FULLY MAGNETICALLY LEVITATED LEFT VENTRICULAR ASSIST SYSTEM FOR TREATING ADVANCED HF

A Multicenter Study

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ABSTRACT

BACKGROUND The HeartMate 3 left ventricular assist system (LVAS) is intended to provide long-term support to patients with advanced heart failure. The centrifugal flow pump is designed for enhanced hemocompatibility by incorporating a magnetically levitated rotor with wide blood-flow paths and an artificial pulse.

OBJECTIVES The aim of this single-arm, prospective, multicenter study was to evaluate the performance and safety of this LVAS.

METHODS The primary endpoint was 6-month survival compared with INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support)-derived performance goal. Patients were adults with ejection fraction <25%, cardiac index <2.2 l/min/m² without inotropes or were inotrope-dependent on optimal medical management, or listed for transplant.

RESULTS Fifty patients were enrolled at 10 centers. The indications for LVAS support were bridge to transplantation (54%) or destination therapy (46%). At 6 months, 88% of patients continued on support, 4% received transplants, and 8% died. Thirty-day mortality was 2% and 6-month survival 92%, which exceeded the 88% performance goal. Support with the fully magnetically levitated LVAS significantly reduced mortality risk by 66% compared with the Seattle Heart Failure Model–predicted survival of 78% (p = 0.0093). Key adverse events included reoperation for bleeding (14%), driveline infection (10%), gastrointestinal bleeding (8%), and debilitating stroke (modified Rankin Score >3) (8%). There were no pump exchanges, pump malfunctions, pump thrombosis, or hemolysis events. New York Heart Association classification, 6-min walk test, and quality-of-life scores showed progressive and sustained improvement.

CONCLUSIONS The results show that the fully magnetically levitated centrifugal-flow chronic LVAS is safe, with high 30-day and 6-month survival rates, a favorable adverse event profile, and improved quality of life and functional status.

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Treatment of advanced heart failure (HF) with a continuous-flow left ventricular assist system (LVAS) is expanding worldwide due to fewer adverse events, improved outcomes, and broader acceptance of the therapy (1–3). Although the majority of patients supported by an LVAS experience extended survival and improved quality of life (QOL), adverse events do occur. Older patients and those with comorbidities carry a high risk of complications (4,5). Gastrointestinal bleeding has emerged as an adverse event in patients with continuous-flow LVAS support (6–8), whereas right HF, infection, stroke, and pump thrombosis continue to be complications associated with significant morbidity and mortality (9–12). Given that patients will present for durable LVAS support with comorbid conditions, and many will require such support for long durations, technological enhancements that address hemocompatibility may help reduce the frequency and severity of these adverse events.

Methods

This single-arm, prospective, nonblinded, nonrandomized study was conducted at 10 centers in 6 countries. The study was conducted in compliance with the Declaration of Helsinki, International Conference on Harmonisation/Good Clinical Practices, and the International Organization for Standardization of medical devices for human subjects, known as 14155:2011, and in accordance with country-specific requirements. Each participating center obtained approval from their respective regulatory bodies and ethics committees. All patients were required to provide written informed consent. The sponsor (St. Jude Medical) managed the study, audited the study centers, and provided data analysis.

The primary endpoint of the study was survival rate at 6 months compared with a performance goal derived using INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support) registry data from patients matched for age, indication for use, intra-aortic balloon pump usage, left ventricular ejection fraction, and supported using the earlier generation of this LVAS. Secondary study endpoints included comparison to the predicted 6-month survival using the Seattle Heart Failure Model (SHFM) (19); QOL (European Quality of Life Questionnaire 5 level); functional status (6-min walk test, New York Heart Association [NYHA] functional class); adverse event rates; and the incidence of device malfunction, reoperation, rehospitalization, and survival free of debilitating stroke (modified Rankin Score >3). INTERMACS adverse event definitions were used in this study (20). Adults with an ejection fraction <25%, cardiac index <2.2 l/min/m² while not on inotropes, or inotrope-dependent status and who were either on optimal medical management for 45 of 60 days or listed for transplant were enrolled in this study. The study had a single set of entry criteria for patients designated for bridge to transplant (BTT) or permanent support (e.g., destination therapy [DT]). Detailed study inclusion and exclusion criteria are presented in the Online Appendix. Patients were followed to the primary endpoint at 6 months or other outcome (transplant, explant, or death), whichever occurred first. Patients

Abbreviations and Acronyms

BTT = bridge to transplant
DT = destination therapy
Full MagLev = fully magnetically levitated
HF = heart failure
INTERMACS = Interagency Registry for Mechanically Assisted Circulatory Support
INR = international normalized ratio
LV = left ventricle/ventricular
LVAS = left ventricular assist system
NYHA = New York Heart Association
QOL = quality of life
SHFM = Seattle Heart Failure Model
vWF = von Willebrand factor

Contemporary axial-flow and centrifugal-flow LVASs pump blood through narrow flow pathways, which contributes to hemolysis, platelet activation, and damage to von Willebrand factor (vWF) (13–17). The HeartMate 3 LVAS (St. Jude Medical, Pleasanton, California) is a new, miniaturized centrifugal-flow device designed to enhance hemocompatibility by minimizing shear force effects on blood components and by incorporating an optimized blood–biomaterial interface (18). Additionally, an artificial pulse may help avoid blood stasis within the left ventricle (LV), allowing the aortic valve to function. These features may potentially limit the major contributing factors to hemorrhagic, thrombotic, and infectious complications.

The purpose of this study was to evaluate the performance and safety of this fully magnetically levitated LVAS in patients with advanced HF. We present the primary endpoint analysis and 6-month results from this study conducted to meet Conformité Européenne (CE) mark requirements.

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with ongoing support at 6 months will be followed for 24 months after implantation or until other outcome.

**DEVICE DESCRIPTION.** The new centrifugal-flow LVAS is intended to provide long-term hemodynamic support in patients with advanced HF. This device is designed for intrapericardial placement, with an inflow conduit inserted into the LV and the outflow graft attached to the ascending aorta (Figure 1). A fully magnetically levitated (Full MagLev) rotor with large blood-flow paths (0.5 mm along the side and 1.0 mm above and below the rotor) minimizes shear forces, which is expected to reduce detrimental effects on blood components (Figure 2). This rotor design avoids the need for mechanical bearings, reducing wear of the moving component and heat generation within the pump. The device’s internal surfaces are textured with titanium microspheres to promote adhesion of patient cells for reduced thrombogenicity. Operating in an artificial-pulse mode, the LVAS’s rotor changes speed every 2 s to generate pulsatile flow. The pump operates at rotor speed in the range of 3,000 to 9,000 rpm, and the maximum flow rate is 10 l/min. The pump motor receives power from a pair of 14V lithium-ion batteries or external AC power sources.

LVAS implantation is accomplished by standard median sternotomy and cardiopulmonary bypass techniques. The apical cuff is sewn to the epicardial surface near the apex of the LV, and a myocardial core is created through the cuff with a circular knife. The outflow graft is anastomosed to the ascending aorta in the standard fashion. The pump is positioned at the apex of the LV; the inflow conduit is inserted into the LV through the apical opening and then secured by the apical cuff. The pump power cable is tunneled and externalized through the abdominal wall and connected to a modular cable. The modular cable is attached to the power and control system.

**FIGURE 1 The Fully Magnetically Levitated LVAS**

The blood pump is positioned within the pericardial space, with its integral inflow conduit in the left ventricle and outflow graft attached to the ascending aorta. The percutaneous power cable is tunneled through the abdominal wall and is attached to the system controller that receives power from 2 lithium-ion batteries. LVAS = left ventricular assist system.

Anticoagulation guidelines include post-operative intravenous heparin to achieve a partial thromboplastin time of 45 to 65 s (1.2 to 1.8 times control) once chest tube drainage is <50 ml/h for 3 h. The heparin is then titrated up over 2 days until the partial thromboplastin time is 55 to 65 s. After the patient is able to take oral medications, aspirin (81 to 100 mg daily) and warfarin (or other vitamin K antagonist) are given throughout the remainder of support with a target international normalized ratio (INR) of 2.0 to 3.0.

**STATISTICAL ANALYSIS.** The primary endpoint for patients supported by the Full MagLev LVAS was compared with HeartMate II LVAS data using appropriately matched contemporary patients (n = 3,103) in the INTERMACS registry. The comparator patients were implanted between January 1, 2012, and June 30, 2014, then followed through December 2014. All patients who did not require intra-aortic balloon use before implantation, with an INTERMACS profile between 2 and 6, age between 19 and 79 years, and a left ventricular ejection fraction <25% were included. Six-month survival for the comparison group was 88%. The Full MagLev LVAS cohort was considered non-inferior to the comparison group if the lower 97.5% confidence limit of the 6-month survival was within 10% of the comparison group. Continuous data are presented as the number of subjects, mean ± SD, or median and range where appropriate. Categorical data are reported as frequencies and percentages. Survival data are presented using the Kaplan-Meier product limit method as well as the percentage of subjects who successfully reached the pre-defined study endpoint. Competing outcome analysis was performed across the study duration. Adverse event data are presented as the number of patients with the event and the percentage of patients with events within 6 months of study duration.
implantation. Survival distribution between actual survival of the novel LVAS patients and predicted survival absent the device using SHFM was compared using an estimated hazard ratio and Z test. Percentage of patients with NYHA functional class I and II at months 1, 3, and 6 were compared to the baseline using the Fischer exact test, whereas the 6-min walk test and QOL data from baseline to 6 months was compared using a paired Student t test. Statistical analysis was completed with SAS version 9.3 (SAS Institute, Cary, North Carolina). No adjustments for multiplicity were made.

RESULTS

Fifty patients were enrolled into the study and implanted with the HeartMate 3 device between June 25, 2014, and November 27, 2014, at 10 centers in Australia, Austria, Canada, Czech Republic, Germany, and Kazakhstan. Six-month follow-up of the last patient was reached on May 26, 2015. The patients were representative of an advanced HF population and the indication for support was a mix of BTT (54%) and DT (46%) patients. Per demographics and baseline data (Table 1), pre-implant hemodynamic values, INTERMACS profile, and medical therapy were consistent with chronic advanced HF. No patients were being treated with a mechanical circulatory assist device at the time of implantation. The majority of patients had 1 or more operative risk factors (Table 2).

OUTCOMES. The 30-day and 6-month survival were 98% and 92%, respectively. The lower 97.5% confidence limit for survival was 83%, which is within 5% of the performance goal of 88%, thus the primary endpoint as specified in the study was met. The SHFM predicted a mean survival rate of 78% on continued medical therapy at 6 months. Thus the Kaplan-Meier actuarial survival of 92% demonstrated a 66% reduction in 6-month mortality risk with support of the Full MagLev LVAS compared with SHFM (hazard ratio: 0.34; p = 0.0093) (Figure 3).

At 6 months, 44 (88%) of the 50 patients were still ongoing with LVAS support, 4 (8%) died, and 2 (4%) were transplanted (Figure 4). Two patients supported for planned BTT underwent transplantation as intended, on post-implant days 50 and 132. The 4 deaths occurred at 2 centers within 6 months, including 1 death within 30 days of support due to cardiac arrest in a patient with immediate post-operative ischemic stroke (day 19). The other deaths were due to circulatory failure subsequent to computed tomography contrast-associated anaphylactic
shock and ischemic stroke determined to be unrelated to the implantation procedure or device (day 48), suicide (day 113), and renal failure with termination of life support (day 144). The indication for the contrast computed tomography scan resulting in anaphylactic shock was suspected pulmonary embolism. The suicide occurred between the 3- and 6-month follow-up and was deemed unrelated to the device or procedure by the study site.

Forty-three (86%) patients were discharged from the hospital at a median of 28 days (interquartile range: 22 to 43 days). Twenty-one (49%) patients were discharged to their home, whereas 22 (51%) were discharged to another intermediate medical facility before going home. Of the 7 patients not discharged, 3 expired during index implantation hospitalization, 1 underwent heart transplantation, and 3 remained hospitalized due to a complicated post-operative course (pneumonia, reoperations, methicillin-resistant Staphylococcus aureus infection, hemorrhagic stroke, or ventilator dependence). Twenty-three of the 43 discharged patients (53%) were readmitted to the hospital. The leading reasons for readmission included...
bleeding \((n=4)\), infection \((n=6)\), anticoagulation adjustment \((n=5)\), volume issue (dehydration \([n=1]\), fluid overload \([n=1]\), and low flow with hyponatremia \([n=1]\)), and chest pain \((n=2)\). By 3 months post-discharge, 5% of the discharged patients were readmitted for 2 device-related or possibly device-related events, and 28% of the discharged patients were readmitted with 14 non-device-related events. By 6 months post-discharge, 28% of patients were readmitted for 15 device-related or possibly device-related events, whereas 35% of discharged patients were readmitted for 24 non-device-related events.

**PUMP PERFORMANCE.** The median duration of Full MagLev LVAS support was 228 days (range 19 to 335 days), with a cumulative time of 31 years. The mean cardiac index before implantation was \(1.82 \pm 0.46 \text{l/min/m}^2\), and it improved to \(2.20 \pm 0.33 \text{l/min/m}^2\) \((p < 0.0001)\) after LVAS support was initiated. During the 6 months of support, average pump flow was \(4.3 \pm 0.6 \text{l/min}\) at \(5,424 \pm 309\) rpm. The artificial pulse mode generated changes in patient arterial pulse pressures (Figure 5). There were no reported events of pump exchange, pump malfunction, or pump thrombosis. There were no reported hemolysis events, as evidenced by lactate dehydrogenase and plasma-free hemoglobin levels through 6 months (Figure 6). Laboratory values reflecting end-organ function at 6-month follow-up are presented in Table 3.

**ADVERSE EVENTS.** Adverse events are listed by their time to occurrence (within the first 30 days of implantation, days 31 through 180, and total time) in Table 4; the majority occurred within 30 days of implantation.

Bleeding was the most common adverse event \((n=19; 38\%)\), with most occurrences during the early post-operative period. There were 6 gastrointestinal bleeding events in 4 patients \((8\%)\): 2 events within 30 days of implantation and 4 events after 30 days. The INR in these patients ranged from 1.3 to 6.7. Seven patients \((14\%)\) required surgical intervention due to bleeding; 5 reoperations took place within 14 days of the implantation. One patient was returned to the operating room on post-implant day 28 to resolve bleeding in the jejunum.

Infection occurred in 18 patients \((36\%)\). Localized infection (e.g., respiratory/pneumonia) accounted for the majority of infections \((28\%)\), followed by sepsis \((16\%)\) and driveline infection \((10\%)\). There were no infections of the implanted pump.

There were 6 strokes in 6 patients \((12\%)\), of which 2 \((4\%)\) occurred in the perioperative period. Four of the 6 strokes \((8\%)\) were considered debilitating (modified Rankin Scale >3). Of these, 1 ischemic stroke occurred the day after index LVAS implantation where there was difficulty in properly engaging the inflow conduit with the apical cuff. This patient expired on day 19. The second that was ischemic in nature was subsequent to anaphylactic shock after the patient received contrast medium for a lung scan. This patient expired on day 48. The third, a hemorrhagic stroke, occurred a day after transcatheter aortic valve replacement. This patient had pre-existing aortic valve disease with bioprosthetic valve replacement during the primary implantation. By month 1, structural deterioration of the valve was observed with moderate aortic regurgitation requiring transcatheter aortic valve replacement. The latter 2 strokes appear to have a temporal relationship with other procedures performed while on LVAS support. The fourth stroke was hemorrhagic in nature and occurred on day 103. This patient further had renal failure with stoppage of life support.

Right HF occurred in 5 patients; 4 instances occurred during the first 30 days of support. Of these, 2 \((4\%)\) patients required right ventricular device implantation during initial implant surgery; of these 2, 1 patient required extracorporeal membrane oxygenation, which was subsequently discontinued (post-implant day 103), and 1 required short-term right ventricular assist device support (CentriMag, St. Jude Medical), which was removed at the time of heart transplantation (post-implant day 50). The remaining patients with right HF were supported with inotropes for >7 days.
In this patient with the fully magnetically levitated LVAS, the arterial pulsatility generated by the device can be seen in the red line (labeled Art). Photo courtesy of the Institute for Clinical and Experimental Medicine, Prague, Czech Republic. LVAS = left ventricular assist system.

There were no hemolysis events per mean (± SD) for lactic dehydrogenase (LDH) and plasma hemoglobin (PlHgb) at baseline to month 6.
TABLE 3 Laboratory Values

<table>
<thead>
<tr>
<th>Baseline</th>
<th>Week 1</th>
<th>Month 1</th>
<th>Month 3</th>
<th>Month 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>AST, U/l</td>
<td>28.9 ± 12.2</td>
<td>48.3 ± 56.7</td>
<td>28.6 ± 14.7</td>
<td>29.9 ± 26.5</td>
</tr>
<tr>
<td>ALT, U/l</td>
<td>33.3 ± 20.8</td>
<td>37.0 ± 50.2</td>
<td>26.9 ± 22.2</td>
<td>24.9 ± 25.0</td>
</tr>
<tr>
<td>Total bilirubin, µmol/l</td>
<td>18.8 ± 10.1</td>
<td>24.0 ± 30.1</td>
<td>11.5 ± 5.5</td>
<td>9.5 ± 4.6</td>
</tr>
<tr>
<td>Creatinine, µmol/l</td>
<td>112.0 ± 31.6</td>
<td>97.1 ± 29.4</td>
<td>101.2 ± 56.7</td>
<td>96.2 ± 28.7</td>
</tr>
<tr>
<td>Hemoglobin, g/dl</td>
<td>13.2 ± 2.0</td>
<td>9.4 ± 1.8</td>
<td>10.3 ± 1.6</td>
<td>11.8 ± 2.0</td>
</tr>
<tr>
<td>Hematocrit, %</td>
<td>39.5 ± 5.6</td>
<td>28.8 ± 3.9</td>
<td>31.5 ± 5.0</td>
<td>36.0 ± 6.3</td>
</tr>
<tr>
<td>Platelets, x10³/µl</td>
<td>231 ± 69.3</td>
<td>212 ± 82.4</td>
<td>322 ± 129</td>
<td>256 ± 83.3</td>
</tr>
<tr>
<td>Sodium, mmol/l</td>
<td>136.0 ± 3.6</td>
<td>137.5 ± 6.6</td>
<td>135.0 ± 5.6</td>
<td>137.5 ± 4.4</td>
</tr>
<tr>
<td>BUN, mmol/l</td>
<td>9.1 ± 5.3</td>
<td>9.4 ± 7.8</td>
<td>8.8 ± 9.5</td>
<td>8.6 ± 7.6</td>
</tr>
</tbody>
</table>

Values are mean ± SD. *p < 0.05 when compared with baseline using the paired Student t test. AST = aspartate aminotransferase; ALT = alanine aminotransferase; BUN = blood urea nitrogen.

TABLE 4 Adverse Events Through 6 Months

<table>
<thead>
<tr>
<th>Days 0-30 (n = 50)</th>
<th>Days &gt;30 (n = 49)</th>
<th>All (6 Months) (n = 50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>Events</td>
<td>Patients</td>
</tr>
<tr>
<td><strong>Bleeding</strong></td>
<td>15 (30)</td>
<td>19</td>
</tr>
<tr>
<td><strong>Requiring surgery</strong></td>
<td>6 (12)</td>
<td>6</td>
</tr>
<tr>
<td>GI bleeding</td>
<td>2 (4)</td>
<td>2</td>
</tr>
<tr>
<td>Cardiac arrhythmias</td>
<td>14 (28)</td>
<td>14</td>
</tr>
<tr>
<td><strong>Infection</strong></td>
<td>10 (20)</td>
<td>14</td>
</tr>
<tr>
<td><strong>Sepsis</strong></td>
<td>4 (8)</td>
<td>4</td>
</tr>
<tr>
<td>Driveline</td>
<td>1 (2)</td>
<td>1</td>
</tr>
<tr>
<td><strong>Stroke</strong></td>
<td>2 (4)</td>
<td>2</td>
</tr>
<tr>
<td>Ischemic</td>
<td>2 (4)</td>
<td>2</td>
</tr>
<tr>
<td>Hemorrhagic</td>
<td>0 (0)</td>
<td>0</td>
</tr>
<tr>
<td>Neurological dysfunction other†</td>
<td>2 (4)</td>
<td>2</td>
</tr>
<tr>
<td>Device thrombosis</td>
<td>0 (0)</td>
<td>0</td>
</tr>
<tr>
<td>Device malfunction</td>
<td>0 (0)</td>
<td>0</td>
</tr>
<tr>
<td>Hemolysis</td>
<td>0 (0)</td>
<td>0</td>
</tr>
<tr>
<td>Psychiatric episode</td>
<td>1 (2)</td>
<td>1</td>
</tr>
<tr>
<td>Renal dysfunction</td>
<td>5 (10)</td>
<td>5</td>
</tr>
<tr>
<td>Hepatic dysfunction</td>
<td>1 (2)</td>
<td>1</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>7 (14)</td>
<td>7</td>
</tr>
<tr>
<td>Right heart failure</td>
<td>4 (8)</td>
<td>4</td>
</tr>
<tr>
<td>Requiring RVAD</td>
<td>2 (4)</td>
<td>2</td>
</tr>
<tr>
<td>Wound dehiscence</td>
<td>2 (4)</td>
<td>2</td>
</tr>
<tr>
<td>Other event†</td>
<td>13 (36)</td>
<td>35</td>
</tr>
</tbody>
</table>

Values are n (%). *Includes 3 procedural-related events: 1 implant issue (difficulty engaging inflow conduit), 1 following anaphylactic shock from contrast media, and 1 following transcatheter aortic valve implantation procedure. †Includes (n = 2) and transient ischemic attack (n = 2). Other adverse events include pleural effusion (n = 1), volume status (n = 5), high/low INR (n = 7), and various (n = 10).

GI = gastrointestinal; RVAD = right ventricular assist device.

Score paired by individual patients improved from 50 at baseline to 70 at 3 months and 75 at 6 months (p < 0.0001).

**DISCUSSION**

This first clinical study with this new centrifugal-flow chronic LVAS has successfully demonstrated the safety and performance of this device in an advanced HF population (Central Illustration), including patients requiring BTT or DT under a single set of entry criteria. Survival rates of 98% at 30 days and 92% at 6 months compare well with the reported survival in prior studies involving BTT or DT indications (1,3,21-31). Additionally, compared with an SHFM-predicted 6-month survival of 78%, support with this new device was associated with a mortality risk reduction of 66%. Patients had marked impairment of functional status and QOL at baseline; both showed significant, progressive, and sustained improvement over time. The device performed as intended, without pump malfunctions requiring pump exchanges, pump thrombosis, or hemolysis. The adverse event types and rates are consistent with expected complications in the advanced HF population.

The most frequent adverse event following LVAS implantation, bleeding, varies by patient-defined variables such as age, sex, body mass index, and etiology of HF (32). The risk of bleeding during LVAS support is also dependent on device- and procedure-related variables, including the extent of surgery for implantation, reactions at the blood-biomaterial interface, and the amount of damage to blood components by shear stress. Reported bleeding rates vary greatly due to differences in definitions and methods, but approximately 60% of all patients implanted with an LVAS experience surgical, gastrointestinal, or other bleeding events during support, with incidence of bleeding peaking within the first 3 months post-implant (33). Early post-operative bleeding requiring reoperation and transfusion has been reported as one of the most common adverse events in previous LVAS studies (22,28,30). Overall bleeding frequency and need for reoperation due to bleeding in this study is considerably less than reported in prior BTT and DT studies (22,23,30,34).

Placement of the Full MagLev LVAS in the thorax eliminates the need to surgically create an abdominal pocket, thereby reducing the amount of surgery required. The wide blood-flow gaps within the rotor, which are 20 times greater than similar devices, might contribute to lower shear stress to minimize hemolysis, platelet activation, and damage to the vWF. Although vWF preservation was not directly evaluated
in this study, the rate of gastrointestinal bleeding we observed (8%) was lower than the 11% to 25% reported for other devices (28,34,35). Reoperations with multiple blood transfusions and prolonged time in intensive care are major contributing factors to the development of infections, a leading cause of morbidity and mortality of LVAS-supported patients. Total infection rates have been as high as 50%, with device-related infection (mostly of the driveline exit site) seen in approximately 20% of patients (1,22,30). The overall infection rate in this study was 36%, with only 10% of patients having a driveline infection. Drivelines were externalized through circular incisions with the same diameter as the driveline, and the silicone portion of the driveline was positioned to be the interface with the subcutaneous tissue, a practice known to help reduce site infection (36). Elimination of the abdominal pump pocket and low bleeding rates, particularly events requiring surgery and transfusion, as well as improved techniques for driveline externalization may have contributed to the low observed rate of infection.

Complete LV unloading during continuous-flow LVAS support often results in constant closure of the aortic valve, with eventual valve commissure fusion and/or aortic insufficiency (37,38). Varying the LV volume and pressure with the artificial pulse mode should facilitate intermittent aortic valve movement to avoid fusion and insufficiency. The effects of the artificial pulse mode could not be assessed due to the short follow-up time.

Stroke occurs in approximately 7% to 15% of patients undergoing long-term LVAS support (3,28). With an overall lower adverse event rate, particularly bleeding and infection, and the absence of hemolysis and pump thrombosis, the 12% stroke rate (8% debilitating stroke) observed in this study was higher than expected. However, one-half (n = 3) of the events appear to be related to an implant procedure issue or other procedures and may not represent recurring risk. A longer follow-up duration and larger future clinical studies with this Full MagLev LVAS will provide an opportunity to better evaluate the frequency of adverse events observed in this study.

Adverse events associated with LVAS support, along with limitations in daily activities due to external drivelines and power supplies, require these patients to make personal adjustments due to their use of this technology. However, with this new LVAS, significant improvement was observed in both functional capacity and QOL in patients with advanced HF, similar to that achieved by other LVASs (28,34).

**STUDY LIMITATIONS.** The main limitation of this study was its lack of randomization and controls. Due to the inclusion of all patients meeting the criteria for advanced HF and without delineation by indication (BTT or DT), direct comparison to other contemporary LVAS studies cannot be done. However, the use of INTERMACS data from the earlier-generation device patients to establish the performance goal was applicable because these patients were supported for both BTT and DT. Although all centers participating in this
study are experienced with LVAS technology and HF care, differences in surgical technique and medical management may exist. The follow-up time presented in this report was short; however, patients will be followed until outcome or 24 months, and a separate randomized clinical trial is ongoing in the United States.

CONCLUSIONS

The first human experience with the new HeartMate 3 LVAS has demonstrated that the pump performs as designed and is safe in an advanced HF population that included a mix of both BTT and permanent-support patients under a single set of study entry criteria. Adequate circulatory support without pump malfunctions requiring pump exchanges, and the absence of pump thrombosis or hemolysis demonstrated device performance. Survival rates at 30 days and 6 months were high, with a favorable adverse event profile. Patient functional status and QOL showed progressive and sustained improvement over time.

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CENTRAL ILLUSTRATION Support With Magnetically Levitated LVAS: HeartMate 3 CE Mark Trial Results Summary

In 50 patients placed on the fully magnetically levitated pump left ventricular assist system (LVAS), use of the system reduced mortality risk and improved functional capacity and quality of life. Although there were no instances of pump failure, thrombosis, or hemolysis, key adverse events including bleeding, infection, and stroke did occur; 14% of patients required reoperation for bleeding. BTT = bridge to transplant; DT = destination therapy; PG = performance goal; SHFM = Seattle Heart Failure Model.

PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Mechanical LVAS are associated with substantial survival benefit compared with medical therapy in patients with end-stage HF, but complications related to hemocompatibility currently limit broader utilization.

TRANSLATIONAL OUTLOOK: Additional research is needed to determine whether LVAS with magnetically levitated rotors will reduce the risks of thromboembolism, bleeding, and structural deterioration of the aortic valve.
REFERENCES


KEY WORDS HeartMate 3, hemolysis, pump, quality of life, thrombosis

APPENDIX For an expanded Methods section, please see the online version of this article.