HEARTMATE 3™ LVAD THERAPY FOR ADVANCED HEART FAILURE **PUBLICATIONS REVIEW**

Select publications reviewing earlier patient identification for advanced heart failure therapies and LVAD therapy

Heart failure is a complex, progressive disease with an alarming increase in mortality rate.[1,2] It has become increasingly important to recognize when heart failure is progressing to advanced stages refractory to medications and to understand the early triggers for referral to a heart failure specialist for advanced treatment options. Earlier referral for evaluation and close follow-up by an advanced heart failure cardiologist can ensure appropriate timing for advanced therapies and avoid missed opportunities for patients to be considered for all available treatment options.

With the increase in heart failure deaths, ineffective medications for NYHA class IV heart failure, and limited availability of heart transplants, the role of LVAD therapy as a long-term treatment option for advanced heart failure is more important than ever to address the clinical gap.

Significant clinical advancements with HeartMate 3™ LVAD therapy support it as an important option to help more patients with advanced heart failure live longer with improved quality of life.[4,5,9] The centrifugal-flow LVAD with magnetic levitation has become the dominant technology, providing long-term survival similar to heart transplantation* and supporting 'Destination Therapy' (or lifelong support) as the most common LVAD implant strategy.[4,7,8]

LEARN MORE ABOUT THE FOLLOWING:

- Heart failure progression and clinical trajectory
- Advancements in LVAD clinical outcomes with the HeartMate 3 LVAD
- LVAD therapy vs. medical management in NYHA class IV advanced heart failure patients

*82% 2-year survival for adult heart transplant patients between 2009 and 2015.[13]

Based on published data from multicenter experience and separate studies, which may involve different patient populations and other variables. Not a head-to-head comparison. Data presented for informational purposes only.

HEART FAILURE PROGRESSION AND CLINICAL TRAJECTORY

Heart failure is a progressive, non-linear disease that can result in sudden patient decline.[2] With a substantially increasing number of deaths associated with heart failure, innovative and effective approaches to treating heart failure are needed.[1] Attention to heart failure clinical trajectory, earlier patient communications for shared decision-making and timely decisions for referral for advanced therapies can help optimize outcomes and treatment opportunities. The Advanced College of Cardiology (ACC) has published an expert consensus on I-NEED-HELP clinical triggers to assist in timely referrals to an advanced heart failure specialist.[3]

Article summaries are taken verbatim from the source articles. Abbott made minor changes only to remove references to other components of the source articles (e.g., reference or supplement numbers) that are not relevant to the content included in this clinical compendium.

ASSOCIATION BETWEEN AGING OF THE US POPULATION AND HEART DISEASE MORTALITY FROM 2011 TO 2017

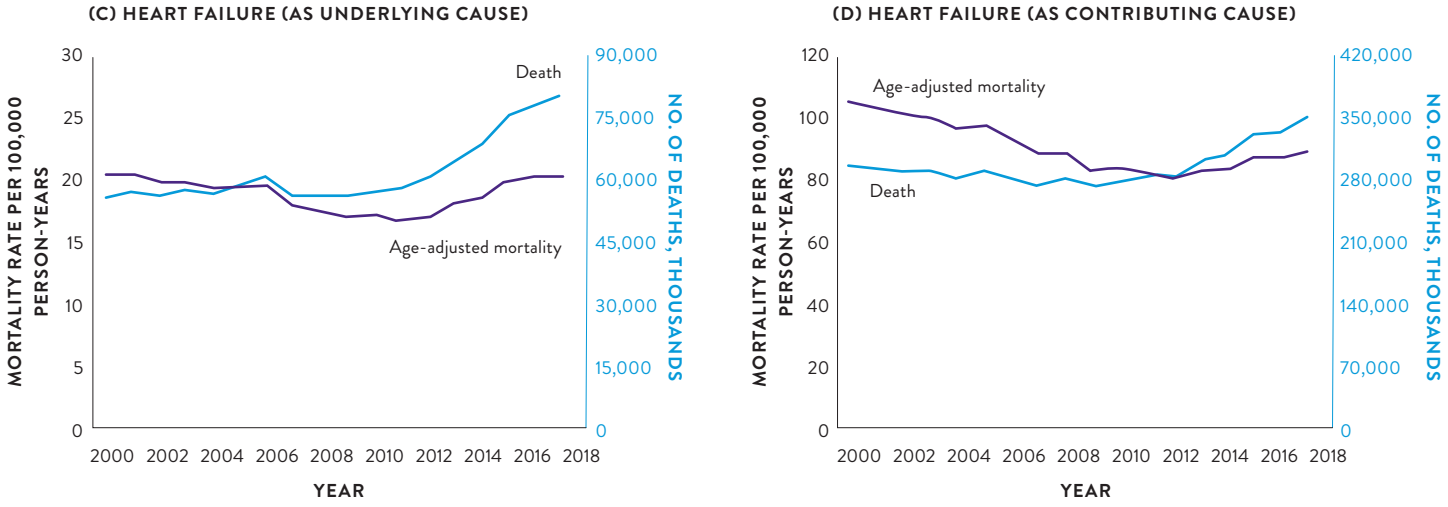
Sidney S, et al. *JAMA Cardiology*. December 1, 2019;4(12): 1280-1286.[1]

- In this quality improvement study, the Centers for Disease Control and Prevention Wide-Ranging Online Data for Epidemiologic Research (CDC WONDER) data set was used to identify national changes in the US population aged 65 years and older and in the age-adjusted mortality rates and number of deaths that were listed with an underlying cause of HD, coronary heart disease (CHD), heart failure, and other HDs from January 1, 2011, to December 31, 2017.
- Overall, the number of deaths increased by 8.5% for heart disease and 38.0% for heart failure, most of which were in the 65 years and older age group.
- With the population of adults aged 65 years and older projected to increase an additional 44% from 2017 to 2030, innovative and effective approaches to prevent and treat heart disease are needed.

CONCLUSIONS:

The substantial increase in the growth rate of the group of adults aged 65 years and older who have the highest risk of HD was associated with an increase in the number of HD deaths in this group despite a slowly declining HD mortality rate in the general population. **With the number of adults aged 65 years and older projected to increase an additional 44% from 2017 to 2030, innovative and effective approaches to prevent and treat HD, particularly the substantially increasing rates of heart failure, are needed.**

Figure. Total Mortality Rates and Number of Deaths, 2000 to 2017



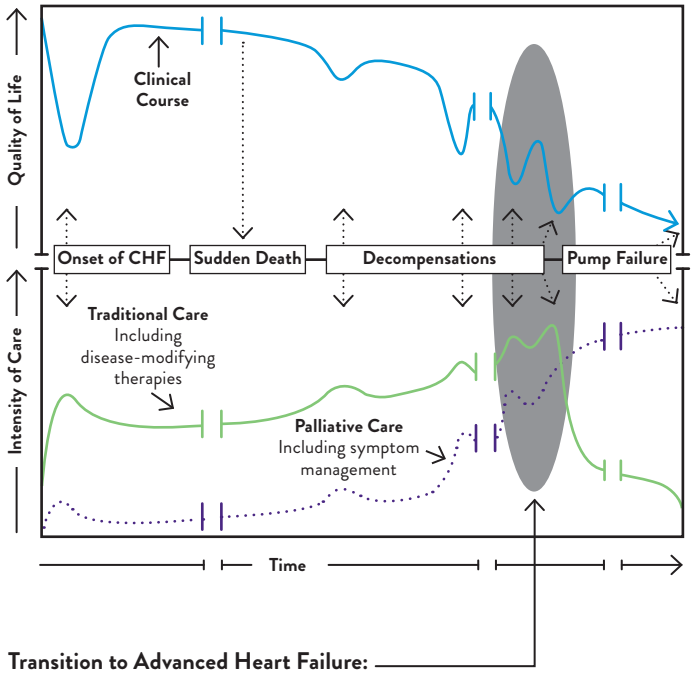
DECISION MAKING IN ADVANCED HEART FAILURE: A SCIENTIFIC STATEMENT FROM THE AMERICAN HEART ASSOCIATION

Endorsed by the Heart Failure Society of America and the American Association of Heart Failure Nurses

Allen LA, et al. *Circulation.* April 17, 2012;125(15):1928-1952.[2]

- Patients tend to follow a progressive, albeit nonlinear, decline in health-related quality of life as the disease progresses; this course can be interrupted by sudden cardiac death caused by arrhythmia or can end in a more gradual death caused by progressive pump failure.

Figure 1. Transition to Advanced Heart Failure



Transition to Advanced Heart Failure:

- Oral therapies failing
- A time for many major decisions
- Consider MCS and/or transplantation, if eligible
- Consider inversion of care plan to one dominated by a palliative approach, which may involve formal hospice

Table 1. Top Ten Things to Know

1	Shared decision making is the process through which clinicians and patients share information with each other and work toward decisions about treatment chosen from medically reasonable options that are aligned with the patients' values, goals, and preferences.
2	For patients with advanced heart failure, shared decision making has become both more challenging and more crucial as duration of disease and treatment options have increased.
3	**Difficult discussions now will simplify difficult decisions in the future.**
4	Ideally, shared decision making is an iterative process that evolves over time as a patient's disease and quality of life change.
5	**Attention to the clinical trajectory is required to calibrate expectations and guide timely decisions, but prognostic uncertainty is inevitable and should be included in discussions with patients and caregivers.**
6	**An annual heart failure review with patients should include discussion of current and potential therapies for both anticipated and unanticipated events.**
7	Discussions should include outcomes beyond survival, including major adverse events, symptom burden, functional limitations, loss of independence, quality of life, and obligations for caregivers.
8	As the end of life is anticipated, clinicians should take responsibility for initiating the development of a comprehensive plan for end-of-life care consistent with patient values, preferences, and goals.
9	Assessing and integrating emotional readiness of the patient and family is vital to effective communication.
10	Changes in organizational and reimbursement structures are essential to promote high-quality decision making and delivery of patient-centered health care.

CONCLUSIONS:

The importance of shared decision making in advanced heart failure cannot be overstated given the complex myriad of treatment options that confront patients, families, and caregivers. We have offered a roadmap for when and how to have conversations with patients to support shared decision making. This process must occur in the context of uncertainties in prognosis, multiple and often competing outcomes, and barriers to communication. Although the promotion of shared decision making may seem daunting to busy practicing clinicians, we have attempted to provide guiding principles and simple tools that can help set future expectations, anticipate major decisions, and promote productive conversations. Our statement is a "call to action," not only to clinicians within our community directly responsible for facilitating shared decision making but also to those on a national level who would reform and restructure the healthcare medical system to truly support patient-centered care.

2021 UPDATE TO THE 2017 ACC EXPERT CONSENSUS DECISION PATHWAY FOR OPTIMIZATION OF HEART FAILURE TREATMENT: ANSWERS TO 10 PIVOTAL ISSUES ABOUT HEART FAILURE WITH REDUCED EJECTION FRACTION: A REPORT OF THE AMERICAN COLLEGE OF CARDIOLOGY SOLUTION SET OVERSIGHT COMMITTEE

Maddox TM, et al. *Journal of the American College of Cardiology*. February 16, 2021;77(6):772-810.[3]

- The 2017 ACC Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment was created to provide a practical, streamlined resource for clinicians managing patients with heart failure with reduced ejection fraction (HFrEF).
- Appropriate and timely referral to an HF specialist and/or HF program is essential in selected patients to optimize therapies and evaluate advanced HF care options.
- Referrals should be made for consultation and, if indicated, for comanagement as well as consideration of advanced therapies (heart transplantation or mechanical circulatory support), recognition and management of specific or unusual cardiomyopathies, or annual review.
- High-risk features (conveniently summarized by the acronym "I NEED HELP" in Figure 4 [...]) should trigger consideration for referral for an advanced HF consultation.

Excerpt from **Figure 4.** Testing and Medication Titration Following Diagnosis of HFrEF

Remember acronym to assist in decision-making for referral to advanced heart failure specialist:

I-NEED-HELP

I	IV inotropes
N	NYHA IIIB/IV or persistently elevated natriuretic peptides
E	End-organ dysfunction
E	Ejection fraction ≤35%
D	Defibrillator shocks
H	Hospitalizations >1
E	Edema despite escalating diuretics
L	Low blood pressure, high heart rate
P	Prognostic medication: progressive intolerance or down-titration of GDMT

ADVANCEMENTS IN LVAD CLINICAL OUTCOMES WITH THE HEARTMATE 3™ LVAD

The HeartMate 3™ LVAD with Full MagLev™ Flow Technology has significantly improved long-term patient outcomes with 'Destination Therapy' (or lifelong support) becoming the most common LVAD implant strategy.[4,5,7-9] Excellent 2-year survival similar to heart transplantation* has been consistently reported in the MOMENTUM 3 randomized controlled trial and Intermacs‡ real-world registry.[4,5,8] Adverse events have also been significantly reduced, with pump thrombosis nearly eliminated, fewer hospitalizations, and stroke rates and GI bleeding lower than ever.[4,5,9]

*82% 2-year survival for adult heart transplant patients between 2009 and 2015.[13]

Based on published data from multicenter experience and separate studies, which may involve different patient populations and other variables. Not a head-to-head comparison. Data presented for informational purposes only

Article summaries are taken verbatim from the source articles. Abbott made minor changes only to remove references to other components of the source articles (e.g., reference or supplement numbers) that are not relevant to the content included in this clinical compendium.

MOMENTUM 3 TRIAL (CAP STUDY PHASE)

PRIMARY RESULTS OF LONG-TERM OUTCOMES IN THE MOMENTUM 3 PIVOTAL TRIAL AND CONTINUED ACCESS PROTOCOL STUDY PHASE: A STUDY OF 2200 HEARTMATE 3 LEFT VENTRICULAR ASSIST DEVICE IMPLANTS

Mehra MR, et al. *European Journal of Heart Failure*. Advance online publication.[4]

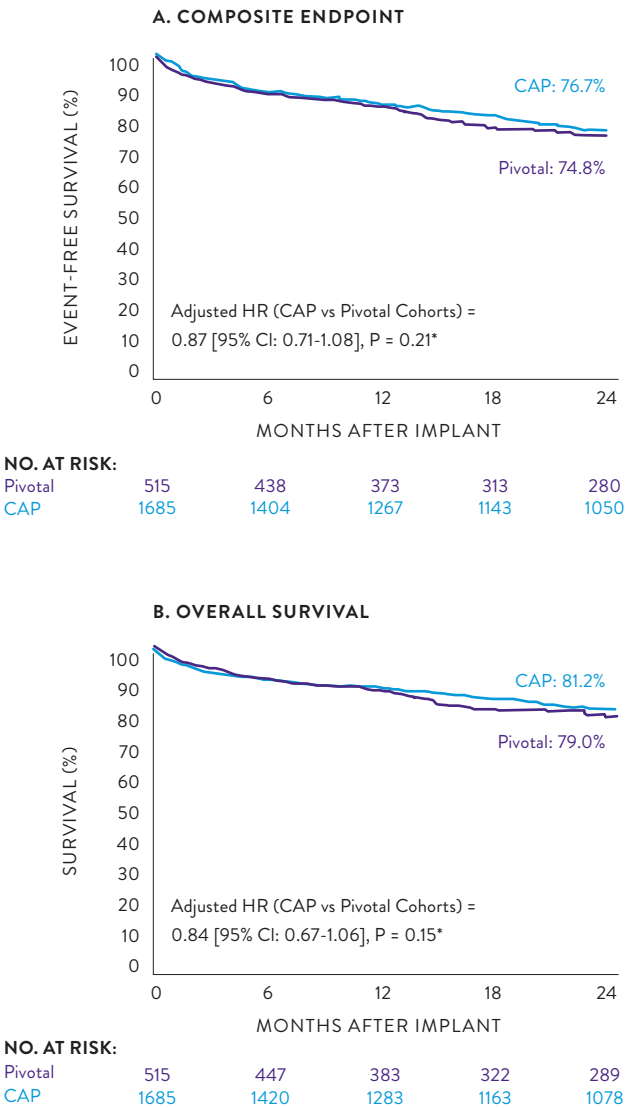
- We now evaluate HM3 LVAD outcomes in a single-arm prospective continuous access protocol (CAP) post-pivotal trial study ... We enrolled 2200 HM3 implanted patients (515 pivotal trial and 1685 CAP patients) and compared outcomes including survival free of disabling stroke or reoperation to replace or remove a malfunctioning device (primary composite endpoint), overall survival and major adverse events at 2-years.
- In this primary results report of the MOMENTUM 3 trial portfolio including the Pivotal and CAP phase, we present the principal 2-year clinical outcomes in the largest reported prospective series of 2200 consecutively enrolled patients implanted with the HM3 LVAD. The main findings include the following:
  1. Survival with the HM3 LVAD approaches or exceeds 80% at 2 years, irrespective of clinical severity of advanced heart failure at the time of pump implantation,
  2. Outcomes by intended goal of implant based on transplant ineligibility (BTT/BTC or DT) are similar between the Pivotal and CAP Cohorts, and specifically, survival of transplant ineligible patients is comparable to that reported with heart transplantation,
  3. Evidence of improving clinical experience is noted by a lower "net-burden" of adverse events in the post-pivotal trial cohort, principally driven by non-hemocompatibility related events, such as infection,
  4. All-cause hospitalizations are fewer in the CAP Cohort.

CONCLUSIONS:

The primary results of accumulating HM3 LVAD experience suggest a lower adverse event burden and similar survival compared to the pivotal MOMENTUM 3 trial.

Figure 1. Composite Endpoint and Overall Survival

Comparison of **(A)** survival free of disabling stroke of reoperation to replace or remove a malfunctioning pump and **(B)** overall survival between Pivotal and CAP Cohorts.



HM3 LVAD = HeartMate 3™ LVAD
BTC = bridge to candidacy
BTT = bridge to transplantation
DT = destination therapy

*Adjusted hazard ratio and P value are calculated with Cox regression. Hazard ratio is presented for CAP vs Pivotal Cohorts and adjusted for age, sex, race (Caucasian, non-Caucasian), intended use (BTT/BTC, DT), and INTERMACS profile (1-3, 4-7). CAP, Continued Access Protocol; CI, confidence interval; HR, hazard ratio.

MOMENTUM 3 TRIAL (FULL COHORT)

A FULLY MAGNETICALLY LEVITATED LEFT VENTRICULAR ASSIST DEVICE — FINAL REPORT

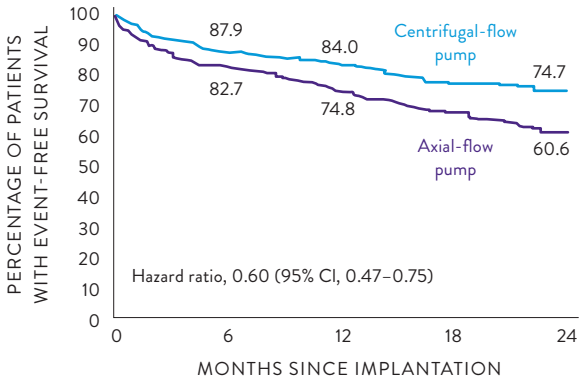
Mehra MR, et al. *New England Journal of Medicine*. April 25, 2019;380(17):1618-1627.[5]

- In the Multicenter Study of MagLev Technology in Patients Undergoing Mechanical Circulatory Support Therapy with HeartMate 3 (MOMENTUM 3), the HeartMate 3 centrifugal-flow left ventricular assist device was compared with the HeartMate II axial-flow device, either as a bridge to transplantation or as destination therapy, in 1028 patients with advanced-stage heart failure.
- The Kaplan–Meier estimates of actuarial event-free survival at 2 years (primary end point) in the intention-to-treat population were 74.7% in the centrifugal-flow pump group and 60.6% in the axial-flow pump group (Fig. 1).*
- In addition to reducing the need for pump replacement (mostly for pump thrombosis), the centrifugal-flow pump was associated with a lower incidence of either ischemic or hemorrhagic strokes of any severity and fewer bleeding events.
- In this final analysis involving the full trial population, we noted that the centrifugal pump was associated with lower rates of bleeding, including gastrointestinal bleeding, which is linked with the unique physiological features of continuous-flow left ventricular assist devices.

CONCLUSIONS:

Among patients with advanced heart failure, a fully magnetically levitated centrifugal-flow left ventricular assist device was associated with less frequent need for pump replacement than an axial-flow device and was superior with respect to survival free of disabling stroke or reoperation to replace or remove a malfunctioning device.

Figure 1. Kaplan–Meier Estimates of the Primary End Point in the Intention-to-Treat Population

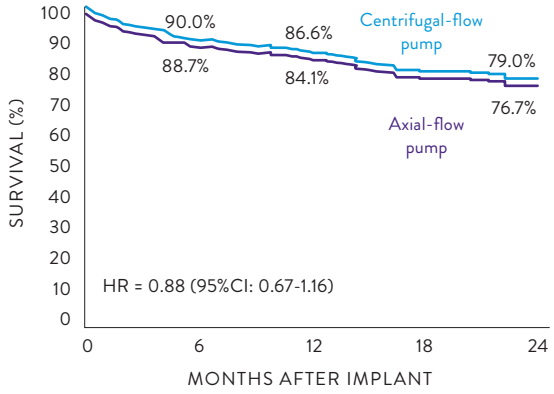


NO. AT RISK:

Centrifugal-flow pump	516	438	373	313	280
Axial-flow pump	512	401	321	264	223

Figure S3. Actuarial Overall Survival (Per Protocol Population)

Source: Supplementary Appendix



NO. AT RISK:

Centrifugal-flow pump	515	447	383	322	289
Axial-flow pump	505	414	339	285	248

*Abbott note: Actuarial overall survival at 2 years per protocol population was 79.0% with the centrifugal-flow pump (Figure S3, Supplementary Appendix).

Centrifugal-flow pump = HeartMate 3™ LVAD
Axial-flow pump = HeartMate II™ LVAD

MOMENTUM 3 TRIAL (SUB-ANALYSIS)

ASSOCIATION OF CLINICAL OUTCOMES WITH LEFT VENTRICULAR ASSIST DEVICE USE BY BRIDGE TO TRANSPLANT OR DESTINATION THERAPY INTENT: THE MULTICENTER STUDY OF MAGLEV TECHNOLOGY IN PATIENTS UNDERGOING MECHANICAL CIRCULATORY SUPPORT THERAPY WITH HEARTMATE 3 (MOMENTUM 3) RANDOMIZED CLINICAL TRIAL

Goldstein DJ, et al. *JAMA Cardiology*. April 1, 2020;5(4):411-419.[6]

- The principal findings of this prespecified analysis of the MOMENTUM 3 trial demonstrate the superiority of the HM3 pump over the HMII LVAD for survival free of a disabling stroke or reoperation to replace or remove a malfunctioning device in either patients who are transplant eligible (or candidates likely to become transplant eligible) or those deemed ineligible by the treating clinician at the time of enrollment.
- The absolute benefit of the HM3 pump was not altered by the intended goal of therapy.
- An equally important observation from this analysis pertains to the fact that the initial intended goal of therapy is not static, as has been observed by other researchers, since nearly 15% of those initially deemed transplant ineligible were eventually transplanted within 2 years of follow-up.
- Of the patients who received HM3 devices, 86 of 198 patients (43.4%) deemed BTT/BTC prior to implant continued to remain on LVAD support at 2 years.*
- Survival was not different between pumps for patients in the BTT/BTC group (HR, 0.93 [95% CI, 0.55-1.59]) or patients in the DT group (HR, 0.87 [95% CI, 0.63-1.20]) (eFigure 2).

CONCLUSIONS AND RELEVANCE:

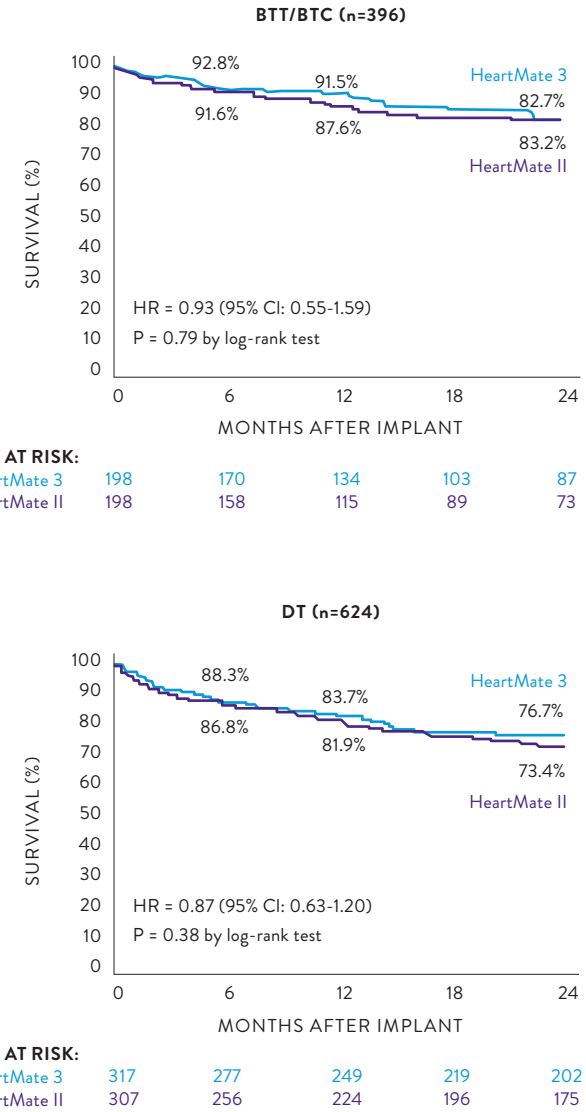
In this trial, the superior treatment effect of HM3 over HMII was similar for patients in the BTT/BTC or DT groups. It is possible that use of arbitrary categorizations based on current or future transplant eligibility should be clinically abandoned in favor of a single preimplant strategy: to extend the survival and improve the quality of life of patients with medically refractory heart failure.

*Abbott note: 40% of BTT/BTC patients were transplanted.

HM3 = HeartMate 3™ LVAD
HMII = HeartMate II™ LVAD
BTC = bridge to candidacy
BTT = bridge to transplantation
DT = destination therapy

eFigure 2. Overall Survival for Patients Receiving the HeartMate 3 and HeartMate II, Stratified by Intended Use

Source: Supplement 1



STS INTERMACS‡ REGISTRY (2019 ANNUAL REPORT)

THE SOCIETY OF THORACIC SURGEONS INTERMACS 2019 ANNUAL REPORT: THE CHANGING LANDSCAPE OF DEVICES AND INDICATIONS

Teuteberg JJ, et al. *The Annals of Thoracic Surgery.* March 2020;109(3):649-660.[7]

- Primary isolated continuous-flow LVAD implants in The Society of Thoracic Surgeons Intermacs registry from January 2014 through September 2019 were evaluated. Survival and freedom from major adverse events were compared between axial-flow, centrifugal-flow with hybrid levitation (CF-HL), and centrifugal-flow with full magnetic levitation (CF-FML) devices.
- Survival at 1-year was significantly higher for CF-FML devices than for CF-HL devices (87% vs 79%, P < .001). For those whose LVAD was implanted as BTT, there was no difference in 1-year survival between the 2 devices, but for DT recipients, the CF-FML devices had significantly higher 1-year survival.
- Freedom from GI bleeding, stroke, major infection, and right heart failure were significantly higher for CF-FML than CF-HL devices for the population who underwent implantation from August 23, 2017, to December 31, 2018.
- As a consequence of the change in the allocation system and reduction of BTT, and to a lesser extent BTC, the field has moved toward DT as the predominant preimplant strategy.

CONCLUSIONS:

Over the past 5 years, centrifugal-flow LVADs have become the dominant technology and DT the most common implant strategy. While outcomes with CF-FML devices are promising, comparisons with other devices from nonrandomized registry studies should be made with caution.

Axial-flow device = HeartMate II™ LVAD
CF-FML device = HeartMate 3™ LVAD
CF-HL device = HVAD‡ LVAD
BTC = bridge to candidacy
BTT = bridge to transplantation
DT = destination therapy

STS INTERMACS‡ REGISTRY (2020 ANNUAL REPORT)

THE SOCIETY OF THORACIC SURGEONS INTERMACS 2020 ANNUAL REPORT

Molina EJ, et al. *The Annals of Thoracic Surgery*. March 2021;111(3):778-792.[8]

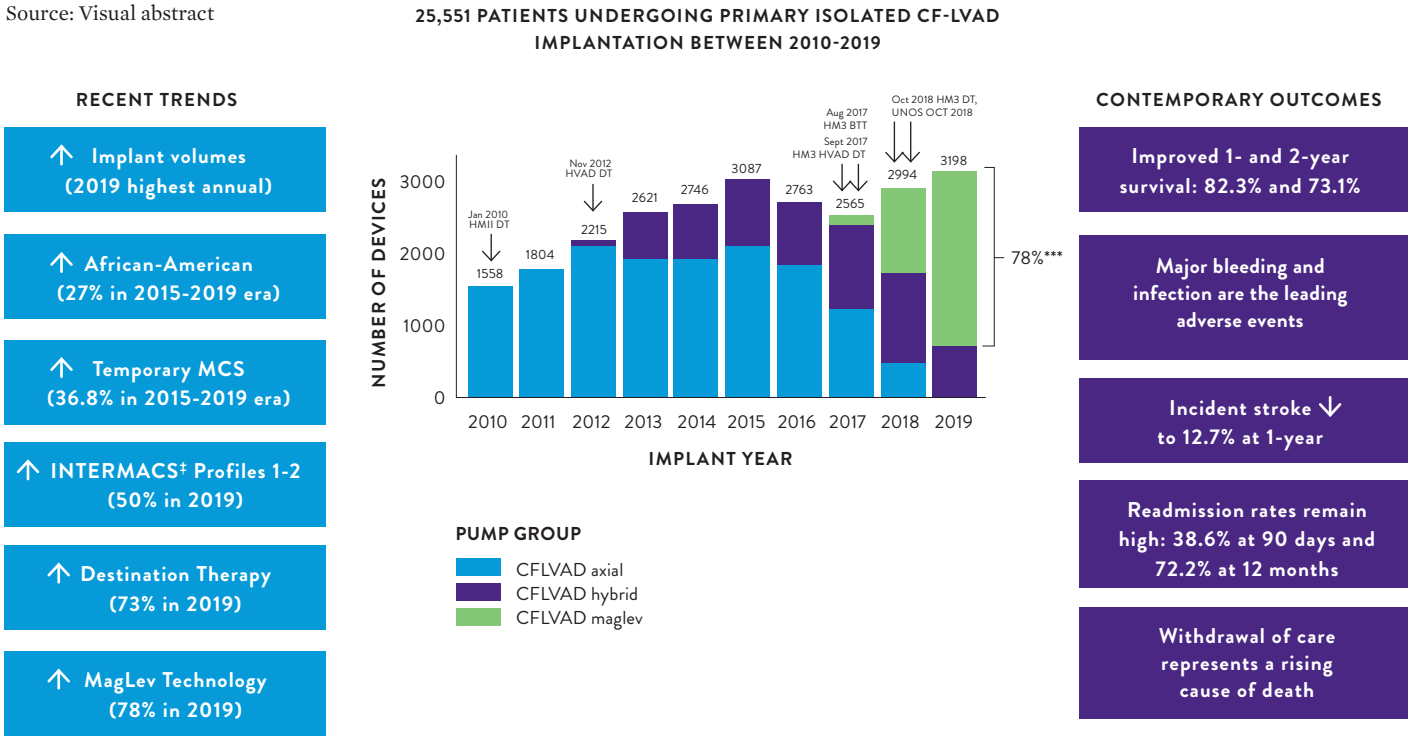
- The Society of Thoracic Surgeons (STS)-Interagency Registry for Mechanically Assisted Circulatory Support (Intermacs) 2020 Annual Report reviews outcomes on 25,551 patients undergoing primary isolated continuous-flow left ventricular assist device (LVAD) implantation between 2010 and 2019.
- Magnetic levitation technology has become the predominant design, accounting for 77% of devices in 2019.
- The 1- and 2-year survival in the most recent era has improved compared with 2010 to 2014 (82.3% and 73.1% vs 80.5% and 69.1%, respectively; P < .0001).
- The most recent report has documented the shifting landscape of devices and indications, including the current predominance of centrifugal-flow technology and a shift toward destination therapy (DT) as the main indication for device implantation.*
- Importantly, neurologic dysfunction is no longer the reported leading cause of death.

SUMMARY:

With the evolution of device engineering and improvements in patient selection and care, average** survival in patients designated for permanent support is now approaching 5 years. The highest risk for mortality and complications continues to occur in the first 3 months after device implantation, supporting the need for ongoing event reporting in short-term and longer-term windows of risk. Hospitalization and serious adverse event burdens remain high after CF LVAD, with stroke, infection, multisystem organ failure, and heart failure contributing the greatest attributable risk to mortality. Stroke has historically been the leading cause of long-term mortality after CF LVAD implant. **As the proportion of patients receiving newer-generation pumps increases, we expect to see a gradual improvement in stroke rates as outlined in the 2019 report.** Withdrawal of care has recently become the leading cause of death in this patient population, a finding that warrants further scientific investigation and clarification. The focus of STS-Intermacs in ensuing years will be to define a multifaceted benchmark for LVAD success that underscores major morbidities, patient-reported outcome measures, and truly long-term (eg, 5-year) outcomes.

Figure from visual abstract.

Source: Visual abstract



*Abbott note: 73% of patients received an LVAD as DT.
**Abbott note: Median.
***Abbott note: 78% of LVAD implantation in 2019 was HeartMate 3™ LVAD.

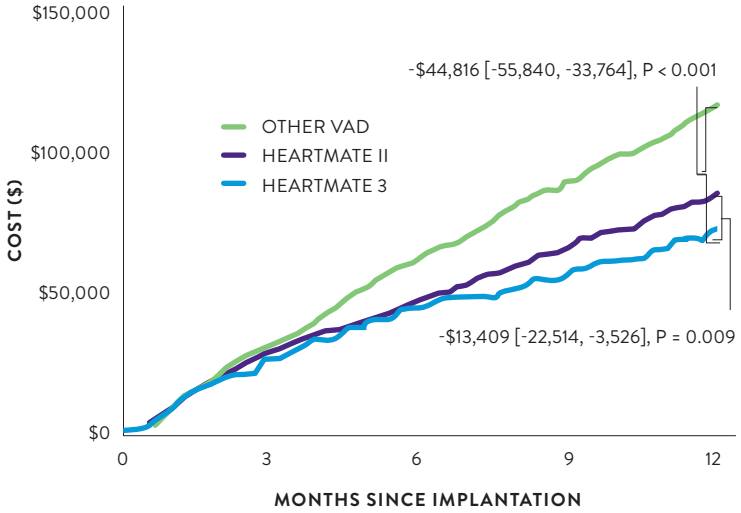
CLEAR-LVAD STUDY

CLINICAL OUTCOMES AND HEALTHCARE EXPENDITURES IN THE REAL WORLD WITH LEFT VENTRICULAR ASSIST DEVICES - THE CLEAR-LVAD STUDY

Pagani FD, et al. *The Journal of Heart and Lung Transplantation*. May 2021;40(5):323-333.[9]

- Using a retrospective observational cohort design, Medicare claims files were linked to manufacturer device registration data to identify de-novo, durable LVAD implants performed between January 2014 and December 2018, with follow-up through December 2019.
- A total of 4,195 de-novo LVAD implants were identified in fee-for-service Medicare beneficiaries (821 HeartMate 3; 1,840 HeartMate II; and 1,534 Other-VADs).
- In a large, real world, United States (U.S.) administrative dataset, we observed the HM3 to have superior survival and lower healthcare expenditures.
- Increasing surgical experience has demonstrated improved outcomes beyond those of the early clinical trials.
- The HM3 LVAD is associated with improved survival and decreased rate of postimplant hospitalizations and days spent in the hospital, when compared to the HMII LVAD, or with other commercially available VADs.

Figure 3 (B). Hospitalization Expenditures Post Discharge Until Death



CONCLUSIONS:

In this analysis of a large, real world, U.S. administrative dataset of durable LVADs, we observed that the HeartMate 3 had superior survival, reduced healthcare resource use, and lower healthcare expenditure compared to other contemporary commercially available LVADs.

HM3 LVAD = HeartMate 3™ LVAD
HMII LVAD = HeartMate II™ LVAD

LVAD THERAPY VS. MEDICAL MANAGEMENT IN NYHA CLASS IV ADVANCED HEART FAILURE PATIENTS

While LVAD therapy is often considered for severe heart failure patients who are in cardiogenic shock or are dependent on continuous IV inotropic therapy, LVAD therapy should also be considered earlier for NYHA class IV heart failure patients for improved survival.[10-12] Despite advances in medications, patients with NYHA Class IV heart failure have low survival. Among ambulatory patients in Intermacs‡ profiles 4 and 5 who are a high risk of progressive worsening heart failure on medical therapy, survival has been shown to be better with LVAD therapy.[10-12] For optimal outcomes and to avoid missed timing opportunities for consideration of all available treatment options, this ambulatory non-inotrope-dependent patient population should be referred as early as possible to an advanced heart failure cardiologist for close follow-up and determination of appropriate timing for advanced therapies.

MEDAMACS REGISTRY

OUTCOMES WITH AMBULATORY ADVANCED HEART FAILURE FROM THE MEDICAL ARM OF MECHANICALLY ASSISTED CIRCULATORY SUPPORT (MEDAMACS) REGISTRY

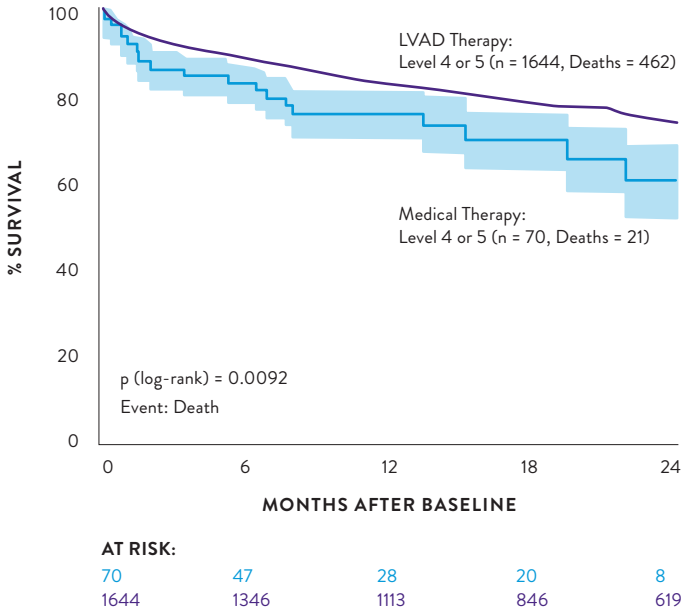
Ambardekar AV, et al. *The Journal of Heart and Lung Transplantation*. April 2019;38(4):408-417.[10]

- The comparison of medical therapy from the 161 patients enrolled in MedaMACS* to LVAD therapy from the 1,753 patients in Profile 4 through 7 enrolled in the INTERMACS registry represents the single largest comparison of medical vs LVAD therapy in ambulatory advanced HF.
- The medical therapy patients who were in Profiles 4 and 5 appeared to be at exceptionally high risk for poor outcomes, and had better survival with LVAD therapy.
- Compared with 1,753 patients with Profiles 4 to 7 receiving LVAD therapy, there was no overall difference in intention-to-treat survival between medical and LVAD therapy, but survival with LVAD therapy was superior to medical therapy among Profile 4 and 5 patients (p = 0.0092).

CONCLUSIONS:

Ambulatory patients with advanced HF are at high risk for poor outcomes, with only 53% alive on medical therapy after 2 years of follow-up. Survival was similar for medical and LVAD therapy in the overall cohort, which included the lower severity Profiles 6 and 7, but survival was better with LVAD therapy among patients in Profiles 4 and 5. Given the poor outcomes in this group of advanced HF patients, timely consideration of transplant and LVAD is of critical importance.

Figure 4 (A). LVAD Therapy and Medical Therapy: Level 4 or 5 Survival[10-12]



*Abbott note: Between May 2013 and October 2015.

STS INTERMACS‡ REGISTRY

INTERMACS (INTERAGENCY REGISTRY FOR MECHANICALLY ASSISTED CIRCULATORY SUPPORT) PROFILING IDENTIFIES AMBULATORY PATIENTS AT HIGH RISK ON MEDICAL THERAPY AFTER HOSPITALIZATIONS FOR HEART FAILURE

Stewart GC, et al. *Circulation: Heart Failure.* November 2016;9(11):e003032.[11]

- The present study represents the largest published cohort of high-risk ambulatory advanced HF patients in INTERMACS profiles 4 to 7 receiving a strategy of oral medical management at VAD/transplant centers. Patients enrolled in this study, each of whom had at least 1 HF hospitalization within the previous year, were not currently receiving MCS for various reasons, including relative contraindications, their own preferences, or their characterization as less sick either by perception or by objective criteria.
- At 1 year, only 47% of this ambulatory advanced HF cohort remained alive on medical therapy. Patients in INTERMACS profile 4 were more likely to die or require mechanical support, with only 52% of these patients alive without support after the first 6 months.
- Lower INTERMACS patient profiles were also associated with a higher risk of death without MCS or transplant. In particular, eligible profile 4 patients should be offered LVAD therapy because continued medical therapy is associated with high event rates and low quality of life.

Table 1. INTERMACS Profile Definitions for Ambulatory Patients on Oral Therapy

PROFILE	SHORTHAND	DEFINITION
4	Resting symptoms	At home on oral therapy but with frequent symptoms of congestion at rest or with any activities of daily living
5	Exertion intolerant	Comfortable at rest but unable to engage in any activity, living predominantly within the house or housebound, but without overt congestion
6	Exertion limited	Comfortable at rest without evidence of fluid overload and able to do some mild activities of daily living, but gets fatigued within a few minutes of any meaningful exertion
7	Advanced NYHA* class III	Clinically stable with a reasonable level of comfortable activity, despite history of previous decompensation that is not recent

INTERMACS indicates Interagency Registry for Mechanically Assisted Circulatory Support.

CONCLUSIONS:

Ambulatory patients with systolic HF, a heavy symptom burden, and at least 1 recent HF hospitalization are at high risk for death or left ventricular assist device rescue. INTERMACS profiles help identify ambulatory patients with advanced HF who may benefit from current mechanical support devices under existing indications.

*Abbott note: This spelling has been corrected from the source article's "NHYA."

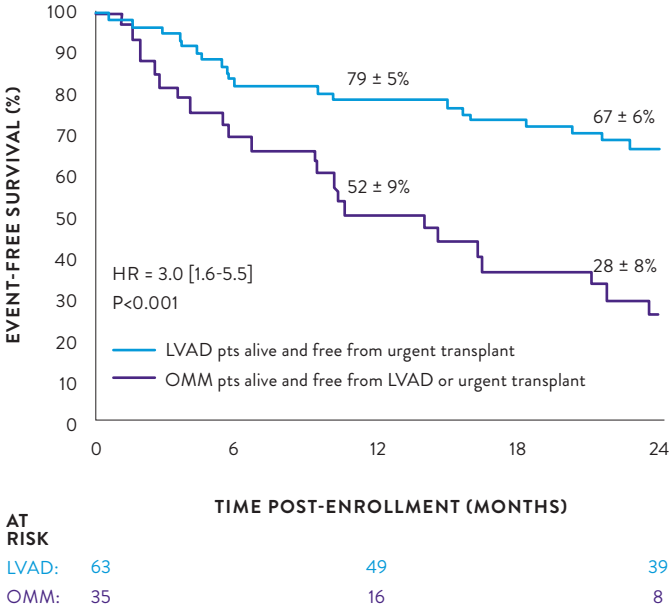
ROADMAP STUDY

LEFT VENTRICULAR ASSIST DEVICES VERSUS MEDICAL MANAGEMENT IN AMBULATORY HEART FAILURE PATIENTS: AN ANALYSIS OF INTERMACS PROFILES 4 AND 5 TO 7 FROM THE ROADMAP STUDY

Shah KB, et al. *The Journal of Heart and Lung Transplantation.* June 2018;37(6):706-714.[12]

- The ROADMAP study showed survival with improved functional status was better with left ventricular assist device (LVAD) therapy compared with optimal medical management (OMM) in ambulatory, non–inotrope-dependent (INTERMACS [IM] Profile 4 to 7) patients.
- Event-free survival on original therapy at 2 years was greater for LVAD than for OMM patients in both IM4 (67% vs 28%; $p < 0.001$) and IM5-7 (76% vs 49%; $p = 0.025$) profile groups.
- When compared with patients who selected medical therapy, patients who received an LVAD were more likely be alive and have an improvement of ≥75 meters in 6-minute walk distance (6MWD) at 12- and 24-month follow-up. In addition, LVAD patients had greater improvement in quality of life, depression and heart failure (HF) symptoms.
- Furthermore, IM4 patients who selected OMM had a high rate of progressive worsening heart failure, whereas only 23% who started on medical management were alive on original therapy at 2 years (40% died, 26% received LVAD, 11% withdrew). The composite AE rates and rehospitalization rates were statistically similar for IM4 patients on LVAD and OMM.

Figure 3 (A). Survival As-treated on Original Therapy in INTERMACS Profile 4 (IM4)



CONCLUSIONS:

LVAD patients in IM4, but not IM5-7, are more likely to meet the primary end-point and have improvements in HRQoL and depression compared with OMM, even with AEs generally being more frequent. **LVAD therapy with current technology may be beneficial in select IM4 patients,** but can be deferred for most IM5-7 patients, who should be followed closely due to the high frequency of treatment failures.

THE VITAL ROLE OF CLINICIANS

MANAGING PATIENTS WITH HEART FAILURE

- Recognize the symptoms of advanced heart failure
- Help patients understand their symptoms and advanced treatment options earlier
- Refer early enough to an advanced heart failure specialist for better outcomes
- Co-manage patients for optimal patient care

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ACRONYM DEFINITIONS

6MWD	6-minute walk distance
ACC	Advanced College of Cardiology
BTC	Bridge to Candidacy
BTT	Bridge to Transplant
CDC WONDER	Centers for Disease Control and Prevention Wide-Ranging Online Data for Epidemiologic Research
CF-FML	centrifugal-flow with full magnetic levitation
CF-HL	centrifugal-flow with hybrid levitation
CHD	coronary heart disease
CMS	Centers for Medicare & Medicaid Services
DT	Destination Therapy
GI	gastrointestinal
HFrEF	heart failure with reduced ejection fraction
HM3	HeartMate 3™ LVAD
HMII	HeartMate II™ LVAD
HRQoL	health-related quality of life
IM	Intermacs‡
IV	intravenous
LVAD	left ventricular assist device
MCS	mechanical circulatory support
NYHA	New York Heart Association
OMM	optimal medical management
VAD	ventricular assist device

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Brief Summary: Prior to using these devices, please review the Instructions for Use for a complete listing of indications, contraindications, warnings, precautions, potential adverse events and directions for use.

HeartMate 3™ LVAS Indications: The HeartMate 3™ Left Ventricular Assist System is indicated for providing short- and long-term mechanical circulatory support (e.g., as bridge to transplant or myocardial recovery, or destination therapy) in adult and pediatric patients with advanced refractory left ventricular heart failure and with an appropriate body surface area.

HeartMate II™ LVAS Indications: The HeartMate II™ Left Ventricular Assist System is indicated for use as a "bridge to transplantation" for cardiac transplant candidates who are at risk of imminent death from non-reversible left ventricle failure. It is also indicated for use in patients with New York Heart Association (NYHA) Class IIIB or IV end-stage left ventricular failure, who have received optimal medical therapy for at least 45 of the last 60 days, and who are not candidates for cardiac transplantation. The HeartMate II Left Ventricular Assist System is intended for use both inside and outside of the hospital, or for transportation of Left Ventricular Assist Device patients via ground ambulance, airplane, or helicopter.

HeartMate 3™ and HeartMate II™ LVAS Contraindications: The HeartMate 3 and HeartMate II Left Ventricular Assist Systems are contraindicated for patients who cannot tolerate, or who are allergic to, anticoagulation therapy.

HeartMate 3™ and HeartMate II™ LVAS Adverse Events: Adverse events that may be associated with the use of the HeartMate 3 or HeartMate II Left Ventricular Assist System are listed below: death, bleeding, cardiac arrhythmia, localized infection, right heart failure, respiratory failure, device malfunctions, driveline infection, renal dysfunction, sepsis, stroke, other neurological event (not stroke-related), hepatic dysfunction, psychiatric episode, venous thromboembolism, hypertension, arterial non-central nervous system (CNS) thromboembolism, pericardial fluid collection, pump pocket or pseudo pocket infection, myocardial infarction, wound dehiscence, hemolysis (not associated with suspected device thrombosis) and possible pump thrombosis.

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