particularly when a composite end point including LVAD placement is used, although in HF ACTION, the SHFM provided appropriate 1-year discrimination and calibration for the composite outcome of death, LVAD implantation, and urgent transplantation. Although it is important to acknowledge this limitation of the SHFM, it is also worth noting that the SHFM was not designed to predict this end point and that today’s LVAD implantation technology was not available in the cohorts from which it was derived. In the derivation of the SHFM, 98% of the events were death, with only 2% urgent transplants and LVADs, and LVADs in that era were often reserved for very high-risk patients (ie, INTERMACS 1).

Regarding risk estimation post–LVAD implantation in ROADMAP patients, the HMRS showed marginal discrimination and poor calibration. The marginal discrimination seems consistent with another report examining INTERMACS 4+ patients and 90-day outcomes, which found HMRS to have moderate discrimination in this group of patients. The calibration issue is not entirely surprising because the HMRS was derived and validated in a much higher risk group of patients, whereas ROADMAP is focused on a narrower range of patients within the lower risk portion of the spectrum. Despite these limitations, the HMRS did identify a high-risk subgroup in terms of 1-year survival after LVAD implantation. This is somewhat surprising because of both the differences in the average patient risk profile (compared with the HMII clinical study) and because the HMRS was originally designed to predict short-term (3-month) survival as opposed to 1-year survival. This is clearly an area in need of further research, that is, to define risk models that predict long-term LVAD outcomes, including in non–inotrope-dependent patients. As clinical practice and outcomes in LVAD patients have improved, optimizing long-term outcomes with good quality of life, rather than just improving short-term survival, is now the primary consideration. This is especially salient for lower risk patients such as those in ROADMAP where the decision to proceed with LVAD implantation is elective, and additional variables beyond medical illness including patient and physician perceptions are operative.
Continued research is necessary to improve risk prediction in patients similar to those enrolled in the ROADMAP study. Specifically, either refinement of existing models or, perhaps more likely, design of new models that can better identify patients likely to have significant progression of HF during an actionable period of time are needed so that timing of LVAD implantation can be optimized to avoid excess perioperative risk caused by worsening clinical status. Moreover, attention in the future needs to be paid to additional patient-centered outcomes of interest such as functional capacity and days alive out of the hospital. Models to predict these would certainly be useful for LVAD decision making and timing. It is intriguing to consider whether the SHFM could provide additional use if applied serially (eg, every 3 months) as its prediction curve for LVAD-free survival was close to that observed for the first 3-month follow-up (Figure 3) and the delayed LVADs within the first year of ROADMAP occurred at a median of 138 days (Q1–Q3, 72–203) after enrollment. Similarly, the HMRS does show some discrimination of risk, and perhaps, a simple recalibration of the risk estimates could produce an improved tool. Our results suggest that the current version of HMRS is of limited use in this group of patients but may help identify patients whose expected post–LVAD implantation outcomes are insufficient to justify early LVAD therapy (ie, HMRS high-risk category).

This study has certain limitations that should be noted. The cohorts for the SHFM and HMRS analyses were just >100 patients each, featuring a relatively narrow range of baseline risk, and the number of deaths (particularly at 3 months post–LVAD implantation) was relatively small. This limits the power of our analysis and creates some subgroups with few subjects/end points (eg, SHFM high-risk group). However, this is the largest prospective study of these types of patients and is likely to be the main trial experience of LVAD implantation in noninotrope advanced HF patients for the foreseeable future. There is a small amount of missing data for our study. Nine patients were excluded from the HMRS analysis because of missing data (n=5) or withdrawal of consent (n=4). Whether these patients differed in a systematic way from those included in the analyses and whether this could impact results is not clear. Another limitation is that the study was observational in nature and thus the 2 arms differed in baseline risk. This creates uncertainty when comparing the outcomes of the 2 arms. However, because our primary aim was to assess model performance within study arms (ie, within OMM or LVAD) this should not impact the primary analysis but should be kept in mind if trying to use these models to compare possible outcomes between different treatment approaches to make clinical decisions.

In conclusion, the SHFM predicted survival in non–inotrope-dependent advanced HF patients but was not able to predict the likelihood of worsening to LVAD implant within a year, a key clinical event for today’s treatment of HF. In similar patients undergoing LVAD implantation, the HMRS had marginal discrimination but poor calibration, overestimating risk of death post–LVAD implantation. There remains a need for refinement of these models or derivation of new ones specific to a non–inotrope-dependent HF population, but the current SHFM and HMRS may help guide patient selection and timing by identifying patients who are at high risk for either OMM or LVAD strategy.

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Disclosures
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References
12. Risk Score may still be useful to identify subgroups of patients who are at relatively higher risk (for either optimal medical management or left ventricular assist device strategy), there remains a need for better risk prediction models specific to a particular patient subgroup. Although both the Seattle Heart Failure Model and Heartmate Risk Score, making its use in this group less clear. Although both Seattle Heart Failure Model and Heartmate Risk Score may still be useful to identify subgroups of patients who are at relatively higher risk (for either optimal medical management or left ventricular assist device strategy), there remains a need for better risk prediction models specific to a non–inotrope-dependent heart failure population to better define optimal treatment strategy and timing of intervention.

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CLINICAL PERSPECTIVE

For patients with severe heart failure who are not dependent on chronic inotropic infusion, this work demonstrates that the Seattle Heart Failure Model can predict survival but not the likelihood of heart failure worsening to the point of left ventricular assist device implantation. High-risk patients deserve vigilant clinical monitoring to detect or prevent this worsening. Similar patients who undergo left ventricular assist device implantation generally had better survival than that predicted by the Heartmate Risk Score, making its use in this group less clear. Although both Seattle Heart Failure Model and Heartmate Risk Score may still be useful to identify subgroups of patients who are at relatively higher risk (for either optimal medical management or left ventricular assist device strategy), there remains a need for better risk prediction models specific to a non–inotrope-dependent heart failure population to better define optimal treatment strategy and timing of intervention.
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SUPPLEMENTAL MATERIALS

Supplemental Figure 1. A) Overall survival of OMM patients, B) LVAD-free survival of OMM patients, and C) survival post-LVAD by INTERMACS profile. Abbreviations: LVAD, left ventricular assist device.

Supplemental Figure 2. OMM survival by SHFM risk group with patients censored at time of delayed LVAD implant.

Supplemental Figure 3. SHFM calibration in the OMM cohort (observed vs. expected event rates) showing overall survival, overall survival censored at delayed LVAD, and LVAD-free survival, according to A) predefined risk groups, and B) tertiles. Error bars indicate SEM. Abbreviations: LVAD, left ventricular assist device; SHFM, Seattle Heart Failure Model.

Supplemental Figure 4. Survival of patients receiving LVAD in the ROADMAP vs. HMII clinical trial. Abbreviations: HMII, HeartMate II; HMRS, HeartMate II Risk Score; LVAD, left ventricular assist device; Med, medium; Risk Assessment and Comparative Effectiveness of Left Ventricular Assist Device and Medical Management in Ambulatory Heart Failure Patients, ROADMAP.
Supplemental Figure 2. OMM survival by SHFM risk group with patients censored at time of delayed LVAD implant.
Supplemental Figure 3

A
Low Risk: SHFM score < 1.5 (n=55)
Med Risk: 1.5 ≤ SHFM score ≤ 2.5 (n=39)
High Risk: SHFM score > 2.5 (n=9)

B
Tertile 1: SHFM score ≤ 1.15 (n=34)
Tertile 2: 1.15 < SHFM score ≤ 1.75 (n=34)
Tertile 3: SHFM score > 1.75 (n=35)
Supplemental Figure 4

Survival (%)

Months Post-Implant

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<thead>
<tr>
<th>HMII Clinical Trial</th>
<th>ROADMAP</th>
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<tbody>
<tr>
<td>Low Risk (n = 455)</td>
<td>Receiving LVAD (n = 116)</td>
</tr>
<tr>
<td>HMRS = 1.03 [0.68-1.32]</td>
<td>HMRS = 1.55 [1.06-2.18]</td>
</tr>
<tr>
<td>Med Risk (n = 422)</td>
<td></td>
</tr>
<tr>
<td>HMRS = 1.96 [1.74-2.19]</td>
<td></td>
</tr>
</tbody>
</table>