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Ventricular Assist Devices: Expanding Role for Long Term Cardiac Support

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1. Introduction

There are more than 5 million people in United States who are diagnosed with heart failure and about 670,000 new cases occur every year in person age > 45 yrs [1]. HF incidence approaches to 10 per 1,000 of population after the age of 65 yrs. It is the most common hospital discharge diagnosis for patients in this age group [1,2]. There have been a number of significant advances in the treatment of heart failure particularly in pharmacological therapy, but despite that many patients become refractory to medical therapy and develop end stage heart failure. About 50,000- 100,000 patients develop end stage heart failure annually and their prognosis remains poor. [1, 2] When HF is refractory to medical therapy than in appropriate candidates, cardiac transplantation is the most effective treatment modality with average survival of 85% at one year. However, the supply of donor hearts is limited. There is also an increase in the number of heart failure patients who are not candidates for cardiac transplantation, mainly due to older age and presence of co-morbidities. [3,4] This has lead to a considerable interest in alternative forms of cardiac replacement therapy like total artificial hearts and ventricular assist devices. In the last few years, ventricular assist devices (VADs) have emerged as an important therapeutic options for patients with advanced heart Failure. The main purpose of a VAD is to unload the failing heart and help maintain forward cardiac output and vital organ perfusion. Originally introduced as a bridge to recovery, and then as bridge to transplantation, VADs have now evolved into permanent or destination therapy for a growing no. of patients with refractory heart failure. [3-5].

2. History and progress in the field of VADs

The first successful cardiac-assist device in humans was implanted by DeBakey at the Texas Heart Institute in 1966 [5]. Early devices were large and cumbersome with extracorporeal placement and provided temporary support only. The technological advancements led to the development of pulsatile LVAD design pioneered in 1976 as the Axio-symmetrical and Pierce-Donachy LVADs. A refined version of the latter device known as the Heartmate (Thoratec) was approved by the FDA as a bridging device to cardiac transplantation in 1994 [5]. Its updated version, the Heartmate XVE was approved as bridge therapy in 1998. The Randomized Evaluation of Mechanical Assistance in Treatment of Chronic Heart Failure (REMATCH) study evaluated the long term benefit of Heartmate XVE placement compared with optimal medical therapy in end-stage heart failure patients. (4) There was 48% reduction in death from all causes, attributable to LVAD therapy compared with best medical therapy in this trial. On this basis, the Heartmate XVE was approved for use as destination therapy in 2002. With time VADs have evolved significantly, with three major changes to date: (a) Transition from pulsatile to continuous-flow devices; (b) Reduction in size with the preference for internal placement of the devices; (c) Use of electricity as a power source [6]. The newest continuous-flow VADs are much smaller in size and owing to less moving parts are silent in operation, leading to significantly greater patient satisfaction and making this therapy more favorable for long-term support. Many newer VADs have been approved by FDA in recent years which includes but not limited to Thoratec Heartmate II (approved in Jan,2010), Heartware Ventricular assist System (approved in Nov,2012) and Jarvic 2000 (approved in Aug,2012).

3. Overview of VADs

3.1. Components of a VAD

VADs support the failing heart by unloading the ventricle and generating flow to the systemic and/or pulmonary circulation. They can be used to support the left ventricle, right ventricle or both the ventricles. LVAD is the main assist device used in clinical practice. Use of isolated right ventricular assist device (RVAD) is a rare event [7]. It is usually inserted around the time of placement of a left ventricular assist device (LVAD) to provide biventricular assistance. Unlike a single VAD, biventricular mechanical devices create a complex system with 2 independent pumps, one right sided and the other left sided which supports both left and right ventricles.

VAD typically has an inflow cannula, an outflow cannula, a pumping chamber, per-cutaneous driveline, a controller and power supply [7]. VADs are usually implanted through a median sternotomy. The inflow cannula is connected to the heart and it decompresses the ventricular cavity and an outflow cannula returns blood to either the ascending aorta or the main pulmonary artery. (9). The pumping chamber of the VAD is implanted sub-diaphragmatically to a pre-peritoneal or intra-abdominal position or may be situated in a para-corporeal position outside the body [7]. A percutaneous driveline, containing the control and power wires, is tunneled through the skin of the abdominal wall. It connects the device to an external portable driver

consisting of an electronic or pneumatic controller and a power supply that may be worn around the waist, carried in a shoulder bag, or contained within a small bedside monitor [7].

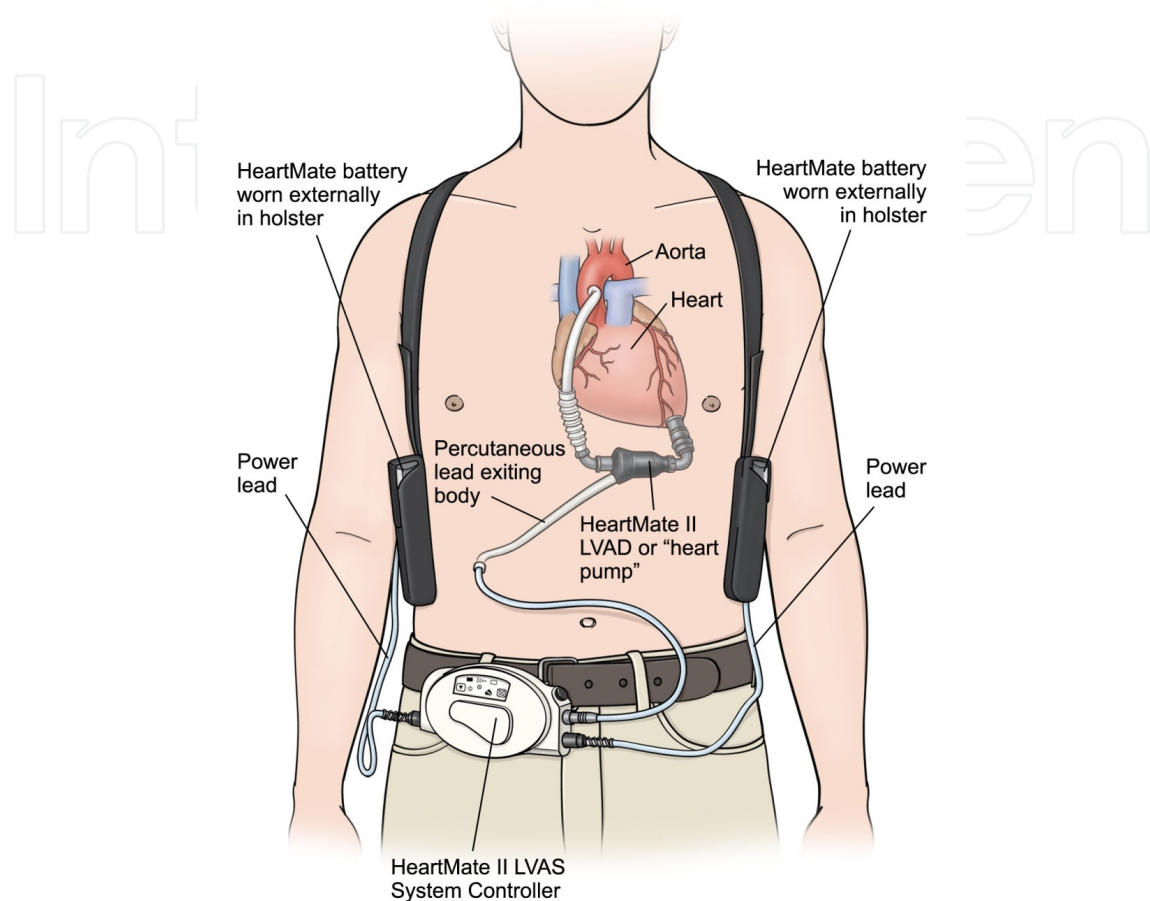


Figure 1. Image showing various components of a Heart Mate II ventricular assist device: Inflow and outflow canula, Heartmate II pump, percutaneous driveline, External portable driver (System controller) (Photo courtesy Thoratec).

3.2. Types of VADs

Many VADs are currently available commercially or in various stages of development. These are developed to satisfy special needs for either short or longer-term support and, therefore, differ markedly in their design characteristics, principles of operation, hemodynamic capabilities, method of insertion, and durability.

3.2.1. Percutaneous short term devices

Percutaneous VADs include devices that are inserted through the femoral artery and advanced to the left ventricle. Examples include Impella 2.5 pump and TandemHeart. Impella 2.5 pump (Abiomed Inc., Danvers, MA) is an impeller-driven, axial flow pump, capable of pumping 2.5 L/min [8,9]. TandemHeart (CardiacAssist, Inc., Pittsburgh, PA) is a low speed centrifugal

continuous-flow pump that drains oxygenated blood through a catheter advanced across the interatrial septum to the left atrium and pumps it back to one or both femoral arteries [10,11].

3.2.2. *Longer term assist devices*

The currently available longer-term VADs are categorized into three generations, reflecting the order in which they were developed and the type of pumping mechanism they use.

3.2.2.1. *First generation or pulsatile flow pumps*

These are pulsatile devices that use pusher plates and have inflow and outflow valves. These devices are efficacious at unloading the left ventricle and maintaining the circulation, with the capacity to pump up to 10 L/min [6]. Examples include the HeartMate® I or XVE (Thoratec Corp., Pleasanton, CA) and the Novacor VAD (WorldHeart Inc., Oakland, California, USA). These implantable VADs are placed intra-abdominally or pre-peritoneally in a pocket under the abdominal rectus muscle and connected to the apex of the left ventricle and to the ascending aorta [12]. There is increased risk of hematomas and infections as they are large in volume, requiring extensive surgical dissection. The percutaneous leads of these devices, especially those of the HeartMate XVE, are large and stiff and contain an air vent channel, which makes the system quite noisy and uncomfortable [12]. All pulsatile devices have biological or mechanical valves to allow a unidirectional blood flow. Anticoagulation is necessary for all devices, except the HeartMate XVE due to a textured inner surface of the pump stimulating formation of a biological layer preventing thrombus formation [11]. After the REMATCH study, Heartmate XVE was approved for use as “destination therapy” in 2002. Although the VAD therapy group had significantly greater survival and quality of life at both one and two years of follow-up, the survival at two years was only 28%. In addition, there were large numbers of readmissions and device-related complications including sepsis and stroke. Therefore, use of Heartmate XVE as destination has not been widely accepted [11]. The first generation devices are also used successfully as a “bridge to transplantation” with a perioperative mortality of 15–20% and an overall survival until device explantation of 60–70%. However, in the majority of studies, the maximal support duration does not exceed 6 months, and in most studies mean support duration ranges only from 50 to 60 days [13–15]. Survival and quality of life has been closely related to adverse events such as bleeding, infections, thrombo-embolic events and technical failures.

3.2.2.2. *Second generation or continuous (axial) flow pumps*

The second generation VADs are much smaller and durable in comparison to the first generation devices. The examples include the HeartMate 2 VAD (Thoratec Inc.), the Jarvik 2000 (Jarvik Heart Inc., New York, New York), Micromed DeBakey VAD and the Berlin Heart Incor (Berlin Heart AG) [11]. They have the continuous flow impeller pumps which are considerably smaller and safer to insert. Because they have only one moving part (the rotor), they are expected to be more durable than first-generation devices. To maintain an international normalized ratio (INR) of 2.0–2.5, the use of these pumps requires full anticoagulant therapy coupled with antiplatelet medications, such as aspirin or clopidogrel [11]. The HeartMate 2 is the most successful second-generation device with over 2500 implants worldwide. It is one-

seventh of the size and one-fourth the weight of the HeartMate XVE. Heartmate II device has been approved by the US FDA for implantation as BTT in April 2008 and as DT in January 2010 [11,12]. The mean duration of support reported from the use of these continuous flow, rotary pumps is considerably longer compared with the first-generation devices (166–236 vs. 50–60 days). Studies show 2 years survival of 65 and 69% with no mechanical failure and low fatal adverse event rates. The incidence of thrombo-embolic events in HeartMate 2 patients is in most studies comparable with those seen with Heart-Mate XVE, however the risk of hemorrhagic stroke rates tend to be higher (2–3%), as a result of the anticoagulation [12].

3.2.2.3. Third generation or continuous (centrifugal) flow pumps

Third-generation VADs are small centrifugal pumps in which the rotor is magnetically or mechanically suspended and, therefore, does not use ball bearings. Drivelines are less thick and more flexible. These features, coupled with the lower number of revolutions per minute, should enhance durability in comparison with the second generation pumps. Examples of such third generation VADs are the VentrAssist VAD (Ventricor Ltd, Chatswood, New South Wales, Australia) [16] and the DuraHeart (Terumo, Somerset, New Jersey, USA) [17]. These devices are thought to last as long as 5–10 years, and their performance is being evaluated in several phase I studies involving the HVAD® (Heart-Ware, Miramar, FL) devices, and more recently the DuraHeart® (Terumo Kabushiki Kaisha, Tokyo, Japan) system. They still carry the risk of neurological complications like stroke as well as risk of infections [11,12].

3.3. Indications for VADs

VADs can be used for a wide spectrum of diseases based on the therapeutic goals of circulatory support as well as the duration of treatment. The major three indications include:

1. Bridge to recovery
2. Bridge to transplantation
3. Destination therapy

4. Bridge to recovery

As name suggests it implies the use of VADs in patients who need only temporary support to provide mechanical unloading of the heart as in cases of acute cardiogenic or post-cardiotomy shock, acute inflammatory cardiomyopathies, and myocardial infarction. This will allow sufficient time for myocardial recovery and eventual removal of device. The ability of LVADs to support an acutely failing heart while it recovers function, is well documented [16–18]. The VAD causes mechanical unloading of the left ventricle, which leads to a reduction in ventricular size and volumes [19] as well as normalization of pressure-volume relationship curves [20]. It also affects myocardial structure by altering both cellular and extracellular component which contributes to recovery of myocardial function at cellular level [21–24]. This process of recovery of ventricular structure and function with the use of VADs is known as 'Reverse remodeling'.

5. Molecular pathways for reverse remodeling

VAD therapy has shown to affect excitation contraction (E-C) coupling in myocardial cells [25]. After VAD treatment, cardiomyocyte contractility is increased [26,27] and the force-frequency relationship is normalized [28,29]. Action-potential duration is also reduced [30,31] mirroring the shortening of the QT interval on electrocardiogram [32]. In addition to E-C coupling mechanisms, several other molecular mechanisms responsible for VAD-induced reverse remodeling have been described. These include effects at the levels of metabolic pathways, alterations in calcium handling proteins, immune and inflammatory responses, transcription factors, the adrenergic system, cytoskeletal proteins, the extracellular matrix, neurohormonal activation, and apoptosis and necrosis signaling [6]. Clinically these changes improve left ventricular function and patients have a dramatic increase in their exercise capacity following LVAD implantation. These findings encouraged the explantation of LVADs in select patients who have demonstrated sufficient recovery of myocardial function. To date clinical results are mixed and although the large number of studies report regression or normalization of the pathological substrate following VAD treatment, the clinical evidence for recovery remains limited. To date, an average of only 5%–10% of patients who undergo mechanical circulatory support demonstrate adequate recovery of ventricular function to allow device explantation [6].

There is also concern that prolonged mechanical unloading reduces cardiac cell function, as well as cell size, in a time-dependent manner which may lead to myocardial atrophy [20–24]. Unloading induced atrophy can be an important impediment to myocardial recovery and removal of the VADs for bridge-to-recovery, limiting the efficacy of VAD treatment [33]. Minimizing unloading-induced atrophy may be an important strategy to obtain the beneficial effects of VADs and, to this end, a pharmacological regimen that includes clenbuterol has been tested in combination with VAD treatment [34–36]. Clenbuterol is a β_2 adrenoceptor agonist that is currently approved only for patients with asthma, but has been shown in animal models to induce hypertrophy of skeletal and cardiac muscle and enhanced mechanical strength of contraction. In a study, a novel combination regimen which included clenbuterol was used in patients with non-ischemic cardiomyopathy who were transplant candidates and required a VAD for refractory heart failure [34–36]. In nearly 70% of patients on the combination therapy, the VAD could be removed within one year. After four years of follow-up, the average ejection fraction had improved from 15% preoperatively to 62%. These encouraging data have prompted the initiation of the Harefield Recovery Protocol Study (HARPS) to assess clinical cardiac recovery and explore molecular mechanisms of clenbuterol [6].

6. Bridge to transplantation

“Bridge-to-transplantation” is the strategy in which VADs are used for improving ventricular function and peripheral perfusion in patients awaiting cardiac transplantation. Several studies have demonstrated that VADs ensure sustained improvement in hemodynamic status and quality of life in patients awaiting cardiac transplantation [37]. More than 80% of VAD-treated patients undergoing cardiac transplantation have a normal or improved post-transplant outcome [38].

When implanted in patients refractory to medical therapy, LVADs lead to improved end organ function as well as overall physical conditioning [11]. LVAD markedly decreases the filling pressures and increases cardiac output by taking over the work of the left ventricle, the. This leads to lower pulmonary vascular resistance and a reduction in afterload for the right ventricle. Additionally, the increase in cardiac output provides additional preload for the right ventricle, which further enhances its function. This improvement in right ventricular function and mechanical replacement of left ventricular output by LVAD results in more efficient delivery of oxygen to end-organ tissues. As a result, the presence of the LVAD can partially or totally reverse functional impairment of these organs. This is most clearly evident in the kidneys, in which renal failure can improve or resolve following the implantation of an LVAD. All organ systems benefit from the increase in perfusion, allowing sick patients to stabilize or improve as they wait for a heart transplant. In addition to providing an increased length of time on the organ waiting list, LVADs significantly improve outcomes by reducing patients' co morbidities at the time of transplant. This makes them better transplant candidates and improves their post transplant outcomes [11, 12].

7. Destination therapy

In "Destination Therapy", VADs are used as an alternative to cardiac transplant to support the patients for their entire life. It involves the largest population of the patients with end stage heart failure who are unable to receive cardiac transplantation [39]. The success of LVAD implantation as "Bridge to transplantation" (BTT) in candidates with refractory heart failure led to the investigations for its use as an alternative to Heart transplantation. The REMATCH trial was one of the most remarkable trials that assessed the feasibility of VADs for Destination Therapy (DT) [40]. The trial was conducted between May 1998 and July 2001 at 20 US hospitals and it *showed significant improvement of the quality of life in patients supported with LVAD and improved one year survival from 25% to 52%. These data led to the US Food and Drug Administration (FDA) approval of the modified HeartMate XVE LVAD for use as DT in November 2002, thus launching a new era of surgical therapy for advanced heart failure* [39,40]. One of the more recent trials, the Heartmate II trial was conducted between March 2005 and May 2007 and it has shown that patients supported with HM II VAD (continuous flow VAD) had significantly improved two-year survival when compared to HM XVE recipients (58% vs. 24%, respectively) and significantly improved probability of freedom from stroke and device failure at two years, as compared to the recipients of pulsatile devices. These data led to approval of Heartmate II VAD for DT by US FDA in January 2010 [39,40].

8. Indications for DT

The criteria for VAD implantation for DT are based largely on the entry criteria into the REMATCH trial [40]. They are:

1. Class IV NYHA symptoms for at least 60 of the last 90 days despite maximized oral therapy, including dietary salt restriction, diuretics, digitalis, beta-blockers, and angiotensin converting enzyme (ACE) inhibitors (if tolerated), or requirement of inotropic support as outlined by the AHA/ACC guidelines for heart failure treatment.
2. LVEF of $\leq 25\%$,
3. Peak oxygen consumption of < 12 mL/kg/min or documented inability to wean intravenous inotropic therapy owing to symptomatic hypotension, decreasing renal function, or worsening pulmonary congestion.
4. Contraindication to HT due to either age greater than 65 years or comorbidities such as insulin-dependent diabetes mellitus with end-organ damage, chronic renal failure, or others, and
5. Appropriate body size (≥ 1.5 m²) to support the LVAD implantation.

9. Survival with DT

As mentioned earlier the results of the REMATCH trial revealed significant improvement in one-year survival from 25% to 52%.with improvement of the quality of life in patients supported with VAD in comparison with optimal medical therapy. In the post rematch era despite improvements in design, there was no significant improvement in clinical outcomes with pulsatile flow devices [39]. Recently published Heart Mate II trial showed that patients supported with continuous flow HM II LVAD had significantly improved two-year survival when compared to pulsatile flow HM XVE recipients (58% vs. 24%, respectively) and significantly improved probability of freedom from stroke and device failure at two years, as compared to the recipients of pulsatile devices[40].

Experiences of the post-REMATCH era have shown that many DT recipients who were initially deemed not transplantable have improved their condition and became eligible for HT; 1 in every 5 recipients of HM XVE in the post-REMATCH era (17% of the 280 studied patients) underwent successful HT within 10 months from device implant [6]. In most of these cases the improvements occurred due to the resolution of deemed irreversible pulmonary hypertension, recovery of renal function, weight loss, achieving cancer-free period, or reversal of other conditions. Therefore, one should not assume that DT would in the future preclude transplantation [39]. Although LVAD implantation in the post-REMATCH era continues to be associated with substantial survival benefit as compared to medical therapy, the outcomes of DT remain substantially inferior to those of HT (85% one-year survival) [39].

Contraindications for LVAD [41,42] therapy

- Irreversible contraindication for heart transplantation if recovery or destination is not the aim
- Biventricular failure in patients older than 65 years
- High surgical risk for successful implantation

- Recent or evolving stroke
- Neurological deficits impairing the ability to manage device
- Significant underlying psychiatric illness or lack of social support that may impair ability to maintain and operate VAD
- Active systemic infection or major chronic risk for infection
- Fixed pulmonary or portal hypertension
- Severe pulmonary dysfunction (eg, FEV₁ <1 L)
- Impending renal or hepatic failure
- Multisystem organ failure
- Inability to tolerate anticoagulation
- Heparin-induced thrombocytopenia

Relative contraindications

- Age >65 years, unless minimal or no other clinical risk factors
- Morbid obesity (BMI>40 kg/m²)
- Chronic kidney disease with serum creatinine level >3.0 mg/dL
- Severe mitral stenosis or moderate to severe aortic insufficiency, or uncorrectable mitral regurgitation
- Severe chronic malnutrition (BMI <21 kg/m² in males and <19 kg/m² in females)

10. Complications associated with VAD therapy

VAD therapy is associated with various long term complications which include bleeding (epistaxis or GI bleed), pump thrombosis, right sided heart failure, arrhythmias, hemolytic anemia etc. It is also associated with perioperative bleeding and infections as well as complications like air embolism and sepsis. The major late complications are mechanical device failure, neurologic events, and infections [43,11].

1. Mechanical Failure:

Device malfunction is an important cause of morbidity and mortality in patients living with VADs, especially with the prolonged support required for both bridge to transplantation and destination therapy [44-46]. In the REMATCH trial, 35% of patients experienced component failure within 24 months of implantation [11]. A contemporary review of 109 pulsatile VADs implanted at a single institution found that the probability of device failure was 6%, 12%, 27%, and 64% at 6 months, 1 year, 18 months, and 2 years, respectively [11]. On the other hand for continuous flow pumps the mechanical durability seems to be markedly improved. In one

study on patients with a HeartMate II VAD as bridge to transplantation, only 5 of 133 (4%) developed either device thrombosis or a complication from surgical implantation necessitating device replacement.

Complications can arise in any component from the portable drive/system controller that controls and powers the device to the inflow and outflow cannulae, valves and batteries [11]. These devices have system controllers and monitors that provide visual and auditory alarms during malfunction. To diagnose suspected device malfunction these alarms must be used in conjunction with clinical, laboratory, and imaging data. For troubleshooting, various catheter, angiography, fluoroscopy, and echocardiography based protocols have been developed to help diagnose common malfunctions [45,46]. If necessary, repair of a dysfunctional VAD or removal and replacement with a new VAD may be performed.

Role of echocardiography in detecting VAD related complications

Echocardiography is one of the important diagnostic tools in detecting VAD related complications. On many instances, it is used as the test of choice in outpatient setting to detect the complications as well as to adjust VAD parameters. Following are some of the examples of complications which can be detected by echocardiography [45,46,59].

- RV failure (decreased RV systolic function, increased RV size, increased right atrial pressure, and increased tricuspid regurgitation)
- Pericardial effusion with or without cardiac tamponade
- LVAD-related continuous aortic insufficiency (aortic regurgitation throughout cardiac diastole and systole)
- Inadequate LV filling (small LV dimensions)
- LVAD-induced ventricular tachycardia (underfilled LV and mechanical impact with septum)
- Intracardiac thrombus (including right and left atrial, LV apical, and aortic root thrombus)
- Continuous pump apical inflow abnormality due to inflow cannula obstruction, malposition, or hyperdynamic apical LV function (color Doppler high-velocity aliased flow at the cannula orifice with a peak Doppler velocity >2 m/s)
- Pulsatile pump apical inflow obstruction (intermittent interruption of usual laminar LVAD diastolic inflow using pulsed-wave Doppler with inflow velocities >2.5 m/s and color flow aliasing at the cannula orifice)
- Pulsatile pump inflow valve regurgitation (apical inflow cannula turbulent flow detected by color Doppler during LVAD ejection, dilated LV, frequent opening of the AV, and reduced outflow graft flow <1.8 m/s)
- Cannula kinking or complete thrombosis (loss of Doppler signal in all echo views and loss of RV outflow tract stroke volume with speed change)

- Hypertensive emergency, continuous flow pump (minimal AV opening, dilated LV, worsening MR, and peak outflow cannula velocity >2 m/s)
- Impeller cessation, continuous flow pump (dilated LV, acute reversal of apical inflow flow direction using spectral or color Doppler, worsening MR, and decreased RV outflow tract stroke volume).

2. Neurologic Events:

Neurologic complications from VAD therapy include cerebro-vascular accidents (both ischemic infarcts and intracranial hemorrhage) as well as non stroke complications like syncope, seizure, brain abscesses, and encephalopathy. Implanted mechanical devices are susceptible to thrombo-embolic events due to their unique properties. The foreign surfaces of VADs and associated turbulent flow can activate the immune system, platelets, and the coagulation cascade which increases the risk of thrombi formation [47]. Moreover, unmasking or inadequate treatment of hypertension, older age, higher VAD flow and pulsatility index, and inadequate anticoagulation further increase the risk for development of neurological events. The incidence of CVAs range from 0.009 to 5.73 events per patient-year [47-49]. The prevalence of neurologic events with destination therapy has ranged from 44% in the RE-MATCH trial (HeartMate XVE) to 57% in the European LionHeart Clinical Utility Baseline Study [11].

Not all devices have the same neurologic event rate. Design modifications like the use of novel biologic materials, textured coatings, and a single moving part, are believed to reduce the risk of thrombus formation. Promising data from the HeartMate II trial demonstrated reduced adverse events per patient year with respect to stroke (0.19 vs. 0.44) and non-stroke (0.26 vs. 0.67) neurologic events compared with a pulsatile flow pump [11]. Appropriate device selection, prevention of infection that can activate platelets, blood pressure control, and meticulous regulation of anticoagulation are all critical for the prevention of cerebro-vascular accidents after VAD implantation [50,51].

3. Infections:

VAD infections occur most frequently between 2 weeks and 2 months after implantation. The predominant organisms are Gram-positive organisms *Staphylococcus epidermidis* and *Staphylococcus aureus* followed by enterococci. Other commonly implicated organisms include Gram negative bacilli such as *Pseudomonas aeruginosa*, *Enterobacter*, and *Klebsiella* species, along with fungi. Frequent use of broad-spectrum antibiotics, particularly during the index hospitalization, is believed to increase susceptibility for fungal infections, which are associated with the highest risk of death [52-58].

The most common site of infection is the percutaneous driveline, which can often be managed successfully with wound care and antibiotics. However, a driveline infection can spread to other components of the VAD resulting in bacteremia, sepsis, and endocarditis. Sepsis in patients with mechanical assist devices has been reported to be the leading cause of death and can result in cerebral emboli and multi-organ failure [52-58]. Other infections, including mediastinitis and peritonitis, have also been reported.

Many strategies have been adopted to try to minimize device-related and wound infections. Proper care of the driveline exit site must be maintained. Strict aseptic technique (e.g., sterile gloves, mask) must be followed when caring for the percutaneous exit site. The site should be gently cleaned with a mild antimicrobial soap and rinsed with sterile normal saline after which a dry sterile dressing should be applied. At all times, the driveline must be secured to minimize the risk of trauma; immobilization can be performed with an abdominal binder, additional gauze, tape, or a stoma-adhesive device [11]. There are also many modifications made to device design to further decrease the risk of infection which include the use of larger single-lead drivelines and drivelines coated with chlorhexidine and silver sulfadiazine. Studies of rotary blood pumps with their reduced surface area for colonization and smaller surgical pump pocket suggest that they are less prone to infection [52-58].

11. Preparing the patients for life outside hospital after VAD implantation

Adequate cardiac rehabilitation including physical, occupational, and nutritional therapy is very important for patient's recovery from VAD implantation.

a. Physical Exercise

It is very important for patients to continue their physical performance. VAD's ability to unload the ventricle leading to profound ventricular pressure and volume changes leads to reversal of neurohormonal activation, impaired metabolic vasodilation, and myocardial remodeling [60].

b. Nutrition

The nutritional status of a VAD patient should be checked periodically. Patients who have malnutrition, particularly cachexia or hypoalbuminemia, may be predisposed to immune system dysfunction, impaired healing, and infection [61,62].

c. Routine self-care

It is important to perform periodic cleaning and maintenance of VAD equipment after discharge including changing the dressing at the exit site, inspecting for signs of infection, measuring daily vital signs, examining the connectors and ventilator filter for dirt or debris, and assessing the status of the batteries [7].

d. Harmful environments

Due to the sensitive nature of these machines, patients should avoid extremes of temperature for prolonged periods of time, operating heavy machinery and must not engage in contact sports or strenuous activities.

e. Responsibility of primary care physicians and nurse associations

Primary health care providers play an important role in successful outpatient management and should be properly instructed in the basic management of VADs. Such providers should be aware of the potential for infection and neurologic complications, as well as pump stoppage.

Primary health care providers should also discuss end of life care options specially for patients who are being considered for "Destination therapy". When patients are considering the VAD therapy, a consult to palliative care team can mobilize important services including symptom management as well as psychological and spiritual support for the patients and their families. After device implant, palliative care team can provide essential support to the patients as needed. If a catastrophic complication occurs after the implant (eg debilitating stroke, overwhelming infection) palliative care experts can play a prominent role in patient management (eg comfort measures, pain control and supportive care) and refer them to hospice care.

f. Role of first responders

Local first responders and emergency department personnel should become familiar with the basic physiology, system operation, and components of a VAD [7].

g. Cardiopulmonary resuscitation and cardioversion

Cardioversion or defibrillation is possible with all technologies, as is intubation. When external defibrillation is required, the VAD system controller should be disconnected before delivering the shock to avoid electronic disruption.

12. Conclusion

With collaboration of multidisciplinary teams composed of engineers, scientists, physicians and nurses, VAD technology and applications continues to evolve. This progress has lead to significant improvement in patient care as well as outcomes of patients receiving this therapy. This technology is becoming a safe alternative to heart transplant for rapidly growing patient population with advance end stage heart failure. With technological advancements, VADs are becoming smaller, more efficient and durable, though challenges are still ahead in making them more safer with less adverse effects. With the encouraging results in terms of survival as well as quality of life, VAD therapy is also being considered for patients with less severe heart failure. As patient population considered for VAD therapy continues to grow, more efforts are needed in educating patients and their families as well as medical care providers to effectively manage the challenges associated with these devices.

Abbreviations

VAD - ventricular assist device

LV- Left ventricle

RV- Right ventricle

LVAD- Left ventricular assist device

RVAD- Right ventricular assist device

FDA- Food and drug administration

BTT - Bridge to transplant

DT- Destination therapy

HF- Heart failure

HT - Heart transplant.

HM XVE- Heart Mate XVE

HM II- Heart Mate II

NYHA- New york heart association

LVEF- Left ventricular ejection fraction

BMI- Body mass index

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