

Circulation

Heart Failure



JOURNAL OF THE AMERICAN HEART ASSOCIATION

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Circ Heart Fail 2012;5;10-16; originally published online November 3, 2011;

DOI: 10.1161/CIRCHEARTFAILURE.111.962951

Circulation: Heart Failure is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75214

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Cost-Effectiveness Analysis of Continuous-Flow Left Ventricular Assist Devices as Destination Therapy

Joseph G. Rogers, MD; Robin R. Bostic, BS; Kuo B. Tong, MS; Rob Adamson, MD; Mark Russo, MD; Mark S. Slaughter, MD

Background—Continuous-flow left ventricular assist devices (LVADs) have become the dominant devices for mechanical circulatory support, but their cost-effectiveness is undetermined. This study assessed the cost-effectiveness of continuous-flow devices for destination therapy versus optimal medical management in advanced heart failure and compared the results with previous estimates for pulsatile devices.

Methods and Results—A Markov model was developed to assess cost-effectiveness. Survival, hospitalization rates, quality of life, and cost data were obtained for advanced heart failure patients treated medically or with a continuous-flow LVAD. Rates of clinical outcomes for all patients were obtained from clinical trial databases. Medicare prospective payments were used to estimate the cost of heart failure admissions. The cost of LVAD implantation was obtained prospectively from hospital claims within a clinical trial. Compared with medically managed patients, continuous-flow LVAD patients had higher 5-year costs (\$360 407 versus \$62 856), quality-adjusted life years (1.87 versus 0.37), and life years (2.42 versus 0.64). The incremental cost-effectiveness ratio of the continuous-flow device was \$198 184 per quality-adjusted life year and \$167 208 per life year. This equates to a 75% reduction in incremental cost-effectiveness ratio compared with the \$802 700 per quality-adjusted life year for the pulsatile-flow device. The results were most sensitive to the cost of device implantation, long-term survival, cost per rehospitalization, and utility associated with patients' functional status.

Conclusions—The cost-effectiveness associated with continuous-flow LVADs for destination therapy has improved significantly relative to the pulsatile flow devices. This change is explained by significant improvements in survival and functional status and reduction in implantation costs. (*Circ Heart Fail.* 2012;5:10-16.)

Key Words: cost-effectiveness ■ heart failure ■ heart-assist device

The burden of advanced heart failure is characterized by excessive morbidity and mortality, poor quality of life, high treatment costs, and limited treatment options. Nearly 6 million Americans have heart failure, and approximately 10% of those have advanced disease.^{1,2} The estimated total annual cost for heart failure in the United States is \$39 billion in 2010, with the advanced heart failure population consuming a disproportionate amount of these healthcare resources.^{1,3} After failing evidence-based medical and electric therapies, these patients have extremely limited treatment options. Heart transplant is considered epidemiologically insignificant as most patients are ineligible for transplant or are unlikely to receive a donor heart resulting from the shortage of suitable organs. Technological innovations and the clinical application of alternative therapies such as mechanical circulatory support devices, including left ventricular assist devices (LVADs), may help bridge this gap of available and effective therapy.

Clinical Perspective on p 16

Several studies have evaluated the long-term outcomes and costs associated with LVAD therapy. Nearly 10 years ago, the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) study randomly assigned patients ineligible for transplant to treatment with an LVAD or optimal medical management (OMM). The LVAD patients had survival rates of 52% at 1 year and 23% at 2 years compared with 25% and 8% in the OMM arm.⁴ The mean cost for the implant-related hospitalization was \$210 187.⁵ A follow-up cost-effectiveness analysis based on the REMATCH trial published in 2004 concluded that the incremental cost-effectiveness ratio (ICER) was \$802 700 per quality-adjusted life year (QALY).⁶ As centers gained more experience with patient selection, device implantation, and postoperative management, costs for the initial implant hospitalization decreased. Miller et al presented

Received May 5, 2011; accepted September 13, 2011.

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DOI: 10.1161/CIRCHEARTFAILURE.111.962951

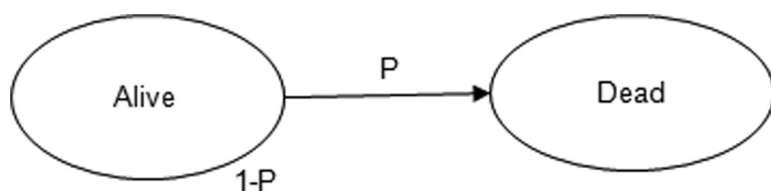


Figure 1. Health state transition model. This model included only 2 health states, alive and dead, with a time-dependent probability of transitioning from alive to dead.

cost data from a cohort of patients implanted with a pulsatile flow LVAD after completion of the REMATCH trial in select high-volume centers and demonstrated that the mean cost for implantation decreased to \$128 048.⁷ In a contemporary review of 6 pulsatile LVAD studies, Clegg et al reported a cost per QALY of \$341 573 and cited a potential improvement in LVAD cost-effectiveness with the introduction of continuous-flow devices.⁸

The HeartMate II Destination Therapy trial randomly assigned patients with advanced heart failure to receive the older pulsatile LVAD used in REMATCH or a new generation continuous-flow LVAD.⁹ Patients who received the continuous-flow device had 1- and 2-year survival rates of 68% and 58%, compared with 55% and 24% with the pulsatile device. The continuous-flow LVAD patients experienced similar long-term improvements in quality of life, exercise performance, and end-organ function to patients supported with pulsatile flow devices.^{10,11} Furthermore, fewer continuous-flow devices required replacement for mechanical failure.

Given the improvement in survival, the reduced need for device replacement, improved quality of life, and a decrease in hospitalization costs associated with newer devices, the cost-effectiveness of LVAD therapy would reasonably be expected to improve. The objective of the current study was to perform a cost-effectiveness analysis of continuous-flow LVADs for destination therapy versus OMM from a third-party payer perspective based on the latest clinical and cost data available and to compare these data to previous estimates of the ICER for pulsatile LVADs.

Methods

Data Sources

Clinical outcomes and costs for this analysis were obtained from several sources. Clinical outcomes for optimal medical therapy were derived from the REMATCH trial ($n=61$, 1998–2001)⁴ and the clinical outcomes of continuous-flow LVADs ($n=134$, 2005–2007) were obtained from the HeartMate II Destination Therapy Trial.⁹

Enrollment criteria in these trials distinguished a high risk patient population. Patients had predominantly New York Heart Association (NYHA) functional class IV symptoms and a left ventricular ejection fraction of $\leq 25\%$. They also had a peak oxygen consumption of < 14 mL/kg/min or required treatment with continuous infusion of positive inotropic agents. These patients were ineligible for heart transplantation because of advanced age or comorbidities that were thought by the investigative site to preclude successful transplant.

The current analysis captured patient-specific clinical events and costs from the time of randomization in a clinical trial through a maximum of 5 years. In REMATCH, the 2-year survival rate was 0.08 for patients receiving OMM and 0.25 for the pulsatile LVAD.⁴ In the HeartMate II Destination Therapy trial, the 2-year survival rate was 0.58 for patients receiving the continuous-flow device.⁹ An indirect comparison of OMM and continuous-flow LVAD outcomes was required using data from REMATCH and the HeartMate II Destination Therapy trial because no trial has directly compared

these treatments. Treatment strategies and protocols for OMM and LVAD destination therapy have been described previously.^{4,9} Baseline patient characteristics were similar between the OMM and continuous-flow LVAD treatment groups except that those in the continuous-flow LVAD group were on average 6 years younger and 25% were classified by investigators as NYHA functional class III, whereas all OMM patients had NYHA class IV disease.^{4,9}

Cost data were obtained from multiple sources, including prospectively collected hospital billing data, Medicare payments for professional services related to LVAD implantation, and Medicare prospective payments for rehospitalizations. A detailed description for each source is provided in later sections.

Model Design and Structure

A decision analytic model was adapted from the Blue Cross Blue Shield Technology Evaluation Center assessment.⁶ After receiving an LVAD for destination therapy or being assigned to OMM, patients were evaluated through a Markov process containing 2 health states: alive or dead. Patients in the OMM and LVAD arms followed the same Markov process with monthly probabilities of transition between health states specific to each treatment group (Figure 1). Costs, QALYs, and life years (LYs) accrued during a patient's model-based lifetime were based on assumptions relating to monthly hospitalization rates and costs, outpatient costs, and the distribution of NYHA Functional Classification (I–IV) health states over time. These parameters and the monthly transition probabilities were informed using data from the REMATCH and HeartMate II Destination Therapy trials, as described below.

Calculation of QALYs and LYs

Cycle-specific survival probabilities were estimated from the Kaplan-Meier survival curves for the OMM cohort in the REMATCH trial and for the continuous-flow LVAD cohort in the HeartMate II Destination Therapy trial. Follow-up in both trials was completed at 24 months, thus requiring survival assumptions beyond this time point. In REMATCH, the survival probability of the OMM cohort at 24 months was 8%.⁴ Extrapolation of survival past 24 months was based on an exponential survival curve using the constant hazard rate observed within 24 months (0.105 per month). For the LVAD treated patients, 3 different methods for survival extrapolation beyond 24 months were used. For the base case analysis, an exponential survival curve was fit to the 24-month data (0.023 per month) from the model. In the sensitivity analysis, the methods of stop and drop (ie, assuming that all patients surviving to 24 months die immediately thereafter) and a linear extrapolation between the observed survival at 24 months of 58% and 40% at 60 months were used (Figure 2).

For both the OMM and LVAD cohorts, QALYs were estimated based on survival adjusted for the cohort's average utility (ie, the preference that an individual or a society places on health outcomes, usually ranging from 0–1) in each cycle. Utility measurements were not collected in the HeartMate II Destination Therapy study or the REMATCH trial, so utility estimates were derived from health states based on NYHA classes.¹² The probability of belonging to a specific NYHA class varied over time. Monthly estimates of these probabilities were obtained from the REMATCH and HeartMate II Destination Therapy trials for the OMM and LVAD arms, respectively (Table 1). When the NYHA classes were not reported, data were interpolated from the immediately preceding month and the month after. The distribution at 24 months was used to estimate NYHA classes beyond 24 months. For the OMM cohort, only the distribution of patients in NYHA classes I/II or classes III/IV were

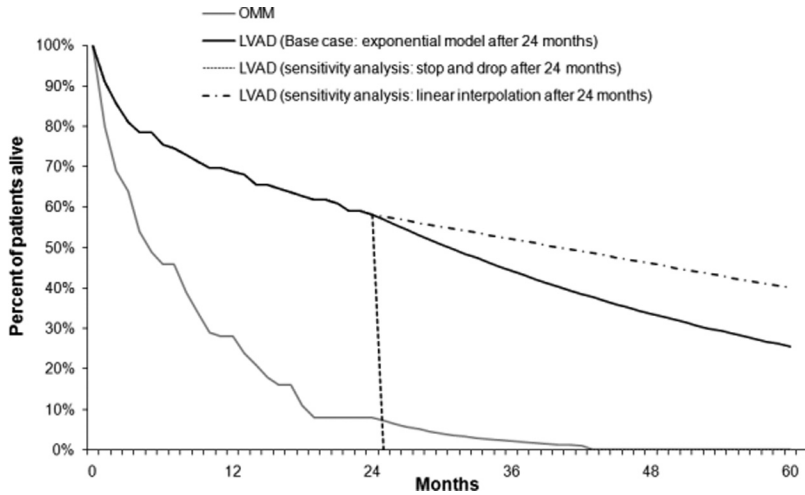


Figure 2. Survival curves for base case and sensitivity analyses. The survival curves for the base case analysis and the 2 sensitivity analyses—stop and drop and linear extrapolation—from 24 to 60 months are shown. OMM indicates optimal medical management; LVAD, left ventricular assist device.

available.⁶ Patients were predominantly classified as classes III/IV during the 24-month trial period, so we assumed that 25% of those had class III and 75% had class IV heart failure. The few patients classified into classes I/II at 3 (3%) and 6 months (9%) were all assumed to have class II disease.⁶ At the 24-month assessment in REMATCH, 1 of the 3 patients who remained alive in the OMM cohort reported NYHA class I/II symptoms. For the purposes of this analysis, the number of OMM patients with NYHA class I/II symptoms at ≥ 24 months was considered to be 0% to be consistent with the observed rates throughout the entire REMATCH trial. Mean utility values of 0.855, 0.771, 0.673, and 0.532 were assigned to NYHA classes I, II, III, and IV, respectively,¹² suggesting that patients with NYHA classes I heart failure were willing to trade, on average, 15% of their remaining years in return for perfect health, and those with NYHA classes IV disease were willing to trade 47% of their remaining life. It was assumed that the utilities for NYHA categories did not differ between the LVAD and OMM patients.

The total LYs and QALYs for the OMM and LVAD cohort in the study period were calculated as the sum of LYs and QALYs accumulated in each cycle and were discounted at 3% per year per

recommendation from the Panel on Cost-Effectiveness in Health and Medicine.¹³

Calculation of Costs

Costs were assessed from the perspective of a third-party payer. Three main categories of costs were included: LVAD implantation and replacement costs, rehospitalization costs, and outpatient costs. Implantation and replacement costs applied only to LVAD recipients, whereas rehospitalization costs and outpatient costs applied to all patients.

LVAD implantation costs included hospital and professional service costs. Hospital costs encompassed the entire hospitalization from implantation to discharge, including the cost of the device, intensive care days, medical/surgical days, operating room, diagnostics, laboratory tests, blood products, drugs, and miscellaneous services. Although patients may incur costs during the preimplantation phase of the hospitalization for heart failure therapy or management of their comorbidities, these costs were not included. Hospital costs were estimated from hospital claims data collected from a subset of patients (83 out of 134) who were representative of all patients receiving a continuous-flow device in the HeartMate II trial.¹⁴ The costs of professional services were obtained from an analysis of Medicare claims submitted by physicians for patients selected from a random sample of Medicare beneficiaries who underwent an LVAD implantation procedure in 2008.¹⁵ The costs included the surgical procedure and follow-up evaluation and management from cardiologists and other physicians in the same quarter that the LVAD was implanted.

The frequency of rehospitalizations for the LVAD cohort was based on data from the HeartMate II Destination Therapy trial in which an annual rehospitalization (including LVAD pump replacement) rate of 2.64 per person and LVAD replacement rate of 0.06 per person was reported.⁹ As hospitalizations for LVAD replacement versus a typical heart failure management are associated with markedly different payments, rates for these hospitalizations were estimated separately. A monthly rehospitalization rate, excluding rehospitalization for LVAD replacement, was estimated at 0.215 per person, and a monthly LVAD replacement rate was estimated at 0.005 per person. For the OMM cohort, the readmission rate in the base case analysis was based on the Comparison of Medical Therapy, Pacing and Defibrillation in Heart Failure (COMPANION) trial, which compared patients with advanced heart failure who received cardiac resynchronization therapy with patients who received optimal pharmacological therapy.¹⁶ In this study, the patients were all in NYHA class III or IV, and the average age was 66 years. For the OMM group, 65% of patients were hospitalized during follow-up, and the average number of hospital admissions per patient-year of follow-up was 1.59. In terms of admissions per month, this equates to 0.1325. The sensitivity analysis tested the assumption based on the 30-day rehospitalization rates for a cohort

Table 1. Probability of Being in NYHA Classes I to IV

NYHA	OMM* ⁶				LVAD† ⁹			
	Class I	Class II	Class III	Class IV	Class I	Class II	Class III	Class IV
Baseline	0%	0%	25%	75%	0%	0%	25%	100%
Mo 1	0%	0%	25%	75%	NR	NR	NR	55%
Mo 3	0%	3%	24%	73%	33%	42%	23%	2%
Mo 6	0%	9%	23%	68%	NR	NR	NR	21%
Mo 9	0%	0%	25%	75%	NR	NR	NR	21%
Mo 12	0%	0%	25%	75%	42%	35%	24%	23%
Mo 18	0%	0%	25%	75%	NR	NR	NR	NR
Mo 24	0%‡	0%‡	25%‡	75%‡	42%	38%	14%	6%

NYHA indicates New York Heart Association; OMM, optimal medical management; LVAD, left ventricular assist device; NR, not reported.

*In the REMATCH trial, only the percentage of OMM cohort in NYHA classes I/II or classes III/IV were reported. In the model, the percentage of patients in classes I/II was assigned to class II, and 25% of those in classes III/IV were assumed in class III and 75% were assumed in class IV.

†For months with missing data, linear interpolation was used in the model.

‡In the REMATCH trial, 33% and 67% of OMM cohort reported NYHA classes I/II and III/IV, respectively. Because of the small sample size (n=3) for OMM patients at 24 mo, the data were reset to 0% and 100% in the model.

Table 2. Model Parameters, Values, and Data Sources in the Base Case and Sensitivity Analysis

	Base Case	Range
24-mo survival for LVAD ⁹	KM curve	NA
24-mo survival for OMM ⁴	KM curve	NA
Long-term survival extrapolation for LVAD	Exponential	Stop and drop, linear (40% at 60 mo)
Long-term survival extrapolation for OMM ⁶	Exponential	NA
LVAD implantation hospital cost ¹⁴	\$193,812	\$122,785–\$264,839*
LVAD implantation professional service cost ¹⁵	\$8,841	NA
LVAD replacement cost ¹⁸	\$131,430	NA
Monthly LVAD replacement rate ⁹	0.005	NA
Rehospitalization cost (per event) ^{5,16}	\$6,850	\$6,850–\$30,627
Monthly rehospitalization rate for LVAD ⁹	0.21	NA
Monthly rehospitalization rate for OMM ¹⁶	0.1325	0.1325–0.26
Monthly outpatient costs ^{20,21}	\$2,331	NA
End-of-life cost ¹⁹	\$44,211	NA
Utility for NYHA Class I ¹²	0.855	0.641–1.0
Utility for NYHA Class II ¹²	0.771	0.578–0.964
Utility for NYHA Class III ¹²	0.673	0.505–0.841
Utility for NYHA Class IV ¹²	0.532	0.399–0.665

LVAD indicates left ventricular assist device; KM, Kaplan-Meier; OMM, optimal medical management; NA, not applicable; OMM, optimal medical management; NYHA, New York Heart Association.

*One standard deviation from the mean cost (\$193,812).

of medically managed heart failure patients in the Medicare fee-for-service program.¹⁷ The cost per rehospitalization was estimated from the average Medicare reimbursement rates for medical severity diagnosis-related group (MS-DRG) 291 (heart failure and shock with major complications and comorbidities) and MS-DRG 292 (heart failure and shock with complications and comorbidities).¹⁸ The cost for LVAD replacement was estimated from the average Medicare reimbursement rates for MS-DRG 1 (heart transplant or implant of heart assist system with major complications and comorbidities).¹⁸ The cost per rehospitalization was assumed to be the same for patients with an LVAD and those receiving OMM, consistent with the prior cost-effectiveness analysis of LVADs.⁶ For patients who died, a 1-time end-of-life cost was added, which was based on the cost of medical management for patients with end-stage heart failure during the last quarter of their lives.¹⁹

Outpatient costs included professional services, laboratory tests, and drugs. In a study of bridge-to-transplant patients, the average weekly outpatient cost was \$352, yielding a monthly cost of \$1531 (1995 US dollars).^{20,21} This amount was revalued in 2009 US dollars using the consumer price index for medical care services.²² Consistent with the prior cost-effectiveness analysis of LVADs,⁶ outpatient costs were assumed to be the same for LVAD and OMM patients. Although these costs were based on a small cohort of bridge-to-transplant patients who were treated more than a decade ago, as these costs were a small fraction of the costs for initial implantation and subsequent hospitalizations, this estimate was unlikely to affect the cost-effectiveness findings.

All costs are in 2009 US dollars. Costs incurred beyond the first year were discounted at 3% per year. Detailed cost parameter values used in the base-case analysis are presented in Table 2.

Table 3. Costs, QALYs, and Life Year Results for the Base Case Analysis

Parameters	OMM	LVAD
Total cost (\$)	\$62,856	\$360,407
Total QALYs (y)	0.37	1.87
Total LYs (y)	0.64	2.42

QALY indicates quality-adjusted life year; OMM, optimal medical management; LVAD, left ventricular assist device; LY, life year.

Base-Case Analysis

The costs and outcomes for the OMM and LVAD cohorts were forecasted over 5 years. The incremental cost-effectiveness ratio (ICER) was calculated comparing the difference in average total costs and the difference in average QALYs or LYs between the OMM and LVAD cohorts. The model was constructed with TreeAge Pro 2006 software (TreeAge Software, Inc, Williamstown, MA).

Sensitivity Analysis

The Blue Cross Blue Shield technology assessment, which used data from the REMATCH study, suggested that the model results were more sensitive to the cost of LVAD implantation and variations in utility for NYHA classes than other parameters. The same model structure was applied in our analysis, and the parameters driving the results remained the same. In addition, alternative assumptions for rehospitalization costs and long-term survival for the LVAD cohort were tested. Alternative costs of rehospitalizations for both LVAD and OMM patients were estimated from the average cost per rehospitalization for the pulsatile device cohort in the REMATCH trial.⁵ Alternative assumptions for long-term survival extrapolation for LVAD patients, such as stop and drop and a linear survival curve, were included in the sensitivity analysis.

Results

Baseline Results

Using the values described for all parameters, at 5 years patients in the LVAD arm gained on average 1.87 QALYs or 2.42 LYs, at a total cost of \$360 407. Medically treated patients gained 0.37 QALYs or 0.64 LYs, at a cost of \$62 856 (Table 3). The ICER for the continuous-flow LVAD compared with OMM was \$198 184 per QALY and \$167 208 per LY.

The baseline results suggested a substantial improvement of continuous-flow devices compared with the previous cost-effectiveness analysis for pulsatile devices, where the total costs were estimated at \$391 906 (2002 US dollars), total QALY at 0.76, and ICER at \$802 674 (2002 US dollars).⁶

Sensitivity Analyses

Results were most sensitive to variations in long-term survival probabilities associated with the LVAD, the cost of LVAD implantation, cost per rehospitalization, and utility for NYHA classes I and II (Figure 3). However, ICERs of \$300 000 or more depended on the improbable assumption that all patients implanted with an LVAD who survived 24 months would die immediately thereafter. In other scenarios, where a wide range of values for the selected parameters were tested, the ICERs for LVAD relative to OMM remained below \$300 000 per QALY.

Discussion

This study demonstrates a meaningful improvement in the cost-effectiveness of mechanical circulatory support in the

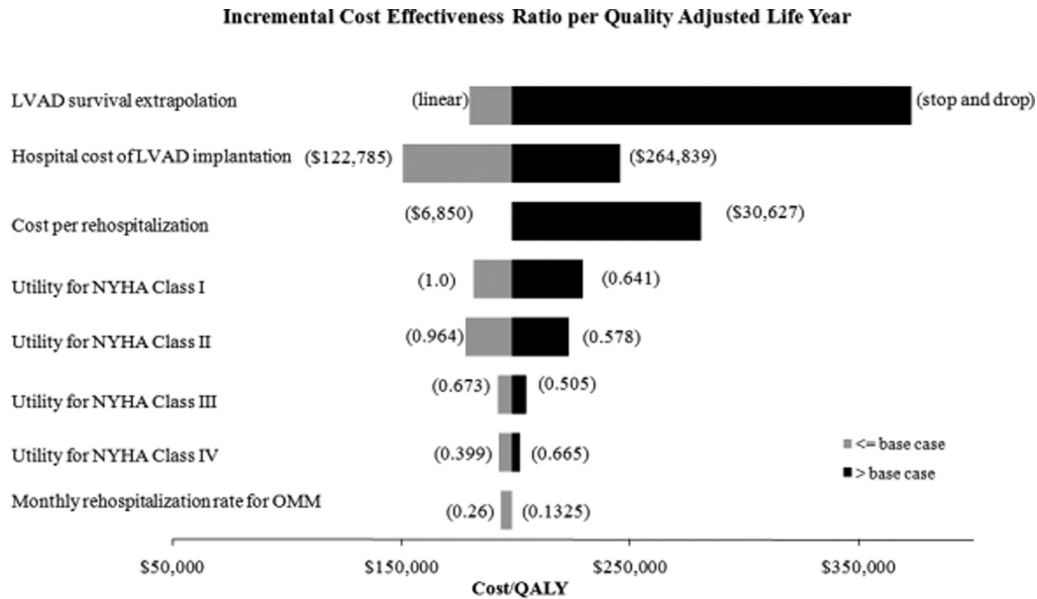


Figure 3. Results of the 1-way sensitivity analyses. In the left ventricular assist device (LVAD) arm, the methods of stop and drop (assuming that all patients surviving to 24 months die immediately thereafter) and a linear extrapolation (assuming a 60-month survival rate of 40%) were used. Utility values for patients with New York Heart Association (NYHA) I to IV heart failure were ranged by plus or minus 25% of the base case estimates. The initial hospital cost of LVAD implantation is varied by 1 standard deviation below or above the mean. The cost per rehospitalization for patients receiving an LVAD from the REMATCH trial (\$30 267) is used in the LVAD and optimal medical management (OMM) arms. The monthly rehospitalization rate for the OMM arm is assumed to be between the rate for the LVAD arm (0.215) and 0.1325.

recent era. These favorable outcomes are largely related to improved survival with continuous-flow LVADs coupled with reductions in implant costs and a persistent improvement in functional abilities in patients treated with mechanically supported circulation. The relative 75% reduction in cost/QALY during the past decade suggests that LVAD therapy continues to evolve in to a mainstream therapy for advanced heart failure.

Advanced heart failure is associated with high residual mortality. For those patients who meet indications, heart transplant remains the gold standard and preferred therapy. However, the shortage of suitable donor organs has limited this option to fewer than 2500 patients each year. A durable and cost-effective mechanical circulatory support treatment option could narrow the chasm that exists between the number of patients with advanced heart failure and the scare resources for transplantation.

Mechanical circulatory support devices were initially designed as pulsatile pumps requiring sufficient size to hold a normal cardiac stroke volume and a complex mechanism to propel the blood that included multiple moving parts. Although these devices were hemodynamically successful, device size and durability, as well as significant adverse events, limited their clinical applicability. Newer pump designs based on continuous flow have permitted miniaturization and design simplification, which has resulted in improved durability and less surgical trauma for implantation. Improved patient-centric care has accompanied these engineering advances. In the latest randomized trial of continuous-flow versus pulsatile LVADs for destination therapy, there was a significant improvement in 2-year survival and reduction in adverse events.²³ LVADs are emerging as the treatment of choice for

patients with advanced heart failure who are ineligible for heart transplantation. However, the relatively high cost of this therapy raises the lingering issue of cost-effectiveness.

In the Medicare population ineligible for transplant, the average cost of treating advanced heart failure with OMM is approximately \$180 000, with the majority being spent in the last 6 months of life.³ In the initial evaluation of costs for pulsatile LVADs, the average cost of LVAD implantation was \$210 187, and an independent technology assessment determined an ICER of \$802 700.^{5,6} In comparison with the pulsatile devices, the hospital costs for continuous-flow device implantation decreased by 50%.¹⁴ Despite the increased survival and quality of life improvements, high treatment costs restricted the adoption of LVAD therapy to a highly selected, extremely sick patient population. Our current cost analysis of patients treated with the new continuous-flow LVADs reveals a significant reduction in the ICER/QALY, from \$802 700 to \$198 184. This ICER/QALY is still significantly higher than the traditionally used threshold of \$50 000 when considering therapies to be cost-effective, but the incremental cost reduction in a relatively short time period is encouraging.

ICERs, as calculated in cost-effectiveness analyses, represent the opportunity cost of resources at margin. However, when applied to orphan disease or other end-of-life treatments, ICERs can be challenged, as the evaluation does not consider the innovative nature of medicine or availability of alternative treatment.²⁴ Although the notion of an ICER threshold value as a guiding principle for resource allocation is subject to debate, cost-effectiveness guided by ICERs continues to be the most commonly used tool in the evaluation of health care practices and new medical technologies.

ICERs less than \$50 000 per QALY are considered cost-effective and those between \$50 000 and \$100 000 are regarded as acceptable. Thus, the use of LVADs for the treatment of advanced heart failure has not yet achieved the currently accepted benchmark. Ongoing improvements in patient survival, reduction in long term complications and readmission rates, and a focus on inpatient and outpatient processes of care would reasonably be expected to result in further declines in the ICER, with the goal of ultimately achieving the current standard for cost-effectiveness.

A number of potential limitations of this study are worth noting. The clinical and economic data for LVADs and OMM were obtained on the basis of reports from different time periods. Survival data for OMM were based on REMATCH performed nearly 10 years ago, whereas the continuous-flow LVAD data were based on the recently completed HeartMate II Destination Therapy trial. Similar to the progress seen with LVADs, one would expect advances in medical management and its outcomes; for example, earlier referral to hospice may have reduced the hospitalization costs, which may lead to a reduction in the overall costs. Furthermore, patients randomly assigned to the OMM arm in REMATCH OMM were older than those treated with continuous-flow LVADs in HeartMate II Destination Therapy trial. If the data on a more recent OMM cohort with a similar age distribution were used, one may anticipate a better survival than currently estimated for the OMM patients. However, given the marked difference in survival and the lack of novel treatments demonstrated to improve the outcomes of patients with this severity of illness, it is reasonable to believe that the results would have been similar if more recent data for OMM were used. Another consideration in the interpretation of this study is the anticipation that long-term mechanical circulatory support will be applied in an older patient population than studied in the HeartMate II Destination Therapy trial. The overall impact of ventricular assist devices on survival, functionality, hospital days, and cost in the elderly may negatively affect the cost-effectiveness of mechanically assisted circulation and should be systematically evaluated. Second, costs of rehospitalizations were not collected in the HeartMate II Destination Therapy trial and were derived by estimation from other sources. The Medicare inpatient prospective payment system uses diagnosis-related groups, which are linked to payment rates for an acute hospital stay based on a patient's clinical condition and treatment strategy, and these were used in this study. As the causes for hospital admissions were unavailable, the analysis only included the payment for a typical episode of heart failure related admission during which medical management is provided. Using MS-DRG payments for heart failure and shock may have overstated the rehospitalization costs for the OMM cohort. It may also have under- or overstated the costs for the LVAD cohort. Although it is reasonable to believe that most admissions would fall under heart failure related MS-DRGs, a recent report from the Interagency Registry for Mechanically Assisted Circulatory Support showed that most readmissions were for nonheart failure reasons. This current estimate for the readmission (\$6850) is substantially lower than the average readmission cost (\$30 627) in the REMATCH trial. REMATCH was

conducted 10 years ago, when the clinical experience with the LVADs remained extremely limited. With the growing clinical experience and the improvement of the device, the implantation cost and the adverse event rates were dramatically reduced. It is reasonable to believe that there was a similar trend for the rehospitalization cost. Furthermore, the REMATCH costing cohort included only 34 patients, and most of them died within 2 years. If we assume that most costs are incurred during the last 6 months of a patient's life, the higher mortality would lead to a higher estimate of average cost per hospitalization.

Utility estimates in the study were not validated for an LVAD population, and LVAD-specific utility estimates are currently not available from the literature. The use of functional class as a surrogate for utility has been used in other clinical heart failure trials and was used in the original cost-effectiveness assessment of LVAD therapy.⁶ Analysis of functional and quality of life outcomes from the HeartMate II clinical trials program demonstrated early and sustained improvements in 6-minute walk distance, as well as Minnesota Living with Heart Failure and Kansas City Cardiomyopathy scores.¹⁰ Thus, it may be anticipated that substitution of another functional or quality of life metric would have yielded similar utility to that observed with NYHA functional class. The Interagency Registry for Mechanically Assisted Circulatory Support registry is collecting the EQ-5D data for the LVAD population; the single-index utility estimates derived from the EQ-5D data, when they become available, can be used to validate the NYHA class-based utility estimates in this study.

Conclusion

Using methods similar to those of the original Blue Cross Blue Shield technology assessment, we have demonstrated a significant improvement in the ICER for LVADs used to treat advanced heart failure in patients who are not eligible for heart transplantation. On the basis of this assessment, it is anticipated that continued refinement of patient selection criteria, technological advances, and improvements in management strategies will converge and result in the demonstration of LVADs as an economically effective treatment option for patients with advanced heart failure.

Sources of Funding

Thoratec, Inc, provided funding support for this research.

Disclosures

Dr Rogers and K.B. Tong have served as consultants for Thoratec. Dr Slaughter has received a research grant from Thoratec. R.R. Bostic is an employee of Thoratec.

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CLINICAL PERSPECTIVE

Mechanical circulatory support has become an accepted treatment for patients with advanced heart failure ineligible for transplantation. It is anticipated that the growing heart failure population coupled with the shortage of suitable donor organs will result in further increases in the use left ventricular assist devices (LVADs) as a means to enhance quality of life and survival. Critical evaluation of new and expanding technologies such as LVADs must include careful analysis of efficacy, safety, and cost-effectiveness. The most comprehensive study of LVAD cost-effectiveness was published 7 years ago based on very early clinical experience with mechanically assisted circulation and older generation devices. High device and implantation costs, as well as relatively modest survival benefits, resulted in an incremental cost effectiveness ratio/quality-adjusted life year of more than \$800 000. To place this in perspective, the per-patient cost of advanced heart failure in a Medicare population treated with standard medical and electric therapies has been reported to be \$180 000, with short anticipated life expectancy and limited likelihood for improvements in quality of life. Thus, the “utility” of standard therapies in these patients is poor. The rapid improvements in LVAD technology, patient selection, center experience, and management strategies would reasonably be anticipated to improve the cost-effectiveness of this therapy by reducing perioperative and long-term mortality, decreasing complications, and enhancing functionality and quality of life over prolonged periods of time.