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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 transplantation[3] 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.[6] Subsequent analyses have further validated the original model discrimination and calibration.[7–9] A recent analysis of the destination LVAD REMATCH study validated the SHFM in survival prediction in both the medically treated and LVAD-treated groups.[10] 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) Class 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%.[11] 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. $p \leq 0.05$ 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