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# Left Ventricular Assist Device: A breakthrough in the Management of End Stage Heart Failure

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**Abstract—***Heart failure (HF) is not a single entity but a clinical syndrome that may vary depending on age, sex, left ventricular ejection fraction (LVEF) status, racial or ethnic origin and etiology with a prevalence of over 23 million cases worldwide. Therapy arsenal for advanced HF involves a gamut of options depending upon the progression of the disease. Optimal medical management (OMM) continues to evolve with new age medication regimens aiming for improving the failing heart's functioning. Cardioverters, defibrillators and resynchronization therapy intervenes when symptoms still advances to New York Heart Association (NYHA) Class III or Class IV category with LVEF less than 25%, resulting in diminished quality -of –life (QOL). Cardiac transplantation option is severely restricted by the availability of donor, immuno-compromised stage or age and compatibility of the candidates. At this debilitating stage, the advent of a promising cutting edge biomechanical technique, Left Ventricular Assist Device (LVAD) enters to add QOL to the patient. LVAD also called a "heart pump" or "VAD" is a mechanical device that assists blood pumping and circulation to a weak heart. Second and third generation LVAD devices like HeartMate II, III along with others are miniaturized implantable and most widely used devices of its kind in the world. The REMATCH study, INTrEPID trial and post-REMATCH study evaluated many models of LVAD's for both Bridge-to-Transplantation (BTT) and Destination Therapy (DT) and were approved by U.S. Food and Drug Administration (FDA) and got CE Mark Authorized. HeartMate II a second-generation axial continuous-flow (CF) pump LVAD outperformed HeartMate XVE, a first-generation pulsatile-flow (PF) pump LVAD. With the new era of this mechanical circulatory support (MCS) technologies, more patients can now significantly improve their NYHA classification, projected survival and QOL.*

## Introduction

Heart failure (HF) is the end stage of all the heart diseases and is a major cause of morbidity and mortality. In today's world deliberate prevalence of heart diseases is shown in the fact that the lifetime risk of developing HF is one in five. HF represents a huge burden to the health-care system with frequent hospitalizations and readmission. Ischemic heart disease, hypertension, coronary artery disease (CAD), smoking, obesity and diabetes pose as potential risk factors and have been well identified to predict the incidence and progression of HF [31,32]. Patients with HF are a heterogeneous group with fluctuating etiology and pathophysiology, which makes the management and treatment optimization a difficult task. A classification system based on etiology, pathophysiology, and genetic factors is certainly of great help in the treatment line and palliative care of HF.

In spite of all the advances in the medical sciences the heart disease progresses to the end stage of failure leading to a debilitating stage of the patient. Non-availability of donor, immuno-compatibility, age related issues and several other restrictive criteria for recipients and donor hamper the heart transplant help. Though transplants offer a plateaued hope for approximately few thousands of advanced heart failure patients each year in the world but over millions of patients have no viable treatment option and are considered at high risk for repeated hospitalizations, poor quality of life (QOL) and even death. There is a clear mismatch in advanced heart failure patients and heart transplantation of below 79 years of age [4,29] .Transplant exclusion reasons or symptoms includes age (39%), obesity issue (12%), pulmonary hypertension (9%), insulin dependent diabetes mellitus (8%) , renal failure (7%), recent history of cancer (7%), patient refusal (7%), social compliances (5%), peripheral arterial disease (5%), sensitization to potential donors (3%) and others (3%) [25]
New York Heart Association (NYHA) has issued a classification of heart failure depending upon the symptoms of the HF patients.

**Table 1. NYHA classification of heart failure [3,27]**

| NYHA Class | Symptoms |
|---|---|
| I | Initiation of cardiac disease, but without any symptoms or limitations in ordinary physical activity, e.g. no shortness of breath when walking, climbing stairs etc. |
| II | Mild symptoms (mild shortness of breath and/or angina) and slight limitation while doing normal routine activities. |
| III | Distinct limitation in activity due to symptoms, even during less-than-ordinary activity, e.g. walking short distances (20–100 m).<br>Comfortable only at rest. |
| IV | Severe limitations as symptoms are experienced even while resting. Mostly bedridden patients. |

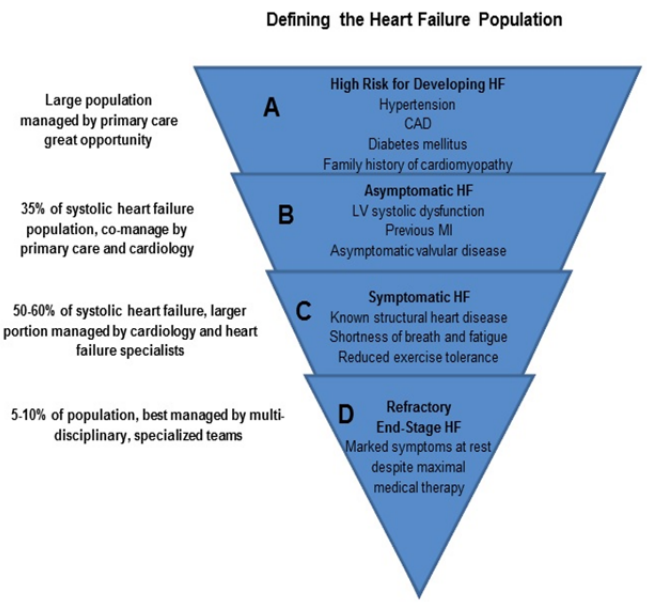


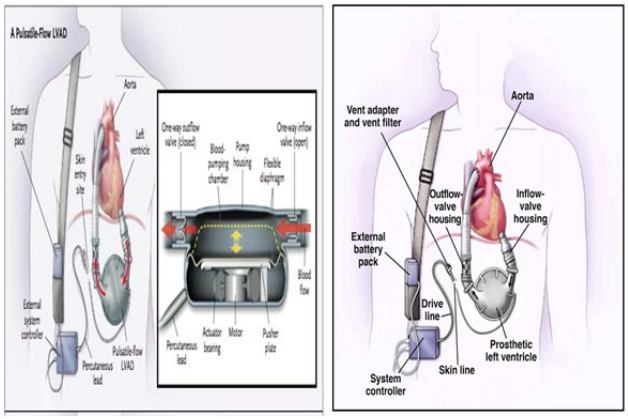

**Fig. 1: Stages and proposed treatment line of Heart Failure [1]**

Adapted from J Am Coll Cardiol.2001; 38; 2101-2113.

American College of Cardiology (ACC) and American Heart Association (AHA) identified four stages of HF. Stage A identifies the patient who is at high risk for developing HF but has no underlying disorder of the heart; Stage B indicates to a patient with a structural disorder of the heart but with no symptoms of HF. Stage C denotes the patient with past or current symptoms of HF associated with underlying structural heart disease and Stage D designates the patient with end-stage disease who requires specialized treatment strategies such as mechanical circulatory support (MCS), continuous inotropic infusions, cardiac transplantation or clinical care. This classification recognizes that there are proven risk factors and structural prerequisites for the development of HF and that therapeutic interventions performed even before the appearance of left ventricular dysfunction or symptoms can reduce the morbidity and mortality of HF. This classification system is intended to complement but not to replace the New York Heart Association (NYHA) functional classification, which primarily gauges the severity of symptoms in patients who are in stage C or D. The NYHA functional classification redirects a subjective assessment by a physician and changes frequently over short periods of time and that the treatments used do not differ significantly across the classes globally [22]. Once the HF progresses to the advance stages with less than 25% left ventricular ejection fraction (LVEF), the rise of machines or MCS renders hope to the thousands of people worldwide who are living with end-stage congestive heart failure. Dr. Michael E. DeBakey successfully implanted a left ventricular assist device for the first time in medical history to a 37-year-old woman in 1966. A paracorporeal external circuit was able to deliver mechanical support for ten days post surgery [16]. The first successful long-term implantation of an artificial LVAD was conducted in 1988 by Dr. William F. Bernhard under a National Institutes of Health (NIH) research contract, which developed Heart-mate, an electronically controlled assist device [28].

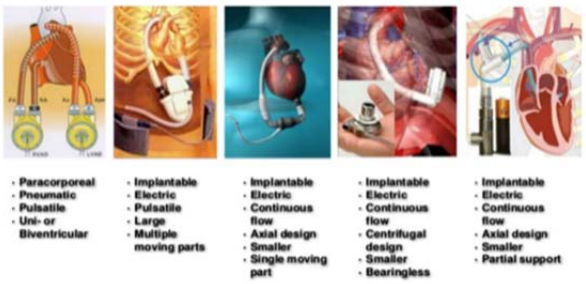
**About the device**

Ventricular Assist Device (VAD) is a mechanical pump that is surgically attached to one of the heart's ventricles to augment or replace native ventricular function. It can be used for the left (LVAD), right (RVAD) or both ventricles (Bi VAD). The LVAD is a biomechanical device which is placed inside a patient's chest where it helps the heart to pump oxygen-rich blood throughout the body. Unlike an artificial heart, the LVAD does not completely replace the heart, but aids in its circulatory job. One end is attached to the left ventricle while another to the aorta, through which blood is circulated to the whole body. A tube called 'drive line' passes from the device through the skin. and it comes out of the body through the abdominal skin and connects the pump to the controller outside which is used for charging the batteries. The outside of the tube is covered with a special material to help in healing and regrowth. LVAD helps in restoring normal blood flow in the body of the recipient whose heart is weakened by the progressive heart disease. It also relieves constant tiredness, body swelling and breathlessness symptoms. In the last few years, LVADs have significantly improved in providing survival and quality of life (QOL) among recipients [20].



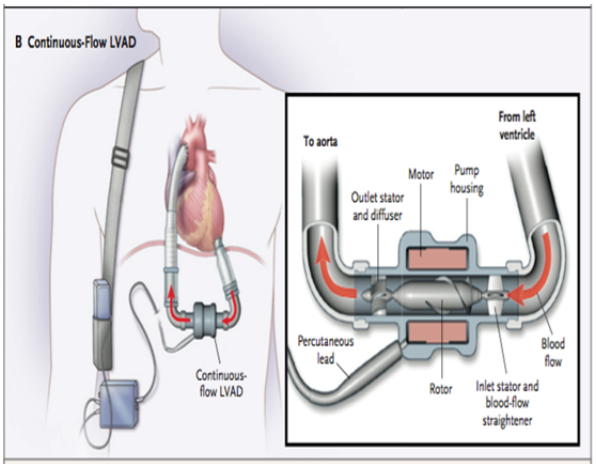

Source : Thoratec .com

**Fig. 2: A LVAD device [30]**




*Source*: Duke Medicine

**Fig. 3: Evolution of Mechanical Support [4,29]**




*Source* www.thoratec.com

**Fig. 4 &5: LVADs with Pulsatile and Continuous flow [30]**

## Approaches and indications of LVAD

LVADs are conventionally used to keep patients alive with a good QOL while they wait for a heart transplantation known as a "bridge to transplantation" (BTT) approach. However, LVADs are sometimes used as destination therapy means that the patient is not undergoing heart transplant, and sometimes as a bridge to recovery [2,7] it also lets the heart recover it's normal function by giving it a chance to rest [20] .BTT is most common and allows rehabilitation from severe cardiac heart failure while waiting for the donor. DT is a permanent device for transplant- ineligible patients. While bridge to recovery (BTR) is unloading the heart for reverse remodeling for a short or long term. Bridge to candidacy (BTC) / Bridge to decision (BTD) is not a true indication for most of the patients where eligibility is unclear in implant.

## Device design

Pumps are the most crucial and important part of any ventricular assist device. It can be internally or externally placed and vary in method of operation, size and placement. Earlier the pumps used in VADs were divided into two main categories – First the pulsatile flow (PF) pumps, that simulate the natural pulsing action of the heart in which the blood volume varies during the pumping cycle, and second the continuous flow pumps [24]. Continuous flow VADs are smaller and have proven to be more durable than pulsatile VADs [26]. They normally use either centrifugal pump or an axial flow pump. Both types have a central rotor containing permanent magnets. In the centrifugal pumps, the rotors are shaped to accelerate the blood circumferentially and thereby trigger it to move toward the outer rim of the pump. Whereas in the axial flow pumps, the rotors are more or less cylindrical with blades that are helical, causing the blood to be accelerated in the direction of the rotor's axis [21]. An important issue with continuous flow pumps is the method used to suspend the rotor. Earlier versions used solid bearings. HeartMate II is a second-generation axial continuous-flow (CF) pump. It is the LVAD that got U.S. Food and Drug Administration (FDA) approval for BTT in April 2008 and approved by FDA in the US for Destination Therapy in January 2010. HeartMate II outperformed HeartMate XVE, a first-generation pulsatile-flow (PF) pump LVAD which got FDA approval for BTT in 2001 and DT in 2003 [8]. While newer third generation pumps, some of which are approved for use in the European Union (EU) like HeartMate III, use either electromagnetic suspension called magnetically – levitated "maglev" [6,10,18,21] or hydrodynamic suspension. HeartMate III is an ultra compact sized device with fully Mag-Lev flow technology that allows device's rotor to be suspended by magnetic force resulting in contact free environment and excellent hemodynamics subsequently. It is intrathoracically placed and also induces a artificial pulse and has a textured blood coating surface that can pump 10L/ min of blood. Low power consumption is another benefit that can crucially prolong the battery life.

*Source*: www.thoratec .com

**Fig. 6. HeartMate III: A fully Mag-Lev LVAD [30]**

**Table 2 : A comparative study of LVAD's evolution and approval [30]**

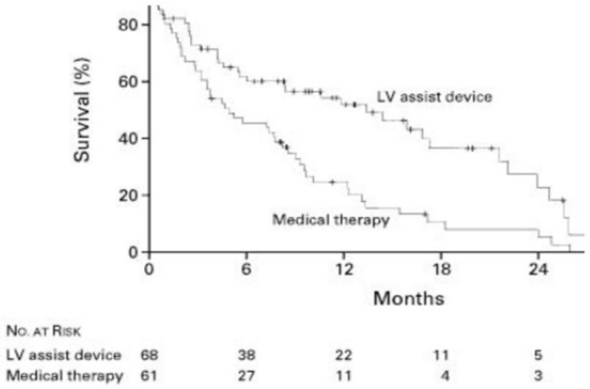
| VAD Models | Start of clinical trials | FDA BTT Approval | FDA DT Approval | EU Approval |
|---|---|---|---|---|
| PVAD (external pump) | 1976 | 1995 | 1998 | 1998 |
| HeartMate IP (implantable pneumatic) | 1985 | 1994 | n/a | 1994 |
| HeartMate VE (vented electric) | 1991 | 1998 | n/a | 1995 |
| HeartMate XVE | n/a | 2001 | 2003 | 2003 |
| HeartMate-II | 2003 | 2008 | 2010 | 2005 |
| HeartMate-III | 2014-Ongoing | Awaited since MOM-ENTU-M 3 IDE trial ongoing | Awaited | CE mark appro-val recent-ly in Dece-mber 2015 |

## Discussion

Various trials have been conducted to evaluate and improve the LVAD implantation performances and outcomes [12].The Harefield Recovery Protocol Study (HARPS) clinical trial evaluated whether advanced heart failure patients requiring VAD support can recover sufficient myocardial function to allow device removal (known as explantation). HARPS combines an LVAD (the HeartMate XVE) with conventional oral heart failure medications, followed by the novel β2 agonist clenbuterol. This opens the possibility that some advanced heart failure patients may waive off heart transplantation as the heart sufficiently regain its function [19].

REMATCH (Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure) study is a randomized control trial of 129 stage IV heart failure patients who were ineligible for cardiac transplantation and received a left ventricular assist device (68 patients) or optimal medical management (61). Kaplan–Meier survival analysis showed a reduction of 48 percent in the risk of death from any cause in the group that received LVAD as compared with the medical-therapy group. The frequency of serious adverse events in the device group was 2.35 Kaplan–Meier Analysis of Survival in the Group that received LVAD and the Group That received Optimal Medical Therapy (OMT) [5].

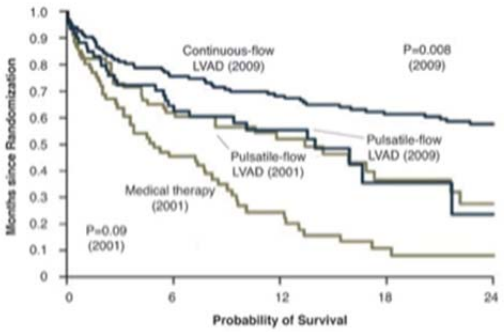
**LVAD vs OMT**




Source Eric A. Rose, et.al, Long-Term Use of a Left Ventricular Assist Device for End-Stage Heart Failure;N Engl J Med 2001; 345:1435-1443 November 15, 2001.

**Fig. 7: Rematch Trial outcome [5]**

**Comparison of OMT vs PF / CF LVAD**




*Source:* James C. Fang, "Editorial: Rise of the Machines- Left Ventricular Assist Devices as Permanent Therapy for Advanced Heart Failure," New England Journal of Medicine 361 (2009): 2282-85

**Fig. 8: Survival rates in various LVAD clinical trials [13]**

The INTrEPID trial (Chronic Mechanical Circulatory Support for Inotrope-Dependent Heart Failure Patients Who Are Not Transplant Candidates) was a prospective, nonrandomized clinical trial comparing LVAD with optimal medical therapy (OMT) .Fifty-five patients with NYHA functional class IV symptoms who failed weaning from inotropic support were offered a Novacor LVAD. Adverse event rates were found to be higher in the OMT group. Eighty-five percent of the LVAD-treated patients had minimal or no heart failure symptoms. Five LVAD patients and 1 OMT patient improved sufficiently while on therapy to qualify for cardiac transplantation suggesting benefits of survival from destination MCS [14, 23].

In post-REMATCH study conducted between November 2001 and December 2005, the in-hospital mortality rate was 27% for 280 patients who underwent HeartMate XVE implantation as DT [5,15].

Data from Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) evaluate various durability issues included pump replacement for infection, hemodynamics study like thrombosis-hemolysis, driveline or pump drive unit failure, and mortality caused by driveline or pump drive unit failure. The Analysis of Interagency Registry for Mechanically Assisted Circulatory Support data showed greater durability for continuous flow than for pulsatile left ventricular assist devices and even longer durations of support can be expected if pump durability improves [9,17].

## Limitations

Major barriers and improvement scope includes exorbitant cost of the device, the lack of public awareness in developing countries, prolonged hospitalization and high rates of readmission. Right Ventricle Dysfunction/Failure, strokes, infection and bleeding are some other adverse events which can be worked upon to make the device more optimum. [11].

## Summary

LVAD therapy is growing tremendously and has become most prominent in non- transplant eligible population. Technological advances and improved patient selection has resulted in increased survival benefits with CF devices. Focus on managing progression of heart failure and LVAD related complications would further improve the outcomes. There is an urgent need for lesser invasive implants, larger datasets from new trials, inventing smaller, cheaper and durable devices with collaborative care outside implanting centers.

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