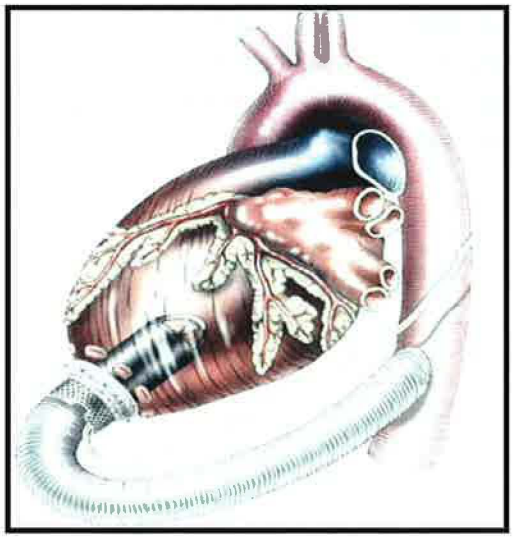
Left Ventricular Assist Device Therapy for Advanced Heart Failure: The End Is The Beginning



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Introduction

Heart failure affects over 5.3 million Americans, resulting in over 1 million hospital discharges and incurring an estimated $39.2 billion in direct and indirect costs in 2009 alone.[1] Heart failure survival has improved over the past two decades with successive introduction of ACE inhibitors, beta blockers, aldosterone antagonists, automated implantable cardioverter-defibrillators, and cardiac resynchronization therapy. Improved survival with CHF and an aging population have resulted in a steady increase in the prevalence of patients with advanced end stage heart failure.

There are approximately 60,000 Americans with end stage heart failure who are refractory to medical therapy.[2] Although cardiac transplantation remains the gold standard for treatment of these patients, it is a scarce option with approximately 2,000 heart transplants performed yearly in the US.[3] This supply-demand mismatch has fueled the development of alternative treatment options including mechanical circulatory support (MCS).

The utilization of left ventricular assist devices (LVADs) has increased over the past two decades given its association with improved survival for transplant and non-transplant candidates. Primary care providers and specialists are having increased exposure to patients supported with LVADs. The purpose of today's grand rounds is to provide an overview of LVAD utilization, patient selection for LVAD therapy and device management.

History of Mechanical Support

The initial application of MCS dates back to the 1930s when experimental surgeon Alexis Carrel and aviator Charles Lindbergh developed a heart perfusion apparatus that successfully externally perfused the thyroid gland of a cat for 18 days.[4] Their results, published in *Science* in 1935, stirred the interest of both researchers and the general public, but unfortunately did not catch on.[5] The initial use of mechanical support was in 1952 when Dr. Forrest Dodrill utilized a mechanical blood pump developed with General Motors to perform a mitral commissurotomy on a 41 year old man during left heart bypass.[6] The machine was utilized as a substitute for the left ventricle for 50 minutes, making it the first clinically successful total left-sided heart bypass. With the addition of an oxygenator for cardiopulmonary bypass, Dr. John Gibbon, in collaboration with IBM, expanded the field by utilizing a heart-lung machine during the repair of a large secundum ASD in 1953.[6] With the growth of open-heart surgery in the 1950s, there became an apparent need for prolonged mechanical support to allow for myocardial recovery in patients who were difficult to wean from cardiopulmonary bypass.[7-10] As a result, the National Heart Institute (predecessor to the NHLBI) established the Artificial Heart Program in 1964 to support further research in short- and long-term circulatory assist devices.[11]

In 1963, Dr. Domingo Liotta and colleagues implanted the first LVAD as acute support in a patient with post-cardiotomy shock.[12] Although the device successfully supported the heart, the patient died four days later from brain damage which occurred during the initial shock.[11] In 1966, the first successful clinical application of a pneumatically driven VAD was utilized in a 37

year old woman who developed heart failure after a mitral and aortic valve replacement. The patient was supported for 10 days until her intrinsic cardiac function recovered. She ultimately became the first long-term survivor of the use of this technology. In 1969, the concept of bridge to transplantation came to fruition, as Dr. Denton Cooley was the first to place an artificial heart in an acutely deteriorating patient, Mr. Haskell Karp, until a heart became available 64 hours later.[13] Although Mr. Karp died soon after heart transplantation, this procedure demonstrated proof-in-concept that mechanical support may be a viable option as a bridge to transplantation.

The failure of cardiac transplantation to provide long term survival in the 1960s and 1970s provided a strong stimulus for the development of LVADs. In 1975, the NHLBI developed the Clinical VAD program and subsequently placed a request for proposal for a pump that could provide support for up to 2 years without external venting.[14] Since the 1980s, the use of MCS has steadily increased. With newer generation devices that are smaller, easier to implant, and more reliable, LVADs have become a viable therapy in transplant candidates and noncandidates with end stage heart failure. To date, over 50,000 LVADs have been implanted (Thoratec and Novacor Registry, 2010).

Device Overview

Although there are multiple devices under use internationally, many have not undergone FDA approval in the US. For purposes of this talk, we will focus on devices evaluated and utilized in the US, particularly the HeartMate VE, HeartMate XVE, and HeartMate II, given that these devices have been utilized at UT Southwestern.

First Generation Devices: Pulsatile Volume Displacement Devices

The first generation VADs are pulsatile volume displacement pumps. They include the Thoratec Paracorporeal and Intracorporeal Ventricular Assist Devices (PVAD/IVAD) (Thoratec, Pleasanton, CA), HeartMate IP/VE/XVE (Thoratec, Pleasanton, CA), and Novacor LVAS (WorldHeart, Oakland, CA). These devices have an internalized pumping chamber and inflow and outflow valves that allow for cyclic filling and emptying (Figure 1). The inflow conduit is inserted in the left ventricular apex and the outflow conduit is placed in the ascending aorta. Most pumps are implanted in a pocket in the left upper quadrant of the abdomen. Pump actuation is supported by either a pneumatic or electrical system that connects to the device through a percutaneous line (drive-line) that is tunneled subcutaneously to exit near the right subcostal margin. In portable electrical devices, these percutaneous wires are connected to a system controller which then connects to either batteries or a power base unit attached to an electrical outlet. The batteries are typically worn on a belt, shoulder bag, or vest.

HeartMate IP/VE/XVE

Until 2008, the HeartMate first generation LVADs were the primary devices utilized at University Hospital/St. Paul for bridge to transplantation and destination therapy. Over the past

15 years, the first generation HeartMate LVAD has transformed from an implantable pneumatic (IP) device to a vented electric (VE) device that was subsequently modified to the XVE.

The pump is made of titanium with a diaphragm and a single pusher-plate actuator.[15] The pusher plate diaphragm mechanically displaces the blood within the chamber either through pneumatic or electrical support. The IP utilizes air to promote displacement of the pusher plate diaphragm. The VE and XVE use an electric motor that rotates and displaces the pusher plates through bearings. Air that is displaced by the diaphragm is "vented" out of the system through the percutaneous driveline. The pump stroke volume is 83 ml and flow is 4-10 L/minute. Pumping may be volume dependent (when 97% of the pump volume is achieved) or fixed at a certain rate. The inflow and outflow conduits have porcine valves. The power is supplied by two external batteries and 300g external controller. Batteries typically last 4-7 hours.

Unlike all other LVADs available currently and in the past, the HeartMate IP/VE/XVE LVAD carries a unique textured inner surface composed of titanium microspheres that allows for support without anticoagulation with warfarin.[16-17] The inner surface promotes formation of a "psuedointimal" layer, composed of collagen, progenitors of fibroblasts, macrophages, and endothelial cells. This layer is resistant to thrombogenesis, allowing management with aspirin alone. The disadvantage of this layer is that it may limit the ability to find an appropriate donor match because this layer is immunologically active.

Because of problems with durability, the VE device underwent multiple modifications and was renamed XVE. Some of the changes include a stronger percutaneous lead to reduce kinking; vent adaptor modification to reduce malfunction; outflow graft "bend relief" to prevent kinking and graft abrasion; increased commissural support of the inflow and outflow valves to prevent dehiscence and valve incompetence; and software changes to decrease stress on the motor, bearings, and diaphragm.

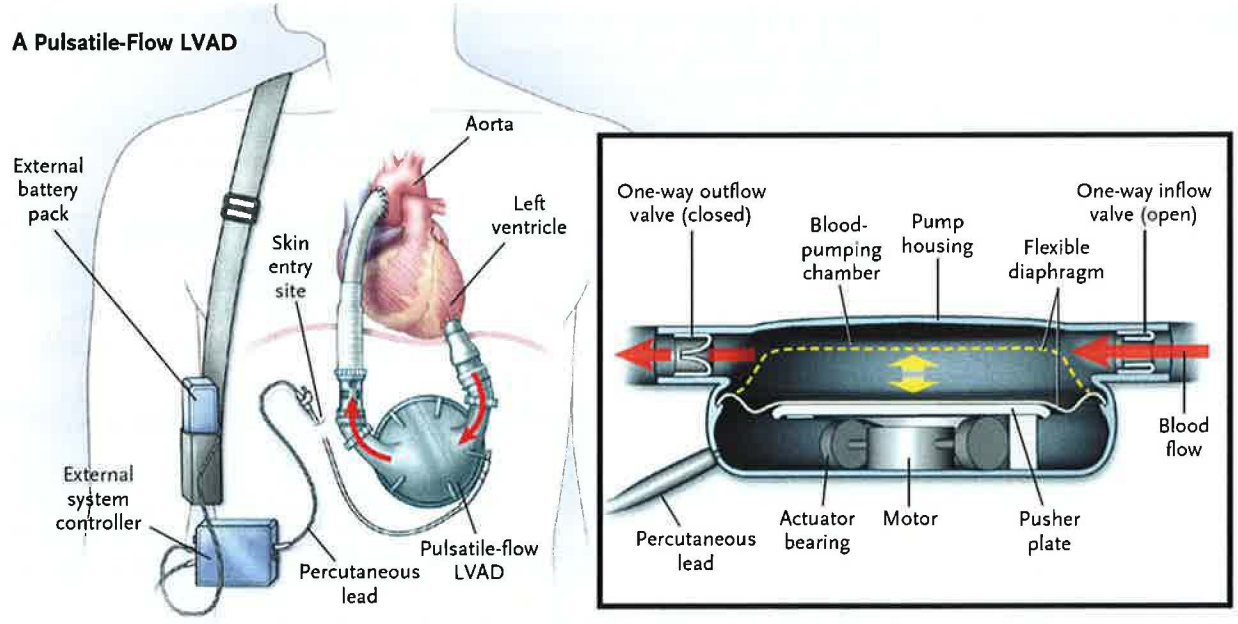


Figure 1: Components of the Pulsatile-Flow Left Ventricular Assist Device[26]

Second Generation Devices: Rotary Assist Devices

The first generation pulsatile devices had multiple design limitations that affected durability and often precluded their practical use for extended mechanical circulatory support (MCS). Primarily, numerous components of the pump contact each other (i.e. the bearings) leading to diminished device longevity. The HeartMate XVE typically lasts only 14-18 months. Other limitations include a large pump size, requirement for extensive surgical dissection within the abdomen, requirement for a BSA ≥ 1.3 mm^2, need for a large-diameter percutaneous lead for venting air, and audible pump operation (Table 1). In addition to these limitations, first generation devices had a high incidence of reoperation for device exchange due to infection or malfunction. These limitations prompted the development of continuous axial flow devices. They include the HeartMate II (Thoratec, Pleasanton, CA), Jarvik 2000 (Jarvik Heart, New York, NY), and Heart Assist 5 (Micromed Cardiovascular, Houston, TX).

Continuous-flow LVADs consist of a pump with a percutaneous drive line that connects to an external system controller and a power source, battery or electrical outlet (Figure 2). The pump is placed to lie parallel to the diaphragm in the subrectus pocket. The outflow conduit is attached to the ascending aorta. The pump provides axial flow, providing continuous unloading of the left ventricle, obviating the need for prosthetic valves. Given axial flow, patients do not have a pulse and only mean arterial blood pressures can be assessed using Doppler. This lack of pulsatility prevents utilization of pulse oximetry to assess oxygen saturations. The axial flow design allows for a significant reduction in size and weight compared to the pulsatile pumps due to the elimination of a blood sac or reservoir needed for the pulsatile systems. These devices are silent during operation.

Table 1. Comparison of Pulsatile and Continuous Flow LVADS[76]

	Pulsatile-flow VAD	Continuous-flow VAD
Size	Large; intracorporeal devices limited to large patients; extracorporeal devices especially suited for smaller patients or for biventricular support	Smaller; accommodates most patients, excluding infants
Blood flow capacity	Up to 10 liters/min	Up to 10 liters/min
Type of pump	Sac or diaphragm	Centrifugal or axial flow by rotating impeller
Implantation	Extracorporeal or intracorporeal types: sub-diaphragmatic intraperitoneal or preperitoneal	Extracorporeal, intracardiac, pericardial, sub-diaphragmatic
Main hemodynamic characteristic	Intermittent unloading of ventricle; pulsatile arterial pressure; asynchronous with heart	Continuous unloading of ventricle
Physiologic flow variables	Preload dependant	Preload and afterload dependant
Mechanical flow variables	Automatic / fixed rate and stroke volume capacity	Set speed of the impeller rotation

HeartMate II (Thoratec, Pleasanton, CA)

Currently, the HeartMate II is the primary pump utilized at University Hospital/St. Paul for bridge to transplantation and destination therapy. The weight of the pump is 350 grams and the size of the pump is 7.0 cm in length and 4 cm in largest diameter.[15] The pump can operate at 6,000-15,000 rpm at flows of up to 10 L/minute. The pump includes an inlet stator (fixed component that forms the pivot or housing for the rotor), a pump rotor (the rotation device that includes impeller blades and pump magnet) and an outlet stator. Electricity moving through the motor winding segment which houses coils creates a spinning magnetic field that drives spinning of the pump magnet. The advantage of this design is that the rotor is the only moving part within the pump, allowing for improved durability. The percutaneous driveline is much smaller than first generation device. Lithium-ion batteries provide 10 hours of support.

Unlike pulsatile pumps which provide exact measurements of cardiac output, the HeartMate II has a flow estimator that estimates output based on a relationship between the pump motor speed (RPM) and time-varying electrical consumption (power). This device also measures a pulsatility index (PI) which is a measure of flow pulse through the pump. The greater the PI, the more intrinsic contractility provided by the heart. This measure may be useful in bridge to recovery.

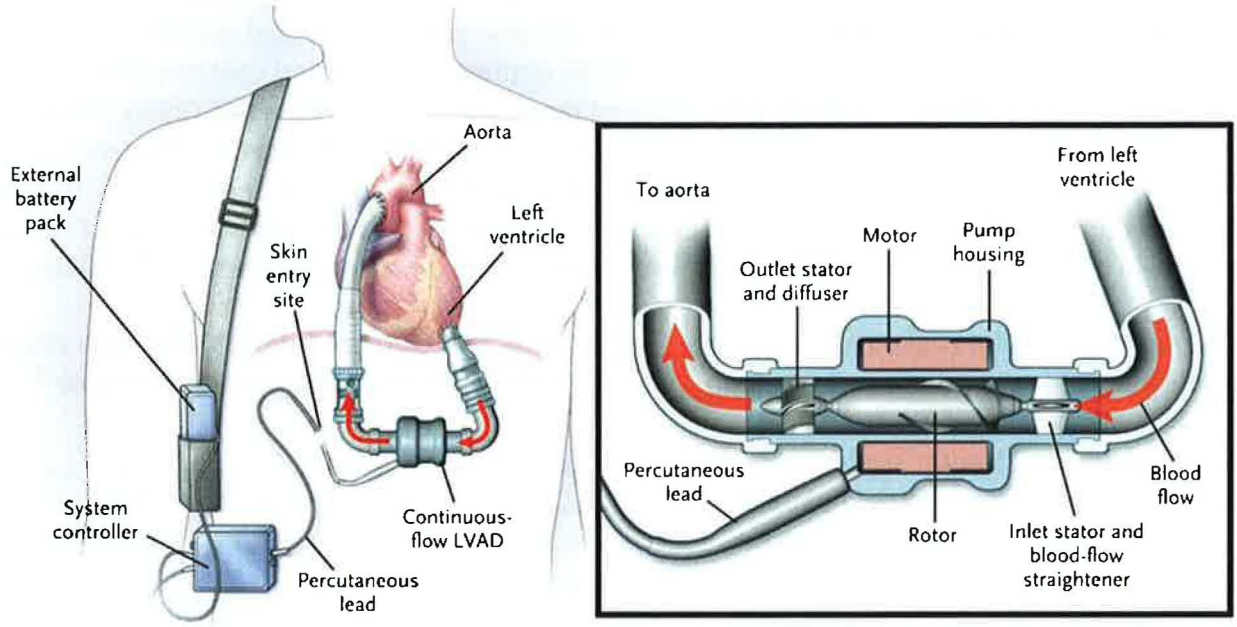


Figure 2: Components of the Continuous-Flow Left Ventricular Assist Device[26]

Clinical Data Supporting Utilization of a Left Ventricular Assist Device

The clinical indications for implementation of MCS with a ventricular assist device have evolved over the past two decades. To date, there are four indications for medium and long-term mechanical support:

1. Bridge to Transplantation (BTT)
2. Destination Therapy (DT)
3. Bridge to Candidacy (BTC)
4. Bridge to Recovery (BR)

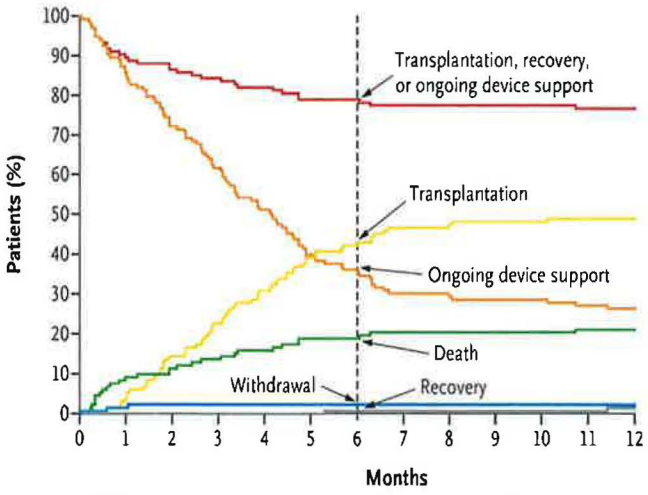
Bridge to Transplantation

Ventricular assist devices can be beneficial for patients with advanced heart failure awaiting cardiac transplant. Benefits include improvement from the deconditioned state, stabilization of renal function, achievement of optimal nutritional status, maintenance of goal levels of physical therapy, and improved hemodynamic parameters prior to transplantation. The proportion of patients undergoing bridge with an LVAD has increased from 3% in 1990 to 35% in 2009.[18]

The first successful cardiac transplant following bridge with an LVAD was in 1984 using the Novacor LVAS.[14] Additional devices immediately followed including the HeartMate IP in 1986. The first IP implantation occurred during one of the first multicenter clinical trials that evaluated the use of these devices as a bridge to transplantation.[19] In this trial 34 patients who were either failing inotropic therapy or on an intra-aortic balloon pump (IABP) underwent implantation of the HeartMate IP. Six controls who were transplant candidates that did not receive the device were included. 65% of the bridged patients underwent transplantation. Of the bridged patients who were transplanted, the one year actuarial survival was 84%. 50% of control patients survived transplantation and 100% of these transplanted controls died within 3 months. Complications for patients who received the device included bleeding (39%), infection (25%) and right heart failure (21%). This study demonstrated that LVAD was an effective tool for supporting end-stage cardiomyopathy patients to transplantation. Due to these results, the FDA initially approved the HeartMate IP for BTT in 1994, leading the way for evaluation and FDA approval of other devices including the Novacor LVAS (1998) and HeartMate VE/XVE (1998).

The first pivotal trial evaluating the safety and efficacy for a continuous-flow pump for BTT was published in 2007.[20] In a prospective, multicenter study without a concurrent control group, 133 patients with end stage heart failure underwent HeartMate II implantation for BTT with a mean duration of support of 168 days. 89% of patients were on inotropes, 11% were intolerant to inotropes and 41% were supported with an IABP. 100 (75%) patients reached the primary endpoint of transplantation, cardiac recovery, or survival with MCS. Of these 100 patients, 56% underwent transplant, 43% continued to receive MCS and were eligible for transplant, and 1% recovered cardiac function (Figure 3).

Figure 3. BTT Outcomes for 133 Patients after Placement of a Continuous-flow Device[20]

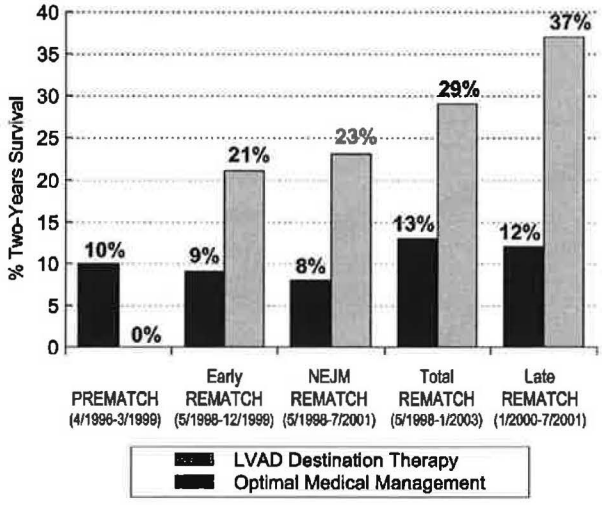


Twenty five patients died before 180 days of support and 5 patients became ineligible for transplantation due to post-operative complications. Overall actuarial survival for patients with MCS was 89% at 1 month, 75% at 6 months, and 68% at 12 months. These values were superior to survival during the pivotal study evaluating pulsatile pump support with the HeartMate VE (53% at 12 months).[21] Morbidity and mortality were greatest early after implantation, supporting the need for improvement in patient selection, timing of LVAD implantation, and surgical placement. There were markedly less deaths during late follow-up (6-18 months) when compared to the HeartMate VE trial suggesting that stroke, infection, and device malfunction were lower with the new design.[22] The causes of death within 180 days included sepsis (5 pts), ischemic stroke (5 pts), multisystem organ failure (4 pts), hemorrhagic stroke (3 pts), anoxic brain injury (2), right heart failure (2), and miscellaneous causes (4). The HeartMate II was approved in April 2008 for outpatient use as a bridge to transplantation.

Destination Therapy

As the durability of the devices improved over the past two decades, the possibility of utilizing LVADs as an alternative to transplantation has become a reality. One of the first trials to evaluate the safety and efficacy of LVAD for DT was REMATCH (Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart failure).[23] In this study, 129 patients with end-stage heart failure who were ineligible for cardiac transplantation were randomized to either the HeartMate XVE (n = 68) or optimal medical therapy (OMT, n = 61). Age was the primary reason for transplant ineligibility with the median age of 67. There was a 48% reduction in the primary endpoint, all-cause mortality at 2 years, in patients receiving LVAD therapy (P = 0.001). The 1 year actuarial survival was significantly greater for the device group (52% vs. 25%, p = 0.002) compared to OMT. However, the survival in both groups was not statistically significant after two years (23% vs. 8%, p = 0.09). The two year survival rates of LVAD recipients were better during the second half compared to the first (37% vs. 23%), but there was no difference in outcomes with medical therapy during the entire study (Figure 4).[24] This suggests that surgical outcomes and LVAD management improved over time as centers developed experience. The improvement in survival was greatest for patients receiving IV inotropic therapy at randomization. Their 1 year mortality was lower with LVAD support (51% vs. 76%, p = 0.001).[25] The two most common causes of death in the VAD group were sepsis and LVAD failure. The probability of infection was 28% at 3 months, bleeding was 42% at 6 months, and device failure 35% at 2 years. HeartMate VE/XVE underwent FDA approval for DT in 2002. With a 2 year survival of 23%, high frequency of serious adverse events, and 2 year device

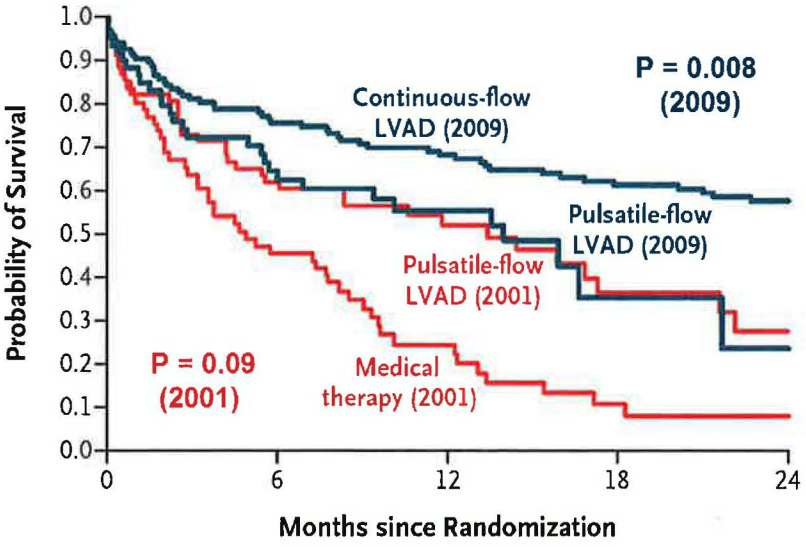
Figure 4. Improved 2 Year Survival Rates During the Second Half of REMATCH[24]



failure rate of 35%, HeartMate XVE for DT was not widely accepted for clinical implementation despite FDA approval.

Attempts to improve outcomes for DT have primarily revolved around improved device design and better patient selection. The only second generation device to receive FDA approval for destination therapy is the HeartMate II. In the prospective, randomized multicenter trial, published in 2009, end stage heart failure patients who were not eligible for transplantation were randomized in a 2:1 fashion with 134 receiving a continuous-flow (HeartMate II) and 66 receiving a pulsatile-flow (HeartMate XVE) device.[26] Age (37%) and obesity (12%) were the primary contraindications for transplantation. The primary endpoint was a composite of survival at 24 months without a disabling stroke or need for reoperation for repair or replacement of the pump. Patients receiving the HeartMate II had a 4-fold increase in achieving the endpoint compared with the HeartMate XVE (46% vs. 11%, $P < 0.001$). Patients receiving the HeartMate II had an 82% reduction in the need to repair or replace the pump (10% vs. 36%, $p < 0.001$) and a 41% reduction in death at 2 years (33% vs. 41%, $p < 0.05$). The actuarial survival at 1 and 2 years for the HeartMate II (68% and 58%) was better compared with the HeartMate XVE (55% and 24%, Figure 5).[27] The leading causes of death with the HeartMate II were hemorrhagic stroke (9% of implanted devices), right heart failure (5%), sepsis (4%), external power interruption (4%), respiratory failure (3%), cardiac arrest (3%), and bleeding (3%). The difference in overall stroke between the two groups was not statistically different (16% vs. 14%). There was a similar significant improvement in measures of functional status and quality of life with both devices, demonstrating that functionality and quality of life were not necessarily dependent on method of blood flow (whether pulsatile or axial). The FDA approved the HeartMate II for destination therapy in January 2010. With a 2 year survival above 50%, it is likely that the HMII will likely become more widely accepted as an alternative for transplantation when compared to the HeartMate XVE.

Figure 5. Survival Comparison of 2 DT Trials: REMATCH (2001) and HeartMate II Pivotal Trial[27]



Bridge to Candidacy

Due to device specific improvements in survival with destination therapy, an additional indication with bridge to candidacy has evolved. Traditionally, obese patients, patients with elevated pulmonary pressures secondary to heart failure, and patients who were actively using

tobacco were not considered transplant candidates. However, given that MCS promotes improvement in functional status allowing for exercise and weight loss[28], provides PVR reduction in patients with pulmonary hypertension because of heart failure[29-30], and gives patients an opportunity to undergo smoking cessation, the indication of bridge to transplant candidacy has become a viable option. This obviously brings up multiple ethical and economic concerns. Is it appropriate to utilize expensive therapies to support a patient while they consider smoking cessation? Is it fair to discuss the option of bridging to transplantation, thereby possibly giving false hope for a morbidly obese patient? While there is little data available describing how many patients initially enrolled as bridge to candidacy successfully progress towards transplantation, further research and guidelines addressing these issues are needed.

Bridge to Recovery

Unloading of the left ventricle (LV) by MCS can reverse adverse remodeling resulting in the normalization of many cellular, electrical, neurohormonal, and functional indices (Figure 6).[31] Decreased cardiac pressure and volume overload in the LV results in decreased ventricular wall tension.[32] This has been shown to be associated with a significant reduction in cell volume, length and diameter.[33] Support with an LVAD has led to a reduction of total collagen content[34], downregulation of matrix metalloproteinases[35], and decreased TNFα[34] levels. Further, increased β-receptor density and improved adrenergic responsiveness following VAD placement, may result in normalization of neurohormones and cytokine levels.[36]

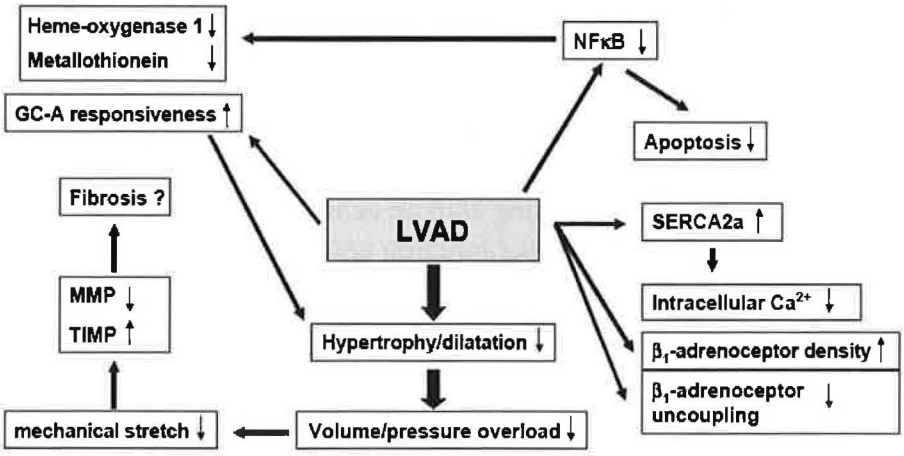


Figure 6: Mechanisms of the Reverse Remodeling Following LVAD Placement[34]

While the benefits of mechanical unloading are evident, determining the appropriate strategy to promote full recovery and identifying patients who could remodel to the point of explantation remain difficult. One of the first studies to introduce pharmacologic based therapy to promote myocardial recovery in mechanically supported hearts was developed by the Harefield group in the U.K. [37] In this prospective, single center, nonrandomized study, enrolled patients underwent two stages of pharmacologic therapy after pulsatile LVAD implantation with the HeartMate XVE. During the first stage, patients bridged with an LVAD were treated with optimal doses of lisinopril, carvedilol, aldactone and losartan. During the

second stage, if regression of LV enlargement was achieved based on echocardiographic measurements of LV dimensions with the pump switched off, the β_2 agonist clenbuterol was administered with the goal of promoting mild hypertrophy and thereby limiting atrophy.[38-39] Explantation was considered in patients who, after the LVAD was turned off for 15 minutes, had the following parameters: LV end-diastolic diameter (LVEDD) < 60 mm, LV end-systolic diameter (LVESD) < 50mm, LVEF > 45% pulmonary capillary wedge pressure < 12mmHg, resting cardiac index > 2.8 l/m/m^2, Maximal $VO_2 \geq 16$ ml/kg/min and $Ve/VCO_2 < 34$.

Five enrolled patients died prior to completion of both stages. Of 15 patients who completed both stages of therapy, 13 had a history of idiopathic dilated cardiomyopathy, 1 chemotherapy induced cardiomyopathy, and 1 post-partum cardiomyopathy. Eleven (73%) patients had appropriate recovery to meet explantation criteria, while 4 were transplanted due to inappropriate recovery. Actuarial survival of explanted patients was 91% at 1 year and 82% at 4 years. Freedom from recurrent heart failure was 100% at 1 year and 89% at four years. One patient died within 24 hours of explantation due to intractable arrhythmia and 1 patient developed a recurrence of heart failure 21 months after explanation. The rate of recovery in this series was significantly higher than in other published studies which ranged from 5-24%.[40-42] It is unclear whether utilization of clenbuterol, a two staged approach, a weaning protocol, or patient selection played a role in this discrepancy. To validate these results, the HARPS (Harefield Recovery Protocol Study) trial was developed and is near completion in 9 US centers using the same protocol.

Utilization of pharmacologic therapy, patient selection and LVAD weaning protocols for recovery need extensive research. Because there are no reliable markers to date that effectively predict the recovery process, consideration for bridge to recovery is on a case by case basis.[43] Patients who have the highest probability of recovery are typically non-ischemics of less than 6 months duration with an LVEDD < 55 mm who are on optimal medical therapy.[44] Such patients should undergo pump weaning with an echo and concomitant right heart catheterization in order to assess myocardial function and hemodynamics during withdrawal of LV support.[45] If echocardiographic and hemodynamic parameters are stable, then the patient may be considered for explant[45].

Patient Selection

Because there are very few prospective trials evaluating LVAD support for BTT and DT, most patient eligibility criteria published by the US Centers for Medicare and Medicaid Services (CMS) are broad and primarily based on experiences of single centers and data from multi-institutional registries.[46] The CMS selection criteria for BTT and DT are listed in table 2.[47] In true clinical practice, determination of candidacy for LVAD therapy involves a more comprehensive evaluation than provided in the CMS criteria. This evaluation includes a clinical assessment of the severity of heart failure, assessment of operative risk, cardiac considerations, and non-cardiac considerations.

Table 2: CMS Selection Criteria for LVAD Placement[47]

CMS Patient Selection Criteria for Bridge to Transplantation:
A. Patient approved/listed for heart transplantation B. The implanting site needs written permission from the transplant center which patient is listed
CMS Patient Selection Criteria for Destination Therapy:
Chronic end-stage heart failure (NYHA Class IV) for at least 90 days with a life expectancy < 2 years and meet all of the following: A. Not heart transplant candidate B. NYHA Class IV heart failure symptoms failed to respond to optimal medical management, including salt restriction, diuretics, digitalis, beta-blockers, and ACE inhibitors (if tolerated) for at least 60 of the last 90 days C. LVEF < 25% D. Peak oxygen consumption of < 12 ml/kg/min or continued need for IV inotropes E. BSA ≥ 1.5 m^2 if a first generation VAD is used

Adapted from National Coverage Determination: Artificial Hearts and Related Devices

Clinical Assessment of Heart Failure Severity:

Clinical assessment of heart failure severity requires a thorough evaluation of clinical presentation, hemodynamic studies and functional studies. It is crucial to consider LVAD implantation prior to the development of end-organ failure or occurrence of irreversible injury due to comorbidities. The Seattle Heart Failure Model[48] and the Heart Failure Survival Score[49] are both predictive models that estimate the expected survival of heart failure patients and may be useful in potentially identifying high-risk patients for LVAD implantation.[50] Given that the clinical spectrum of patients who are considered for MCS vary, these models are primarily limited in that they derive risk in ambulatory patients.

Table 3. INTERMACS Patient Profiles

INTERMACS Level	Hemodynamic status	Time to MCS
1 "Crash and burn"	Critical cardiogenic shock despite escalating inotropes and IABP	Within Hours
2 "Sliding on inotropes"	IV inotropes with deterioration in nutrition, renal function, or fluid retention.	Within a Few Days
3 "Stable inotropes"	Stabile but dependent on mild-moderate inotrope dose (hospitalized or at home)	Within a Few Weeks
4 "Frequent flyer"	Recurrent decompensation – "recurrent" rather than "refractory"	Within weeks to months
5 "Housebound"	Severe limited tolerance for activity but comfortable at rest	Variable
6 "Walking wounded"	Exertion limited, completes mild activity but fatigued within minutes of exertion	Variable
7 "Too Well"	Clinically stable, completes reasonable activity without recent decompensation	Not an MCS Candidate

Adapted from Stevenson et.al. [51]

The Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS), a national registry for patients receiving mechanical support, derived a scale to classify different degrees of clinical severity of ambulatory and hospitalized patients with stage D heart failure and NYHA Class IV symptoms (Table 3).[51]

INTERMACS 1 and 2

Patients classified as INTERMACS I carry the most advanced "crash and burn" profile during which patients have life-threatening hypotension despite inotropic support, often with an IABP and critical organ hypoperfusion. INTERMACS 2 patients are "dependent on inotropes" and showing signs of continuing deterioration involving renal dysfunction, fluid retention, and impaired perfusion. MCS should be urgently considered for INTERMACS 1 and 2 patients as a means of rescue therapy. INTERMACS 1 and 2 status accounted for 72% of patients who underwent LVAD placement in the INTERMACS registry.[18]

INTERMACS 3

Patients who are dependent but "stable" on inotropes are classified as INTERMACS 3. Often, these patients can go home with continuous infusion of a single low dose inotrope. Given that inotrope dependence is associated with < 50% six month survival[52-53], LVAD therapy should be considered electively for these patients. Elective device placement should also be considered in patients on inotropes with anticipated long waiting time to heart transplantation, including patients who are blood type O or with increased anti-HLA antibodies.[46] INTERMACS 3 status accounted for 14% of patients who underwent LVAD placement in the INTERMACS registry.[18]

INTERMACS 4-6

INTERMACS 4-6 patients are non-inotrope dependent with NYHA class IIIB and IV symptoms. The correct timing of LVAD implantation remains controversial for these patients. Although placement of a device in INTERMACS 4-6 patients could be justified by CMS criteria, there are no prospective trials to date looking at whether LVAD is beneficial in these patients and whether early device placement for these patients is beneficial. Post-hoc analysis of the REMATCH trial demonstrated that patients with greater than INTERMACS 3 status did not derive survival benefit with LVAD implantation.[25] However, post-REMATCH assessment of patients undergoing DT with the HeartMate XVE VAD showed that deferring implantations until patients progress to biventricular and end-organ failure may increase the operative risk.[54] Whether LVAD implantation for DT in patients with less severe heart failure surpasses outcomes with optimal medical therapy has to be determined and requires further assessment, especially during the clinical implementation of second and third generation devices.

Assessment of Operative Risk

Numerous studies have developed predictive models for operative mortality during LVAD placement.[54-56] In an analysis of 222 patients in the HeartMate XVE LVAD DT registry, Lietz and

Miller established a risk score to estimate 90 day survival after implantation.[54] They determined that the most important predictors of mortality were poor nutrition, hematologic abnormalities, markers of end-organ or right ventricular dysfunction, and lack of inotropic support (Table 4). Low (n=65), medium (n=111), high (n=28), and very high (n=18) risk was associated with 90 day survival rates of 94%, 87%, 39% and 18%; and 1-year survival rates of 81%, 62%, 28%, and 11%, respectively.

Table 4. Lietz-Miller Score[54]

Risk Factor	Score
Platelet count $< 148 \times 10^3$ / µL	7
Serum albumin < 3.3 g/dL	5
INR > 1.1	4
Vasodilator therapy	4
Mean pulmonary artery pressure < 25 mm Hg	3
Aspartate aminotransferase > 45 U/ml	2
Hematocrit < 34%	2
BUN > 51 mg/dL	2
No Intravenous Inotropes	2

Risk: Low 0-8, Medium 9-16, High 17-19, Very High > 19

High and very high risk patients may benefit from preoperative optimization of nutritional and hemodynamic measures in order to lower risk scores to become better candidates for LVAD support. Similar survival trends were seen when evaluating the INTERMACS registry. INTERMACS I and II patients had lower adjusted 30- and 90- day survival (54% and 41%) compared with INTERMACS III and IV patients (80% and 72%, $p < 0.05$).[57] These data suggest that placement of LVADs earlier in the course of heart failure could potentially improve outcomes.

Cardiac Considerations for LVAD Eligibility:

Right Ventricular Failure

The primary cardiac structural abnormality that influences the efficacy of device placement involves right ventricular (RV) failure. Acute unloading of the left ventricle after LVAD placement leads to decompression of the left ventricle and leftward shift of the septum, altering RV shape, size, and contractility.[58] RV dysfunction may lead to inadequate filling of the left ventricle and septal shift into the LV inflow cannula (termed "suction event"). The RV is a major determinant of early post-implantation outcomes because there are no current outpatient biventricular support devices approved for DT. Biventricular support requires inpatient ICU stay with a paracorporeal right ventricular support device.

Approximately 20-35% of patients who undergo LVAD implantation develop RV failure whether supported with a pulsatile or axial flow pump.[59-60] Although several clinical predictors for post-operative RV failure have been developed though single-center series [59-63], prospectively determining who is likely to have RV failure is difficult. Recently, in a prospectively collected single center LVAD study, independent predictors of RV failure included a vasopressor requirement (4 points), AST ≥ 80 IU/L (2 points), bilirubin ≥ 2.0 mg/dL (2.5 points), and creatinine ≥2.3 mg/dL (3 points).[60] The odds ratio for RV failure for patients with a score of 3, 4-5, and ≥ 5.5 were 0.49, 2.8, and 7.6 respectively. The 180 day survivals were 90%, 80%, and 66%, respectively ($p < 0.01$). While this score has been clinically helpful, it has yet to be

validated in a large study. Other risk factors which appear to be important in other studies include right atrial pressures > 20 mmHg, low mean pulmonary artery pressure < 25 mmHg, central venous pressure to pulmonary capillary wedge pressure ratio > 0.63, low right ventricular stroke work index, severe tricuspid regurgitation, renal dysfunction, and hepatic dysfunction.[59-63] In the event that the RV deteriorates post-operatively, RV function can be supported with inotropes, pulmonary vasodilators such as inhaled nitric oxide and/or temporary placement of a right VAD.[64]

Valve Competency:

Significant valvular abnormalities can lead to important adverse events in patients undergoing LVAD therapy and may require repair or replacement (Figure 7).[65] Although isolated aortic stenosis is not a contraindication to LVAD implantation, moderate to severe aortic insufficiency can markedly impact the hemodynamics of the pump.[66] Left ventricular decompression after placement of an LVAD results an increased gradient across the aortic valve leading to increased aortic insufficiency. The recirculation leads to a increasing pump work, decreasing effective forward blood flow, and decreasing systemic perfusion.[67] In this case, the flow registered by the device may artificially be 1.5-2 L higher than true cardiac output. Surgeons have addressed this issue by either placing a bioprosthetic valve or over-sowing the aortic valve during LVAD implantation.[68] Moderate to severe mitral stenosis should be corrected during LVAD implantation to allow for adequate left ventricular and pump filling. Mitral regurgitation, on the other hand, usually improves after VAD placement due to left ventricular decompression.[64] Patients with severe tricuspid regurgitation can have impaired forward blood flow from the right side of the heart especially in the setting of elevated pulmonary pressures. Patients with baseline tricuspid regurgitation may develop worsened regurgitation post-operatively due to increased RV dysfunction in the setting of leftward shift of the interventricular septum.[69] Given that this may decrease left sided filling, tricuspid valve repair should be considered.

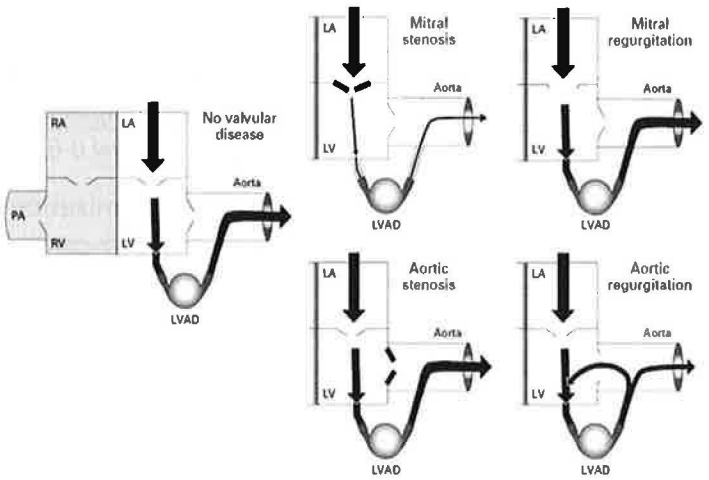


Figure 7. Effect of Valvular Abnormalities on LVAD Flow[65]

Intracardiac Shunts:

Patent foramen ovale, atrial septal defects, and ventricular septal defects must be identified prior to initiation of mechanical support. If a defect is present and not corrected, there can be reversal of flow through the defect during LV decompression with the LVAD, leading to a right-to left shunt and systemic hypoxemia[67].

Arrhythmias:

Both atrial and ventricular arrhythmias are common in patients with cardiogenic shock and advanced cardiomyopathies. Often, these arrhythmias improve after support with the LVAD due to LV decompression and withdrawal of inotropes. Ventricular arrhythmias after LVAD implantation are generally well tolerated and have not been associated with worsening hemodynamics or clinical deterioration.[70] In fact, LVAD therapy is considered a viable option for support in patients with refractory ventricular arrhythmias.[71-73] Antiarrhythmic therapy is often considered in patients with persistent ventricular tachycardia supported by the ventricular assist device if mild alterations in flow and power are present. In stable patients, the AICD is often turned off to prevent inappropriate discharge. Atrial arrhythmias may affect RV filling but is generally well tolerated in VAD recipients. Electrical or pharmacologic cardioversion is considered either pre- or post-VAD implantation to avoid thrombus formation and improve exercise tolerance.

Non-cardiac Considerations for LVAD Eligibility

General considerations:

Physiological age is an important consideration for LVAD eligibility. LVAD support is much more challenging physically, psychologically, and emotionally for elderly patients compared to younger patients.[46] Patients with life-limiting comorbidities including advanced pulmonary disease, irreversible CKD, cancer, peripheral vascular disease or limiting stoke should not be considered LVAD candidates.

Renal function

24% of patients with pulsatile-flow devices and 16% of patients with continuous-flow devices developed renal failure in the pivotal HeartMate II DT study.[26] Although renal dysfunction secondary to reduced cardiac output is reversible, it has been associated with adverse outcomes in patients supported with an LVAD.[74-75] The nephrologist should assess whether renal insufficiency is secondary to poor perfusion and whether it is irreversible. Patients with a creatinine level > 2.5 mg/dL, BUN > 40 mg/dL, estimated GFR < 0.5 ml/kg/min or on chronic dialysis are at greatest risk for adverse outcomes.[76] Optimization of renal function preoperatively is imperative.

Hepatic function

Hepatic dysfunction is associated with adverse outcomes after LVAD implant, primarily due to increased risk of bleeding.[77] Increased transfusions due to perioperative bleeding can result in worsening right heart failure, often requiring need for RVAD support. ALT or AST greater than 3 times normal, INR > 1.5, and total bilirubin > 5 mg/dL are the strongest markers of hepatic impairment associated with mortality.[64] Given that right sided heart failure leads to hepatic dysfunction in patients with advanced heart failure, it is important to differentiate hepatic

congestion with cirrhosis by either utilizing hepatic ultrasound or a liver biopsy prior to VAD placement. Patients with primary portal hypertension or cirrhosis are not candidates for VAD support. Optimization of hepatic function prior to LVAD implantation by reducing right heart filling pressures is imperative. In addition, supplemental vitamin K may be useful in malnourished heart failure patients in order to replete vitamin K dependent coagulation factors prior to surgery.

Nutrition:

Due to the metabolic deficiencies in patients with advanced heart failure[78], patients must undergo evaluation and optimization of nutritional status. Malnutrition increases patient risks for infection, decreases the likelihood of postoperative recovery, and is associated with poor outcomes.[79] Pre-albumin levels of <15 mg/dL at 2 weeks of VAD implantation are associated with high risk of dying before discharge.[80] Other markers of poor nutritional status associated with increased mortality after VAD placement include cachexia (BMI < 21 in males or 19 in females), low albumin, low total protein, and low absolute lymphocyte count.[81] To reduce the risk of postoperative morbidity and mortality, malnourished patients who are stable should undergo optimization of nutritional status prior to LVAD placement.[79] Often, an enteral feeding tube may be needed to provide support. During hyperalimentation, the pre-albumin level should be checked often and should exceed 15 mg/dL before implant.

Neurological / Psychosocial function:

Given the complex management involved with LVAD care, patients who have neurologic disease that compromises their ability to care for the device are poor candidates for MCS. Patients with history of TIA or stroke should undergo CT or MRI scanning and undergo formal evaluation by a neurologist and psychiatrist. Patients with advanced age, diabetes, or peripheral vascular disease should also have a carotid ultrasound.

Patients with psychiatric disorders, history of drug abuse, and other psychosocial issues need to be assessed for ability to manage the device and comply with care instructions. These issues are often more important for VAD candidates than heart transplant candidates because of the complexities of device management. Active drug users are typically not appropriate candidates for LVAD therapy. On the other hand, current smokers who demonstrate an interest in cessation can undergo bridge to candidacy with the understanding that transplantation will only be offered after abstinence for 3-6 months[82] Having strong family support is crucial for success. We typically require 24 hour family support for a minimum of 3 months after LVAD placement for DT and until transplantation for BTT.

Patient/Family/Physician Expectations:

It is important that patients and their physicians have realistic expectations and full understanding of goals when considering mechanical support. Because of the strong desire of physicians to "save" their patients, maintaining objectivity to avoid getting trapped in futile

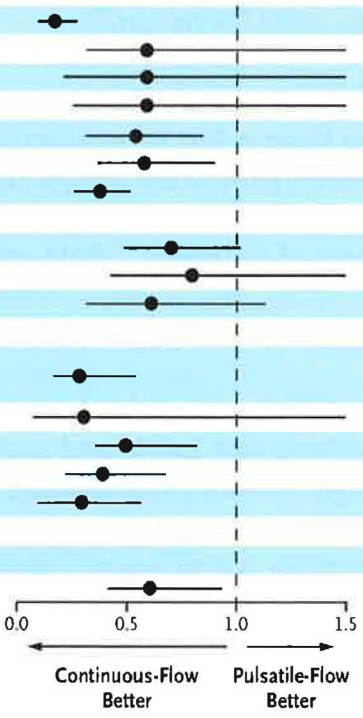
situations is crucial.[83] Not maintaining objectivity may create situations in which standard of care is not followed and emotions influence patient selection criteria. Proceeding with caution is particularly important in situations where the patient is young; the heart failure is unexpected; and when physicians feel they have invested in a good amount of patient care.[83] Because LVADs have the ability to maintain stable hemodynamics despite unanticipated complications such as stroke, anoxia, or progression of renal failure, there is a possibility for patient suffering despite having adequate hemodynamic support. To avoid confusion, creation of a living will and documentation of patient's and family's end of life desires should be obtained prospectively.[84] Further, patients should undergo formal discussions about other options besides mechanical support, including hospice. Ethicists and palliative care physicians are often helpful in these discussions because of their advanced training in futility and comfort care.[85-86]

Perioperative and Postoperative Complications and Management

The benefits of MCS must be tempered by the risks of device placement and postoperative complications. In the pivotal HeartMate II DT trial, the leading cause of death in: 1) the pulsatile-flow device group were hemorrhagic stroke (10% of patients who underwent implantation), right heart failure (8%), multi-system organ failure (7%), and ischemic stroke (5%); and 2) continuous-flow group were hemorrhagic stroke (9% of implanted devices), right heart failure (5%), sepsis (4%), external power interruption (4%), respiratory failure (3%), cardiac arrest (3%), and bleeding (3%, Table 5).[26]

Table 5. Adverse Events and Relative Risk Stratified by Treatment Group[26]

Subgroup	Continuous-Flow LVAD (N=133) (211 patient-yr) no. (%)	no. of Events/ Patient-Yr	Pulsatile-Flow LVAD (N=59) (41 patient-yr) no. (%)	no. of Events/ Patient-Yr	Relative Risk (95% CI)	P Value fo Interactio
Pump replacement	12 (9)	0.06	20 (34)	0.51		<0.001
Stroke	24 (18)	0.13	8 (14)	0.22		0.21
Ischemic	11 (8)	0.06	4 (7)	0.10		0.38
Hemorrhagic	15 (11)	0.07	5 (8)	0.12		0.33
LVAD-related infection	47 (35)	0.48	21 (36)	0.90		0.01
Local non-LVAD infection	65 (49)	0.76	27 (46)	1.33		0.02
Sepsis	48 (36)	0.39	26 (44)	1.11		<0.001
Bleeding						
Bleeding requiring PRBC	108 (81)	1.66	45 (76)	2.45		0.06
Bleeding requiring surgery	40 (30)	0.23	9 (15)	0.29		0.57
Other neurologic event	29 (22)	0.17	10 (17)	0.29		0.14
Right heart failure						
Managed with extended use of inotropes	27 (20)	0.14	16 (27)	0.46		<0.001
Managed with RVAD	5 (4)	0.02	3 (5)	0.07		0.12
Cardiac arrhythmia	75 (56)	0.69	35 (59)	1.31		0.006
Respiratory failure	50 (38)	0.31	24 (41)	0.80		<0.001
Renal failure	21 (16)	0.10	14 (24)	0.34		<0.001
Hepatic dysfunction	3 (2)	0.01	0	0.00		
LVAD thrombosis	5 (4)	0.02	0	0.00		
Rehospitalization	107 (94)	2.64	42 (96)	4.25		0.02



Right Ventricular Failure

RV failure requiring the management of extended use of postoperative inotropes ranges from 20-27% and support with an RVAD is less than 5%.[26] As discussed before, LV unloading causes the interventricular septum to bulge away from the RV, reducing RV efficiency.[58] This is further exacerbated by increased venous return provided by the LVAD which may rise beyond the capability of the right ventricular pump. Myocardial stunning, ischemia, arrhythmias, and increased PVR are other factors that may affect the RV.[87] If needed, RV function can be supported with inotropes, pulmonary vasodilators such as inhaled nitric oxide and/or temporary placement of an RVAD[64].

Stroke/Thromboembolism:

The reported incidence of postoperative cerebral thromboembolism ranges from 3-49%.[88] Thromboembolic complications occur because contact between the pump surface and the patient's blood activates coagulation pathways and attracts platelets and complement, initiating clot formation.[16] In order to limit clot formation, all VAD types except the HeartMate XVE require anticoagulation with warfarin and antiplatelet medications. The HeartMate XVE is the only device that does not require warfarin because it has a unique interior lining that promotes endothelial cells adherence and decreases thrombogenicity.[89] Despite its unique interior lining, 14% of patients receiving the HeartMate XVE in the REMATCH trial had either an ischemic or hemorrhagic stroke with approximately ½ of the events occurring within the first 30 days.[88] Interestingly the HeartMate II had similar stroke rates of 18% during its pivotal DT trial and 8% during its pivotal BTT trial despite requiring anticoagulation.[20, 26] The stroke rates of both devices were higher than that reported in another trial of patients with medically managed advanced heart failure[90] but similar to a post-hoc analysis of heart failure patients treated for atrial fibrillation.[91]

Thromboembolism may also be associated with pump thrombosis which typically manifests as decreased flows in first generation pumps and increased power consumption and estimated flow in second generation pumps. Utilization of antiplatelet agents with clopidogrel or thrombolytics have been reported; however pump thrombosis more often requires surgical replacement of the pump.[92] Both approaches are associated with high mortality.

Hemorrhage

Postoperative bleeding is frequent in patients undergoing VAD placement. It can occur in up to 80% of patients with LVADs and approximately 15-30% of patients undergo reoperation to treat hemorrhage.[26] Factors that increase risk for postoperative bleeding include need for anticoagulation, prolonged surgical procedure with cardiopulmonary bypass, extensive surgical dissection often due to a prior sternotomy, and preoperative hepatic congestion.[93] Limiting bleeding is particularly important in patients awaiting bridge to transplantation as blood transfusions increase risk for HLA sensitization which, in turn, limits the likelihood of matching with a potential donor.

Infection

Infection is the leading comorbidity and a significant cause of death in patients undergoing LVAD therapy. The REMATCH trial demonstrated a 28% probability of LVAD infection within the first 3 months after implant.[23] 41% of patients randomized to VAD therapy died due to complications of sepsis. The types of infections may be non-VAD related (pneumonia, urinary tract infection, line sepsis) or device related (driveline infection, pump pocket infection, surgical site infection and endocarditis). The high rate of infection in LVAD patients is likely related to the preoperative malnourished state.[94] Poor management of the percutaneous driveline may also be a source of infection. The two primary organisms that cause VAD related infections include *Staphylococcus epidermidis* and *Staphylococcus aureus*.[95] Risk factors for VAD related infections include patient comorbidities such as diabetes and obesity as well as other factors such as length of hospital stay, indwelling catheters and need for surgical reexploration.[95-96] Immobilization of the driveline, patient education, and nutrition are the most important components of postoperative infection prevention[97].

Driveline infections are the most common type of device related infections with rates ranging from 18-52%.[94, 98] They often remain localized and can be successfully treated with antibiotic treatment and appropriate wound care; however relapse is common.[99] Pocket infections comprise 11-31% of VAD infections and are primarily managed through debridement procedures, open drainage, and irrigation.[98] Patients who have recurrent device infections or septicemia often require chronic suppressive antibiotic therapy until a heart transplant can be performed or a new device can be implanted.[94] Patients must undergo extensive teaching for percutaneous lead care focusing on drive-line immobilization, nontraumatic cleansing of the exit site, and sterile dressing changes. Additional approaches to reducing infection risk include decreasing driveline diameter and better antimicrobial prophylaxis. LVAD related infections have been shown to be lower in the continuous-flow devices when compared to the pulsatile devices.[26] Despite these improvements, the rate of device-related infection still remains unacceptably high and limits the implementation of long-term device therapy.

GI Bleeding

GI bleeding has become more of a concern with the utilization of continuous-flow devices. Approximately 15% of patients with continuous-flow devices have problems with GI bleeing.[100-101] Proposed mechanisms for bleeding include 1) warfarin use, 2) arteriovenous malformation in the setting of nonpulsatility, in a mechanism similar to that of Heyde's syndrome[101] and 3) development of acquired von Willebrand disease, possibly due to increased shear stress involved with axial flow pumps.[102-104] Whether assessment of the GI tract preimplantation is needed has yet to be determined. Given that AVM's are hard to detect in the absence of active bleeding, it is unclear whether endoscopic evaluation prior to LVAD placement would be helpful. If GI bleeding occurs after LVAD implantation, anticoagulation is typically held or decreased. At our institution, persantine and aspirin are first held. If the bleeding persists or is brisk, warfarin is also held. In the setting of recurrent bleeding despite anticoagulation cessation, the only option available is to proceed with a heart transplant or major GI surgery.

Device Failure

LVAD failure was the second leading cause of death in the REMATCH trial.[23] 35% of patients experienced device failure during the 24 months after implant. Of these, 52% involved the external components and 48% involved the internal components (pump, inflow, or outflow conduit). The device had to be replaced in 15% of patients. Mechanical failures occur because of the wear and tear on the parts of the device. Causes of failure of internal components for first generation devices include bearing wear (often detected by the presence of dust in the vent filter), device diaphragm fracture (resulting in air embolus), valvular dysfunction (resulting in regurgitation and decreased flow), kinking or malfunction of the inflow or outflow conduit, and motor failure.[105] Causes of external failure include malfunction of the controller, batteries, stroke-volume limiter, and power base unit; and fracture of the y-connector or driveline. Incidence of pump replacement in the continuous flow devices were 1/8 that of pulsatile devices in the HeartMate II pivotal DT trial.[26] Damage to the percutaneous lead was the primary cause of device replacement in the HeartMate II arm. There were no primary-pump or bearing failures in patients with continuous-flow VADs.

Psychosocial problems

Although placement of an LVAD has been associated with improved functional status and quality of life,[20, 23, 26] these devices can introduce new stressors to patients and caregivers, especially in patients undergoing DT. Caregivers have been shown to experience significantly more psychological distress compared to their partners both early after implantation and longterm.[106] Early involvement from social workers, palliative care, psychiatry, and support groups is important to provide patients and their families a fulfilling life.

To minimize stressors, health care professionals should design specific discharge planning and educational programs to prepare patients and their families. At our institution, we provide classes educating patients and families on how to operate the device, how to interpret and respond to the alarms, and how to provide care in case of emergency. They are taught safety precautions including avoidance of immersion in water, avoidance of static electricity, and prevention of water getting into the vent filter. They are taught how to wash or shower without jeopardizing the device. They must learn sterile technique for driveline dressing changes. Mastery of all of these components is required through formal testing. Prior to discharge, VAD coordinators will complete an inspection of the patient's home, checking for any electrical hazards and confirming electrical outlets are grounded. They also train and provide emergency contact numbers to medical personnel, EMS, and fire station personnel near the patient's residence. They help patients identify locations for backup generators in case of power outage and contact the patient's electrical company and notify them of the need for electricity to maintain a vital state. Finally, prior to discharge, patients must undergo 2-3 outings with the VAD coordinator to ensure patient and family confidence with device management.

Economic Burden

LVAD therapy has the potential to have a marked financial impact on the medical community, hospital providers, third-party payers and society. Given the increasing incidence of advanced heart failure and the expanding indications for LVAD placement, it is important to determine whether this therapy is cost-effective, especially in light of increasing health care costs.

Currently, there are limited data available evaluating this issue primarily because determination of the costs and benefits of MCS have been a moving target. Initially, studies evaluating first generation VADs suggested that LVAD placement was associated with longer length of stay, higher total hospital costs, and lower revenue when compared with heart transplantation.[107] However, more recently, Miller, et. al. showed that increased experience and volume may have a positive influence on financial efficiency.[108] Total index hospital costs (mean) for the HeartMate XVE in the two highest enrolling US centers were 40% lower in the Post-REMATCH era when compared to the REMATCH cohort ($148,350 vs. $210,187, $p = 0.053$). Much of this cost benefit was due to a trend towards greater survival to discharge (87% vs. 67% $p = 0.09$) and decreased length of hospital stay (33 vs. 44 days) in the post-REMATCH group. Post-REMATCH patients who survived to discharge derived 50% lower hospital costs when compared to those who died ($114,979 vs. $215,476, $p < 0.01$). Utilization of a multidisciplinary team has also been shown to decrease overall hospital costs by approximately $40,000 in one study, primarily by decreasing length of stay during non-ICU care (7 vs. 35 days $p = 0.03$).[109]

As devices improve, surgical times decrease, and complications become less, this technology has the potential to be beneficial from a financial standpoint. To date, there are no large scale cost analysis studies assessing second and third generation devices, but one would speculate that these newer devices would likely further decrease the costs of device implementation.

Future of VAD Therapy

Adverse events and device durability have limited the widespread use of MCS. Third generation ventricular assist devices have attempted to improve upon these issues and have entered clinical trials in the United States. These devices are primarily centrifugal flow pumps often with magnetically levitated impellers. Theoretically, due to a bearingless design, these devices have long term durability (> 10 years). The smaller pump sizes also decrease blood to pump exposure leading to decreased risk of pump thrombosis.

Further research has focused on the development of a fully implantable system. The LionHeart LVAS (Arrow International, Limerick, PA) was one of the first devices to be a fully implantable system by using a transcutaneous energy transmission system (TETS).[110] In TETS technology, battery packs are connected to a transformer coil worn on the outside of the chest. When the external transformer coil is placed over the implanted transformer coil, it produces an electrical current that keeps the pump running. Although Arrow dissolved its LionHeart program, other companies are working on implementation and improvement of TETS technology with their third generation devices.

Conclusion:

Left ventricular assist device therapy is effective for management of end stage heart failure as a bridge to transplantation and destination therapy. Appropriate patient selection and optimization of risk factors are crucial for successful therapy. Management involves a multidisciplinary approach involving cardiologists, cardiothoracic surgeons, LVAD coordinators, nurses, dietary services, rehabilitation, and social workers. The direction of technological and scientific innovation in the field of mechanical circulatory support is enigmatic, but exciting. As technology improves, further questions regarding indications, implementation, and utilization will certainly arise.

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