JACC: HEART FAILURE VOL. 5, NO. 2, 2017

ISSN 2213-1779/$36.00
http://dx.doi.org/10.1016/j.jchf.2016.09.008

CLINICAL RESEARCH

# Cost-Effectiveness of Left Ventricular Assist Devices in Ambulatory Patients With Advanced Heart Failure

Jacqueline Baras Shreibati, MD, MS,[a] Jeremy D. Goldhaber-Fiebert, PhD,[b] Dipanjan Banerjee, MD, MS,[a] Douglas K. Owens, MD, MS,[b,c] Mark A. Hlatky, MD[a]

## ABSTRACT

**OBJECTIVES** This study assessed the cost-effectiveness of left ventricular assist devices (LVADs) as destination therapy in ambulatory patients with advanced heart failure.

**BACKGROUND** LVADs improve survival and quality of life in inotrope-dependent heart failure, but data are limited as to their value in less severely ill patients.

**METHODS** We determined costs of care among Medicare beneficiaries before and after LVAD implantation from 2009 to 2010. We used these costs and efficacy data from published studies in a Markov model to project the incremental cost-effectiveness ratio (ICER) of destination LVAD therapy compared with that of medical management. We discounted costs and benefits at 3% annually and report costs as 2016 U.S. dollars.

**RESULTS** The mean cost of LVAD implantation was $175,420. The mean cost of readmission was lower before LVAD than after ($12,377 vs. $19,465, respectively; $p < 0.001$), while monthly outpatient costs were similar ($3,364 vs. $2,974, respectively; $p = 0.54$). In the lifetime simulation model, LVAD increased quality-adjusted life-years (QALYs) (4.41 vs. 2.67, respectively), readmissions (13.03 vs. 6.35, respectively), and costs ($726,200 vs. $361,800, respectively) compared with medical management, yielding an ICER of $209,400 per QALY gained and $597,400 per life-year gained. These results were sensitive to LVAD readmission rates and outpatient care costs; the ICER would be $86,900 if these parameters were 50% lower.

**CONCLUSIONS** LVADs in non-inotrope-dependent heart failure patients improved quality of life but substantially increased lifetime costs because of frequent readmissions and costly follow-up care. LVADs may provide good value if outpatient costs and adverse events can be reduced. (J Am Coll Cardiol HF 2017;5:110–9)


The U.S. health care system spends more than $26 billion annually for patients with heart failure (HF) (1). Nearly 250,000 of the approximately 6 million patients with HF have advanced disease with frequent hospital admissions, low quality of life, and high mortality (2). The left ventricular assist device (LVAD) is an established treatment option for patients with inotrope-dependent HF,

From the [a]Division of Cardiovascular Medicine, Department of Medicine, Stanford University School of Medicine, Stanford, California; [b]Center for Health Policy and Center for Primary Care and Outcomes Research, Department of Medicine, Stanford University, Stanford, California; and the [c]Veterans Affairs Palo Alto Health Care System, Palo Alto, California. Dr. Banerjee has received research support and consulting fees from HeartWare and Thoratec Corp. Dr. Owens has received consulting fees from Zoll, Inc. Dr. Hlatky has received research support from HeartFlow, Inc.; and consulting fees from Acumen, Inc. and Jansson. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received June 14, 2016; revised manuscript received September 7, 2016, accepted September 11, 2016.

but use of LVADs as destination therapy (DT) is less common among ambulatory patients with advanced HF who are not dependent on intravenous inotropes (3).

Patients with non-inotrope-dependent HF have shorter lengths of stay for LVAD implantation and better survival than patients with inotrope-dependent HF, yet they still face considerable ongoing risks due to device complications (4,5). A recent study reported that readmission rates were higher after LVAD implantation than among patients who received medical therapy (5).

DT-LVADs do not appear to be cost-effective in patients with inotrope-dependent HF (6–8), although the incremental cost per quality-adjusted life-year (QALY) gained has become more favorable with second-generation devices and improved patient selection. There are no randomized studies comparing LVADs with medical therapy in ambulatory patients with advanced HF. It is not known whether LVADs would provide good value if used in these patients.

SEE PAGE 120

In this analysis, we documented costs of care from Medicare patients who received LVADs and combined these data with evidence from published studies to estimate the cost-effectiveness of LVADs in patients with non-inotrope-dependent advanced HF. We also examined the cost-effectiveness of LVADs in patients who are not ideal candidates for the device and tested alternative scenarios to identify when LVADs provide the most value.

## METHODS

**MEDICARE COST ANALYSIS.** We obtained costs for patients with advanced HF receiving medical management and from those receiving LVAD by analyzing claims from Medicare beneficiaries before and after LVAD implantation. We derived costs from a cohort that had characteristics similar to the registry participants featured in our cost-effectiveness analysis (Online Table S1) (5).

We identified fee-for-service Medicare beneficiaries who received an implantable VAD in 2009 or 2010. We identified implant hospitalizations by using an International Classification of Diseases, 9th edition procedure code, in any position on the claim, of 37.66.

Non-inotrope-dependent patients tend to have shorter lengths of stay for LVAD implantation than inotrope-dependent patients (4), so to identify less acutely ill patients at the time of implantation, we selected implantation hospitalizations using the diagnosis-related group (DRG) code 002 ("Heart transplant or implant of heart assist system without major complications or comorbidities"), rather than DRG code 001 ("Heart transplant or implant of heart assist system with major complications or comorbidities"). We excluded implantations if heart transplantation occurred during the same admission.

We determined costs from Medicare claims from 2008 to 2011 by using a 100% sample of inpatient claims (Part A) and a 20% sample of physician/carrier (Part B), durable medical equipment, hospice, outpatient, and home health agency claims. We included reimbursements and deductibles paid for by patients (Online Table S2) (9) and adjusted costs to 2016 U.S. dollars, using the Consumer Price Index (10).

Applying these criteria to the 100% Medicare inpatient claims sample, we identified 220 beneficiaries with inpatient claims for LVAD in 2009 or 2010, 20% of whom (n = 45) also had outpatient costs.

**COSTS AND LENGTH OF STAY.** We calculated the average readmission cost and length of stay for medical management, using inpatient claims from the 12 months prior to LVAD. For LVAD, we used claims from the 12 months after implant discharge. We calculated stroke (DRG codes 061 to 069) separately because stroke can lead to profound decrements in quality of life. We calculated pump replacement (International Classification of Diseases, 9th edition procedure codes 37.53, 37.54, and 37.63) separately because this hospitalization costs substantially more than other LVAD-related adverse events, such as bleeding and driveline infection (11). We identified readmission for bleeding as DRG codes 377, 378, 379, 811, or 812.

We obtained average monthly outpatient costs for medical management by using claims from the 12 months leading up to implantation. For LVAD, we used claims from the 12 months after implantation discharge if patients were alive and free of heart transplant at the beginning of each monthly interval. Cost and length-of-stay data were compared using the non-parametric Wilcoxon rank sum test.

The Institutional Review Board at Stanford University School of Medicine approved the cost analysis. All p values were 2-sided, and p values ≤0.05 were considered statistically significant. All data were analyzed using SAS version 9.2 (Cary, North Carolina).

**MODEL-BASED COST-EFFECTIVENESS ANALYSIS.** We developed a Markov model to estimate survival, quality of life, hospital readmissions, and costs

### ABBREVIATIONS AND ACRONYMS

**DT** = destination therapy

**DRG** = diagnosis-related group

**HF** = heart failure

**ICER** = incremental cost-effectiveness ratio

**INTERMACS** = Interagency for Mechanically Assisted Circulatory Support

**LVAD** = left ventricular assist device

**MedaMACS** = Medical Arm of the Mechanically Assisted Circulatory Support

**QALY** = quality-adjusted life-year

**TABLE 1 Base Case Model Input Parameters**

| | Medical Management | LVAD | Ref. # |
|---|---|---|---|
| Age, yrs | 61 | 61 | (12,14) |
| Readmission | | | |
| Medical management total (per patient-year) | | | |
| Low-risk patients | 0.84 | | (12) |
| High-risk patients | 1.8 | | (12) |
| LVAD total, per patient-yr* | | 2.0 | (3,16) |
| LVAD pump replacement, per patient-yr | - | 0.05 | (29,30) |
| Stroke, per patient-yr | 0.02 | 0.09 | (5,31) |
| % Proportion major stroke | 40 | 40 | (32) |
| Treatment change | | | |
| % LVAD received, annual | 2.4 | | (12) |
| % Heart transplant received, annual | 2.4 | 2.4 | (5,12) |
| Survival | | | |
| % Medical management survival at 1 yr | | | |
| Low-risk patients | 84 | | (12) |
| High-risk patients | 73 | | (12) |
| % LVAD survival at 30 days | | 95 | (33,34) |
| % LVAD survival at 3 months | | 93 | (14) |
| % LVAD survival at 1 yr | | 83 | (14) |
| % LVAD survival at 2 yrs | | 75 | |
| % Severe stroke survival at 1 yr | 1 | 1 | (35) |
| % Heart transplant survival at 30 days | | 95 | (36) |
| % Heart transplant survival at 1 yr | 85 | 85 | (37,38) |
| % Heart transplant survival at 7 yrs | 45 | 45 | (37,38) |
| Quality of life | | | |
| Baseline utility | 0.40 | 0.40 | (19) |
| Utility after LVAD implant, 2–5 months | | 0.66 | (19) |
| Utility after LVAD implant, ≥6 months | | 0.70 | (19) |
| Utility after heart transplant, ≥2 months | 0.76 | 0.76 | (39) |
| Utility after major stroke | 0.30 | 0.30 | (20) |
| Utility during any hospitalization | 0 for length of stay | 0 for length of stay | (21), **Table 2** |

Medical management cohorts were derived from the MedaMACS registry. Low-risk are likely LVAD- eligible patients, and high-risk are likely LVAD-ineligible patients, as determined by the practicing HF clinician. LVAD survival is free from heart transplant. Medical management survival is free from heart transplant or LVAD. *Rate inclusive of stroke and pump replacement readmissions.

HF = heart failure; LVAD = left ventricular assist device; MedaMACS = Medical Arm of the Mechanically Assisted Circulatory Support.

among non-inotrope-dependent HF patients receiving DT-LVAD and compared them with costs incurred by patients receiving medical management (Online Figure 1, **Table 1**). We performed the analysis from a societal perspective.

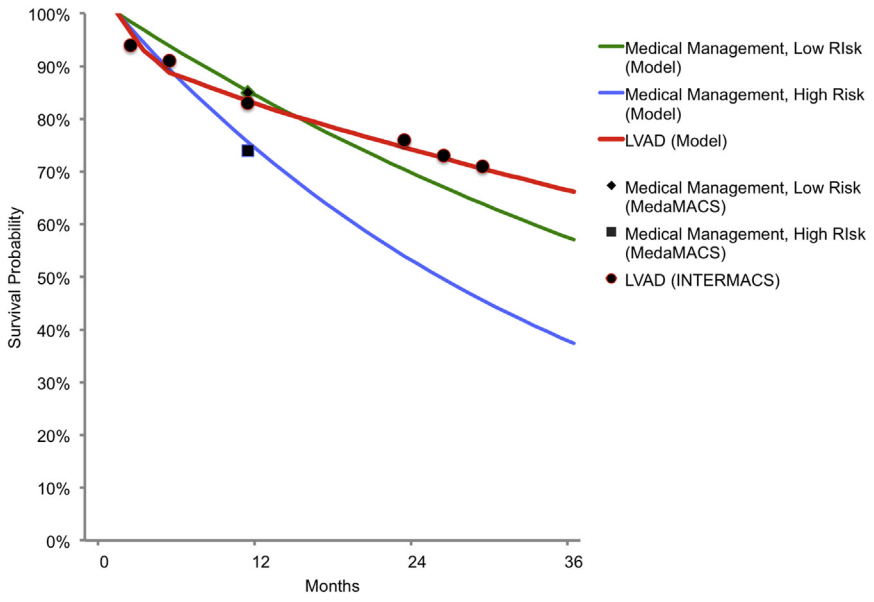
Patients entered the model at age 61, equal to the mean age in the registries and Medicare cohort. Each month, patients were at risk for death and for readmission for HF and other reasons, which lowered quality of life and was costly. Patients receiving medical management were eligible to receive an LVAD. Patients in the LVAD group underwent device implantation, and survivors remained at risk for readmissions as well as for LVAD complications. Less than 3% of ambulatory patients with DT-LVADs or medical therapy receive a heart transplant each year, and our model incorporated this small risk (5,12). The model followed patients over their remaining lifetimes (13). We discounted utilities and costs at 3% annually and rounded incremental cost-effectiveness ratios (ICER) to the nearest $100. The model was implemented using TreeAge Pro 2016 software (Williamstown, Massachusetts).

We estimated parameters for the model from the INTERMACS (Interagency for Mechanically Assisted Circulatory Support) and the MedaMACS (Medical Arm of the Mechanically Assisted Circulatory Support) registries (3,12,14). INTERMACS includes more than 2,000 patients with non-inotrope-dependent HF who have received mechanical circulatory support since 2006. MedaMACS includes 144 patients with non-inotrope-dependent advanced HF, followed between May 2013 and February 2015. Patients in MedaMACS were stratified by their HF clinician into 1 of 3 groups: likely transplant eligible, likely DT-LVAD eligible, and likely DT-LVAD ineligible. Perceived poor candidacy for LVAD was associated with higher mortality and worse prognosis (12). For our base case, we used data from the LVAD-eligible group (designated herein as "low risk"). Because some programs implant LVADs in patients with multiple comorbidities, we performed a complementary analysis using data from the likely LVAD ineligible ("high-risk") patients.

Participants in INTERMACS and MedaMACS were predominately male and white, older than 60 years of age, had ischemic HF, a creatinine concentration of 1.4 mg/dl, and high use of HF medications at the time of enrollment (Online Table S1). The high-risk patients in MedaMACS were less likely to be white and take HF medications.

**SURVIVAL.** We matched published survival curves by varying model parameters for LVAD and medical management mortality rates (**Figure 1**). We used different mortality rates among 3 months, 1 year, and 2 years for LVAD to more accurately reflect the course reported in INTERMACS. We assumed the rate of cardiovascular mortality was constant beyond survival data available from INTERMACS (3 years) and MedaMACS (10 months). We accounted for age-specific, noncardiovascular mortality, using 2010 U.S. life tables for white men (Online Appendix) (15).

**FIGURE 1 Comparison of Model Survival Curves With Registry Data**




The survival curves for LVAD and medical management are based on INTERMACS and MedaMACS registry data, respectively (12,14). INTERMACS = Interagency for Mechanically Assisted Circulatory Support; LVAD = left ventricular assist device; MedaMACS = Medical Arm of the Mechanically Assisted Circulatory Support.

**READMISSIONS.** For medical management in low-risk patients, we used a total readmission rate of 0.84 per patient-year; for high-risk patients, we used a rate of 1.8 per patient-year (12). Total readmission rates after LVAD for all-comers are reportedly between 1.6 and 2.6 per patient-year (11,16-18); LVAD readmission rates for non-inotrope-dependent HF patients are not well described, although 60% of these patients in INTERMACS have had at least 1 readmission by 6 months (3). For the main analysis, we used a total readmission rate of 2.0 per patient-year. We included separate readmission rates for stroke and for pump replacement. We assumed readmission rates remained constant over the patients' remaining lifetimes.

**QUALITY OF LIFE.** Each health state was associated with a quality-of-life value ranging from 0 to 1, where 0 represents death and 1 represents ideal health (13). We obtained utility data from non-inotrope-dependent HF patients in the INTERMACS registry (19). We used a baseline utility of 0.40 and assumed utility would improve to 0.70 at 6 months after LVAD but would not improve with continued medical management. We assumed patients who had experienced major stroke had a utility of 0.30 for their remaining lifetimes (20). For readmissions, we applied a utility value of 0 for the days spent in the hospital (21). We obtained hospital lengths of stay from our Medicare claims analysis, which were consistent with those from published reports (11).

**SENSITIVITY AND UNCERTAINTY ANALYSES.** We conducted 1-way deterministic sensitivity analyses to assess the relative impact of each model parameter and of key model assumptions. We performed scenario analyses in which several parameters were varied simultaneously. Finally, we performed a probabilistic sensitivity analysis to account for the influence of simultaneous changes in correlated and uncertain model inputs, using a gamma distribution to reflect uncertainties in costs and a beta distribution to reflect uncertainties in transition probabilities and utilities (22). We ran 10,000 independent simulations in which we sampled from the parameters' uncertainty distributions to estimate the proportion of ICERs that fell below a particular willingness-to-pay threshold (23).

## RESULTS

**MEDICARE COST ANALYSIS.** The 220 Medicare patients with LVADs implanted in 2009 to 2010 were mean 61.0 years of age, 78% were male, and 80% were white. The mean cost of LVAD implantation was

**TABLE 2** Cost* and Length of Stay Data From Medicare Beneficiaries Receiving an LVAD

| Outcome | Cost Before LVAD (n = 220) | Cost After LVAD (n = 220) | p Value |
|---|---|---|---|
| LVAD implantation | - | 175,420 ± 93,274 [151,353] | - |
| LVAD pump replacement readmission | - | $90,147 ± 7,539 [$90,147] | - |
| Stroke readmission | $10,970 ± 7,431 [$8,465] | $12,648 ± 13,230 [$10,285] | 0.76 |
| All-cause readmission | $12,377 ± 12,630 [$8,715] | $19,465 ± 34,636 [$10,027] | <0.001 |
| Length of stay, days | | | |
| LVAD implantation | - | 23.7 ± 26.2 [21] | - |
| LVAD pump replacement readmission | - | 9.5 ± 2.1 [8] | - |
| Stroke readmission | 3.7 ± 4.3 [2] | 8.3 ± 7.6 [6] | 0.14 |
| All-cause readmission | 5.0 ± 4.5 [4] | 8.5 ± 12.3 [5] | <0.001 |
| Monthly outpatient costs | 3,364 ± 5,436 [1,619] | 2,974 ± 3,344 [1,576] | 0.54 |

Values are mean ± SD [median]. *Values are in 2016 U.S. dollars. p values were obtained from the Wilcoxon test. All-cause readmission is exclusive of stroke or pump replacement. Hospitalization costs were obtained from claims from a 100% sample of Medicare beneficiaries. Outpatient costs were obtained from claims from a 20% random sample of beneficiaries.

LVAD = left ventricular assist device.

$175,420, and the mean cost of pump replacement was $90,147 (Table 2). These patients had a combined 529 admissions in the year before LVAD and 589 admissions in the year following LVAD. Hospitalizations for bleeding comprised 1.2% of admissions before LVAD and 12.9% of admissions after LVAD ($p < 0.0001$) (Online Table S3). All-cause readmission after implantation had $7,088 higher costs and was 3.5 days longer than before implantation (both: $p < 0.001$). Most readmissions were for cardiovascular disease and were longer and more costly after LVAD than before, particularly admissions for "Heart failure and shock with complication/comorbidity" ($12,696 vs. $7,394, respectively; $p < 0.0001$) and for "Cardiac arrhythmia and conduction disorders with complication/comorbidity" ($8,180 vs. $5,832, respectively; $p < 0.0001$) (Online Table S4). Average monthly outpatient costs of approximately $3,000 were not significantly different after LVAD than before ($p = 0.54$).

**MODEL-BASED COST-EFFECTIVENESS ANALYSIS. Life expectancy.** The model projected the discounted life expectancy after LVAD to be 6.28 years with 1-year and 2-year survival (censored at transplantation) of 83% and 75%, respectively. The discounted life expectancy for medical management in low-risk patients was 5.67 years, with 1- and 2-year survival (censored at LVAD or transplant) of 84% and 69%, respectively (Figure 2). The discounted life expectancy for medical management in high-risk patients was 3.44 years, with 1- and 2-year survival of 73% and 53%, respectively.

**Projected economic and health outcomes.** LVAD cost $726,200 over 6 years. Cumulative readmission costs after LVAD implantation were higher ($268,700) than the cost of outpatient care ($219,500) and either device implantation ($175,400) or heart transplantation ($62,600).

Compared with medical management, LVADs increased survival in low-risk patients by 0.61 life-years and 1.74 QALYs at an additional cost of $364,400 (Table 3). Taken together, the DT-LVAD in ambulatory patients with advanced HF cost $209,400 per QALY gained and $597,400 per life-year gained, relative to medical management.

Compared with medical management, LVADs increased survival in high-risk patients by 2.84 life-years and 2.78 QALYs, with an additional cost of $475,500. The ICER for LVAD was $171,000 per QALY gained and $167,400 per life-year gained.

**Sensitivity analyses.** The cost-effectiveness ratio was most sensitive to LVAD total readmission rate, LVAD outpatient costs, and LVAD readmission costs (Figure 2). Compared with medical management in low- and high-risk patients, the ICER for LVAD was <$150,000 per QALY gained when the readmission rate was 1.3 per person-year or less, when outpatient costs were below $1,500 per month, or when the cost of readmission was below $10,000. The ICER of LVAD versus medical management in low-risk patients was more sensitive to changes in utility parameters because survival was similar between the 2 strategies. For instance, if the baseline utility was 0.5, the ICER for LVAD in low-risk patients increased to $280,500, whereas the ICER in high-risk patients increased to $188,800. The ICER was not sensitive to costs and probabilities of infrequent events, such as pump replacement or receipt of heart transplant (Online Table S5).

For LVAD versus medical management in low-risk patients, we explored various "best-case scenarios" incorporating lower LVAD readmission rates and outpatient costs (Table 4). When the LVAD total readmission rate and outpatient costs were decreased by 50%, the ICER dropped to $86,900 per QALY gained.

In the observational study of LVADs in non inotrope-dependent HF, ROADMAP (Risk Assessment and Comparative Effectiveness of Left Ventricular Assist Device and Medical Management), patients in the LVAD group were more severely ill than those in

**FIGURE 2** **Tornado Diagram: Series of 1-Way Sensitivity Analyses**


Bars indicate the cost per QALY gained with LVAD compared with medical management in low-risk **(A)** and high-risk **(B)** patients across a range of values. The **gray solid line** indicates the model's incremental cost-effectiveness ratio. PPY = per-patient year; QALY = quality adjusted life years; y = years; other abbreviations as in Figure 1.

the medical group (5). Furthermore, 22% in medical management crossed over to LVAD. When we used inputs from ROADMAP in our model (Online Tables S6 and S7), LVAD had higher costs and worse outcomes than medical management.

In the probabilistic sensitivity analysis, LVAD was preferred for low-risk patients in 33% of simulations at a willingness-to-pay threshold of $100,000 per QALY gained and in 44% of simulations at a threshold of $150,000 (Figure 3).

## DISCUSSION

Our analysis suggests that patients with advanced HF who are not dependent on intravenous inotropes would live 0.61 years longer, with improved quality of

life (1.74 QALYs added), and incur an additional $364,400 in lifetime costs, if treated with DT-LVAD rather than medical management. These estimates imply that LVAD has an ICER of $209,400 per QALY gained for low-risk patients. In higher risk, potentially LVAD-ineligible patients, we found that LVAD had an ICER of $171,000 per QALY gained. Across a spectrum of advanced HF patients, we found that the high frequency of readmissions and the high cost of outpatient care over a longer period of survival were the largest determinants of the relatively low value provided by LVAD therapy.

This cost-effectiveness analysis of LVADs is unique because it is based on comprehensive cost data from Medicare beneficiaries who underwent LVAD implantation. These data are, to our knowledge, the first to characterize spending before and after LVAD implantation. We found that readmissions after implantation were generally more costly and longer in duration, whereas monthly outpatient spending was comparable, approximately $3,000, before and after implantation.

Sensitivity analyses demonstrated that outpatient and inpatient LVAD spending substantially influenced the cost-effectiveness of LVADs. We also found that readmissions for patients after LVAD were significantly costlier and longer than before the device was implanted. This may be because patients were sicker or because more studies of the LVAD patient were performed. Currently there is little guidance for clinicians as to how often tests, such as echocardiography, should be performed to monitor LVADs (24). As a result, there is substantial variation in treatment practices. Studies should be done to show what tests are needed in LVAD recipients to ensure adequate outcomes and reduce unnecessary spending.

LVADs in patients with non-inotrope-dependent HF appear to provide comparable value as LVADs in patients with inotrope-dependent HF. Using INTERMACS data, Long et al. (8) estimated an ICER of $212,100 (2016 U.S. dollars) for DT-LVADs in patients taking inotropes. In an older study, Rogers et al. (7) also evaluated LVADs in patients taking inotropes, with substantially higher mortality (92% at 2 years for medical management and 42% for LVAD) and reported an ICER at 5 years of $220,000 (2016 U.S. dollars).

Readmission rates after LVAD vary widely. So far, studies do not support the notion that patients with a better clinical profile at implantation have fewer readmissions; rather, adverse event rates appear to depend on hospital volume, outpatient support, and distance from implantation hospital (16). As

**TABLE 3 Projected Health and Economic Outcomes**

| | Medical Management | | |
|---|---|---|---|
| | Low Risk | High Risk | LVAD |
| Readmissions | | | |
| Total | 6.35 | 5.96 | 13.03 |
| Stroke | 0.19 | 0.10 | 0.58 |
| LVAD pump replacement | 0.02 | 0.01 | 0.18 |
| LVAD | 0.13 | 0.07 | - |
| Heart transplant | 0.15 | 0.08 | 0.17 |
| Life-years | 5.67 | 3.44 | 6.28 |
| Quality-adjusted life-years | 2.67 | 1.63 | 4.41 |
| Lifetime costs, U.S. $ | 361,800 | 250,700 | 726,200 |
| Incremental cost per life-year and quality-adjusted life-year gained, LVAD versus medical management, U.S. dollars | | | |
| Cost/life-year gained | 597,400 | 167,400 | |
| Cost/quality-adjusted life year gained | 209,400 | 171,000 | |

Values on 2016 U.S. dollars.
Abbreviation as in Table 2.

LVAD technology evolves, there may be a significant decrease in the rate of adverse events that contribute to mortality and readmission. For example, a fully implantable system could eliminate driveline infections, the addition of pulsatility to the current generation of devices could decrease gastrointestinal bleeding, and remote monitoring could reduce pump thrombosis requiring exchange. If future improvements were to eliminate LVAD adverse events completely, the ICER would be as low as $58,000 per QALY gained. This hypothetical scenario, however, does not capture the additional expenditures needed for the cost of the new technology as well as increased outpatient support to keep LVAD recipients healthy and outside the hospital (25).

Although LVADs do not appear to provide high value by current benchmarks (26), there are currently few other effective treatments for the 250,000 patients with advanced HF. Providing access to therapies that prolong survival in this population may be an important consideration for coverage and reimbursement policies (13). Currently, <1% of patients with advanced HF will receive 1 of the 2,200 adult heart transplants that take place each year in the United States (27). If all of these patients were to receive a DT-LVAD, an estimated 100,000 new patients annually, the additional cost would be roughly $36 billion per year, nearly 6% of the entire Medicare budget (28).

**STUDY LIMITATIONS.** First and foremost, we focused on LVAD in Medicare-eligible patients, which represents approximately 45% of all implantations and which is likely to be a highly selected population (3). Second, there have been no randomized trials of

**TABLE 4 Scenario Analyses**

| Scenario | Lifetime Costs ($) | | | QALY | | | ICER ($/QALY) |
|---|---|---|---|---|---|---|---|
| | LVAD | Low-Risk Medical Management | Δ | LVAD | Low-Risk Medical Management | Δ | |
| LVAD implant cost $0 | 550,800 | 339,900 | 210,900 | 4.41 | 2.67 | 1.74 | 121,200 |
| LVAD outpatient costs reduced by 50% and readmission rate 1 PPY | 493,800 | 333,900 | 159,900 | 4.52 | 2.69 | 1.84 | 86,900 |
| LVAD readmission rate 2 PPY for the first 6 months, then 1 PPY thereafter* | 620,900 | 349,800 | 271,100 | 4.41 | 2.67 | 1.74 | 155,800 |
| Medical management readmission increases 0.2 PPY per year, and utility decreases 0.02 per year† | 726,200 | 361,800 | 364,400 | 4.41 | 2.29 | 2.13 | 171,100 |

*Scenario derived from Hasin et al. (17). †Scenario derived from Russo et al. (40). Low-risk medical management was derived from patients in the MedaMACS registry deemed likely to be LVAD eligible. Values are in 2016 U.S. dollars.

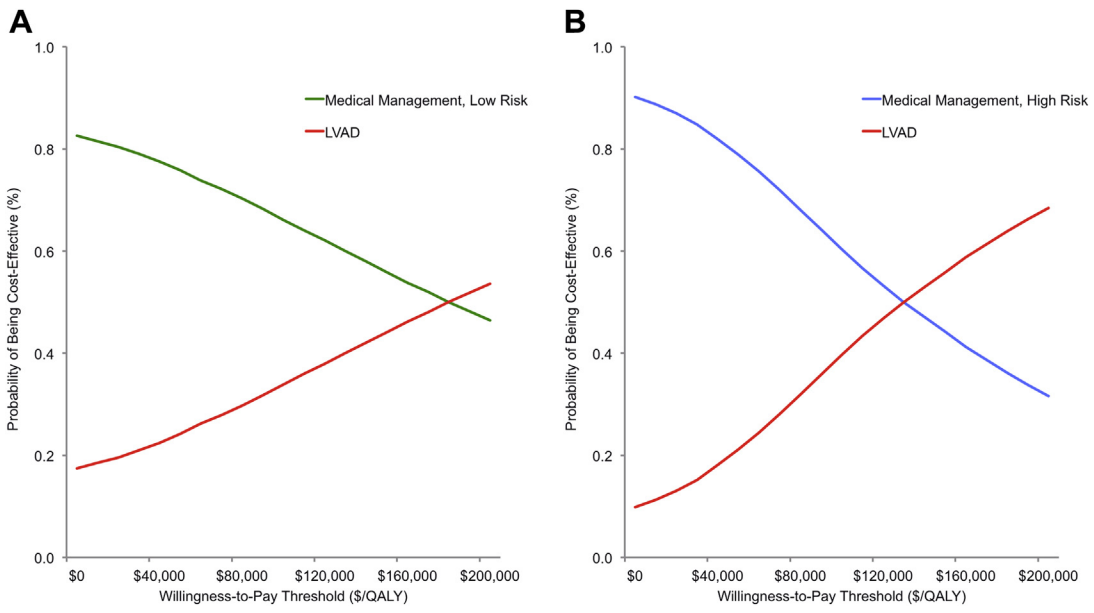
ICER = incremental cost-effectiveness ratio; PPY = per patient year; QALY = quality-adjusted life-year; other abbreviations as in Table 2.

LVADs in ambulatory patients with advanced HF; hence, we estimated model inputs from registries and administrative claims. Although there was heterogeneity across sources, we selected studies with comparable patient characteristics. Furthermore, despite uncertainty in our model inputs, in most sensitivity analyses, which covered a broad range of model inputs, the ICER of LVADs remained between $150,000 and $250,000.

There are limitations associated with our Medicare cost analysis. The spending was derived from 2008 to 2011 claims; however, reimbursement did not substantially change over this period. Second, the outpatient cohort was small (n = 45), and generalizability may be limited. Third, we assumed that patients with a lower acuity DRG code for LVAD implant were less acutely ill, but we were unable to confirm whether they had been receiving inotrope therapy pre-implantation. The claims only allow for the identification of implantable ventricular assist devices; however the majority (>95%) of ventricular assist devices are LVADs (3). Finally, we did not have access to pharmacy data to include outpatient pharmacy expenditures.

We modeled our cohort from registries that were composed predominantly of white male participants.

**FIGURE 3 Probabilistic Sensitivity Analysis**




The curves illustrate the proportion of samples in which LVAD or medical management in low-risk **(A)** and high-risk **(B)** patients is the preferred strategy at a given willingness-to-pay threshold. Abbreviations as in Figure 1.

Thus, our findings may be somewhat less applicable to women and minority groups. Our model simplified the complex progression of heart transplantation and of medically managed end-stage HF. We assumed that costs, readmission rates, and quality of life for medical management would be constant in follow-up and that LVAD survival would be similar in the low-risk and high-risk models because there are limited data on which to base trends.

## CONCLUSIONS

The value provided by LVADs in ambulatory patients with advanced HF does not appear to be favorable by conventional standards but may be acceptable in patient subgroups that have lower adverse event rates or in settings where LVADs can be managed at a lower cost. Further research of how to care for LVAD patients longitudinally and reduce device complications will be important for policymakers and payers alike as the indications for implantation continue to broaden.

**REPRINT REQUESTS AND CORRESPONDENCE:** Dr. Jacqueline Baras Shreibati, Division of Cardiovascular Medicine, Department of Medicine, Stanford University School of Medicine, HRP Redwood Building, T150A, 150 Governor's Lane, Stanford, California 94305-5405. E-mail: Jacqueline.shreibati@gmail.com.

## PERSPECTIVES

**COMPETENCY IN MEDICAL KNOWLEDGE:** The use of LVADs in patients with advanced HF who do not require inotropes at the time of implantation is not cost-effective by conventional criteria. LVADs may provide good value in patients with less severe HF if the cost of follow-up care and the frequency of adverse events can be reduced.

**TRANSLATIONAL OUTLOOK:** Randomized studies are needed to define the benefits, risks, and costs of LVADs in patients with non–inotrope-dependent HF.

## REFERENCES

**1.** Heidenreich PA, Albert NM, Allen LA, et al. Forecasting the impact of heart failure in the United States: a policy statement from the American Heart Association. Circ Heart Fail 2013;6:606–19.

**2.** Miller LW, Guglin M. Patient selection for ventricular assist devices: a moving target. J Am Coll Cardiol 2013;61:1209–21.

**3.** Kirklin JK, Naftel DC, Pagani FD, et al. Seventh INTERMACS annual report: 15,000 patients and counting. J Heart Lung Transplant 2015;34:1495–504.

**4.** Boyle AJ, Ascheim DD, Russo MJ, et al. Clinical outcomes for continuous-flow left ventricular assist device patients stratified by pre-operative INTERMACS classification. J Heart Lung Transplant 2011;30:402–7.

**5.** Estep JD, Starling RC, Horstmanshof DA, et al. Risk assessment and comparative effectiveness of left ventricular assist device and medical management in ambulatory heart failure patients: results from the ROADMAP study. J Am Coll Cardiol 2015;66:1747–61.

**6.** Slaughter MS, Rogers J. Editorial commentary: determining the cost-effectiveness of mechanical circulatory support. J Heart Lung Transplant 2012;31:448–9.

**7.** Rogers JG, Bostic RR, Tong KB, Adamson R, Russo M, Slaughter MS. Cost-effectiveness analysis of continuous-flow left ventricular assist devices as destination therapy. Circ Heart Fail 2012;5:10–6.

**8.** Long EF, Swain GW, Mangi AA. Comparative survival and cost-effectiveness of advanced therapies for end-stage heart failure. Circ Heart Fail 2014;7:470–8.

**9.** Cipriano LE, Romanus D, Earle CC, et al. Lung cancer treatment costs, including patient responsibility, by disease stage and treatment modality, 1992 to 2003. Value Health 2011;14:41–52.

**10.** Consumer Price Index Inflation Calculator. Bureau of Labor Statistics. U.S. Department of Labor. Available at: http://www.bls.gov/data/inflation_calculator.htm. Accessed May 15, 2016.

**11.** Akhter SA, Badami A, Murray M, et al. Hospital readmissions after continuous-flow left ventricular assist device implantation: incidence, causes, and cost analysis. Ann Thorac Surg 2015;100:884–9.

**12.** Ambardekar AV, Forde-McLean RC, Kittleson MM, et al. High early event rates in patients with questionable eligibility for advanced heart failure therapies: results from the Medical Arm of Mechanically Assisted Circulatory Support (MEDAMACS) registry. J Heart Lung Transplant 2016;35:722–30.

**13.** Gold MR, Siegel JE, Russel LB, Weinstein MC. Cost-Effectiveness in Health and Medicine. New York, NY: Oxford University Press; 1996.

**14.** Cowger J, Shah P, Stulak J, et al. INTERMACS profiles and modifiers: Heterogeneity of patient classification and the impact of modifiers on predicting patient outcome. J Heart Lung Transplant 2016;35:440–8.

**15.** Arias E. United States life tables, 2010. Natl Vital Stat Rep 2014;63:1–63.

**16.** Hasin T, Marmor Y, Kremers W, et al. Readmissions after implantation of axial flow left ventricular assist device. J Am Coll Cardiol 2013;61:153–63.

**17.** Smedira NG, Hoercher KJ, Lima B, et al. Unplanned hospital readmissions after HeartMate II implantation: frequency, risk factors, and impact on resource use and survival. J Am Col Cardiol HF 2013;1:31–9.

**18.** Slaughter MS, Rogers JG, Milano CA, et al. Advanced heart failure treated with continuous-flow left ventricular assist device. N Engl J Med 2009;361:2241–51.

**19.** Grady KL, Naftel D, Stevenson L, et al. Overall quality of life improves to similar levels after mechanical circulatory support regardless of severity of heart failure before implantation. J Heart Lung Transplant 2014;33:412–21.

**20.** Post PN, Stiggelbout AM, Wakker PP. The utility of health states after stroke: a systematic review of the literature. Stroke 2001;32:1425–9.

**21.** Sanders GD, Hlatky MA, Owens DK. Cost-effectiveness of implantable cardioverter-defibrillators. N Engl J Med 2005;353:1471–80.

**22.** Briggs AH. Handling uncertainty in cost-effectiveness models. Pharmacoeconomics 2000;17:479–500.

**23.** Doubilet P, Begg CB, Weinstein MC, Braun P, McNeil BJ. Probabilistic sensitivity analysis using Monte Carlo simulation. A practical approach. Med Decis Making 1985;5:157–77.

**24.** Feldman D, Pamboukian SV, Teuteberg JJ, et al. The 2013 International Society for Heart and Lung Transplantation guidelines for mechanical circulatory support: executive summary. J Heart Lung Transplant 2013;32:157–87.

**25.** Wilson SR, Givertz MM, Stewart GC, Mudge GH Jr. Ventricular assist devices the

challenges of outpatient management. J Am Coll Cardiol 2009;54:1647–59.

**26.** Anderson JL, Heidenreich PA, Barnett PG, et al. ACC/AHA statement on cost/value methodology in clinical practice guidelines and performance measures: a report of the American College of Cardiology/American Heart Association Task Force on Performance Measures and Task Force on Practice Guidelines. J Am Coll Cardiol 2014;63:2304–22.

**27.** Yusen RD, Christie JD, Edwards LB, et al. The Registry of the International Society for Heart and Lung Transplantation: Thirtieth Adult Lung and Heart-Lung Transplant Report—2013; focus theme: age. J Heart Lung Transplant 2013;32:965–78.

**28.** Kaiser Family Foundation. The Facts on Medicare Spending and Financing. Available at: http://kff.org/medicare/fact-sheet/medicare-spending-and-financing-fact-sheet/. Accessed May 18, 2016.

**29.** Pagani FD, Milano C, Tatooles A, et al. HeartWare HVAD for the treatment of patients with advanced heart failure ineligible for cardiac transplantation: results of the ENDURANCE destination therapy trial. Paper presented at the 35th Annaul Meeting of the International Society of Heart and Lung Transplantation and Scientific Session. Nice, France; 2015.

**30.** Kirklin JK, Naftel DC, Pagani FD, et al. Pump thrombosis in the Thoratec HeartMate II device: an update analysis of the INTERMACS registry. J Heart Lung Transplant 2015;34:1515–26.

**31.** Freudenberger RS, Hellkamp AS, Halperin JL, et al. Risk of thromboembolism in heart failure: an analysis from the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT). Circulation 2007;115:2637–41.

**32.** Freeman JV, Zhu RP, Owens DK, et al. Cost-effectiveness of dabigatran compared with warfarin for stroke prevention in atrial fibrillation. Ann Intern Med 2011;154:1–11.

**33.** Pal JD, Klodell CT, John R, et al. Low operative mortality with implantation of a continuous-flow left ventricular assist device and impact of concurrent cardiac procedures. Circulation 2009;120:S215–9.

**34.** Milano C, Pagani FD, Slaughter MS, et al. Clinical outcomes after implantation of a centrifugal flow left ventricular assist device and concurrent cardiac valve procedures. Circulation 2014;130:S3–11.

**35.** Holloway RG, Benesch CG, Burgin WS, Zentner JB. Prognosis and decision making in severe stroke. JAMA 2005;294:725–33.

**36.** Healy AH, Stehlik J, Edwards LB, McKellar SH, Drakos SG, Selzman CH. Predictors of 30-day post-transplant mortality in patients bridged to transplantation with continuous-flow left ventricular assist devices—an analysis of the International Society for Heart and Lung Transplantation transplant registry. J Heart Lung Transplant 2016;35:34–9.

**37.** Lund LH, Edwards LB, Kucheryavaya AY, et al. The registry of the International Society for Heart and Lung Transplantation: Thirty-second Official Adult Heart Transplantation Report-2015: focus theme: early graft failure. J Heart Lung Transplant 2015;34:1244–54.

**38.** Russo MJ, Hong KN, Davies RR, et al. Post-transplant survival is not diminished in heart transplant recipients bridged with implantable left ventricular assist devices. J Thorac Cardiovasc Surg 2009;138:1425–32.

**39.** Moreno SG, Novielli N, Cooper NJ. Cost-effectiveness of the implantable HeartMate II left ventricular assist device for patients awaiting heart transplantation. J Heart Lung Transplant 2012;31:450–8.

**40.** Russo MJ, Gelijns AC, Stevenson LW, et al. The cost of medical management in advanced heart failure during the final two years of life. J Card Fail 2008;14:651–8.

**KEY WORDS** cost-effectiveness analysis, heart failure, left ventricular assist device, Medicare

**APPENDIX** For supplemental tables and a figure, please see the online version of this article.