

QUARTERLY FOCUS ISSUE: HEART FAILURE

Ventricular Assist Devices

The Challenges of Outpatient Management

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The need for mechanical assistance of the failing heart, whether acute after a myocardial infarction or permanent in patients with end-stage heart failure, has increased with improvements in medical therapy and a growing aged population. Over the past few decades, much progress has been made in the development and refinement of ventricular assist devices (VADs), medical devices capable of maintaining circulatory output of the diseased ventricle. Initially designed as a temporary support to allow ventricular recovery or as a bridge for patients to cardiac transplantation, these devices are now being used as a permanent form of “destination” therapy. Improvements in technological design, durability, and medical management have allowed individuals with VADs to be managed in their communities. Although these devices provide excellent hemodynamic support and enhance patient functional status, discharged individuals face many unique challenges. In this article, we discuss 1) the spectrum of VADs for outpatient therapy, including their basic physiology and hemodynamics; 2) the multidisciplinary approach required to care for a patient with such a device in the community; 3) routine general cardiac issues that are encountered; 4) associated long-term device and nondevice-related complications; and 5) the reported overall improvements in quality of life. (J Am Coll Cardiol 2009;54:1647–59) © 2009 by the American College of Cardiology Foundation

Despite widespread use of evidence-based therapies to reduce the morbidity and mortality of heart failure, the incidence of heart failure has not changed, and it remains the most common hospital discharge diagnosis for patients older than 65 years of age (1–5). Heart failure is a progressive disease, and individuals at the end of life have few options, given the limitations of intravenous positive inotropes and a finite number of donor organs (6). Multiple different mechanical devices for long-term circulatory support have been developed, ranging from total artificial hearts to ventricular assist devices (VADs). 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 temporary bridge to recovery and then as a bridge to transplantation, VADs have evolved into permanent or “destination” therapy for a growing number of patients with refractory heart failure (7). After VAD placement, many patients are discharged to their home communities. Once outpatients, individuals with an implanted VAD, whether indicated as a bridge to recovery or transplantation or as destination therapy, face similar lifestyle

modifications and long-term management issues. Although these patients will always require the attention of specialized heart failure centers, they also rely on the support of their community medical care providers. This review describes the current state of VAD technology and the challenges of caring for patients with a VAD living outside the hospital.

Overview of VADs

Indications for device therapy. Mechanical devices may be considered for a wide spectrum of diseases based on the anticipated duration and therapeutic goals of circulatory support. The classification is typically broken down into 3 categories: bridge to recovery, bridge to transplantation, and destination therapy. Bridge to recovery is reserved for patients who need only temporary support for days to weeks during which time reversibility of ventricular insult may occur followed by weaning and removal of device. This includes patients with acute cardiogenic or post-cardiotomy shock, acute inflammatory cardiomyopathies, and myocardial infarction. The second cohort is bridge to transplantation. These patients meet the criteria but need additional circulatory support while awaiting transplantation. Destination therapy categorization is reserved for patients who are not candidates for transplantation yet require the use of a VAD as a final therapy until death.

Components of a VAD. VADs used in the outpatient setting are implanted devices placed through a median

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Abbreviations and Acronyms

ICD = implantable cardioverter-defibrillator

LVAD = left ventricular assist device

QOL = quality of life

RVAD = right ventricular assist device

VAD = ventricular assist device

real position outside the body. Smaller devices are being developed for thoracic implantation, some with outflow to the descending aorta. 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 (Fig. 1).

Physiology of VADs. RIGHT OR LEFT VENTRICULAR SUPPORT. VADs support the failing heart by unloading the ventricle and generating flow to the systemic and/or pulmonary circulation. This creates parallel pumping chambers that compete for the same venous return (pre-load) and face the arterial resistance (afterload) of their respective pulmonary and systemic vascular beds. Under optimal conditions, the native ventricle is a passive conduit through which the

mechanical pump fills throughout the cardiac cycle, and the decompressed ventricle should contribute little to the systemic cardiac output. If a ventricular stroke volume is generated and the aortic/pulmonic valve leaflets are seen to open on echocardiography, either return of native ventricular function or inadequate decompression of the native ventricle and device dysfunction should be suspected.

Isolated right ventricular dysfunction requiring insertion of a right ventricular assist device (RVAD) to support the failing ventricle is a rare event. Cases have been reported post-cardiotomy after an acute myocardial infarction, coronary artery bypass grafting, and valvular surgery. More commonly, an RVAD may be inserted around the time of placement of a left ventricular assist device (LVAD) to provide biventricular assistance.

BIVENTRICULAR SUPPORT. The unique physiology created by a mechanical pump is further complicated if biventricular support is need. Unlike a single VAD, biventricular mechanical devices create a complex system with 2 independent pumps, one right sided and the other left sided. Left atrial venous return is normally greater than right atrial pre-load because of the bronchial circulation, so overall left-sided output (LVAD plus native left ventricle) must always be greater than right-sided output (RVAD plus native right ventricle) or else pulmonary edema may develop. In addition to navigating complex biventricular cannula insertion anatomy, native right and left ventricular function may also recover at different rates.

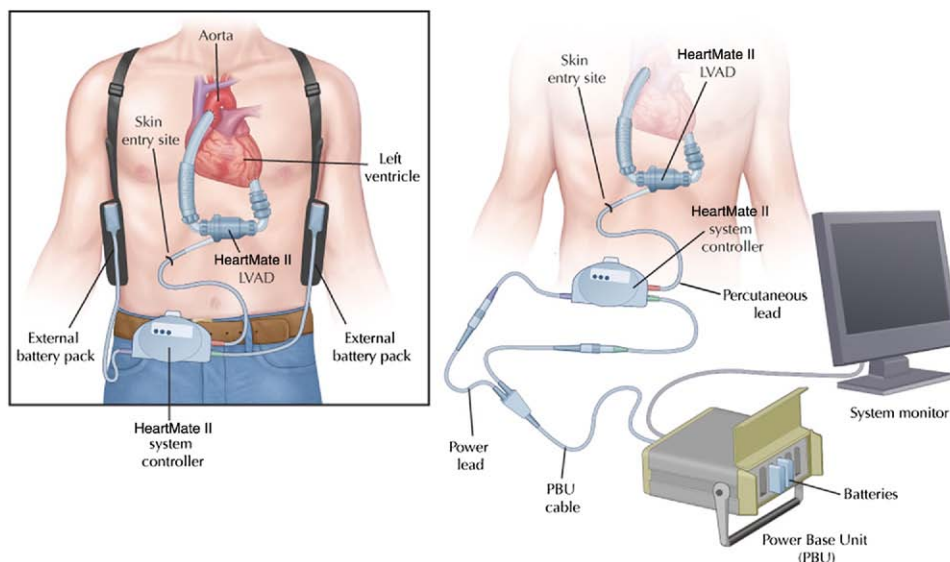


Figure 1 Components of a Continuous Flow VAD

A continuous flow ventricular assist device (VAD) consists of a pump connected to the heart and aorta via an inflow cannula and an outflow cannula, respectively, an external driveline that powers the motor within the device, and a system controller. Power may be delivered through a power base unit (PBU) or battery packs, allowing increased mobility. Figure illustration by Rob Flewell. LVAD = left ventricular assist device.

Table 1 Mechanical Cardiac Support Devices

	Volume-Displacement Pumps (First-Generation Devices)	Rotary Blood Pumps (Second-Generation Devices)	
		Axial Flow Pumps	Centrifugal Flow Pumps
Method of displacement	Pulsatile chamber or sac that fills passively or by suction and is compressed by external pusher plate	Continuous flow driven by a spinning rotor around a central shaft	Continuous flow driven by a hydrodynamic or electromagnetic suspended spinning rotor
Blood pressure	Cyclic, pulsatile flow	Constant, nonpulsatile flow	Constant, nonpulsatile flow
Valve	Inflow and outflow prosthetic valves	No valves	No valves
Devices implanted during cardiac surgery	HeartMate XVE, Novacor, Thoratec PVAD or IVAD, Abiomed 5000, LionHeart*	HeartMate II, Jarvik 2000,* MicroMed DeBakey,* Incor*	VentrAssist,* HVAD,* Terumo Dura Heart,* HeartWare,* HeartQuest,* MTIHeart LVAD*

*Investigational (not approved by the U.S. Food and Drug Administration) devices.

HVAD = HeartWare ventricular assist device; IVAD = implantable ventricular assist device; LVAD = left ventricular assist device; PVAD = paracorporeal ventricular assist device.

Device type. These devices can be broadly categorized as either displacement pulsatile or rotary continuous flow pumps (Table 1).

PULSATILE PUMPS. Pulsatile or displacement pumps have been the most commonly used devices in the U.S. These pumps consist of inflow and outflow conduits, unidirectional valves, a pumping chamber, a battery pack, and a system controller and may be driven pneumatically or electrically (Fig. 2). Pneumatic pumps, such as Thoratec's Paracorporeal Ventricular Assist Device and Implantable Ventricular Assist Device (Thoratec Corporation, Pleasanton, California) send a predetermined air pressure through tubing to fill a sac cyclically, which displaces a stroke volume. In contrast, the pulsatile HeartMate XVE (Thoratec Corporation) uses an electromagnetic pusher plate to drive blood flow.

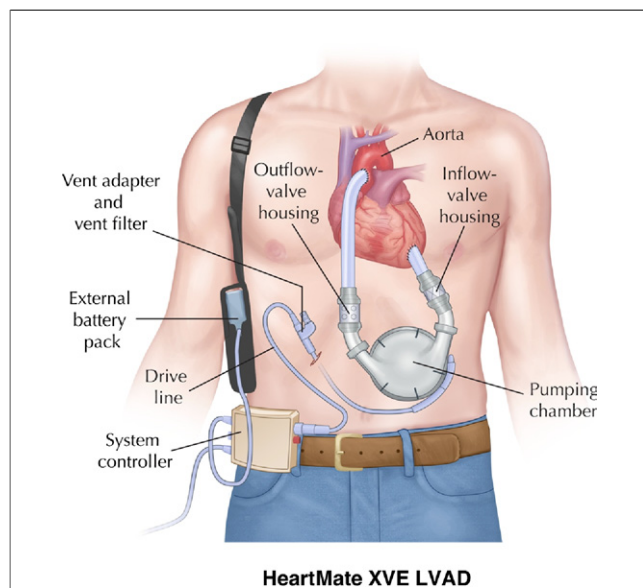


Figure 2 Components of a Pulsatile VAD

A pulsatile VAD consists of a pump, battery pack, and controller. An LVAD decompresses the ventricle into a pump that directs blood into the aorta. The inflow cannula is surgically implanted into the ventricular apex and the outflow cannula is inserted into the ascending aorta. Figure illustration by Rob Flewell. Abbreviations as in Figure 1.

With each ejection, the pulsatile pumps impart a stroke volume, producing a pulse pressure that mimics systole and diastole of the native heart. Pulsatile devices are typically not phased to the contractions of the heart but can capture the entire cardiac output and are often operated with a fixed stroke volume and variable beat rate. Despite the improvements in cardiac function and systemic blood flow seen with pulsatile VADs, their adoption has been constrained by their size and weight and the need for extensive surgical dissection at the time of implantation.

CONTINUOUS FLOW PUMPS. Continuous flow rotary pumps have become increasingly available, and many are now the subject of ongoing clinical investigations, including the Thoratec HeartMate II Left Ventricular Assist System, the MicroMed DeBakey Ventricular Assist Device (MicroMed Microvascular Inc., Houston, Texas), and the Jarvik 2000 Heart (Jarvik Inc., New York, New York) (8–11). This technology accelerates blood through only 1 bearingless central rotor powered by a miniaturized motor (Fig. 1). These pumps are driven by either a spinning impeller (axial flow pumps) forcing blood along the axis of the rotor or concentric cones (centrifugal pumps) accelerating the blood circumferentially.

The generation of continuous blood flow in a nonphysiologic manner eliminates the need for valves or compliance chambers. To mimic physiologic flow, continuous flow VADs have a mode of operation (pulsatility index) that permits aortic valve opening during systole by adjusting the rotations per minute of the device. The pulsatility index (range 1 to 10) is representative of the magnitude of flow pulse generated by the pump through each cardiac cycle. The pulsatility index represents the balance of native ventricular function and unloading by the continuous flow VAD. The pulsatility index is routinely monitored and adjusted to ensure safe automatic flow control and may be a useful piece of information when assessing a change in clinical status. Potential advantages of axial flow pumps include smaller size, easier surgical implantation, quieter vibration-free operation, enhanced patient comfort, and extended durability (11). Much is being learned about the physiologic and pathologic effects of continuous flow devices for cardiac support. Initially, many questions and

concerns were raised regarding the impact of a continuous flow device on the systemic circulation and post-transplantation outcomes (12,13). Recently published literature suggests that continuous compared with pulsatile VADs provide favorable hemodynamic circulatory assistance to support end-organ function and functional status (11,14,15).

Programmable functions of VADs. VADs have programmable functions including mode of operation, device rate, drive pressure, vacuum pressure, and duration of systole for the pneumatic pump, along with rotary speed for continuous flow pumps (Table 2).

Approved VADs. Multiple VADs are approved by the U.S. Food and Drug Administration for bridge to transplantation or recovery. These include the pulsatile Thoratec paracorporeal VAD and the implantable LVAD and RVAD, Novacor LVAD (Novacor, Rueil-Malmaison, France), HeartMate XVE LVAD (Thoratec Corporation), Jarvik 2000 (Jarvik Inc.), and HeartMate II LVAD (Thoratec Corporation) (Fig. 3, Table 3). The only device currently approved for destination therapy is the HeartMate XVE LVAD. The HeartMate II is an axial flow pump recently approved for bridge to transplantation, and it and the Jarvik 2000 are under investigation for destination therapy. Each of these devices may be encountered in the outpatient setting. Additionally, there are many ongoing clinical trials examining the next generation of VADs along with potential strategies to improve the long-term outcomes of these patients (Table 4).

Changes in Ventricular Function After Implantation

Histologic and biochemical signs of recovery. Although the major purpose of a VAD is to assume the pumping function of the heart, the reduction in myocardial stretch after VAD decompression may lead to a recovery process referred to as reverse ventricular remodeling (16). Improvement in intrinsic myocyte function may occur because of alterations in abnormal gene expression, changes in collagen content, regression of cellular hypertrophy, and reduction in myocytolysis and inflammatory cytokines (17–20). Although such changes may occur, most patients do not fully recover and are ineligible for explantation (21).

Clinical approach to encourage myocardial recovery. The rate of clinical recovery leading to device explantation is low and dependent on the wide heterogeneity and severity of medical conditions for which VAD support is used. To help promote reverse remodeling, efforts are under way to assess the use of disease-altering pharmacologic regimens in VAD patients. It is hoped that such therapies in conjunction with ventricular decompression by VAD support will act as a bridge to recovery. At the present time, all patients who appear to be bridge to recovery candidates are restarted on neurohormonal antagonists, which are then up-titrated to published guidelines as tolerated. It is not yet understood which heart failure patients are the best candidates for the institution of additional aggressive adjunctive therapies. Active clinical research to help determine who would benefit from such strategies is ongoing.

In 2006, Birks et al. (22) reported the successful reversal of remodeling in selected VAD patients with nonischemic cardiomyopathy treated with clenbuterol, a selective β_2 -agonist. The researchers devised a 2-stage pharmacologic management approach after implantation, along with diagnostic functional and echocardiographic criteria for weaning patients from VAD support (Table 5). Building on these promising data, the Harefield Recovery Protocol Study has begun to enroll LVAD patients with a history of chronic refractory heart failure. This study is examining whether adjunctive clenbuterol treatment leads to sufficient improvement in myocardial function to allow device removal. There is hope that further combinations of mechanical unloading and drug therapy may enhance myocardial recovery and allow device explantation.

Preparing for Life Outside of the Hospital

The ultimate success of a VAD depends on appropriate preparation of patients and their caregivers for the return home from the hospital. Proper training of both the patient and the community allows for a smooth transition to life outside the hospital, increasing patient satisfaction and quality of life (QOL) (23).

Training for discharge. PSYCHOLOGICAL RECOVERY AND PREPARATION OF PATIENT AND FAMILY. VAD patients face a unique set of challenges and stressors: loss of work

Table 2 Modes of VAD Operation

	Modes of Operation	Timing of Support	Indication(s) for Use
Volume displacement pumps	Asynchronous	Rate of VAD is fixed and asynchronous to native QRS complex	Initiation of mechanical support, weaning from device, and during times of hemodynamic instability
	Volume or automatic*	Asynchronous from native QRS complex, pumping is adjusted passively according to the left ventricular filling volume	Outpatient routine operation, exercise
	External synchronous*	Synchronized to native QRS complex	Weaning from device
Rotary blood pumps	Fixed rate	Constant pump speed (rotations/min)	Initiation of mechanical support, weaning from device
	Variable rate	Speed of pump adjusts to the activity level of patient and cardiac contractility	Outpatient routine operation, exercise

*A backup device rate is needed when placing patients in either volume or external asynchronous modes of support. Backup rates are typically pre-set at 50 to 60 beats/min.

VAD = ventricular assist device.

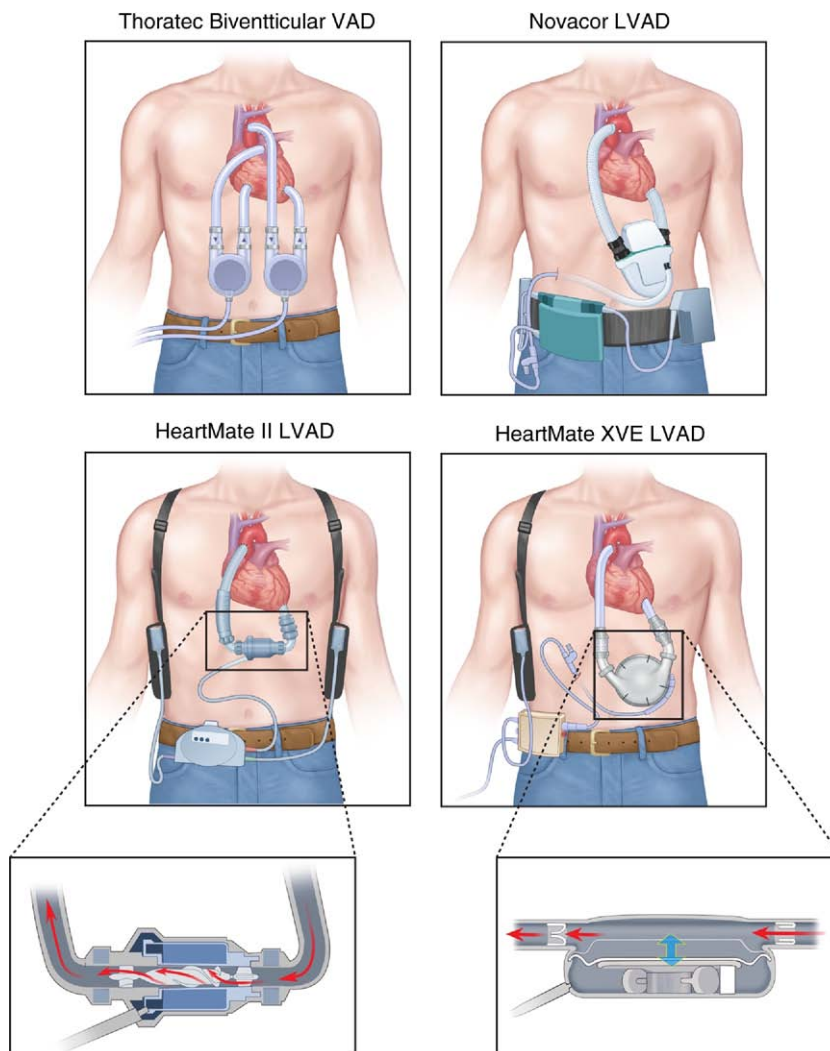


Figure 3 Schematics of Commonly Used VADs

Mechanical support systems: Thoratec VAD (**top left**), Novacor LVAD (**top right**), HeartMate II LVAD (**bottom left**), and HeartMate XVE LVAD (**bottom right**). Illustrations depicting the mechanisms of action of an axial flow and volume displacement pumps are shown for the HeartMate II and HeartMate XVE devices. The axial flow pump is a small device consisting of a continuously spinning impeller along a central shaft. Blood is drawn from the spinning blades of the impeller and propelled at 4 to 6 l/min with minimal hemolysis. The pulsatile pump of the HeartMate XVE uses an electromagnetic pusher plate to cyclically expand and decompress a chamber. The pusher plate can provide between 5 and 10 l/min of pulsatile blood flow. Figure illustration by Rob Flewell. Abbreviations as in Figure 1.

and independence, concern with burdening caregivers, fear of complexity in managing the device or related equipment, change in family dynamics, strain on finances, and fear of dying. Patients must be screened for emotional and psychological readiness, family and social support, and home safety (24,25). Before discharge, a VAD patient and his or her caregivers must be comfortable and competent to assume responsibility for daily monitoring, device maintenance, and independent performance of activities of daily living. The home environment is assessed, and family and friends are educated about the major system components and how to identify and respond appropriately to alarm symbols and audible tones.

REHABILITATION. Adequate cardiac rehabilitation including physical, occupational, and nutritional therapy is a central part of the patient's recovery from VAD implantation. Although this is often achieved during hospitalization after surgery, long-term rehabilitation needs may persist for some patients who have not demonstrated satisfactory self-care and ability to live independently. Unfortunately, this may be impossible to arrange in a typical community setting. Most rehabilitation facilities are unwilling to take VAD patients due to a lack of training or knowledge about the technology, although in our experience this can be overcome with a strong collaborative relationship.

Table 3 Comparison of Current VAD Technology for Outpatient Care

	HeartMate XVE	WorldHeart Novacor	Thoratec VAD System	HeartMate II	Jarvik 2000
Position	Internal	Internal	Internal or external	Internal	Internal
Patient size	Large	Large	Small to large	Small to large	Small
Power	Electric	Electric	Pneumatic	Electric	Electric
Capability	LVAD	LVAD	LVAD, RVAD, or BIVAD	LVAD	LVAD
Duration	Yrs	Yrs	Possibly yrs	Yrs	Possibly yrs
Recommended anticoagulation					
Antiplatelet therapy	Yes	No	No	Yes	No
Warfarin therapy	No	Yes	Yes	Yes	Yes

BIVAD = biventricular assist device; LVAD = left ventricular assist device; RVAD = right ventricular assist device; VAD = ventricular assist device.

Physical exercise. Once discharged, it is highly recommended that patients continue to improve their physical performance. If deconditioned, patients should be sent to an outpatient cardiac rehabilitation program to help them work on gaining strength and improving their endurance and energy capacity. Compared with ambulatory patients with severe heart failure, VAD patients have improved rest and exercise hemodynamics, as demonstrated by an increase in peak oxygen consumption ($\dot{V}O_2$), decrease in peak minute ventilation/carbon dioxide production ($\dot{V}E/\dot{V}CO_2$), increase in cardiac output, and reduction in mean pulmonary artery and wedge pressures (15,26). These improvements in maximal exercise capacity suggest that the 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 (27,28).

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 (29,30). Assessment by a nutritionist may be necessary along with appropriate supplementation. Changes in inflammation can be used to monitor the metabolic response to nutritional support by measuring plasma levels of C-reactive protein and prealbumin. If the C-reactive protein increases or the negative acute-phase reactive prealbumin decreases, more nutritional support may be necessary. Other parameters including low lymphocyte count and total cholesterol can be of assistance to ensure optimal recovery (31).

Routine self-care. Once discharged home, patients and family members are required to perform periodic cleaning and maintenance of VAD equipment. This includes 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. Patients are permitted to shower only after the surgery site has healed completely. Because VAD components are not waterproof, it is critical to keep the vent filter, system controller, and batteries dry. Specially designed covers made from wetsuit material are used to protect the conduits, providing independence and allowing

patients to feel comfortable around water. Swimming or taking a bath is not permitted, and water in the device may cause the pump to stop.

Harmful environments. As outpatients, VAD patients may resume many of their previous normal activities, but there are some restrictions that must be maintained to ensure their well-being and optimal device function. Due to the sensitive nature of these machines, patients should avoid extremes of temperature for prolonged periods of time. Because VAD patients remain permanent susceptible hosts to infection, they should be cautious in surroundings that can place them at a greater risk (e.g., day care facilities, contact with sick individuals, crowded living conditions, poor hygiene). Patients should avoid operating heavy machinery and must not engage in contact sports or strenuous activities. Serious injury may occur if patients undergo a magnetic resonance imaging study. Additionally, it is recommended that individuals avoid power stations and power lines for possible electrical interference.

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, but should not be asked to assume primary responsibility for long-term VAD care or fully understand the nuances of device technology. A visiting nurse association will be uniformly asked to provide home support for all VAD patients. Meticulous attention must be paid to wound care to avoid driveline infections, and, in addition, there are frequent blood draws for laboratory tests, medication adjustments, and routine contact with the VAD team.

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. Many VAD programs have established outreach programs that teach first responders basic issues concerning troubleshooting and pump stoppage (32–34). When an emergency does occur, emergency medical services should bring all components of the device (e.g., hand pumps, extra batteries, and primary and backup drivers) to the local emergency

Table 4 Current Clinical Studies of VADs

Name of Trial	Study Objectives
CentriMag Ventricular Assist System in Treating Failure-to-Wean From Cardiopulmonary Bypass	Nonrandomized trial to determine the safety and efficacy of the Levitronix CentriMag ventricular assist system in hemodynamically unstable patients with cardiac dysfunction who cannot be weaned from cardiopulmonary bypass for up to 30 days
EXCOR Pediatric Ventricular Assist Device (VAD) as a Bridge-to-Cardiac Transplantation	Prospective multicenter, historical control, single-arm study to examine the safety and potential benefit of the Berlin Heart EXCOR Pediatric VAD as a bridge to cardiac transplantation in children
HARPS (Harefield Recovery Protocol Study for Patients With Refractory Chronic Heart Failure)	Nonrandomized, open-label, multicenter trial to assess the percentage of HeartMate XVE patients who, when treated with clenbuterol in conjunction with conventional oral heart failure medications, recover adequate cardiac function to be removed from VAD support and not require heart transplantation
Evaluation of the HeartWare Left Ventricular Assist Device for the Treatment of Advanced Heart Failure	Open-label, nonrandomized study to establish the safety and effectiveness of the HeartWare LVAD system in refractory heart failure patients listed for cardiac transplantation
Jarvik 2000 Heart as a Bridge to Cardiac Transplantation—Pivotal Trial	Phase II and III study to ascertain the safety and effectiveness of the Jarvik 2000 Heart as a bridge to heart transplantation in end-stage heart failure patients who are approved transplantation candidates
Evaluation of Myocardial Improvement in Patients Supported by Ventricular Assist Device Under Optimal Pharmacological Therapy	Randomized, single-blind trial designed to assess the recovery of myocardial function in VAD bridge to transplantation patients treated with either high- or standard-dose pharmacologic therapy
Thoratec HeartMate II Left Ventricular Assist System (LVAS) for Destination Therapy	Prospective, multicenter, noninferiority trial evaluating the efficacy and safety of the HeartMate II in ineligible transplantation patients with NYHA functional class III or IV heart failure. Patients will be randomized in a 2-to-1 basis to the HeartMate II and the HeartMate XVE
VentrAssist LVAD for the Treatment of Advanced Heart Failure	Multicenter, prospective, randomized, controlled clinical trial to explore the use of the VentrAssist LVAD in patients with chronic stage D heart failure who are ineligible for a heart transplantation
VentrAssist LVAD as a Bridge to Cardiac Transplantation—Feasibility Trial	Nonrandomized, historical control phase II and III clinical trials of the VentrAssist LVAD, a centrifugal flow pump, to determine the safety and feasibility in patients who require an LVAD as a bridge to cardiac transplantation

This table lists current ongoing trials of VADs. Final results of these clinical investigations have not yet been published.

NYHA = New York Heart Association; other abbreviations as in Table 3.

department. VAD patients should be transported to hospitals that have device expertise and are adept with their emergency needs. However, this is not always feasible.

First responders need to be aware of the necessary steps to follow when a VAD stops operating due to a mechanical or power failure including changing batteries, connecting to an alternative means of alternating current (AC) power, and the techniques for hand pumping a pulsatile device (Fig. 4). They should be taught to anticipate that patients with axial

flow technology are usually pulseless and that no backup support is available.

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. Health care workers should be instructed not to treat a cardiac arrhythmia or perform cardiopulmonary resuscitation in an asymptomatic individual if the device is functioning properly. Chest compression may lead to dislodging of the tubing or damage to the device itself. Most importantly, emergency personnel should always listen to the patient and keep his or her companions close by for they have been educated on the therapies that can or cannot be delivered.

Electrical utilities. Electric utility companies are notified to place VAD patients on a list for priority power restoration in the event of a power outage as well as to arrange for portable generators. Power companies are asked to prevent planned outages at the patient's home and be advised not to shut off electricity for nonpayment of electric bills. The local community police and fire departments should be aware of the VAD patients in their district and in extreme circumstances may be alerted to provide emergency backup power. Before leaving the hospital, the electrical supply at a patient's residence must undergo a safety check, with proper grounding provided for battery rechargers.

Table 5 Proposed Medical Management and Structural and Functional Targets* for VAD Explantation

Pharmacologic Management	
Stage 1: After discontinuation of inotropic therapy	
Lisinopril 40 mg daily	
Carvedilol 50 mg twice daily	
Spironolactone 25 mg daily	
Losartan 100 mg daily	
Stage 2: Normal left ventricular end-diastolic diameter for a minimum of 2 weeks	
Carvedilol discontinued and bisoprolol initiated	
Clenbuterol 40 µg twice daily (titrated to 700 µg 3 times daily)	
Assessment Modality	Target
Echocardiography	
Left ventricular end-diastolic diameter, mm	<60
Left ventricular end-systolic diameter, mm	<50
Left ventricular ejection fraction, %	>65
Cardiac catheterization	
Pulmonary capillary wedge pressure, mm Hg	<12
Resting cardiac index, l/min/m ²	>2.8
Cardiopulmonary exercise test	
Peak $\dot{V}O_2$, ml/kg/min	>16
$\dot{V}E/\dot{V}CO_2$ slope	<34

Modified from Birks *et al.* (22). *All measurements must be made when the LVAD has been off for 15 minutes.

$\dot{V}O_2$ = oxygen consumption; $\dot{V}E/\dot{V}CO_2$ = minute ventilation to carbon dioxide production; other abbreviations as in Table 3.

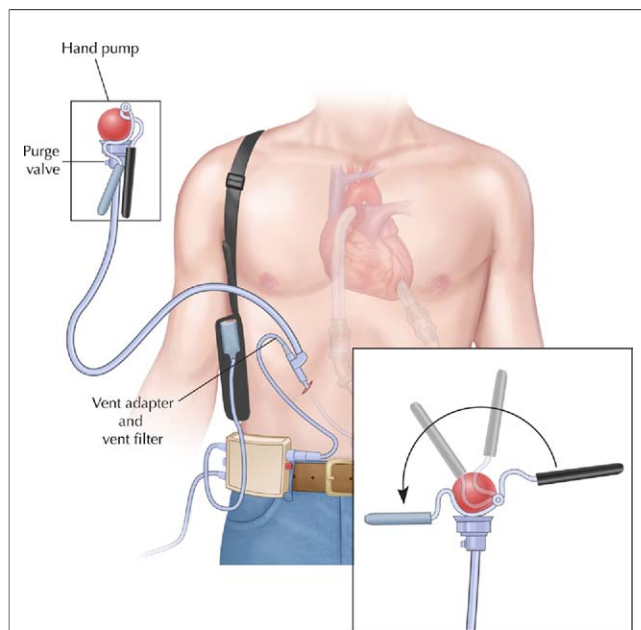


Figure 4 HeartMate XVE Hand Pump

In cases of an emergency such as a failure of the primary and backup drivers, a hand pump should be used immediately to restore flow to a pulsatile ventricular assist device (VAD). To use a hand pump properly, the system controller must be disconnected from the power source. Next, the hand pump bulb should be connected to the end of the driveline vent filter and the system primed by holding down the purge valve on the pump and collapsing the bulb. The hand pump delivers pulses of air to the pusher plate, generating a stroke volume. One hand pump is needed for each VAD. The pump should be squeezed approximately 60 to 90 times per minute to empty and fill the blood chambers. Figure illustration by Rob Flewell.

General Medical Care of the VAD Patient

Longitudinal outpatient management of VAD patients is crucial for a successful outcome. This care is typically led by the cardiology service along with a team of members including a nurse or VAD coordinator, primary care physician, surgeon, and specialists. All coexisting noncardiac medical conditions, such as diabetes, must be aggressively managed.

Blood pressure. Blood pressure needs to be carefully measured because systemic hypertension has been seen in both ischemic and nonischemic cardiomyopathy patients with pulsatile VADs. Obtaining systolic pressure by radial artery palpation is preferred over brachial artery auscultation for conventional pulsatile technology because the device itself can transmit sounds that can be confused with Korotkoff sounds. With axial flow pumps, no audible aortic valve closure sound occurs because there is no or minimal pulse pressure. The Korotkoff sound heard upon auscultation is actually the mean blood pressure. When defining the blood pressure, it is recommended that a Doppler flow probe be used to help define the blood pressure. If present, hypertension should be treated aggressively to help reduce the incidence of neurologic events, end-organ damage, or VAD dysfunc-

tion. In patients with a continuous flow pump, we aim for a mean blood pressure between 70 and 90 mm Hg. This sometimes will necessitate the use of multiple agents.

Anticoagulation and antiplatelet therapy. Anticoagulation or antiplatelet therapy is a central component of outpatient management because thromboembolism is associated with all devices. International normalized ratios of 1.5 to 2.5 are currently targeted for pneumatically driven pulsatile devices. In patients with a continuous flow pump, some VAD centers are now recommending a lower international normalized ratio of 1.7 to 2.3. If an individual experiences a neurologic event, a higher international normalized ratio may be targeted. Clinicians must carefully weigh the chance of a thromboembolic event against the vulnerability of a bleed associated with excessive anticoagulation. Such patients should be monitored closely to minimize the risk of a gastrointestinal or intracranial bleed or severe epistaxis. Adjustments to the warfarin regimen may be directed by the community physician in conjunction with a patient's specific needs and the established practicing patterns of the implant center.

Most device manufacturers also recommend antiplatelet therapy with aspirin because patients always remain at risk of stasis thrombus, hemolysis, and shear-induced platelet dysfunction. Additionally, studies on platelet function have shown that after VAD insertion, an up-regulation of platelet activation markers and function occurs (35,36). Due to the reported risk of aspirin resistance, which may occur in as many as 40% of individuals, all VAD patients should have their platelet responsiveness to aspirin determined (37). To help individualize therapies, studies have assessed the use of thromboelastographic monitoring to guide therapy and decrease the risk of thromboembolic events and prevent bleeding complications (38). Additionally, these drug regimens can be modified based on the patient's history (e.g., drug-eluting stent).

Data from newer and next-generation devices along with individual institutional experiences demonstrate lower rates of thromboembolic and cerebrovascular events, suggesting that less stringent anticoagulation requirements may be necessary in selected populations. The HeartMate XVE VAD can be managed with antiplatelet therapy alone because of its unique surface that allows for neointima formation and the presence of bioprosthetic unidirectional valves. Warfarin may be added in patients with a HeartMate XVE VAD if they have another indication for anticoagulation (e.g., atrial fibrillation or venous or systemic thromboembolism).

Bleeding. Bleeding after VAD insertion may be related to systemic anticoagulation or potentially acquired von Willebrand disease (39). Additionally, higher rates of gastrointestinal bleeds have been reported in patients with nonpulsatile VADs (40). The lower pulse pressure of nonpulsatile devices may lead to hypoperfusion of the bowel wall leading to vascular dilation and angiodysplasia (41). If significant

bleeding occurs, anticoagulation can often be withheld for weeks to months safely, and patients must be immediately stabilized. Future decisions about reinstitution of anticoagulation should be made by the primary VAD team. Patients with nonthreatening gastrointestinal bleeds (e.g., guaiac-positive stools, slight decrease in hematocrit) can safely undergo upper and lower endoscopy by local care providers. If localization of the bleed cannot be determined, further evaluation at the VAD center may include small bowel capsule endoscopy to assess for arteriovenous malformations. At such time, close observation must be maintained due to the potential risk of interference between the electromagnetic devices (42).

Cardiac pacemakers and implantable cardioverter-defibrillators (ICDs). ICD management may present challenges. There have been reports from clinical trials that, due to electromagnetic disturbances, a minority of ICDs and pacemakers cannot establish telemetry and be reprogrammed. However, the majority of ICDs do not interact with normal VAD operation and vice versa (43). If an incompatible device is present, an alternative device should be inserted in the majority of patients requiring ICD protection.

Ventricular arrhythmias. Ventricular arrhythmias are not uncommon in VAD patients, especially in those with an underlying ischemic cardiomyopathy (44). Often, ventricular tachycardia or fibrillation may cause little change in VAD flow, with relative preservation of cardiac output and consciousness (45). These arrhythmias, however, are associated with a more malignant course and an increased mortality risk and suggest that the use of ICDs in this setting is appropriate (46,47). Unique to the axial flow pumps, excessive ventricular unloading leading to suction of the left ventricular wall or septum into the draining cannula can induce ventricular tachycardia. This is the most common cause of ventricular tachycardia in axial pumps and terminates after clearance of suction (48). If suspected, an echocardiogram should be performed.

Long-Term Complications

Since the publication of the landmark REMATCH (Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure) trial in 2001 (7), refinement in devices and the adoption of best practice management techniques have improved the short- and long-term care of patients (49,50). Perioperative complications include hemorrhage, right ventricular failure, sepsis, air embolism, and kinking of conduits. The most common late complications are mechanical device failure, neurologic events, and infection (7,51,52).

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. In the REMATCH trial, 35% of patients experienced compo-

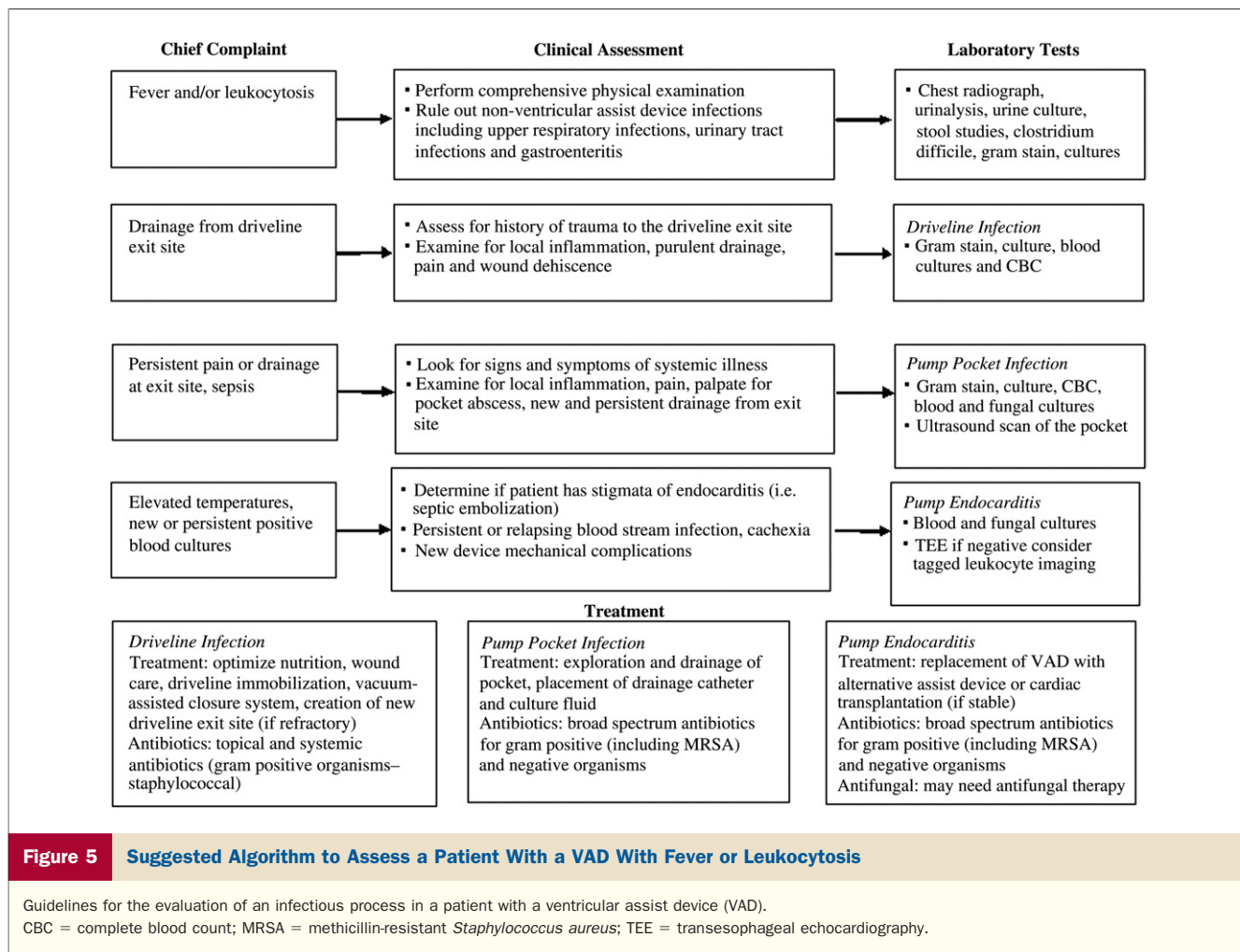
nent failure within 24 months of implantation (7). A contemporary review of 109 pulsatile VADs implanted at a single institution found that the probability of device failure was 6%, 12%, 27%, and 64% at 6 months, 1 year, 18 months, and 2 years, respectively (53). Mechanical durability of continuous flow pumps seems to be markedly improved. In a bridge to transplantation study, only 5 of 133 (4%) patients with a HeartMate II VAD developed either device thrombosis or a complication from surgical implantation necessitating device replacement. Such devices are constructed from fewer components subject to mechanical failure (11).

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, batteries, and the VAD itself. All devices have system controllers and monitors to provide visual and auditory alarms during malfunction. These alarms must be used in conjunction with clinical, laboratory, and imaging data to diagnose suspected device malfunction. For troubleshooting, systematic catheter-, angiography-, fluoroscopy-, and echocardiography-based protocols have been developed to help diagnose common malfunctions (54–57). If necessary, repair of a dysfunctional VAD or removal and replacement with a new VAD may be performed.

Neurologic events. Implanted mechanical devices are susceptible to thromboembolic events due to their unique properties. The foreign surfaces of VADs can activate the immune system, platelets, and the coagulation cascade. In addition, the blood-contact surfaces of VADs along with turbulent blood flow increase the risk of shear stress on blood and thrombi formation (58). Other risk factors for the development of neurologic events include the unmasking or inadequate treatment of hypertension, older age, higher VAD flow and index, and inadequate anticoagulation.

Neurologic complications from VAD therapy include cerebrovascular accidents and transient ischemic attacks, with an incidence ranging from 0.009 to 5.73 events per patient-year (58,59). The prevalence of neurologic events with destination therapy has ranged from 44% in the REMATCH trial (HeartMate XVE) to 57% in the European LionHeart Clinical Utility Baseline Study, with 21% and 43%, respectively, resulting in permanent neurologic injury (58,60). Intracranial hemorrhage, syncope, seizure, brain abscesses, and encephalopathy have all been reported. These data are mostly from the bridge-to-transplantation experience and may not apply to destination therapy patients who are generally older and have more comorbidities and longer implantation periods (60).

Not all devices have the same neurologic event rate. Design modifications incorporated in the newer generation of VADs, including 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 recently completed HeartMate II trial demonstrated reduced adverse events per patient year with respect to stroke (0.19 vs. 0.44) and nonstroke (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 cerebrovascular accidents after VAD implantation (61,62).

Infection. INFECTIONS ASSOCIATED WITH VADS. VAD infections can occur at any time, but occur most frequently between 2 weeks and 2 months after implantation (63). Device-related infections are caused predominantly by the Gram-positive organisms *Staphylococcus epidermidis* and *Staphylococcus aureus* followed by enterococci (64–66). Other commonly implicated organisms include Gram-negative bacilli such as *Pseudomonas aeruginosa*, *Enterobacter*, and *Klebsiella* species, along with fungi (65,67). 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 (67,68).

LOCATION OF INFECTIONS. The entire VAD is susceptible to infection including the surgical site, device pocket, driveline, valves, and conduits. The most common site of infection is the percutaneous driveline, which can often be managed successfully with wound care and antibiotics (69). However, a driveline infection can spread to other components of the VAD resulting in bacteremia, sepsis, and endocarditis (Fig. 5) (70). Sepsis in patients with mechanical assist devices has been reported to be the leading cause of death and can result in cerebral emboli and multiorgan failure (65,67). Other infections, including mediastinitis and peritonitis, have also been reported.

STEPS FOR THE PATIENT AND CAREGIVERS TO REDUCE RISK OF INFECTIONS. Many strategies, primarily based on clinical experience, have been adopted to try to minimize device-related and wound infections. Proper care of the driveline exit site must be maintained. Every day patients or their caregivers must strictly adhere to aseptic technique (e.g., sterile gloves, mask) 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 (71,72). Injury to the delicate exit site through either a shearing traction or torsion injury is the initiating mechanism for most late driveline infections (73). Patients should be educated to monitor for any changes to the exit site and to notify their health care team immediately if there are signs of infection.

INFECTION-ASSOCIATED DESIGN MODIFICATIONS. Since the introduction of VADs, many modifications to device design have been made to further decrease the risk of infection. These include the use of larger single-lead drivelines and drivelines coated with chlorhexidine and silver sulfadiazine to reduce colonization and augment initial tissue ingrowth (67,73). 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 (74,75). Future research to reduce device-related infections will focus on the influence of the pump surfaces on the native immune system to develop more biocompatible materials (76–78). It is hoped that one day, a completely implantable device without a driveline will be inserted and will dramatically reduce device-related infections.

QOL

Despite potential complications, VADs significantly improve QOL in patients with end-stage heart failure. When surveyed about lifestyle changes, VAD patients highlight the ability to drive, exercise, travel, return to work or school, and engage in hobbies and sexual activity as major contributors to improved QOL (79,80). In the REMATCH study, scores on the physical-function and emotional-role subscales of the Short Form Health Survey and the New York Heart Association functional class were all better with the HeartMate XVE VAD at 1 year (7). In addition, the Minnesota Living With Heart Failure Questionnaire score was improved with destination VAD compared with optimal medical management (34 points vs. 13 points, respectively) (7). This magnitude of QOL improvement surpasses that achieved with adjunctive pharmacologic or cardiac resynchronization therapy in patients with advanced heart failure (81,82).

More recently, in patients awaiting heart transplantation, the HeartMate II continuous flow device improved QOL at 3 months on multiple validated indexes (–27 on the Minnesota Living With Heart Failure Questionnaire and +22 on the Kansas City Cardiomyopathy Questionnaire) (11). The impact of different devices on QOL has not been compared directly in clinical trials to date. In theory, QOL may be even greater with rotary devices because of their smaller size and quieter operation compared with pulsatile VADs. Given the rapid evolution of mechanical circulatory support, QOL outcome measures have be-

come an integral part of all clinical trials and registries involving VADs (83).

Conclusions

As VAD technology progresses, collaboration of multidisciplinary teams composed of engineers, scientists, physicians, and nurses will continue to refine the technology and improve patient care and outcomes. Advances in device design will allow easier implantation and create smaller, more efficient, durable, and reliable units. The National Heart, Lung and Blood Institute in collaboration with the Centers for Medicare & Medicaid Services and the U.S. Food and Drug Administration has established a national registry called INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support) (83). Most VAD implantation hospitals are members, and patients who receive a U.S. Food and Drug Administration–approved mechanical circulatory support device are entered and followed prospectively. This registry will be used to help refine selection criteria for VAD therapy, inform best practice guidelines, and allow clinicians to provide patients more information about device comfort, QOL, and survival after VAD implantation. In light of the growing population of patients with advanced heart disease, the shortage of suitable donors, and evolving technology, mechanical circulatory support devices will play an ever-increasing role in the care of patients with end-stage heart failure.

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