Predictive value of the Seattle Heart Failure Model in patients undergoing left ventricular assist device placement

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BACKGROUND: Left ventricular assist devices (LVADs) are increasingly used in advanced heart failure patients. Despite proven efficacy, optimal timing of LVAD implantation is not well defined.

METHODS: Patients receiving an LVAD were prospectively recorded. Laboratory and clinical data were extracted and used to calculate the predicted survival with medical therapy using the Seattle Heart Failure Model (SHFM). This was compared with observed survival, hospital length of stay and timeliness of discharge.

RESULTS: We identified 104 patients. Survival with an LVAD vs SHFM predicted survival was 69% vs 11% at 1 year, corresponding to a hazard ratio of 0.17 (p < 0.0001). SHFM-estimated 1-year survival with medical therapy increased from 4% in 1997 to 2004 to 25% in 2007–2008 (p < 0.0001). Subgroup analysis of higher vs lower risk LVAD patients showed observed 1-year survival of 83% vs 57% (p = 0.04). The lower risk group had a shorter length of stay (46 vs 75 days, p = 0.03), along with higher rates of discharge prior to transplant (88% vs 61%, p = 0.01) and discharge within 60 days of LVAD placement (77% vs 52%, p = 0.03).

CONCLUSIONS: The SHFM allows prediction of important features of a patient’s hospital course post-operatively, including length of stay and 1-year survival. Given evidence of improved survival and shorter hospital stay in lower risk patients, earlier LVAD placement based on a prediction model like the SHFM should be considered in advanced heart failure patients. The SHFM may have utility as a virtual control arm for single-arm LVAD trials.

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Heart failure hospitalizations have more than doubled in the last two decades to over 1 million admissions annually, whereas both survival and the cost of care of heart failure patients have increased significantly.1 For patients with heart failure refractory to optimal medical management, transplantation has been an option for several decades. Unfortunately, there has been a worsening imbalance between the number of patients listed for transplant and the number of donor hearts.2 Ventricular assist devices have increasingly become an option for both prolonging survival as a bridge to heart transplantation3 and as a definitive destination therapy in the terminally ill heart failure patient not eligible for transplant.4 The American College of Cardiology and American Heart Association (ACC/AHA) suggested that a predicted mortality of >50% at 1 year is an appropriate threshold for consideration of placement of an LVAD.5


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The Seattle Heart Failure Model (SHFM) is a well-validated tool for predicting heart failure survival in a wide variety of settings, with the original cohort dataset and 5 validation data sets including >10,000 patients. Subsequent analyses have further validated the original model discrimination and calibration. A recent analysis of the destination LVAD REMATCH study validated the SHFM in survival prediction in both the medically treated and LVAD-treated groups. Other important considerations include quality of life, hospital length of stay and the ability to discharge from the hospital without transplant as a rescue therapy from the LVAD. We sought to use a real-world dataset to validate use of the SHFM to describe the risk of patients receiving an LVAD at a single institution, including mortality, length of stay and likelihood of timely hospital discharge. We estimated a hazard ratio for LVAD therapy using the SHFM as a virtual control arm.

Methods

Patients undergoing LVAD placement are prospectively collected in a limited database. A review of patients receiving an LVAD between 1997 and 2008 was undertaken after approval by the institutional review board of the University of Washington. The sole inclusion criterion was a diagnosis of heart failure for at least 30 days prior to the implantation of an LVAD. Patients receiving an LVAD as a temporary or peri-operative stabilizing measure (“bridge to re-evaluation”) were excluded. Data were obtained in best approximation to LVAD insertion. Laboratory biomarkers (percent lymphocytes, uric acid, hemoglobin, sodium and total cholesterol) were recorded as the most recent values within 30 days prior to surgery. Vital signs (systolic blood pressure, heart rate and weight) were averaged over the 24 hours prior to surgery, whereas patient medications (including daily diuretic doses, presence of intravenous inotropic or vasoactive medications and the use of an angiotensin-converting enzyme inhibitor [ACE-I], angiotensin receptor blocker [ARB], aldosterone receptor antagonist, beta-blocker, statin or allopurinol) were recorded for the 48 hours prior to surgery. Age, gender, ejection fraction, implantable cardiac defibrillator or cardiac resynchronization therapy, and requirement for dialysis, ventilator or a medically necessary intra-aortic balloon pump (IABP), were noted in the 48 hours prior to surgery. All patients were New York Heart Association (NYHA) Stage IV. Other data not a part of the SHFM were collected for descriptive purposes of the patient population.

The SHFM was updated as applied in REMATCH with a hazard ratio of 2.92 for IABP/ventilator and 1.17 for each inotrope. In addition, given our recent research showing a primary prevention implantable cardioverter-defibrillator (ICD) has no benefit in patients with an estimated mortality of >25%/year, we applied a variable ICD benefit for patients with an annual mortality of ≤25% and no ICD benefit for an annual mortality of >25%. All variables included in the SHFM were available for 101 patients. The mean value was used for rare missing variables in the 3 remaining patients. The devices used varied over the time period and included the HeartMate Intraperitoneal (n = 17), HeartMate VE/XVE (n = 51), Abiomed (n = 1), Thoratec IVAD (n = 2) and HeartMate II (n = 33). Patients with a HeartMate VE/XVE/II or Thoratec IVAD who did not require a right VAD (n = 4) were considered potentially eligible for discharge (n = 82).

Statistical analysis was carried out with SPSS 16.0 software (SPSS, Inc., Chicago, IL). Fisher’s exact test was used for simple comparisons of categorical variables, whereas Student’s t-test was used for continuous variables. Survival was analyzed using Kaplan–Meier survival curves and statistical significance via log-rank tests. Estimated hazard ratios were performed using the Z statistic. Patients who received transplantation were censored as alive for analysis purposes, p ≤ 0.05 was considered statistically significant. We used an empiric cut-point of ≤20% mortality at 30 days (corresponding to approximately 75% mortality at 180 days) to describe our lower risk population.

Results

One hundred fifty-four patients received an LVAD during the study period; 104 met the inclusion criteria. Ninety-three percent of the patients received the device as a bridge to transplantation, whereas 7% received the device as destination therapy. Baseline characteristics of the population are shown in Table 1. Average age was 53 years, with a mean ejection fraction of 18%. All patients were NYHA Stage IV, with 46% having an ischemic etiology to their heart failure. Fifty-three percent had an ICD and/or biventricular pacemaker ICD, and 77% were dependent on an IABP prior to surgery. Eighty-eight percent were on dobutamine and/or milrinone. Forty-nine percent tolerated an ACE-I or an ARB, whereas 13% were on a beta-blocker. They had markedly abnormal laboratory biomarkers with low hemoglobin, percentage lymphocytes, sodium and cholesterol, along with high creatinine, brain natriuretic peptide (BNP) and uric acid. The furosemide total diuretic daily dose was 7.8 mg/kg (approximately 640 mg/day).

The average duration of LVAD support was 147 ± 143 days for a total support time of 41.9 years. Average duration of LVAD support varied by HeartMate (HM) device with: VE/XVE < IP II (99 ± 85, 125 ± 94 and 235 ± 194 days, HM II vs VE/XVE, p < 0.001). Of the 97 patients implanted as a bridge to transplant, there were 9 deaths (9%), 86 transplants (89%) and 2 patients awaiting transplant at time of data analysis. The 180-day observed Kaplan–Meier survival did not differ significantly by LVAD type (IP: 94%; VE/XVE: 79%; II: 86%). The percentage of patients discharged prior to transplant was similar for the HM II vs VE/XVE (73% vs 61%, p = 0.27).

Figure 1 shows the distribution of SHFM 1-year predicted survival with medical management alone. Eighty-two percent of the patients had an SHFM-estimated 1-year survival of <25%. Ninety-two percent of patients met the
ACC/AHA criteria of <50% expected 1-year survival, with 83% having <50% 180-day survival, and 37% having <50% survival at 30 days. Survival with LVAD was markedly improved over predicted survival with medical management alone. Figure 2 shows the observed Kaplan–Meier survival curve for patients receiving LVAD vs the SHFM predicted survival with medical management alone. The observed survival with an LVAD vs predicted survival by the SHFM was 95% vs 54% at 1 month, 84% vs 20% at 180 days and 69% vs 11% at 1 year. LVAD implantation was associated with an estimated hazard ratio of 0.12 at 30 days.

0.11 at 180 days and 0.17 at 365 days (all \( p < 0.0001 \)). We noted a change in the risk profile of patients undergoing LVAD placement in the earlier vs later period of the study, as shown in Figure 3. One-year estimated survival with medical management increased from 6.5% in 1997 to 1998 to 25.4% in 2007–2008 (\( p < 0.0001 \)).

We performed a subgroup analysis on the 82 patients who had an LVAD that was capable of outpatient management. LVAD patients with devices capable of discharge were divided into a lower risk (\( n = 26 \)) and higher risk (\( n = 56 \)) group with a cut-point based on SHFM risk score that corresponded to 30-day mortality of \( \leq 20\% \) vs >20% (corresponding to approximately 25% 180-day survival). Figure 4 shows the Kaplan–Meier survival curve for the two subgroups. Survival was 100% in the lower risk group as compared with 80.3% in the higher risk group at 6 months and 83.3% vs 57.2% at 1 year (\( p = 0.039 \)). Patients in the lower risk group had an 88% chance of a hospital discharge within 60 days of LVAD placement, whereas patients in the higher risk group had a 61% chance of a discharge within 60 days.
days ($p = 0.01$). Calculation was then made for length of hospital stay after LVAD placement, with exclusion of patients who died in the hospital. The lower risk group had a mean length of stay of 46 days, as compared with 75 days in the higher risk group ($p = 0.03$).

The ultimate survival, combining the period in which the LVAD was used as a bridge to transplantation (BTT) with the post-transplant period, is shown in Figure 5. Patient survival in LVAD patients after transplantation was 91% at 1 month, 86% at 1 year, 75% at 5 years and 66% at 10 years. Including the period of support with an LVAD as BTT, survival was 79% at 1 year, 68% at 5 years and 60% at 10 years.

Discussion

Emerging data have continued to show the efficacy of LVAD therapy in the treatment of refractory heart failure: the original REMATCH data comparing destination LVAD with medical management demonstrated a 52% 1-year survival in the LVAD group as compared with 25% survival in the medically managed group, whereas subsequent post–end-point analysis confirmed continuing improved survival in the LVAD treatment group. Data from the INTERMACS self-reported database of 75 centers implanting VADs showed 78% survival at 6 months for patients receiving an LVAD as a bridge to transplant and 75% survival in patients receiving an LVAD as destination therapy. A recently published study of a newer generation continuous-flow device showed a continued improvement in outcomes with a 58% 2-year survival. Our study has described LVAD outcomes in a real-world population and, by comparing with predicted survival (a “virtual control”), further validates the life-prolonging benefit of LVAD therapy in a critically ill heart failure population outside the scope of a clinical trial. In fact, Kaplan–Meier analysis of our population demonstrated slightly higher 180-day survival compared with findings from REMATCH, HeartMate II Bridge to Transplant and INTERMACS.

The efficacy of LVAD therapy is proven unequivocally, but optimal placement timing remains poorly defined. As a result, accurate risk prediction tools are needed to select appropriate patients. The INTERMACS database includes a classification dividing patients receiving LVADs into seven profiles based on generalized categories of heart failure, such as critical cardiogenic shock vs stable but inotropic-dependent vs exertion intolerant. This schema has discriminant power in differentiating outcomes in critically ill vs relatively stable patients receiving LVADs, although the classification was not predictive of outcomes in our critically ill patient population. Schaffer et al recently compared four risk prediction scores in patients with advanced heart failure receiving an LVAD at a single institution. In their study, the SHFM was the best predictor of mortality. Some have argued that the ACC/AHA guidelines are too restrictive in their definition of appropriate timing for LVAD placement. It is notable that our population was more critically ill than populations in previous studies. In the REMATCH analysis, for example, 19% of patients had SHFM predicted 1-year survival of $>50\%$, approximately double the rate in our study. The vast majority of our patients met both Medicare criteria and the more restrictive ACC/AHA criteria for LVAD placement. Furthermore, the lower risk subgroup of our population had better outcomes after LVAD placement.

Not only is there a proven survival benefit in appropriately selected advanced heart failure patients, but patient quality of life post-LVAD has been shown to be better than quality of life in medically managed patients. Our study, the SHFM not only predicted mortality in LVAD patients, but also important proxy measures for morbidity in the post-LVAD hospital course. Patients with less advanced heart failure, as defined by lower SHFM score, benefited from a nearly 50% reduction in hospital days post-LVAD placement, and a 67% reduction in risk of a >60-day post-operative hospital course. In critically ill patients, an LVAD may keep critically ill patients alive, but not improve quality of life by allowing ultimate hospital discharge. It is very important in destination therapy LVADs to avoid placement

![Figure 4](image4.png)

**Figure 4** Kaplan–Meier survival analysis comparing higher and lower risk LVADs based on pre-operative SHFM score of $\geq 20\%$ vs $>20\%$ mortality at 1 month (equivalent to $\sim 25\%$ survival at 180 days or $\sim 7\%$ survival at 1 year).

![Figure 5](image5.png)

**Figure 5** Kaplan–Meier survival analysis with the LVAD BTT approach from the time of LVAD with continued survival observation after transplant (includes all deaths after LVAD including those post-transplant).
in patients who are ultimately unable to be discharged from the hospital as they do not have the option of transplant as rescue therapy from the LVAD. Given the outcomes in patients receiving LVADs at our institution and others, perhaps it is not necessary to wait for patients to become so critically ill (1-year survival <50%) before advising placement of an LVAD.

The observation that patients with lower risk of death have improved outcomes supports the concept of an early vs delayed LVAD implantation in patients with a 1-year medical survival of ~70% to 80% (data pending from the REVIVE-IT study). Lower risk patients identified by the SHFM at our medical center, Johns Hopkins, University of Minnesota and in the ongoing HeartWare European/Australian Bridge to Transplant Trial all suggest an ~80% to 85% 1-year survival with LVAD therapy in this lower risk population. The SHFM is a widely validated risk model with excellent calibration that can be used to identify ambulatory heart failure patients who are at high enough risk to place an LVAD, while excluding those patients with low peak VO₂ and significant symptoms who do not have a high risk of death to justify an LVAD (possibly <30% to 40% annual mortality).

Strengths of our study included narrow exclusion criteria along with thorough follow-up data and an entire population derived from a single academic medical center. The demonstrated positive effects of LVAD placement as compared with medical survival must be offset against the relatively low number of patients in our population able to tolerate a full regimen of life-prolonging heart failure medications. For example, in comparison to the HeartMate II clinical trial, more of our patients were on an ACE-I or ARB (49% vs 35%), whereas significantly fewer were on a beta-blocker (38% vs 13%).

In conclusion, the SHFM can describe the risk for patients receiving LVADs and may allow for comparison between trials using LVADs as BTT where there is no control arm. It may have significant utility in identifying ambulatory non-inotrope-dependent patients who may be appropriate for elective LVADs. The variables used to calculate the SHFM score are inexpensive and should be collected in LVAD trials and in the INTERMACS registry to allow risk characterization of the patient populations.

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References