End-Stage Congestive Heart Failure in the Adult Population: Ventricular Assist Devices

39

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Abstract

Congestive heart failure (CHF) is a major cause of morbidity and mortality within the adult population. If these patients progress to the end stages of this disease, then heart transplantation or ventricular support devices are required. However, due to a shortage of donor hearts, the use of ventricular assist devices (VADs) as either a *bridge to transplant* or *destination support* has grown dramatically as a therapy. Furthermore, with the increased use of these devices, there have been major efforts to develop these technologies as well.

Keywords

Congestive heart failure • Ventricular assist device

39.1 Introduction

Approximately five million Americans have congestive heart failure (CHF), and approximately 50,000 new cases are diagnosed every year. Furthermore, CHF is the most frequent cause of hospital admissions in patients older than 65 years, and it is the largest single expense for Medicare [1]. To date, with current medical management the 5-year mortality rate of CHF can be as high as 50 %. Fortunately, advances in medical therapy such as biventricular pacing, defibrillator implantation, and the ability to successfully perform surgery in high-risk patients have revolutionized the management of patients with CHF and greatly delayed the progression of CHF to end stage. Note that once a patient develops end-stage CHF, the treatment options are limited and typically ineffective, and thus subsequent mortality is high. In such patients, heart transplant becomes the last resort. Yet, in general, it is a very effective therapy which offers an excellent short-term and long-term survival benefits (over 90 and 50 % survival rates at one year and 10 years, respectively); most patients enjoy a near-normal lifestyle after heart transplant [2]. However, the donor hearts available for transplantation are limited to an average of 2200 per year, compared to over 35,000 people per year who could benefit from such a therapy [1].

Besides the scarcity of donor hearts, many patients die each year while waiting for an acceptably matched donor heart. Importantly in the past fifteen years, ventricular assist devices (VADs), especially left ventricular assist devices (LVADs), have been increasingly used to support such patients as a *bridge to transplant* [3]. After the landmark REMATCH trial, the LVAD has been used more and more as the *destination therapy* for end-stage CHF [4, 5]. In addition to the increased use of these devices, newer generations of VADs with better mechanics, smaller size, and longer durability have been developed in recent years [6–11]. Nevertheless, the ultimate goal of future VAD development is to produce a small, totally implantable, biocompatible, and durable heart pump that can physiologically function like a human heart. Clinically effective VADs should be judged by a variety of mechanical and physiological performance parameters; specifically, they should: (1) provide sufficient cardiac output to allow patients to perform their usual daily activities, (2) have a low risk of thromboembolism and pump or driveline infections, (3) have a low incidence of device malfunction, (4) be easily implantable and removable, and (5) be small in size.

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39.2 Classification of VADs

In general, VADs can be classified based on: (1) their internal mechanics (volume displacement, axial flow, or centrifugal), (2) therapeutic purposes (temporary, bridge to decision, bridge to recovery, bridge to transplant, and destination), (3) sites of support (LVAD, right VAD, or BiVAD), (4) location of the pump (implantable, paracorporeal, or extracorporeal), and/or (5) implanting approaches (sternotomy, thoracotomy, laparotomy, subcostal, or percutaneous).

39.3 VADs Defined by Mechanics and Clinical Applications

39.3.1 Volume Displacement Pumps (Pulsatile Pumps)

The functioning human left and right ventricles are physiologic volume displacement pumps. During each cardiac cycle, they generate over 60 cc of stroke volume, and each ventricle has a pair of inflow and outflow valves to maintain a unidirectional blood flow. The end result is that a human heart generates a pulsatile blood pressure and yet a steady cardiac output. The mitral and tricuspid valves function as the inflow valves, while the aortic and pulmonary valves function as outflow valves. A volume displacement VAD functions exactly like human ventricles; it has a pump chamber that generates a stroke volume between 40 and 80 cc during each cardiac cycle, and it has two artificial valves—either bioprostheses or mechanical valves.

The valves used inside VADs (i.e., bioprosthetic versus mechanical) are considered to ultimately determine the durability of the VAD and the need for anticoagulation. More specifically, bioprostheses may have the advantage of not requiring anticoagulation therapy, thus reducing the patient's risk for thromboembolism. However, the valve's limited life span inside the VAD may result in premature VAD failures, thus requiring VAD replacement. On the other hand, mechanical valves have the advantage of being durable, but then the patient will require adequate anticoagulation therapy to prevent clotting. Under- or over-anticoagulation treatment can increase the risk of thromboembolism or bleeding which can subsequently affect the patient's outcome.

Typically one of the two mechanisms is used to eject blood in this type of VAD: (1) compressed air is employed to squeeze the blood-filled sac or to displace a flexible diaphragm within a hard shell to generate stroke volume, or (2) a slow torque electrical motor is used to displace a flexible diaphragm inside the implantable unit within a hard shell to generate stroke volume. In general, the compressed air approach seems to provide a simple and reliable way of either moving the diaphragm or compressing the sac, with a pressure more comparable to a physiologically acceptable waveform. However to date, this design has required a bulky driving console, compromising the patient's mobility. In addition such driving consoles typically will make loud noises. If the diaphragm is propulsed by an electrical motor within a noncompressible metal chamber, the early systolic pressure generated by this pump is much higher than the pump driven by the compressed air. It has been found that such unphysiologically high pressures can speed the calcification process in the inflow bioprostheses and/or even cause early valve failures [12].

The blood to pump contact surface interaction plays an important role in determining the relative degree of resultant thrombogenicity of the pump and therefore the required needs for anticoagulation. This is particularly important for volume displacement pumps, because of their relatively large contact surface areas with blood, as compared to an axial flow pump. Historically, first the smooth surface was pursued during VAD design and then manufactured to avoid thrombosis, but later it turned out that an evenly distributed textured surface actually generated less thrombosis. More specifically, such textured surfaces promote early platelet and fibrin depositions during initial contact with blood, which in turn results in formation of stable pseudointima which subsequently prevents the formation of thrombosis [13].

Common volume displacement pumps include: (1) HeartMate® XVE LVAD (Figs. 39.1 and 39.2) and (2) Thoratec VAD (Fig. 39.2) (Thoratec Corp., Pleasanton, CA, USA). The HeartMate XVE was once the mostly implanted and most studied pulsatile LVAD worldwide until axial flow pumps, the second-generation LVAD such as HeartMate II, demonstrated the superiority in durability, easy to implant, and pump-related complications. It was approved by the FDA for use as both a bridge to heart transplant and as destination therapy for end-stage CHF. This system is driven by an electrical motor, but it can also be driven by compressed air if and when the electrical motor wears out. It is implantable and powered through the driveline which exits from the abdominal wall; common implant locations are in the abdomen or in the preperitoneal space. The inflow cannula is inserted into the left ventricle via an opening in the left ventricular apex, and the outflow graft is connected in the proximal ascending aorta. It has textured interface surfaces and thus has a very low risk of thromboembolism (Fig. 39.3). Therefore, patients with these implanted systems do not need to be anticoagulated with coumadin or Plavix, yet it is recommended that they take aspirin once a day.

The HeartMate XVE LVAD is no longer used in the adult clinical setting, yet it played a very significant historical role in demonstrating that end-stage CHF patients could be successfully supported with an LVAD. When compared to maximal medical management including home inotropic therapy, the use of the HeartMate XVE LVAD significantly improved the quality of life and survival of end-stage CHF patients [5].

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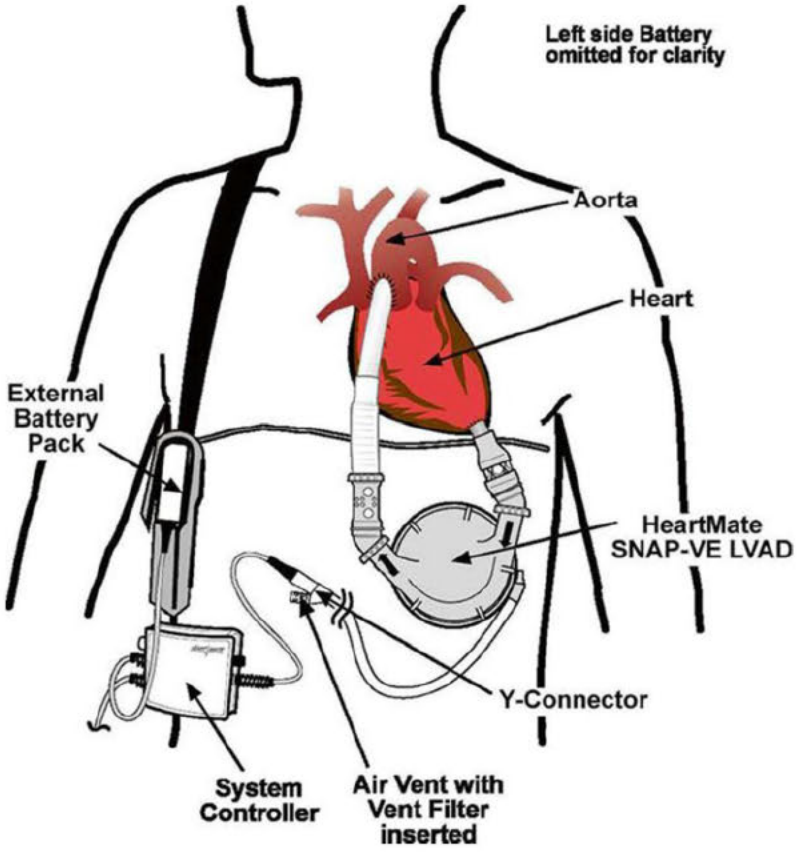


Fig. 39.1 Schematic of a HeartMate SNAP-VE ventricular assist device system. One can see the internal connections at the apex of the left ventricle where there is inflow into the device and outflow connected directly to the aorta. This system utilizes an external battery pack and controller system. *LVAD* left ventricular assist device

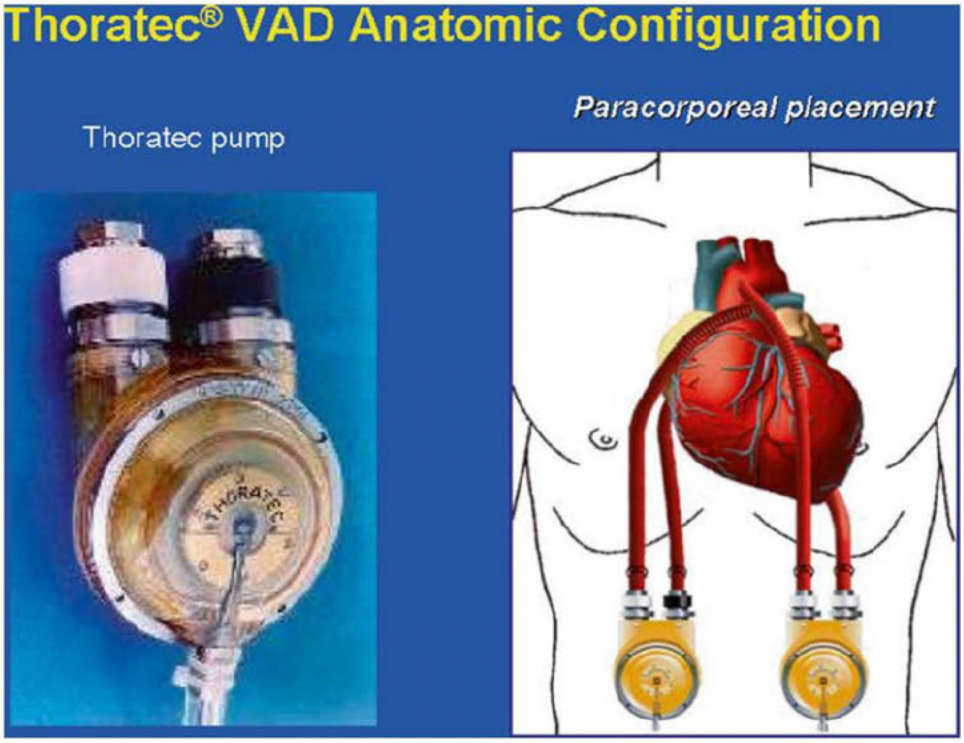


Fig. 39.2 Thoratec ventricular assist device (*VAD*). *Left*: pump with both inflow and outflow valve housing connectors pointing upward and the compressed air driveline pointing downward. *Right*: cannulas and grafts are implanted inside the body cavity, while the pumps are connected outside the body cavity

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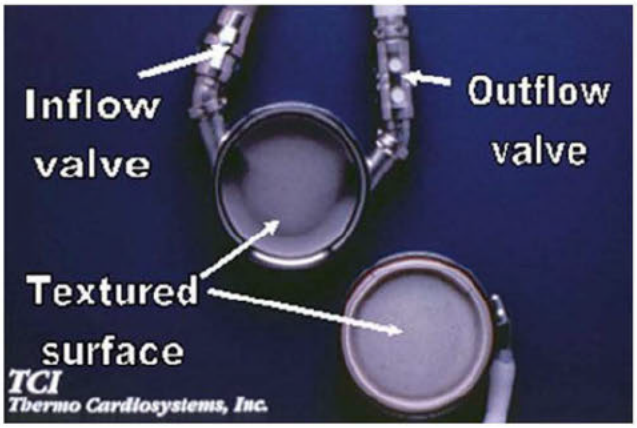


Fig. 39.3 Textured inner surface of HeartMate XVE left ventricular assist device. The textured surface promotes formation of pseudointima which subsequently prevents thrombosis formation

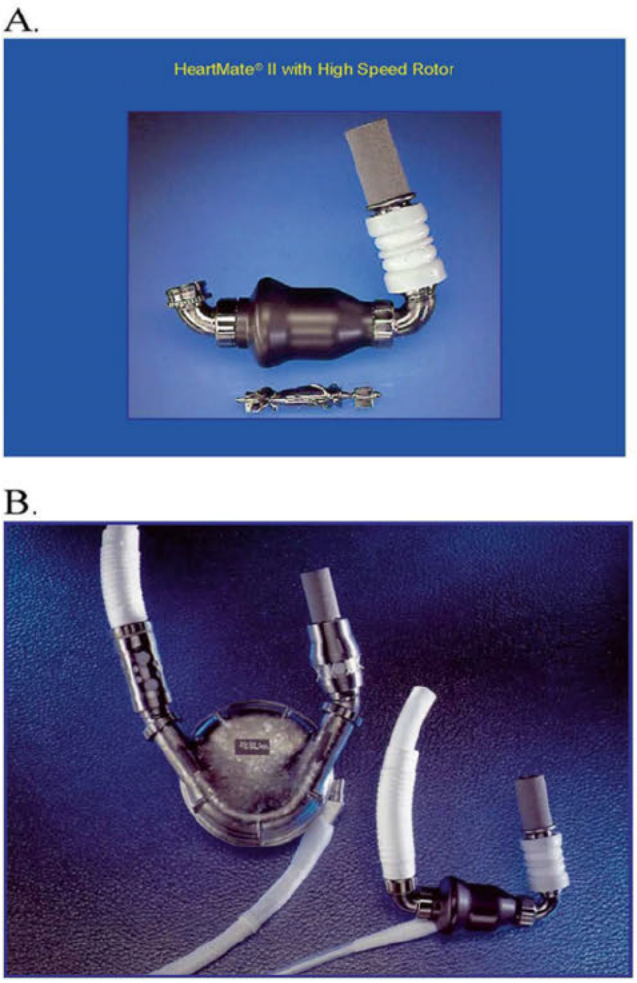


Fig. 39.4 HeartMate II left ventricular assist device. (**A**) HeartMate II pump and the high-speed rotor. The inflow cannula is connected to the pump. (**B**) Size comparison between the HeartMate VE and HeartMate II pumps. The inflow cannulas of both pumps are the same

It is the first implantable LVAD that was approved as the destination therapy for end-stage heart failure in the USA. However, the disadvantages of this system include (1) its overall heavy weight, (2) its bulky size, and (3) frequent inflow valve and/or electrical motor failures, after an average of 12 months of implantation [3–5, 14, 15].

The Thoratec VAD [16] can be used as an LVAD, RVAD, or BiVAD. It is commonly described as an implanted paracorporeal pump, with the inflow cannula inserted in the left ventricle via the left ventricular apex and the outflow graft sewed to the ascending aorta when used as an LVAD (or the inflow cannula inserted in the right atrium and the outflow graft sewed to the pulmonary artery as an RVAD). This system allows for numerous cannulation options. Its pump is made of a flexible sac housed in a plastic ball-shaped container. Currently, the sac material is composed of Thoralon which has a smooth surface to reduce the risk of thrombosis. This sac is squeezed by the compressed air via an air-driven console, and it has two mechanical valves, one as an inflow and the other an outflow valve. Importantly, these units can be implanted in small- or large-size patients (weight between 17 and 144 kg) and can be readily employed for short-term as well as long-term support. To date, this device is approved by the FDA to be used as a bridge to heart transplant and as postcardiotomy support to recovery. The disadvantages of this system include the paracorporeal pump being attached outside the body, which can be inconvenient to patients, and patients require anticoagulation with coumadin to maintain an INR between 2.5 and 3.0 to prevent thromboembolism.

39.3.2 Continuous Flow Pumps: Axial Design

The axial flow pumps are typically regarded as second-generation VADs, as compared to the first generation of volume displacement pumps. Such pumps incorporate both continuous flow and rotary pump technologies as the foundation of their design and construction. They have an impeller inside the pump that can generate high-speed rotations in a blood system (Fig. 39.4). Depending on the motor capacity and rotational speed, an axial flow pump can function either as a partial-flow or full-flow support VAD. The speed of a rotor can reach an RPM of 9000, and it can generate up to 10 L/min of flow with a mean pressure of 100 mmHg.

Initially, serious doubts about the utility of such pumps were raised due to the concerns of red blood cell destruction and heat generated by the high-speed motor inside the blood system. But (starting with conjunction) such theoretical concerns were discarded when a Hemopump was successfully used in a clinical setting without significant hemolysis [17]. The Hemopump thus set the stage for evaluation of other types of axial flow pumps that could be used to pump blood in the human body [6, 7, 9–11].

The common features of axial flow pumps include the following: (1) the simpler design of continuous flow rotary

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pump technology promises increased long-term mechanical reliability; (2) they do not require valves to create a unidirectional flow nor do they require an external vent or a compliance chamber, thus making them more likely to be used as the platform for future development of a totally implantable VAD; (3) the inflow cannulas are inserted into the left ventricular apexes or totally inside the left ventricle, and the outflow grafts can be connected to either the ascending or descending thoracic aorta (i.e., which is important if abnormalities in the ascending aorta exist); (4) the size of such pumps is relatively small, one-fifth to one-seventh the size of the volume displacement pumps, thereby extending therapy to underserved patient populations including women and even some children; and/or (5) these pumps are associated with minimal noise generation and overall greater patient comfort [6, 7, 9–11, 14, 15].

The HeartMate II LVAD (Thoratec Corp.), the DeBakey MicroMed LVAD (MicroMed Cardiovascular, Inc., Houston, TX, USA), and Jarvik 2000 (Jarvik Heart, Inc., Manhattan, NY, USA) are currently available representatives of this group of VADs. Among them the HeartMate II and the DeBakey MicroMed LVAD have many similarities: (1) they are about the same size, (2) both devices consist of an internal blood pump with a percutaneous lead that connects the pump to an external system driver and power source, and (3) both pumps can generate up to 10 L/min of flow. The initial results appeared to be encouraging, with data supporting effective circulatory support and durability [6, 7, 9–11, 14, 15]. Of particular interest is that the diminished pulse pressures that are associated with utilizing an axial flow pump seemed to be tolerated well in patients, at least for the short term. Importantly, the long-term consequences of using axial flow pumps have yet to be evaluated. Additionally, hemolysis associated with the use of axial flow pumps has been detectable, yet the level has been considered clinically insignificant. Nevertheless, these pumps seem to activate platelets because of the physical strain on blood cells; such activation could be an important source of intravascular thrombosis and/or embolic complications. It should be noted that the incidence of thromboembolism seems to be particularly high for the MicroMed LVAD. Therefore, intense anticoagulation regimens targeting platelet activation and clotting cascade have been employed to deal with these potential problems. A combination of coumadin and Plavix has been recommended for patients who have been provided with a MicroMed LVAD.

The HeartMate II LVAD has shown improved clinical outcomes both as bridge to transplant and destination therapy, with markedly better functional status and quality of life. An actuarial survival of 89 % at 1 month and 75 % at 6 months was reported [14]. The HeartMate II LVAD has proven to be safe and effective as bridge to transplantation. Furthermore, compared to HeartMate XVE, the HeartMate II significantly reduced the device- and surgery-related complications. It is considered that the lower incidence of postoperative bleeding and device-related infection may be due to its smaller size and the lack of need for a large pocket to house its pump and smaller driveline. The absence of a large preperitoneal pocket (which was required with the larger pulsatile devices) has reduced: (1) the need for extensive dissection, (2) postoperative bleeding, and (3) LVAD pocket hematomas and the development of pocket infection. Based on multiple clinical trial outcomes [14, 15, 18], the FDA approved the HeartMate II LVAD to be used as bridge to transplant as well as destination therapy for end-stage CHF patients in 2008 and 2010, respectively. To date, the clinical use of the HeartMate II LVAD has increased rapidly since FDA approval, and thus far over 17,000 patients have received implantation of the HeartMate II LVAD worldwide.

39.3.3 Continuous Flow Pumps: Centrifugal Design

The continuous flow pumps with centrifugal designs are considered the third-generation VADs. The technology used in these pumps includes noncontact bearings and hydrodynamic levitation that offer the advantages of (1) minimizing the friction of blood flow, (2) reducing platelet damage, and (3) reducing wear of the rotor (Fig. 39.5). The HeartWare pump (HeartWare, Framingham, MA, USA) is representative of this type of LVAD.

Compared to the HeartMate II system, the HeartWare pump is smaller and can fit inside the pericardial space; anatomically, it can fit into smaller adults as well as congenital patients. The pump can be inserted via a minimally invasive procedure, and this, in turn, potentially minimizes blood transfusions. Today, this is the only pump that can be readily used as an implantable RVAD and thus can be used for BiVAD support in those patients requiring such therapy.

Initial clinical trials of the HeartWare LVAD as bridge to heart transplant showed that patients' 30-day and 1-year survival rates were 99 and 86 %, respectively [19]. The pump received FDA approval for implantation as bridge to heart transplantation in 2012 and currently is in clinical trials to assess its use as destination therapy for end-stage CHF patients. So far over 6000 thousand patients have received HeartWare LVAD implantation worldwide.

39.4 VAD Implantation Techniques

In general, the implantation techniques currently employed for these three types of VADs are not very different from each other. The implantation for the latter two VADs is

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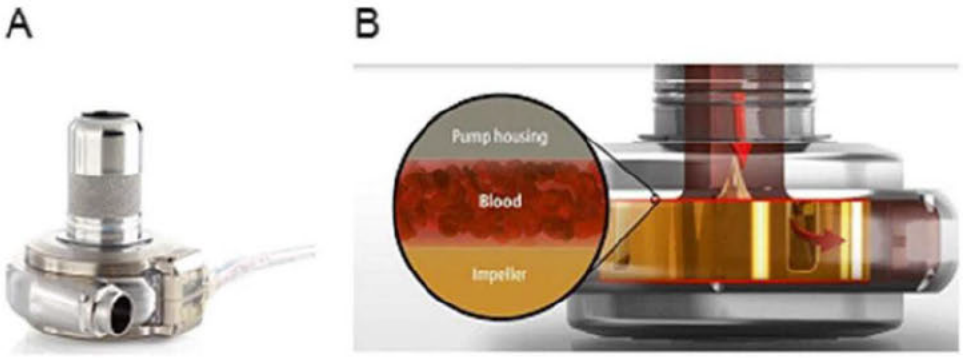


Fig. 39.5 HeartWare left ventricular assist device pump. (**A**) HeartWare pump. (**B**) Cross section of the inside structure of the pump showing the contactless design as well as magnetic and hydrodynamic bearings

probably easier because the need for tissue dissection is less for the smaller pumps and subsequently there is less bleeding. Typically a median sternotomy is made, and the patient is placed on cardiopulmonary bypass. The HeartMate II pump is inserted in the pre-created preperitoneal pocket, below the posterior rectus sheath. The HeartWare LVAD is inserted inside the pericardial space. The inflow cannula is inserted through a cored out portion of the apex of the left ventricle. The outflow graft is sewn to a longitudinal aortotomy in the proximal ascending aorta. Following appropriate connections, the patient is weaned off cardiopulmonary bypass, and the pump is started. Optimizing pump speed is performed under echocardiographic guidance, as well as by continuously monitoring the patient's hemodynamic status. Adequate flow is achieved by adjusting pump speed and by ensuring adequate preload and appropriate inotropic support for right ventricular function. After meticulous hemostasis is achieved, the chest is closed with appropriately placed chest tubes. The HeartWare LVAD can be inserted via a combination of left mini-thoracotomy and upper sternotomy or right mini-thoracotomy.

39.5 Device Management

It is imperative that standard postoperative care is used in the management of these patients. First, device settings can be monitored and adjusted based on patient hemodynamics as well as echocardiographic findings. Additionally, a combination of aspirin and warfarin is typically used as part of the anticoagulation protocol to maintain an INR between 2.5 and 3.5 for all the devices, except for patients with the HeartMate XVE for which only aspirin is needed. The VAD flow is generally maintained above 4 L/min, and the mean blood pressure is maintained over 60 mmHg. After LVAD placement, typically a patient does not change defibrillator and/or biventricular pacing settings if s/he had such a device implanted prior to VAD implantation. Finally, all patients undergo a standard postoperative rehabilitation program.

39.6 University of Minnesota VAD Experience

The University of Minnesota VAD and heart transplant program is one of the largest programs in the world. We have been among the participating centers and leaders in multiple NIH-sponsored clinical trials. Ten different types of VADs had been tried or used at our center. Since 1995, we have implanted 700 VADs, including over 250 continuous flow VADs for bridge to heart transplantation, bridge to bridge, bridge to recovery, and/or for destination therapy. We developed an effective VAD implantation algorithm to successfully treat patients with refractory acute cardiogenic shock and multiorgan failure who would typically die (Fig. 39.6) [20]. We also pioneered a minimally invasive LVAD exchange technique to avoid sternotomy (Figs. 39.7 and 39.8) [21].

39.7 Summary

Over the last 15 years, VADs (especially continuous flow LVADs) have been increasingly used in the clinical management of the chronic heart failure patient, as either a bridge to transplant or as the destination therapy. Abundant and important knowledge and experience has been obtained from the early clinical use of VADs. We believe that the future of VADs is very promising. The ideal design of any future VAD should embody, at a minimum, the following features:

1. It can provide adequate blood flow to meet the various physiological requirements.
2. It must be reliable and durable. For a VAD to be used as a destination therapy, 5–7 years has been suggested as an acceptable length of time for durability.
3. It must be biocompatible with the host patient and also require no, or minimal, anticoagulation therapy.

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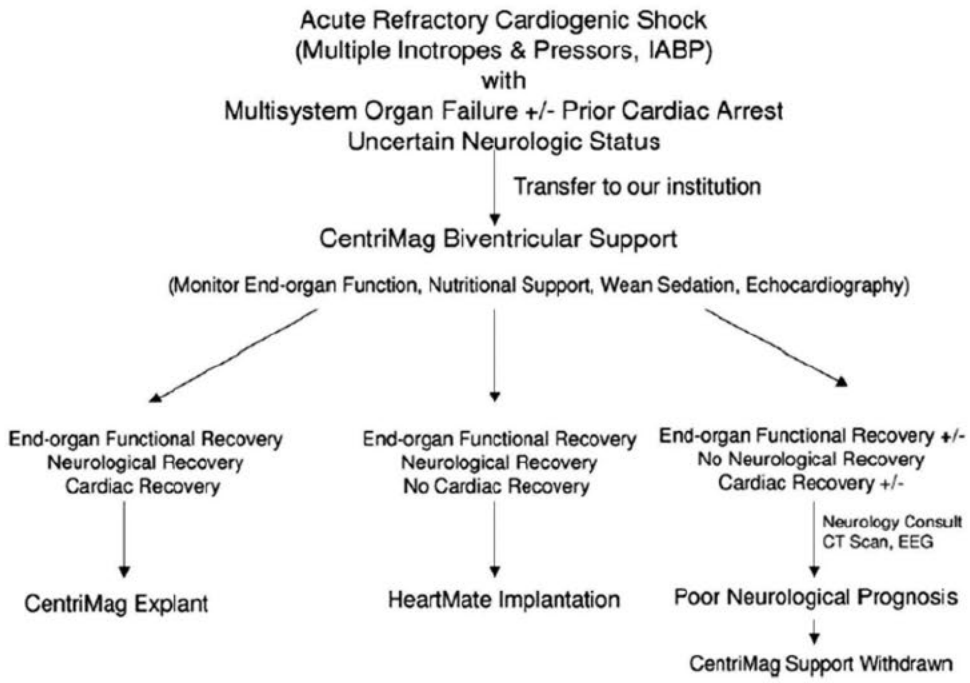


Fig. 39.6 Algorithm depicting the management of patients with refractory acute cardiogenic shock with multiorgan failure

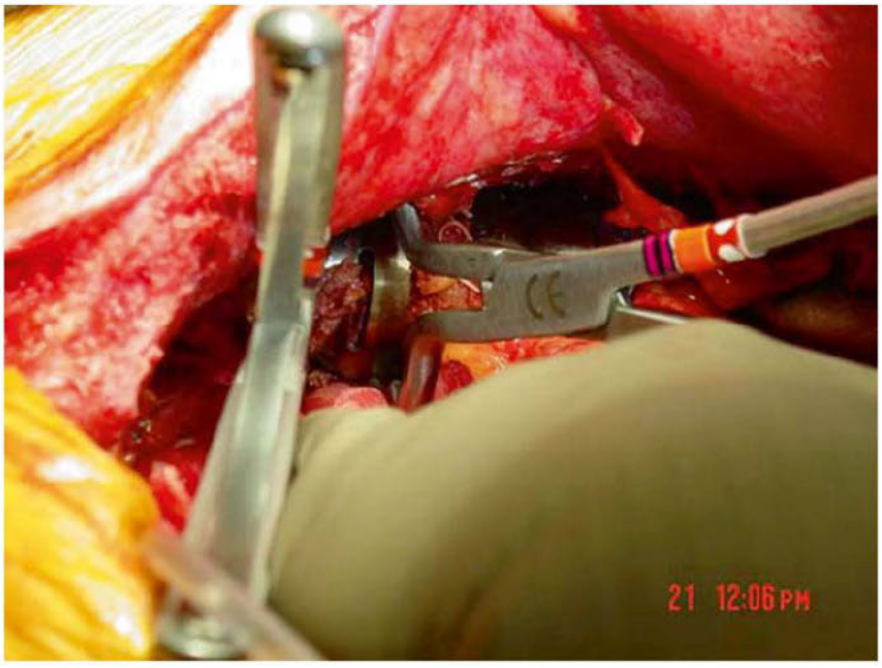


Fig. 39.7 Left ventricular assist device exchange is performed via laparotomy only; sternotomy is avoided

4. It must be small in size to minimize patient discomfort and ensure an improved quality of life.
5. It should be easy to implant, preferably through developing minimally invasive approaches.

It is considered that within the next ten years, we will see the birth of the "dream" VAD that meets these criteria. Perhaps one day implanting a VAD will be similar to implanting a prosthetic valve. Ultimately, the future of treating end-stage CHF lies in the cell therapy which can either reverse myocardium remodeling or regrow new myocardium, yet such a therapy may require VAD support of the patient during administration. For additional information on LVADs and their use in congenital populations, the reader is referred to Chap. 11.

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Fig. 39.8 Patient who received the fifth left ventricular assist device (*LVAD*) exchange. Photo was taken together with the author/surgeon 3 weeks after his fifth LVAD exchange surgery

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