Demise of HVAD: The only constant is change

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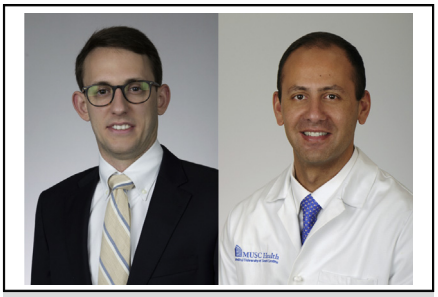
We are frequently reminded of the adage "the only constant is change" in medicine. In the field of mechanical circulatory support, innovation and progress in device technology and patient management have been exponential. The HeartMate II (Abbott) left ventricular assist device (LVAD) was the predominant durable device just a decade ago.[1] The introduction of smaller profile intrapericardial pumps that obviated the need for a preperitoneal pocket were revolutionary. The HeartWare HVAD (Medtronic) durable LVAD was approved for a bridge to transplant indication in 2012 and subsequently for destination therapy in 2017, and has been implanted in approximately 20,000 patients worldwide.[2,3]



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CENTRAL MESSAGE

The HVAD provided survival benefit and improvement in quality of life for many heart failure patients. Its demise is a result of significant progress in the field of mechanical circulatory support.

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PREVIOUS HVAD TRIALS

Published in 2017, the The HeartWare Ventricular Assist System as Destination Therapy of Advanced Heart Failure, ENDURANCE, trial compared the HVAD against the durable axial flow device of the time (HeartMate II) in a 2:1 fashion in adults undergoing implantation for destination therapy. The primary end point was 2-year survival with freedom from disabling stroke or need for device removal for malfunction or failure. Results showed noninferiority of the HVAD group with less need for device removal or exchange but more than twice the stroke rate.[3] Indeed, 30% of HVAD patients experienced a stroke in this study.

Because of this discrepancy in stroke rates for the 2 devices, a post hoc analysis of stroke data from the ENDURANCE trial was conducted and showed that blood pressure was an important independent variable associated with stroke risk, leading to the ENDURANCE supplemental trial.[4] In the ENDURANCE supplemental trial, the primary end point was 12-month incidence of transient ischemic attack or stroke with residual deficit 24 weeks post event. The secondary end point was a composite outcome of freedom from death, disabling stroke, and need for device replacement or urgent transplantation. The study failed to demonstrate noninferiority of the HVAD to the HeartMate II device with regard to the primary end point, but did show superiority of the HVAD with regard to the secondary end point. The rates of stroke in HVAD subjects was reduced 24% compared with those in the ENDURANCE trial. Although it remains unknown why the differences in stroke rate exist for the 2 devices even with strict blood pressure control in the HVAD cohort, the differences in hemocompatibility and flow dynamics for the various pump designs might contribute.

The most promising data for the HVAD device came from the A Prospective, Single-Arm, Multi-Center Study in Collaboration With INTERMACS to Evaluate the Thoracotomy Implant Technique of the HeartWare HVAD System in Patients With Advanced Heart Failure, LATERAL, trial, which was a multicenter, prospective, nonrandomized single-arm trial published in 2019 including 144 patients who received the HVAD via a lateral thoracotomy approach from 26 centers.[5] The primary end point was a composite outcome of being alive with the original device at

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180 days and free of disabling stroke, which was achieved in 88.1% of patients. This led to the HVAD being the first LVAD to be approved by the Food and Drug Administration (FDA) for implantation via thoracotomy later that year. Two-year follow-up of the LATERAL trial showed that these favorable outcomes persisted longitudinally, with a 2-year freedom from disabling stroke of 95%.[6] These outcomes, along with other accumulating evidence, also led to a refueled discussion about whether durable LVAD therapy is superior to optimal medical therapy in terms of survival and/or quality of life in patients with ambulatory, noninotrope-dependent advanced heart failure.[7]

THE HeartMate 3 (ABBOTT)—A FORMIDABLE COMPETITOR

In 2019, the publication of the final results of the Thoratec Corporation MOMENTUM 3, Multi-center Study of MagLev Technology in Patients Undergoing MCS Therapy With HeartMate 3 IDE Clinical Study Protocol, MOMENTUM III, trial brought to full bear the competitor of the HVAD—the HeartMate 3.[8] The trial was a randomized trial in which the magnetically levitated centrifugal flow rotor pump design of the HeartMate 3 was compared with the mechanically driven axial pump design of the HeartMate II in a 1:1 fashion. Over 2 years, the HeartMate 3 devices were superior in terms of survival without pump removal or replacement and freedom from disabling stroke. HeartMate 3 implantation was also associated with a lower rate of stroke of any severity, major bleeding, and gastrointestinal hemorrhage. Although the HVAD device had shown noninferiority compared with the older generation axial flow device, the HeartMate 3 showed superiority across all domains. Despite initial technical concerns because of a higher-profile device, several reports were subsequently published showing the feasibility and safety of a thoracotomy approach for the HeartMate 3 device, leading to FDA approval of this technique in 2020.[9,10]

RECALL OF THE HVAD

In parallel with increasing use of the HeartMate 3 came an increase in device-related recalls from the FDA on the HVAD device. These ranged from issues with battery cables and connectors to major pump failures and failed restarts. The company received >100 reports of failed or delayed restarts resulting in 14 patient deaths and 13 device removals. This combined with the failure of the device to match the neurological outcomes of the HeartMate 3 led to an FDA distribution of a class 1 recall of the HeartWare devices on June 3, 2021, accounting for >4000 implanted devices across the nation.[11] This recall stopped implantation of the devices effective immediately and soon after, Medtronic stopped distribution of the devices worldwide, which has carried through to the present.

WHAT NOW?

Removal of the HVAD device from the market led to several concerns from the heart failure community. These concerns were addressed in a webinar sponsored by the Society of Thoracic Surgeons and the International Society for Heart and Lung Transplantation that was well attended and included key members of industry, heart failure cardiology, and cardiac surgery.[12] An example of a topic discussed included patients with small body surface area for whom some clinicians believed the HVAD offered an advantage over the HeartMate 3 device. This concern also relays from the pediatric community in that many pediatric cardiac surgeons preferentially were using the HVAD in smaller pediatric patients. Multiple reports have recently been published establishing the feasibility and safety of HeartMate 3 implantation in smaller patients and/or those with smaller left ventricular chamber size, including in the pediatric population.[13,14]

Another important topic relates to LVAD exchange in patients currently supported with the HVAD device. In an analysis of the Society of Thoracic Surgeons Interagency for Mechanically Assisted Circulatory Support (INTERMACS) registry 3 cohorts were compared to address this scenario: (1) those with a primary HVAD implant (n = 3797), (2) those undergoing HVAD to HeartMate 3 exchange (n = 45), and (3) those undergoing HVAD to HVAD exchange (n = 234).[15] A major finding was that patients who underwent LVAD exchange with either a HeartMate 3 or HVAD had worse survival compared with patients who retained their primary HVAD. This supports the notion that "prophylactic" exchange should not be performed. The authors also reported that in those who underwent exchange, exchange to a HeartMate 3 was associated with better survival post exchange than exchange to another HVAD.

There are specific technical considerations revolving around exchange of an HVAD to a HeartMate 3. A thoracotomy approach allows for less tedious mediastinal adhesiolysis with less operative burden than a redo sternotomy in patients who had their primary HVAD implanted with a sternotomy. As with other LVAD exchanges, this of course would be limited to patients without mediastinal infection, outflow graft compromise, or other issues that would necessitate full explant of the original device with replacement. A thoracotomy approach for HVAD to HeartMate 3 exchange would entail a graft-to-graft anastomosis, which would create a "step-down" in size from the 14-mm outflow graft of the HeartMate 3 to the 10-mm outflow graft diameter of the HVAD. There is a concern that this would generate increased afterload and result in running the HeartMate 3 pump speeds at higher rates, although these data are in evolution. Whether this approach should be abandoned and a redo sternotomy, with removal of the entirety of the primary HVAD outflow graft and re-anastomosis of the new HeartMate 3 outflow graft to native aorta in all cases of HVAD to HeartMate 3 exchange, remains to be elucidated.

ADDITIONAL CONCERNS

Other important concerns have been voiced regarding the removal of the HVAD from the market. One of which is that Abbott now essentially monopolizes the durable LVAD market. The lack of competition in this area might stall the push for device improvements, slow clinical trial development, and delay the goal of developing a fully implantable device. This combined with allocation changes in heart transplantation are likely leading to a shift in durable LVADs toward an older destination therapy population. These factors have led to a concern that the potential lack of drive to innovate with the current monopoly, lower implant volumes with the decrease of the bridge to transplant population, the push toward more acute support with temporary devices to expedite transplantation, and the development of effective advanced heart failure medications such as sacubitril-valsartan and SGLT2 inhibitors will lead to stagnancy in the durable LVAD field.

CONCLUSIONS

Although the downfall of the HVAD device closes a chapter in the mechanical circulatory support story, it marks the start of another. The new generation of magnetically levitated centrifugal flow devices has raised the bar in the world of durable LVADs. This reflects the natural ebb and flow of technological advancement in clinical medicine. As physicians, scientists, and innovators across the world work diligently for better outcomes for our patients, we will continue to evolve as a field with new devices, techniques, and care paradigms in hopes of providing better outcomes for the communities for which we provide care.

Conflict of Interest Statement

Arman Kilic is a speaker/consultant for Abiomed and Abbott. Walker Blanding reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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