Are LVADs Ready to be Mainstream?

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What is required of a treatment modality before it should be considered for mainstream usage within a given patient population? Certainly, a strong record of clinical success demonstrated in a large patient population and a compelling benefit-risk profile are the minimum requirements before any therapy is broadly adopted. Until recently, left ventricular assist devices (LVADs) did not meet this threshold, as the published clinical evidence suggested limitations with respect to device reliability and an association with numerous complications. As a result, usage of these technologies has been largely limited to our most dire cases of advanced heart failure.

However, the advent of continuous-flow LVADs has dramatically changed the benefit-risk profile of this therapeutic intervention. Indeed, the short- and long-term outcomes demonstrated in contemporary multi-center evaluations of the HeartMate II® LVAD have the heart failure clinical community reexamining the role of LVADs in the spectrum of heart failure care and revisiting the question as to whether this particular modality is ready for mainstream usage within the advanced heart failure patient population.

HeartMate II was approved in the United States in April 2008 to be used as a bridge-to-transplantation (BTT) for advanced heart failure patients. In January 2010, it gained a second indication as destination therapy (DT) for those Class IIIB or IV advanced heart failure patients who are ineligible for transplantation. The device is also approved and being distributed in Europe, Asia, Australia, and Canada.

Clinical experience

To date, the clinical experience with HeartMate II includes more than 6,000 patients at 254 centers worldwide. About 700 patients have been supported for longer than 2 years, and more than 60 have been on HeartMate II support for longer than 4 years, with the longest continuing on support for the past 6 years. Device recipients range in age from 9 to 91 and size from 1.1 to 3.2 BSA.

In terms of peer-reviewed publications, the clinical experience with HeartMate II has been reflected in more than 120 articles in several prominent journals, including *The New England Journal of Medicine, The Journal of the American College of Cardiology, Circulation, The Journal of Heart and Lung Transplantation, The Annals of Thoracic Surgery* and *The Journal of Cardiovascular Surgery.*

Compelling data

Bridge-to-Transplantation. The first major study evaluating usage of HeartMate II was the United States Multi-center Pivotal BTT Trial.[1] The results from this study resulted in FDA approval of the device for this indication. The most contemporary BTT results for this therapy were recently accepted for publication and feature patients enrolled in a multi-center post-approval study. As shown in the graph below, 180-day survival (to cardiac transplantation, recovery and device explantation, or ongoing device support) has improved substantially with experience, despite an extremely ill heart failure patient population.[1-3]

This is particularly impressive given that the post-approval protocol was designed to offer the HeartMate II to a broader patient population that was representative of real-life practice. More than half (61%) of post-approval patients were classified as INTERMACS 1 or 2, meaning that they were in either critical cardiogenic shock or progressively declining on intravenous inotropic therapy. This most recent cohort of patients demonstrated 90% successful outcomes at 6 months, and 85% at 1 year.

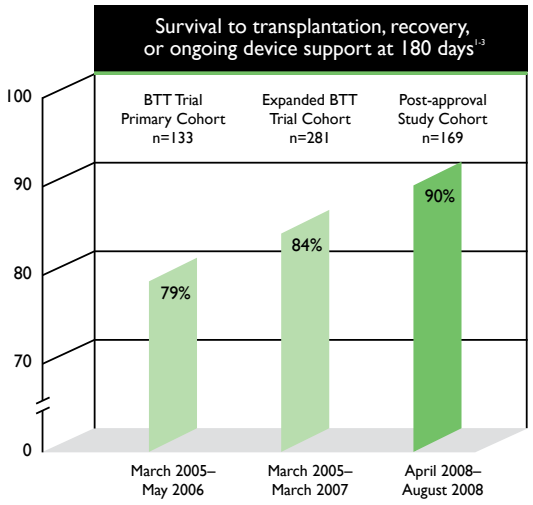

Figure 1. Improvements in BTT results over time.

Adverse event rates have also continued to drop among BTT patients. Between the BTT pivotal trial and post-approval study, stroke rates (ischemic, hemorrhagic, and

total) declined, as did the rate of right ventricular failure and the need for extended inotropic support (Table 1).

Device: Experience: Enrollment Period:	HeartMate II BTT Pivotal Trial 2005–2008	HeartMate II Post-Approval Study Cohort Mid-2008
Stroke		
Ischemic	0.09	0.06
Hemorrhagic	0.05	0.01
Total	0.14	0.07
RV Failure		
RVAD	0.09	0.04
Extended Inotropes	0.20	0.15

Events per patient year.

Table 1. HeartMate II adverse event rates from the BTT post-approval study.[3]

Destination Therapy. The HeartMate II Pivotal DT trial enrolled individuals with NYHA class IIIB and IV heart failure who were ineligible for cardiac transplantation and randomized them 2:1 to receive either the continuous-flow HeartMate II or its predecessor, the pulsatile-flow HeartMate® I.[4] The trial investigators discovered that the HeartMate II offers significantly better and event-free survival, with less risk of pump failure, infection, rehospitalization, or right-heart failure. These results have led to a dramatic shift in LVAD usage, with continuous-flow devices now representing 98% of LVADs implanted in the United States.[5]

The DT trial also had an expanded cohort of patients after the initial cohort.[6] This more contemporary experience shows that, as with the BTT experience, DT outcomes have continued to improve. Survival in the expanded DT cohort rose to 74% at 1 year from 68%, and 64% at 2 years from 58%. The more contemporary cohort also experienced a 50% reduction in hemorrhagic stroke, a 35% reduction in device-related infections, and a 25% reduction in sepsis compared to earlier HeartMate II DT recipients. This provides evidence of not only an improved device, but also represents timelier patient referral, better patient selection, and improved patient management.

Early and sustained improvements in quality of life

HeartMate II patients do more than survive longer than their medically treated counterparts—they experience early and sustained improvements across an array of functional capacity and quality of life (QoL) measures. Early last year, we published data from advanced heart failure patients enrolled in both the BTT and DT trials, all of whom had NYHA class IIIB or IV symptoms at baseline.[7] Following implant, 82% of BTT patients and 80% of DT patients at 6 months and 79% of DT patients at 24 months improved to NYHA class I or II. Mean 6-minute walk distance in DT patients improved from 204 meters at baseline to 350 meters at 6 months and 360 meters at 24 months, clearly showing the sustained nature of the functional capacity improvements seen with the HeartMate II. Significant improvements were also noted for BTT and DT patients in terms of mean QoL scores using both the Minnesota Living with Heart Failure and Kansas City Cardiomyopathy questionnaires.

Beyond improved quality of life, a percentage (4%–9.3%) of HeartMate II recipients experience sufficient ventricular recovery to warrant device explantation.[8,9] The effects of LVAD support on myocardial recovery are being actively investigated,[10,11] and I suspect that at some future point, our goal in LVAD implantation might be to allow for concurrent treatments that will allow the failing heart to heal, negating the need for permanent assistance or replacement.

In summary, we appear to be moving rapidly away from historical LVAD technologies that have major limitations and are therefore constrained to usage in the sickest of patients and performed only at select centers, to a therapy that has now been demonstrated to be efficacious and safe in an expanded advanced heart failure population. Notably, HeartMate II has proven to be highly reliable and demonstrate dramatic improvements in functional capacity and quality of life.

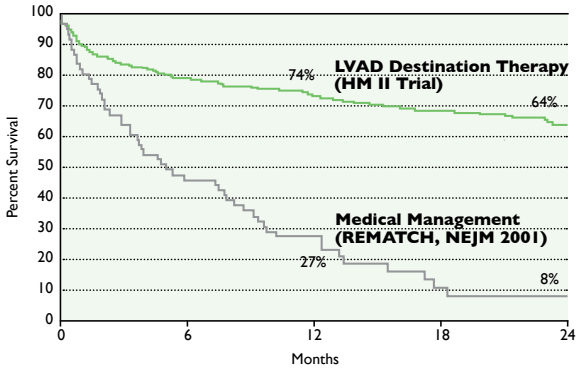

Figure 2. LVAD survival compared to medical management.[6-12]

With the wide gap in survival (Figure 2) and quality of life between other treatment options and continuous-flow LVAD support, the HeartMate II is quickly becoming an attractive treatment option for large numbers of patients with advanced heart failure and beginning to be accepted as a mainstream treatment modality for select advanced heart failure patients.

References

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