Advances in Mechanical Circulatory Support

Cost of Ventricular Assist Devices
Can We Afford The Progress?

Leslie W. Miller, MD; Maya Guglin, MD, PhD; Joseph Rogers, MD

The societal cost of heart failure (HF) is matched by few other medical conditions. More than 670,000 new cases will be diagnosed this year. It commonly affects the aged and is associated with other chronic illnesses. Despite significant improvements in outcomes associated with contemporary medical and electric therapies, HF tends to be a progressive condition with a median survival of only 2 to 3 years after diagnosis. In addition, HF is the second most costly condition for Medicare. The total expenditure on this disease in the United States is estimated between $20 to $39 billion, which corresponds to 1.5% to 4% of total health care costs.

Further, the majority of medical financial resources are consumed in the final 2 years of life, a cost estimated at nearly $155,000.

Patients with advanced HF failing optimal treatments have limited therapeutic options. A small subset may qualify for cardiac transplantation, but stringent candidacy criteria and a limited supply of donor hearts limits its value to the larger HF population. In the past 5 years, improvements in left ventricular assist devices (LVAD) have made this a viable option to bridge a patient to transplant (BTT) or as permanent therapy (Destination Therapy, DT). The inability to define the size of the population that may ultimately be candidates for VAD therapy, particularly as DT, has led to widespread angst about the health care cost implications of this technology. The primary focus of this article is to critically review the available literature on the cost of VADs as well as alternative treatments for advanced HF.

Patients with advanced HF have a 1-year survival of only 10% to 25%. Initial clinical trials of older pulsatile flow LVADs used as destination therapy demonstrated 1-year survival of 52%, and more recent studies of continuous flow pumps, used for the same indication, showed 1-year survival of 73%. These studies also documented improvements in functionality and quality of life relative to that seen with medically-treated HF. With the observed gains in longevity, functionality, and quality of life in destination VAD recipients, mechanical circulatory support compares favorably with heart transplantation, the only long-term solution for patients with end-stage HF just a decade ago. Better technology with better outcomes and fewer adverse events, as well as smaller devices fitting into more patients, has prompted growth in the number of LVAD implants and the number of centers implanting these devices. Estimates of the number of potential VAD recipients in the United States may be as high as 250,000 to 300,000. The cost of managing advanced HF patients on traditional medications is relatively inexpensive, because medication costs are low and survival is short, although resource consumption increases substantially in the last 2 years and especially in the final 6 months of life. Prolonging life and restoring functional capacity with either VAD therapy or transplantation is expensive. The critical questions are the actual cost of these therapies, future savings attributable to fewer readmissions and improved quality of life on mechanical circulatory devices, and the willingness of society to pay for them upfront.

Cost of HF Treatment

Different metrics are used to compare the cost of medical interventions. Traditionally, the cost effectiveness of renal hemodialysis is used as the benchmark of acceptable expense, with a cost of about $40,000 for each year of life gained. Costs and cost effectiveness of treatment modalities are commonly evaluated and compared using quality-adjusted life years (QALY), which takes into account both survival benefit and improved quality of life. The cost–utility ratio is the cost of 1 QALY. The incremental cost-effectiveness ratio of a treatment represents a cost difference between a new and an established treatment divided by gained QALY.

It has been suggested that a cost-effectiveness ratio < $20,000 per QALY is very attractive, a ratio of $20,000 to $60,000 per QALY is acceptable, a ratio of $60,000 to $100,000 per QALY is higher than desirable, and > $100,000 per QALY is unattractive. Therefore, the incremental cost-effectiveness ratio of LVADs would need to be at least < $100,000 per QALY to be considered a more or less cost-effective therapy, although still more expensive than desirable.

In the case of medical therapy, the average cost for enalapril maleate therapy is $959 per year, and the cost of hydralazine plus isosorbide dinitrate therapy is $437 per year. Considering the morbidity, mortality, and quality of life benefits of these agents from clinical trials, the cost effectiveness of enalapril is $9700 per year of life gained, and the cost effectiveness of hydralazine–isosorbide therapy is $5600 per year of life gained. The addition of carvedilol to HF therapy is associated with an incremental cost-effectiveness ratio of $29,477 per life-year.
Heart failure (HF) treatments before the LV ADs. The overall conversion and should be considered a rough approximation. The societal cost of heart transplant will never be prohibited simply because the volume of transplantations is primarily determined by the limited availability of donor hearts. At least 16,500 individuals per year in this country would be suitable candidates for cardiac transplant but the scarce supply of donor hearts at $22,000 a year limits the number of procedures performed.

Evolution of the Field: Milestones in Mechanical Circulatory Support

To fully appreciate the current status of mechanically assisted circulation and its associated costs, the rapid progress in this field will be reviewed. To date, the majority of patients enrolled in clinical VAD trials have failed standard medical treatments and are in cardiogenic shock treated with either continuous infusion inotropic support or an intra-aortic balloon pump.

From the end of the twentieth century to the present, there have been several important milestones in LVAD development. The field has evolved from large devices that created pulsatile flow like the human heart delivering a normal stroke volume with each mechanical contraction of the pump to small, fully implantable continuous flow devices that move blood continuously. In 2001, the Randomized Evaluation of Mechanical Assistance in the Treatment of Congestive Heart Failure (REMATCH) trial established the superiority of a pulsatile flow VAD to medical treatment of patients with advanced HF who were ineligible for cardiac transplantation. The favorable outcomes of REMATCH resulted in Food and Drug Administration approval of the HeartMate XVE (Thoratec Corporation, Pleasanton, CA) as DT. At that time Blue Cross and Blue Shield Association’s Technology Evaluation Center also expanded coverage for DT LVADs in end-stage HF, despite the estimated cost/QALY of $803,000. After REMATCH, LVAD therapy was reserved for the sickest patients in a limited number of centers. As such, the overall financial burden to the healthcare system was similar to other orphan diseases using novel therapeutics such as Fabrazyme for Fabry disease. The individual patient cost is high but the population is so small that society can afford it. Subsequent improvements in survival and quality of life with newer continuous flow LVAD technologies have widened the outcome disparity between LVADs and medical therapy in patients with advanced HF. Thus, it appears unlikely that a direct comparison of these treatment strategies will be tested again and prospective healthcare cost comparisons of these two patient cohorts will always contain a number of assumptions that may alter the accuracy of the calculations.

The demonstration that adjunct pharmacotherapy may promote durable improvements in left ventricular function sufficient to allow removal of an LVAD popularized the concept of bridge to recovery. Birks and colleagues demonstrated that aggressive use of standard neurohormonal blockade combined with the β-2 agonist, clenbuterol, resulted in stable recovery in 11 of 15 nonischemic patients. Similar improvements have been reported with concomitant cell-based therapies, a concept currently being studied in a National Institutes of Health (NIH)-funded trial. The notion that VADs may be used in combination with adjunctive treatments to recover the failing ventricle may ultimately represent the future of this therapy, at least for selected patients with nonischemic cardiomyopathy and recent onset of HF. If effective, expansion of the indications for VADs and the cost would require careful study.

The past 5 years has witnessed a dramatic increase in the number of VAD implants in the United States, and the concept of orphan disease is no longer applicable to the therapy. In addition, VADs are increasingly being implanted in the larger advanced HF population who are less ill. It certainly expands the potential pool of patients, but it also makes outcomes better and reduces length of stay, which typically drives the cost. As an example, avoidance of VAD implantation in patients with cardiogenic shock and multisystem organ failure appears to have important implications for both outcomes and cost. Boyle and colleagues recently presented a retrospective analysis of 101 LVAD patients stratified by INTERMACS patient profiles (INTERMACS 1: critical cardiogenic shock; INTERMACS 2–3: inotrope-dependent severe heart failure; INTERMACS 4–7: noninotrope dependent advanced HF). The 3-year survival was 95% in the INTERMACS 4 to 7 patients versus 51% and 69% in the INTERMACS 1 and 2 to 3, respectively. Further, the length of stay for the index hospitalization was 27 days shorter in the less sick patients. Eckman et al grouped LVAD patients into those treated with inotropes before implant (INTERMACS 1–3) and those who were not (profile 4–6). Median length of stay was 29 days for the first group versus 16 days for noninotrope dependent patients. Direct costs were $216,902 versus $175,397, respectively. Thus, refined candidate selection that minimizes the number of patients with critical cardiogenic shock and
end-organ dysfunction can reasonably be anticipated to reduce index hospitalization length of stay, mortality, and cost of mechanically assisted circulation.

The growth of this field has forced a re-evaluation of the absolute costs of mechanical circulatory support and the costs relative to other infrequently used life saving therapies like chemotherapy for colon cancer,26 hemodialysis, renal transplantation,27 medical management of heart failure,7 or heart transplant28 (Figure 2).

During the past decade, the Centers for Medicare and Medicaid Services have changed coverage for LVADs several times to recognize both growing survival benefit29 and the costs associated with this treatment. In 2002, hospital reimbursement was provided under a new diagnosis-related group (Heart Assist System Implant), and the amount per device increased by 100% between 2000 and 2003. In response to studies demonstrating that LVADs were poorly reimbursed relative to heart transplantation,16 VADs became reimbursable under the same diagnosis-related group as heart transplantation in 2004. As a result, current reimbursement is 240% more than in the year 2000.30

Cost-Effectiveness of Pulsatile LVADs

Pulsatile Flow LVADs as Bridge to Transplant

As the clinical relevance of artificial blood pumps became clear, the question of their cost-effectiveness was raised. Early comparisons were made between pulsatile LVADs used as a BTT and cardiac transplantation. Investigators at Columbia University demonstrated that LVAD implantation was associated with longer length of stay (36.8 days versus 18.2 days), higher readmission rates, and higher cost for initial hospitalization ($169,535 versus $124,830). Overall cost for the 123 days of care including initial hospitalization was $197,957 for LVADs and $151,646 for heart transplant.16 A subsequent study from the same group defined the first-year costs for LVAD at $222,460 including professional fees and $192,154 excluding professional fees compared with the average first-year costs for cardiac transplantation of $176,605 without professional fees.31 As with transplant, the first year of LVAD support that includes the initial implantation is the most expensive, and the high cost is offset by lower costs in subsequent years. More recently, Adamson et al32 observed a significant reduction in average hospital costs of 41% while the transplant costs increased by 17%. Moreover, VAD/transplant hospital cost ratio was 3.14 in 2006 and 1.6 in 2010. Although the absolute cost remains high, the evolution demonstrates favorable trends in the cost of VAD therapy.

Pulsatile Flow LVADs as Destination Therapy

The intuitive comparator for LVAD as destination therapy is medical management of LVAD-eligible patients. The best group for such comparison is the medical management arm of the REMATCH trial represented by patients with advanced HF and very high mortality who were placed in the conservatively managed arm by randomization. According to the analysis by 1 of the coauthors of this study, medically treated patients gained in the trial 0.37 QALYs at a cost of $62,856 over 5 years, or $=125,500 per year of life.33

Analyzing data from LVADs used in the UK, Clegg et al34 derived a cost per quality adjusted life year of £170,616 ($263,875), although the same authors’ estimate for pulsatile devices used only as BTT was much more modest at £65,242 (£=100,000). It was proposed that the cost-effectiveness did not reach current acceptability standards in the UK and that LVAD survival would need to improve by 60% relative to that achieved in the REMATCH trial, and device costs would need to decrease by 60% to achieve the generally accepted cost-effectiveness thresholds (£30,000 or $=46,000 per QALY).34

As overall experience with the clinical application of LVADs has grown, the cost has decreased. An analysis of
Cost-Effectiveness of Continuous Flow LVADs

Continuous Flow LVADs as Bridge to Transplant

The initial cost-effectiveness of continuous flow LVADs came from the British BTT experience. The mean cost per QALY was £258,922 ($414,275), which included the device acquisition cost of £94,200 ($150,720). This estimate exceeds the standard of £30,000 for cost-effective treatment. Sensitivity analysis highlighted 2 determinants of poor cost-effectiveness: improved survival of advanced heart failure patients awaiting transplant and the high cost of the LVAD. Understanding cost-effectiveness of LVADs from BTT trials is challenging because the high upfront costs of implantation are included but the support duration is often shortened by subsequent transplantation. Further analysis of the dataset with an extended bridging interval of 18 months more fully captured the survival gains with LVAD therapy and the overall cost dropped to incremental cost-effectiveness ratio of £133,860 ($214,176). Conclusions from this study should be interpreted cautiously because the probabilistic Markov model used requires multiple assumptions that may be inaccurate. For example, a hypothetical control cohort was taken from the United Network for Organ Sharing registry waiting list for Status 1A and 1B patients. It was assumed that these patients’ survival was the result of conventional medical therapy, although many of these patients actually received LVADs. Consequently, the survival benefit calculated by authors likely underestimated the actual cost-effectiveness of LVADs in this population.

In the analysis based not on a model but on a real life experience, length of hospital stay, number of readmissions, and 1-year survival was similar between patients receiving a continuous flow LVAD as a bridge and those going straight to heart transplant. Cost comparison between the 2 strategies demonstrated a higher cost of the initial hospitalization in bridged patients resulting from the high cost of the device itself, which was $197,000±$38,000. The cost of initial admission with heart transplant in that study was $128,000±$44,000, P=0.001. However, inpatient costs after the index hospitalization were similar, at $33,000±$70,000 for bridge to transplant and $38,000±$48,000 for cardiac transplantation (P=0.81). Immunosuppressive drugs and right heart catheterization with biopsy were not included in the analysis and would likely substantially increase the cost of heart transplant.

Continuous Flow LVADs as Destination Therapy

The affordability of LVADs will not ultimately be determined by their function as a BTT but by their role in long-term mechanical circulatory support as DT. Recent trials have provided, for the first time, some valuable insights into this issue.

The HeartMate II Destination Therapy trial compared clinical outcomes and the costs of a continuous flow LVAD with a pulsatile flow LVAD in patients ineligible for transplant. Hospital mortality and length of stay (27 versus 34 days) were lower for the continuous flow LVAD patients. Analysis of billing data for the implant hospitalization demonstrated significantly lower mean costs for patients on continuous flow support compared with pulsatile support ($193,812 versus $384,260, respectively; P<0.001). Adverse perioperative events including bleeding, respiratory failure, and infection were identified as important factors associated with incremental cost.

Thus, the decade that spanned from pulsatile LVADs to continuous flow LVADs was associated with a 50% reduction in the cost of implant hospitalization; a remarkable improvement considering acquisition cost of the device was similar. Postoperative costs primarily driven by lengths of stay in the intensive care unit and step-down units appear to have been critical for the observed cost reductions with continuous flow devices.

Using a more inclusive dataset from the HeartMate II DT trial that included initial hospital stay, rehospitalizations, and Medicare payments for professional services, the cost of LVAD therapy was compared with the cost of medical therapy to treat advanced HF. Continuous flow LVAD patients had higher quality-adjusted life years (1.87 versus 0.37), and life years (2.42 versus 0.64), as well as higher 5-year costs ($360,407 versus $62,856). The incremental cost-effectiveness ratio of the continuous flow LVAD was $198,184 per QALY and $167,208 per life year, which was equivalent to a relative 75% reduction in incremental cost-effectiveness ratio from $802,700 per QALY in 2004. This recent data demonstrate that LVAD therapy has not achieved definitional cost-effectiveness in the United States (<$100,000/incremental cost-effectiveness ratio), but the improvements gained in the short-term are encouraging. Key determinants of cost effectiveness using current methodology are total cost, survival, and quality of life. If patient-perceived quality of life remains stable, combinations of cost reduction and improved survival will favorably impact cost-effectiveness. It is reasonable to assume that there are opportunities to reduce cost of VAD therapy focused on process of care improvements. Further, using the same HeartMate II data-set and modeling techniques, a 20% improvement in 2-year survival (58% to 70%) would reduce the ICER to $100,000.

Given variability of the results based on mathematical model chosen by authors of the cost-effectiveness studies, there is value in examining the raw data. Recently, Goldstein et al simply calculated all direct and indirect costs through 1 year in 20 recipients. For ease of analysis, LVAD costs were segmented by phase of care: initial admission (preimplant, implant, postimplant) and postdischarge, including readmissions. The median preimplant length of stay was 7.5 days with an associated cost of $46,141±$35,087. Professional fees plus room and board accounted for the majority of the cost in this phase. Total implant day costs for the 20 patients were $290,734 or 32% of total yearly costs, mostly related to the cost of device and surgical supplies. Median postimplant length of stay was 23 days (range 13 to 113), and was primarily determined by room and board. Almost all patients (85%) were readmitted during the first year, although overall they spent 82% of their time outside the hospital. Aggregated 1-year total costs from day of implant totaled $80,689,994.
Interestingly, none of the articles analyzing costs of LVADs describe driveline infection as a major contributor to expenses.

Goldstein’s article describes targets for cost reduction: the postimplant hospital stay and readmissions. The time from LVAD implantation to hospital discharge is medically, physiologically, and psychologically complex. These patients have typically suffered from severe advanced heart failure with compromised end-organ function, profound physical debilitation, and malnutrition. They are challenged to recover from the operative procedure and rehabilitation to achieve self-care. Families and the patients also undergo extensive education to ensure safe device operation outside the hospital setting. Novel processes of care are required to facilitate and expedite this recuperative phase. For example, the use of VAD rehabilitation wards with lower level of intensity would be potentially cost saving. Prevention of readmissions needs to also become a priority for this patient population.

As the field moves away from implanting devices into extremely sick and debilitated INTERMACS profile 1 and 2 patients, and shifts toward less ill electively implanted candidates who come from home and do not require ICU stay before surgery, cost reduction on the initial admission is also going to be tremendous.

Although nearly all centers with cardiac transplantation capabilities implant VADs, a growing number of new centers with expertise in HF and cardiac surgery are starting LVAD programs. The growth of the field in to these centers will undoubtedly increase the number of LVADs implanted and may impact outcomes. As the field expands, ongoing cost-effectiveness analysis will be required.

In this article, we have demonstrated that cost-effectiveness of mechanical circulation support is extremely dynamic and rapidly changing. The poor cost-effectiveness of the first generation of pulsatile pumps was driven by modest patient outcomes and high cost. The advent of continuous flow devices with improved outcomes in the past 5 years has made the data pertaining to the pulsatile pumps obsolete. Several upcoming events are likely to continue to shape VAD cost-effectiveness.

The FDA advisory panel approval of HeartWare HVAD in April 2012 hopefully will lead to full approval of this device for commercial use in near future. Until now, there has only been one implantable continuous flow device available to clinicians. Competition and device pricing may favorably impact the cost of the therapy.

Further development and clinical application of partial circulatory support with miniaturized continuous flow pumps (Circulite, CircuLite Inc, Saddle Brook, NJ) may once again change the field. It is anticipated that these small devices that augment cardiac output less than currently available LVADs but can be placed less invasively may expand the number of patients for whom mechanical circulation is beneficial.

Progress in the field of transcutaneous energy transmission may eventually eliminate the need for an external driveline. Also not a major player in driving up the costs, line infection certainly contributes to readmissions, patient satisfaction, and overall quality of life. How this technology will translate into cost saving is speculative because it is currently unavailable.

As mentioned above, it is reasonable to anticipate a focus on process improvement in the next decade that is aligned with many other initiatives in cardiovascular medicine. Reductions in unnecessary hospital days, development of more robust strategies to manage common medical conditions in an outpatient setting, development of best practices, and, above all, better patient selection focusing on more stable elective candidates will all improve cost-effectiveness.

Conclusions

Cost analysis of any treatment is challenging and has inherent limitations. Complex and variable economic relationships, ever-changing health care regulatory policies and budgets, and a paucity of publications with methodological differences confound attempts to understand true cost effectiveness. Definition of a uniform methodological approach to cost effectiveness research would be an important contribution that would ultimately allow a greater understanding of this field. Sociological and philosophical approaches to healthcare in each country also influence cost-effectiveness. In the United States, individual contracts between hospitals and manufacturers and insurance carriers differ from state to state making any analysis only somewhat valid.

Regardless, current data suggest that the cost effectiveness of VAD therapy as DT is improving but has yet to achieve the goal of <$100,000 USD/QALY. Further refinements in patient selection and management as well as a renewed focus on patient care processes should have a favorable impact on the total cost of this therapy. When coupled with more robust data on long-term survival and quality of life, it is reasonable to anticipate that mechanically assisted circulation will ultimately achieve definitional cost effectiveness. Further progress in this groundbreaking area will depend on the willingness of the society to pay for the progress, to cover higher than standard cost of LVADs today to support looming breakthroughs in technology that eventually will result in cost-effective mechanically circulatory support.

Disclosures

Joseph Rogers is a consultant for Thoratec.

References


Cost of Ventricular Assist Devices: Can We Afford The Progress?
Leslie W. Miller, Maya Guglin and Joseph Rogers

Circulation. 2013;127:743-748
doi: 10.1161/CIRCULATIONAHA.112.139824
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2013 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/127/6/743

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org/subscriptions/