Ventricular Assist Devices Today and Tomorrow

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THE NUMBER OF people worldwide with heart failure (HF) is increasing at an alarming pace. In the United States alone, there are approximately 5.3 million people who have HF, with a prevalence estimated at 10 per 1,000 in people over the age of 65.1 It is now estimated that there are 660,000 new cases of HF diagnosed every year for people over 45 years of age. In 2008, there were more than 1 million hospital admissions for HF at a cost of $34.8 billion. Currently, preventative measures, optimal medical therapy, and heart transplantation are not effectively reducing the overall morbidity and mortality of this syndrome.

The American College of Cardiology/American Heart Association (ACC/AHA) have classified HF in 4 stages based on the progression of the disease (Table 1).2,3 Early in the course of the disease (stages A and B), symptoms are absent or mild, but the patients are at high risk of developing symptomatic or refractory disease. As the disease progresses through stage C, ventricular function is maintained by adrenergic stimulation, activation of renin-angiotensin-aldosterone, and other neurohumoral and cytokine systems.4,5 These compensatory mechanisms become less effective over time, and cardiac function deteriorates to the point where patients have marked symptoms at rest (stage D). The ACC/AHA-recommended therapeutic options for patients with stage D symptoms are continuous inotropic support, heart transplantation, mechanical circulatory support, or hospice care.

Standard HF medical therapies such as angiotensin-converting enzyme inhibitors, β-blockers, diuretics, inotropic agents, and antiarrhythmics may relieve symptoms, but the mortality rate remains unaffected. Optimal medical therapy does not halt the progression toward stage D HF symptoms, and when this occurs, there is a greater than 75% 2-year mortality risk, with surgical intervention being the only effective treatment. Cardiac transplantation is an effective therapy for terminal HF and is associated with excellent 1-year survival (93%), 5-year survival (88%), and functional capacity.5 However, there are approximately 2,200 donors available for as many as 100,000 patients with advanced-stage HF.7 Moreover, donor hearts are usually reserved for patients <65 years of age even though older patients have the highest prevalence of HF. Patients over 65 years of age and those with other comorbidities are often ineligible for transplantation, creating a considerable need for alternative therapies.

VENTRICULAR ASSIST DEVICES

Mechanical circulatory support (MCS) includes a wide variety of devices that can provide short- or long-term support. Short-term MCS is used for severe acute HF and is intended to rest the ventricle, promoting recovery of its function. Sufficient recovery of myocardial function may occur after brief MCS or in cases of chronic HF recovery may be seen after many months of support. Numerous studies have shown that the myocardium is able to repair itself during varying periods of unloading; after which patients experience an improvement in quality of life.5-15 Ventricular assist devices (VADs) have 3 main clinical applications: bridge to transplant (BTT), bridge to recovery (BTR), and destination therapy (DT).16,17 Because of the severe limitation in the number of heart transplants that can be performed, the BTT application is limited. BTR is also limited and depends on the extent of myocardial damage and the etiology. However, the greatest potential for VAD therapy is for the HF population who are not heart transplant candidates, have not recovered myocardial function, and may benefit from long-term support as DT.

Device and patient selection are critical factors that affect the outcome of MCS.5 Factors that need to be taken into consideration during the device selection process are the expected duration of support, type of support needed (right, left, or biventricular assist), cost, mobility, and Food and Drug Administration (FDA) approval status. Proper patient selection for DT is one of the most important factors that determine success.18 There is now a substantial amount of evidence that indicates that VAD support earlier in the progression of HF will result in better outcomes. In the setting of acute HF, initial options for ventricular support include intra-aortic balloon pump and percutaneous VADs.
such as TandemHeart (Cardiac Assist Inc, Pittsburgh, PA) and Impella (AbioMed, Inc, Danvers, MA). When improvement in cardiac function is delayed despite adequate immediate support, either short- or long-term MCS should be instituted before severe end-organ dysfunction ensues. The usual contraindications for device implantation include irreversible organ failure, advanced pulmonary disease unrelated to cardiac function, sepsis, and metastatic cancer.

**CLASSIFICATION OF DEVICES**

There are currently 3 generations of VADs either available for clinical use or in preclinical trials. The first generation (Table 2) predominantly includes pneumatic or electrically driven pumps that generate pulsatile flow; whereas the second generation (Table 3) includes rotary-pump designs that provide continuous flow. The third generation (Table 4) includes the most sophisticated designs, implementing technologies such as magnetically suspended impellers, but because these are still in development they will be discussed later in this article (see section on New VAD Technology). Reference to generation is the primary method of classification for devices although they may also be subdivided according to other characteristics including the location of device (intra-, extra-, or paracorporeal), the source of driving power (pneumatic or electric), the level of anticoagulation required, and the length of time the device can adequately provide support. These aspects of the individual devices are included in the descriptions later.

**First-Generation Devices**

**Thoratec Paracorporeal VAD**

The Thoratec paracorporeal VAD (PVAD) is a pneumatically driven, pulsatile pump that has been used for more than 20 years and is FDA approved for short- to intermediate-term support in the setting of BTT and BTR. The pump consists of a rigid plastic housing chamber that contains a blood-pumping sac made of a polyurethane multipolymer (Fig 1). Air from a pneumatic driver externally compresses the sac by pressurizing the surrounding chamber, ejecting blood each cycle. Mechanical valves are situated in the inflow and outflow ports to allow unidirectional flow. The device rests in a paracorporeal position (the pump housing rests externally against the chest wall) with the inflow and outflow cannulae connecting to the heart and great vessels transcutaneously. The driver console provides alternating pneumatic pressure and vacuum in a pulse-like fashion for ejection and filling in 3 modes: asynchronous (fixed rate), synchronous (timed to patient heart rate), and volume mode. The volume mode, which is the recommended mode for patient support, refers to the “fill-to-empty” function of the device; the casing of the pump has a sensor that detects when the pumping sac is filled and then triggers an ejection. This mode is dependent on preload (ie, increased preload allows for faster filling) and thus an increase in rate of ejection. The PVAD has an approximate stroke volume of 65 mL, a maximum rate of 100 beats/min, and a maximum cardiac output of 6.5 L/min.

There are several advantages of the design of the PVAD. The paracorporeal location allows for right, left, or biventricular support and ease of exchange in the event of device malfunction, thrombosis, or infection. Likewise, there is not a restriction based on patient size as with the intracorporeal devices, with successful placement in patients as small as 17 kg. The longest duration of support to date is 1,204 days, and a portable driver is available so patients can be discharged to home with the device. In comparison to the analogous Abiomed BVS5000 (discussed later), the PVAD offers higher pump output, greater patient mobility, longer duration of support, and less morbidity.

Anticoagulation in the postoperative period with heparin and long-term with warfarin is necessary, and in select patients aspirin prophylaxis is initiated as well. Postoperative anticoagulation regimens for the different VADs are discussed in the Postimplantation Issues and Outcomes in the VAD Recipient: Postoperative Anticoagulation section.

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**Table 1. ACC/AHA Classification of Chronic Heart Failure**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>A</td>
<td>High risk for developing HF</td>
</tr>
<tr>
<td>B</td>
<td>Asymptomatic HF</td>
</tr>
<tr>
<td>C</td>
<td>Symptomatic HF</td>
</tr>
<tr>
<td>D</td>
<td>Refractory end-stage HF</td>
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</table>

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Hypertension, diabetes mellitus, CAD, family history of cardiomyopathy</td>
</tr>
<tr>
<td>B</td>
<td>Previous MI, LV dysfunction, valvular heart disease</td>
</tr>
<tr>
<td>C</td>
<td>Structural heart disease, dyspnea and fatigue, impaired exercise tolerance</td>
</tr>
<tr>
<td>D</td>
<td>Marked symptoms at rest despite maximal medical therapy</td>
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</table>

**Abbreviations**: CAD, coronary artery disease; LV, left ventricle; MI, myocardial infarction.

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**Table 2. First-Generation VADs**

<table>
<thead>
<tr>
<th>Device</th>
<th>Length of Support</th>
<th>Position</th>
<th>Ventricles Supported</th>
<th>Drive Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thoratec PVAD and IVAD</td>
<td>Short to medium</td>
<td>PVAD extracorporeal, IVAD</td>
<td>LV, RV, BV</td>
<td>Pneumatic, pulsatile</td>
</tr>
<tr>
<td>HeartMate I (XVE)</td>
<td>Long (BTT and DT)</td>
<td>Infracorporeal, abdominal</td>
<td>LV</td>
<td>Electric, pulsatile</td>
</tr>
<tr>
<td>Abiomed BVS5000 and AB5000</td>
<td>Short</td>
<td>Extracorporeal</td>
<td>LV, RV, BV</td>
<td>Pneumatic</td>
</tr>
</tbody>
</table>

**Abbreviations**: LV, left ventricle; RV, right ventricle; BV, biventricular.
Thoratec Implantable VAD

The Thoratec implantable VAD (IVAD) was developed out of the need for an intracorporeal (pump housing located inside the patient’s body) version of the PVAD to facilitate patient discharge from the hospital and improve mobility and thus quality of life.23 It is the only intracorporeal device capable of biventricular support and is FDA approved for intermediate-to-chronic circulatory support in the settings of BTT and BTR.27 The mechanism of the pump is functionally similar (Fig 1), but the chamber housing is a titanium alloy to allow for implantation with shorter cannulae and a longer, transcutaneous drive line.23

In comparison to the PVAD, the IVAD weighs less (339 v 419 g) and is smaller (252 v 318 mL), but patient size still limits candidacy for implantation with smaller patients being ineligible. The IVAD has comparable survival and reduced complication rates compared with the PVAD.23 The longest duration of support to date is 979 days, and experience thus far is in excess of 500 patients.28 The anticoagulation regimen is the same as for the PVAD, again with select patients receiving aspirin prophylaxis in addition to warfarin therapy. Although the second-generation devices offer more sophisticated and efficient pump designs, the Thoratec IVAD remains the only intracorporeal option for biventricular support.

During in-hospital use, the PVAD and the IVAD are powered by the Thoratec Dual Drive Console (DDC), a wheel-mounted, 231-kg unit with a small battery allowing for short-term mobility.25 The console can operate left- and right-sided pumps independently when biventricular support is performed. Stroke volume and VAD output are displayed, and there are controls for the adjustment of certain pump parameters such as operating mode (asynchronous, synchronous, or automatic), pump rate, ejection drive pressure, vacuum pressure, and ejection time (Fig 2). The ejection drive pressure must be at least 10 mmHg above the patient’s systolic pressure and is commonly set to 230 to 245 mmHg. Vacuum pressure is suction applied to the pump diaphragm during diastole and may be increased to assist with filling of the pump sac; typical vacuum pressure is between −25 and −40 mmHg. The minimum recommended ejection time for complete emptying is 300 milliseconds.25

Thoratec also offers the TLC-II portable driver, a console that allows for patients to be discharged to home with either the

<table>
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<tr>
<th>Table 3. Second-Generation VADs</th>
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<tr>
<td>Device</td>
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<tr>
<td>--------</td>
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<tr>
<td>Impella Recover LP 2.5, 5.0, and LD</td>
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<tr>
<td>Levitronix CentriMag</td>
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<tr>
<td>TandemHeart (pVAD)</td>
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<tr>
<td>HeartMate II</td>
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<tr>
<td>Jarvik 2000</td>
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<tr>
<td>MicroMed DeBakey</td>
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Abbreviations: LV, left ventricle; RV, right ventricle, BV, biventricular; LVAD, left ventricular assist device; pVAD, percutaneous ventricular assist device.

<table>
<thead>
<tr>
<th>Table 4. Third-Generation VADs</th>
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<tbody>
<tr>
<td>Device Name</td>
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<tr>
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</tr>
<tr>
<td>HVAD</td>
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<tr>
<td>DuraHeart LVAS</td>
</tr>
<tr>
<td>VentrAssist</td>
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<tr>
<td>Synergy</td>
</tr>
<tr>
<td>PediVAS/UltraMag</td>
</tr>
<tr>
<td>Novacor II LVAS</td>
</tr>
<tr>
<td>Levacor</td>
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<tr>
<td>HeartMate III</td>
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</table>

Abbreviations: HVAD, HeartWare ventricular assist device; LVAS, left ventricular assist system; DT, destination therapy; BTT, bridge-to-transplant; RVAD, right ventricular assist device; CPB, cardiopulmonary bypass.
PVAD or IVAD. Unlike the DDC, the TLC-II permits operation in only 2 modes (asynchronous or automatic).

HeartMate I/Extended Lead Vented Electric Left Ventricular Assist System

The first-generation HeartMate is manufactured by the Thoratec Corporation and is an intracorporeal device approved for intermediate-to-chronic support as BTT or DT for patients ineligible for transplantation. The XVE is electrically driven by a motor located within the pump housing, which is separated from the blood-pumping sac by a diaphragm that divides the pump into 2 chambers. The motor compresses a pushing plate against the diaphragm, and blood is ejected from the device through the outflow valve and into the aorta. Filling is accomplished by recoil force inherent in the diaphragm because it is manufactured in the “full” position and returns to this position once the drive from the motor stops. The negative pressure created by the recoil of the diaphragm is enough to assist filling of the device even in the setting of a completely flaccid left ventricle. For the diaphragm to function properly, the chamber housing the motor must be vented to air to maintain atmospheric pressure within the casing. This is accomplished by a single percutaneous tube that combines the electric cable and the air vent and allows for displacement of the volume of air required for each filling of the blood sac. The tube is coated with woven polyester that is designed to encourage skin ingrowth, anchoring the tube into the integument and decreasing the risk of infection. The device has porcine valves, and all of the internal surfaces are made of textured materials to promote the deposition of a stable biologic lining, creating a pseudoneointima similar to the lining of natural blood vessels and thus eliminating the need for long-term anticoagulation.

When in auto mode, the device responds to increased left-sided venous return by increasing the pump rate and output, similar to the volume mode of the PVAD and IVAD. The XVE is implanted in a preperitoneal or intraperitoneal pocket (Fig 3) and because of size can only provide univentricular support and cannot be implanted in patients with a BSA less than 1.5 m². Frequently, patients with this device experience early satiety and can be predisposed to malnutrition as a result. Experience with the XVE is in excess of 4,500 patients, and the longest duration of support is 1,854 days. It has a higher maximum cardiac output than the IVAD or PVAD, with a stroke volume of 83 mL and a maximum rate of 120 beats per minute. The system controller can be worn on a belt or holster and powered with a portable battery pack, so this device allows the most mobility of the first generation of LVADs. The HeartMate XVE is the only pulsatile device.
available for intermediate-to-chronic circulatory support that requires no systemic anticoagulation.\textsuperscript{30} AbioMed Biventricular Support 5000

The AbioMed BVS5000 was the first extracorporeal VAD available and is FDA approved for BTR in the setting of potentially reversible HF.\textsuperscript{33} The BVS5000 is located external to the patient and mounted on a pole. It is designed for short-term use, and the typical length of support is 7 to 10 days. The pump is a pneumatically driven, 2-chambered device that supports 1 side of the heart but can be used in tandem for biventricular support. The pump casing is clear plastic, which permits visualization of the chamber contents (Fig 4). Inflow and outflow cannulae are transcutaneously tunneled, and unidirectional valves direct flow to and from the pump casing.\textsuperscript{34} When the device is being used for biventricular support, the respective heights of the right and left devices can be adjusted to maintain balanced flows and prevent pulmonary edema because filling is by gravity drainage.\textsuperscript{35} AbioMed makes 3 different driver consoles: the BVS5000i, the BVS5000t, and the AB5000, all of which can be used for the AbioMed BVS5000 pump in either uni- or biventricular arrangement. The consoles offer subtle differences, but all adjust the pump rate and systolic-to-diastolic time ratio based on air flow into and out of the pump.\textsuperscript{34} Output of the pump depends on intravascular volume status and downstream vascular resistances, and the driving console automatically adjusts the rate of pumping to provide up to 5 L/min of cardiac output based on these detected parameters.\textsuperscript{36}

Anticoagulation is necessary with the BVS5000 and should be initiated within 24 hours of placement. Heparin should be titrated to an activated coagulation time (ACT) of 180 to 200 seconds.\textsuperscript{38} Experience supports its indication for reversible HF because it is relatively simple to implant, provides pulsatile flow believed to have beneficial effects for organ recovery, and is less expensive than the Thoratec PVAD. Long-term use is associated with high morbidity because of sepsis, multiorgan failure, and cerebral infarction, and, thus, careful selection of recipients for the AbioMed BVS5000 is key to the success of device implantation.\textsuperscript{26}

AbioMed AB5000

The AB5000 is the ambulatory version of the BVS5000. Clinical experience has shown the 2 devices to have similar survival outcome and adverse event data, with the AB5000 offering the advantage of patient mobility and longer duration of support. It is indicated for short-term use, with the longest single pump duration of 57 days. The cannulae for the BVS5000 are interchangeable with the AB5000, so exchanging the devices can be done with relative ease. The device is a single-chambered, pneumatically driven device located in a paracorporeal position to provide uni- or biventricular support.\textsuperscript{37} The pump is a rigid chamber made of epoxy, aluminum, polycarbonate, and titanium that houses a polyurethane bladder (Fig 4). Polyurethane unidirectional valves promote unidirectional flow through the device. In an alternating fashion, the console drives compressed air into the chamber and then allows for return air to be vented to atmospheric pressure or a vacuum, thus allowing for pulsatile ejection and filling. Increasing preload or adjusting the level of vacuum applied to the chamber will alter the rate of filling, which, in turn, affects the rate of
ejection of the device as the bladder only ejects once full.38 Like the BVS5000, the AB5000 is compatible with all 3 of the AbioMed consoles, but the AB5000 console is the only one that allows for ambulation and mobility and is therefore primarily used.

Anticoagulation with heparin is necessary with the ACT titrated to 180 to 200 seconds.37 Like the BVS5000, the AB5000 functions only in “volume mode” for a maximum output of 6 L/min.36,39 Although it is technically approved for short-term support, the durability of the AB5000 is likely comparable to longer-term devices because each pump is one half of the recently approved AbioCor Implantable Replacement Heart.36

Second-Generation Devices

The Impella Recover LP 2.5

The Impella 2.5 is an intravascular microaxial pump that is manufactured by AbioMed and is approved for partial circulatory support for up to 6 hours. The device is a percutaneous catheter placed through the femoral artery and retrograde past the aortic valve to rest in the left ventricle (Fig 5). Blood is aspirated from the left ventricle catheter inlet, through an encapsulated axial motor, and pumped into the ascending aorta, thus augmenting cardiac output by up to 2.5 L/min.40 The catheter tip is continuously purged with a dilute heparin solution to prevent clot formation inside the motor. Patients must be heparinized before Impella placement because the purge solution does not produce systemic anticoagulation. The Impella offers ease of placement, low rates of hemolysis and stroke, and effective unloading of the left ventricle.41 The disadvantage to the device is that it can only provide partial support.

AbioMed recently completed a clinical trial showing the safety and efficacy of the device in high-risk percutaneous coronary intervention42 and is currently conducting 2 US studies comparing the device to the intra-aortic balloon pump.43 The FDA likewise just approved 2 additional Impella devices, the Impella 5.0, which is implanted by surgical cut down via the femoral artery, and the Impella LP, which is implanted via surgical thoracotomy. Both devices provide higher flows up to 5.0 L/min for short-term support.44

The console of the Impella devices displays a pressure waveform measured from the device tip, which can be used to help position the catheter across the aortic valve. Also displayed are flow rate (in liters per minute) and performance level (P0 through P9). The performance level is derived from motor speed, and the recommended performance level for all types of Impella devices is P8, which corresponds to a flow rate of 1.9 to 2.5 L/min and 50,000 revolutions per minute (RPM) in the
Impella 2.5, and a flow rate of 3.2 to 4.9 L/min and 30,000 RPM in the Impella 5.0 and LP models.40,45

Levitronix CentriMag Blood Pumping System

The CentriMag blood pump (Levitronix LLC, Waltham, MA) is manufactured by Levitronix and distributed by the Thoratec Corporation. It is an extracorporeal centrifugal pump that propels blood with the rotary motion of a spinning impeller (Fig 6). The pump housing contains the rotor that is magnetically levitated, and the magnetic field is electronically regulated with an external electric processor that controls radial rotor position and speed. Blood is directed at the axis of the rotating impeller and through the centrifugal force of the impeller is directed out of the pump housing with augmented flow. The pump is bearingless, with the rotor floating within the magnetic field of a stator with which it has no mechanical contact.46 This offers the advantages of decreased potential for hemolysis and thrombus formation.47

Blood flow through the pump depends on the motor speeds, venous return into the pump, and the intravascular and circuit pressures for both inflow and outflow limbs of the device. The console control panel (Fig 7) permits adjustment of pump speed (range of 0 to 5,500 RPM) and displays the resulting pump flow (0-9.9 L/min). The pump flow is measured directly with an ultrasonic flow probe.46

The device is designed for short-term support in the setting of acute HF and can provide left, right, or biventricular support. The CentriMag is frequently used as a bridge to the placement of a longer-term device (“bridge to decision”). Currently, the device is indicated for support of up to 6 hours, but clinical trials are presently underway to evaluate usage for up to 30 days.48

TandemHeart Percutaneous VAD

The TandemHeart pVAD is a continuous-flow centrifugal pump approved for short-term support for up to 14 days. It is an extracorporeal device that can be used in the same manner as other available centrifugal assist devices but has the unique capability of being inserted percutaneously in the catheterization laboratory.59 The TandemHeart is dual-chambered with an upper and lower housing assembly. The upper portion accommodates the magnetically driven impeller and its directed blood flow, whereas the lower portion receives an infusion line of heparinized saline to provide a hydrodynamic bearing, cooling of the apparatus, and anticoagulation of the system. If placed percutaneously, the venous inflow cannula is placed into the left atrium via transseptal puncture, whereas the outflow cannula returns blood via the femoral artery (Fig 8).50 The TandemHeart can deliver flows up to 5 L/min percutaneously or up to 8 L/min when direct surgical cannulation is used.51
HeartMate II Left VAD

The HeartMate II LVAD is manufactured by the Thoratec Corporation and is an intracorporeal continuous-flow device indicated for intermediate-to-chronic support, extensively studied as BTT and currently in clinical trials for DT.52 The device is an axial flow blood pump that contains a titanium-coated internal rotor with helical blades that curve around a central shaft.20 An electrically powered motor within the pump housing generates a magnetic field that induces rotary motion and torque of the magnet-cored rotor, thus generating blood flow (Fig 9). Like the HeartMate I (XVE), the inflow and outflow conduits are coated with a textured material to encourage the deposition of a pseudoneointima.53 Recent results indicate that the HeartMate II has a low incidence of thromboembolism; however, anticoagulation with warfarin, aspirin, and dipyridamole is still required.54 A percutaneous lead supplies direct-current wires and control signals to the device, and using the HeartMate I design it is coated with woven polyester designed to encourage skin ingrowth. It can generate up to 10 L/min of blood flow.53

Because of its smaller size in comparison to its predecessor, the device can be used in much smaller patients including women and adolescents. Experience is extensive with more than 1,600 patients implanted worldwide and the longest duration of support of 4 years.54 Although it has an improved safety profile from the HeartMate I, long-term support does introduce physiologic changes and clinical problems, including aortic valve fusion, thrombosis of coronary sinuses, arteriovenous malformations, and gastrointestinal bleeding.54

The HeartMate II Display Module can be used to evaluate device function or to program the pump settings (Fig 10). The module displays current mode, pump speed in RPM, pulsatility index, estimated flow in L/min, and power in Watts.53 The device has 2 modes of operation: fixed (set to a fixed RPM between 6,000 and 15,000) and an emergency “power-saver” mode (8,000 RPM or the fixed speed if it is <8,000). The continuous flow through the Heartmate II device is augmented with each contraction of the native ventricle, creating a variation in flow (“flow pulse”) that is quantified by the pulsatility index (PI), a dimensionless value between 1 and 10. The PI is determined by the interaction among ventricular preload, myocardial contractility, and the amount of assistance provided by the device. When the myocardial fibers are stretched by increased preload, contractility is augmented (via the Frank Starling mechanism) and the PI goes up; this is observed even in hearts with end-stage disease. A higher PI occurs when ventricular filling is increased or the device is providing a low level of support, whereas a lower PI occurs when the ventricle is
underfilled or the device is providing a high level of support. The PI should be monitored routinely and should not vary greatly. During clinical use, the PI typically ranges between 3 and 4. The flow is estimated based on the pump speed and the power input. Except for very low or high pump speeds, there is a linear relationship between power and flow at a given speed. The pump power is the amount required to power the motor and is within a range of 0 to 25.5 W.

The Jarvik 2000 Flowmaker

The Jarvik 2000 (Jarvik Heart, Inc, New York, NY) is designed for intermediate-to-chronic support, and although it has a potential role for DT and BTR, it is currently undergoing FDA-approved clinical trials for BTT in the United States. It is an axial flow device with a titanium shell housing a direct-current motor, a rotor supported by 2 ceramic bearings, and a spinning titanium impeller that pumps blood from the left ventricle into the aorta (Fig 11). The device is powered by a transcutaneous cable through the abdominal wall or through a connector mounted on the head behind the ear. Patients can control flows up to 7 L/min by adjusting the RPM of the device, with the output dependent on the pressure gradient from the ventricle to the aorta as well as the set pump speed. The controller automatically slows the rotational speed of the impeller for 8 seconds of every 64-second cycle, allowing for regular periods of brief ejection to reduce blood stasis in the ventricular apex and in the ascending aorta.

The Jarvik 2000 is distinguished from other assist devices by its size; the pump measures 2.5 × 5.5 cm and weighs only 90 g, allowing for its implantation in smaller individuals including pediatric patients. Its size also allows for implantation either by the routine median sternotomy approach or by left thoracotomy, with or without the use of cardiopulmonary bypass. The pump housing resides completely within the left ventricle secured with a polyester sewing ring through the ventricular wall and a fabric graft channels flow from the pump into the aorta. The device has successfully supported a patient for 7.5 years, which is longer than any other type of support device available, and to date there have been no reported mechanical failures in the more than 200 patients with a Jarvik 2000 pump.

The MicroMed DeBakey Axial Flow Pump

The MicroMed DeBakey ventricular assist device, now marketed as the HeartAssist 5 (MicroMed Cardiovascular, Inc, Houston, TX), is an axial flow pump that has been in development since 1988. It is very similar in design to the Jarvik 2000, offering a small size of 30.5 × 76 mm and 93 g. It is also electromagnetically driven, with a spinning impeller directing forward flow of blood. It is implanted in the pericardial space rather than within the ventricle and has a titanium inflow cannula and a Vascutek Gelweave vascular graft outflow conduit (Terumo CardioVascular Systems Corp, Ann Arbor, MI) directing flow into the ascending aorta (Fig 12). Unique to this device is an ultrasonic flow probe placed around the outflow graft that communicates with the external control system. The pump can generate maximum flows of 5 L/min with a motor speed of up to 10,000 RPM. Because of its size, it can be used in the pediatric population and is the only device that is FDA approved for this indication. The HeartAssist 5 is currently undergoing FDA studies for its use in the adult population and is already being used for pediatric and adult patients in Europe.

ANESTHETIC MANAGEMENT: PREOPERATIVE ASSESSMENT

The patient who presents for LVAD placement is typically suffering from end-stage HF, the advanced phase of a myriad of
conditions including coronary artery disease, hypertension, valvular disease, idiopathic cardiomyopathy, and congenital heart disease. Whatever the cause may be, cardiac function has deteriorated to the point that systolic and diastolic failure are inseparable, leading to inadequate cardiac output and the potential for widespread end-organ dysfunction. The surgical candidate may have respiratory failure and be dependent on supplemental oxygen. Patients with advanced disease may present with pulmonary hypertension, which can be either passive or fixed. Inadequate cardiac output may also lead to renal insufficiency and hepatic dysfunction. Damage to these organs may result in abnormal electrolytes and altered drug pharmacokinetics, reflected in a decreased volume of distribution and diminished clearance. Thus, the anesthesiologist should expect conventional doses to produce higher-than-normal drug concentrations. Most end-stage HF patients present with a history of prior cardiac surgery, blood transfusion, and exposure to heparin. As a result, difficulties with blood cross-matching and the presence of heparin-induced thrombocytopenia (HIT) may complicate the clinical scenario. Strategies for managing the HIT-positive VAD candidate may include the substitution of heparin with direct thrombin inhibitors or platelet inhibitors (see the section on Choice of Monitors and Conduct of Anesthesia for a discussion on HIT management).

The typical LVAD candidate has poor cardiopulmonary reserve with elevated filling pressures. During the induction of anesthesia, a decrease in preload may occur, leading to a decrease in cardiac output. Conversely, preload augmentation in the presence of adequate left ventricular preload does not improve cardiac output because the Starling curve is rightward shifted and nearly flat. Increases in afterload are poorly tolerated because cause stroke volume falls remarkably. Patients with end-stage HF have a relatively fixed cardiac output and a reduced stroke volume with the heart rate being the critical determinant of cardiac output. Bradycardic episodes are poorly tolerated because the failing heart is unable to compensate by increasing stroke volume, and tachycardia may be associated with decreased stroke volume because of reduced diastolic filling time. Therefore, the maintenance of optimal heart rate in patients with end-stage HF is crucial for preserving adequate cardiac output.

Medical therapy for HF is directed at modulating neurohumoral systems. To manage excessive preload, patients are placed on a sodium-restricted diet and treated with loop diuretics and venodilators (nitrates). When diuretic intolerance occurs, ultrafiltration (via peripherally inserted catheter) may be performed to reduce circulating volume. When possible, afterload is reduced with β-blockers, angiotensin-converting enzyme inhibitors, and arterial vasodilators (such as hydralazine or sodium nitroprusside); the typical LVAD candidate, however, is intolerant of afterload reduction therapy because of hypotension. The patient presenting for LVAD insertion will likely be receiving chronic inotropic therapy (dobutamine and milrinone) and may have an intra-aortic balloon pump. To control life-threatening arrhythmias, the patient may be taking antiarrhythmic medication (amiodarone) or have an automatic implanted cardioverter/defibrillator. Finally, many patients with advanced HF undergo cardiac resynchronization therapy in which biventricular pacing is used to restore the normal sequence of activation and contraction of the ventricles.
CHOICE OF MONITORS AND CONDUCT OF ANESTHESIA

In addition to the standard American Society of Anesthesiologists monitors, the patient who presents for LVAD insertion should have an arterial catheter and introducer with a pulmonary artery (PA) catheter. Placement of these monitors before anesthesia allows the anesthesiologist to quickly detect hemodynamic perturbations that may occur during induction. A PA catheter with the ability to monitor continuous cardiac output and mixed venous oxygen saturation is preferable.

Hemodynamic stability during the induction of general anesthesia is achieved by paining attention to factors that may adversely affect preload, afterload, heart rate, and pulmonary vascular resistance (PVR). HF patients are frequently vasoconstricted and tachycardic because of high sympathetic tone; anesthetic agents may interrupt the sympathetic output and trigger decreases in preload and heart rate. Intubation, surgical stimulation, hypoxia, and hypercarbia may increase systemic vascular resistance and PVR. Before induction, any pre-existing inotropic agents or IABP support should be maintained and optimized. Large-bore intravenous access, rapid-volume infusers, fluid warmers, and blood products should be available.

After preoxygenation, the induction of general anesthesia can be performed using small, titrated doses of an induction agent (etomidate), fentanyl, and a muscle relaxant. In patients with a severely depressed left ventricular ejection fraction (<15%), a technique based on midazolam and fentanyl may be indicated to avoid cardiac depression. Rapid-sequence induction is indicated when the patient has a full stomach or the anesthesiologist desires to minimize hypventilation. If the patient has an AICD, the antitachycardia program should be deactivated before the use of electrocautery.

The most common cause of death in patients with LVADs is sepsis, with a peak hazard occurring approximately 3 weeks after implantation. Sepsis in LVAD recipients may represent poor infection control at the time of surgery. The leading pathogens isolated in LVAD patients with bloodstream infection are staphylococci and Candida species. The recommended regimen of antibiotic and antifungal prophylaxis, which must be administered before incision, consists of the following drugs: vancomycin, levofloxacin, rifampin, fluconazole, and topical mupirocin.

Implantation of the LVAD requires full systemic heparinization with 300 to 400 U/kg of heparin before the initiation of cardiopulmonary bypass (CPB). Either an ACT greater than 480 seconds or a heparin blood concentration greater than 3 units/mL is desired. The management of intraoperative anticoagulation in the HIT-positive patient is controversial and may include the substitution of heparin with a heparin alternative. Direct thrombin inhibitors, such as bivalirudin, are associated with an increased risk of bleeding and lack rapid pharmacologic reversibility, whereas platelet inhibitors, such as prostacyclin, may cause severe systemic hypotension. Given the drawbacks of heparin alternatives, some clinicians will administer a bolus of heparin to patients with a history of HIT if current HIT antibodies are undetectable. Alternatively, if HIT antibodies are present, preoperative plasmapheresis can be performed to reduce HIT antibodies and subsequently permit intraoperative heparin use. In either case, postoperative anticoagulation should be done with a heparin alternative because HIT antibodies rapidly reform.

Surgical implantation of most LVADs may be performed via median sternotomy. Aortic cross-clamp is not performed, cardioplegia is not administered, and hypothermia is not necessary. A brief period of fibrillation may be used to reduce the risk of air entry into the left ventricle when the inflow cannula is inserted. The compact design of the Jarvik 2000, in which the body of the pump is positioned inside the cavity of the left ventricle, allows implantation via median sternotomy, left thoracotomy, or subcostal/extrathoracic approach. The left thoracotomy approach may be chosen when median sternotomy is technically difficult. One-lung ventilation and lateral decubitus positioning are required, and the outflow cannula is anastomosed to the descending aorta rather than the ascending aorta. Additionally, the Jarvik 2000 can be implanted without CPB via any of the previously described approaches. For off-pump insertion, the dose of heparin is reduced to 150 U/kg, and the femoral vessels are cannulated in case CPB becomes necessary. Esmolol given at the time the Jarvik 2000 is inserted into the left ventricle can aid in insertion by reducing the forcefulness of ventricular contractions.

Bleeding is a common problem after the insertion of an LVAD. Exposure of the patient’s blood to nonbiological extracorporeal surfaces induces a “total body inflammatory response” characterized by widespread activation of coagulation, fibrinolysis, and inflammation. Other factors that promote coagulopathy include hepatic congestion caused by pre-existing right-heart failure (RHF), preoperative use of antiplatelet and anticoagulant drugs, hypothermia, and dilution of blood components after the injudicious administration of crystalloid solutions. Pharmacologic therapy to reduce bleeding includes the antifibrinolytic drugs epsilon-aminocaproic acid and tranexamic acid, which are widely used but not well supported in terms of efficacy, and the hemostatic agent desmopressin, which may slightly reduce bleeding and transfusion requirements. Nonsurgical, coagulopathic bleeding has been successfully stopped with recombinant activated factor VII. The administration of blood products to correct coagulopathy should be algorithm based and guided by point-of-care testing and blood conservation techniques (cell-saving devices and salvage of pump blood) should be used. Priming of the bypass pump with fresh frozen plasma is advocated by some clinicians. Off-pump implantation and selection of devices that do not require extensive surgical dissection may play a role in reducing coagulopathy.

PREBYPASS TRANSESOPHAGEAL ECHOCARDIOGRAPHIC EXAMINATION

Transesophageal echocardiography (TEE) plays a critical role in managing intraoperative hemodynamics and identifying abnormalities that may complicate LVAD placement. The transesophageal echocardiographic probe is placed shortly after induction. Transgastric short-axis views of the left ventricle are useful for assessing preload and guiding fluid administration during the prebypass period.

The heart should be inspected for intracardiac shunts, of which patent foramen ovale (PFO) is the most common type encountered. PFO, found in nearly 25% of the population,
can be a source of paradoxical embolism and hypoxemia in the LVAD recipient. The interatrial septum can be interrogated using the midesophageal 4-chamber, right ventricular inflow/outflow, and bicaval views. Color Doppler, with aliasing velocity reduced to 30 cm/s, can visualize the lower velocity flow of a PFO. In the typical LVAD recipient, the left atrial pressure far exceeds right atrial pressure, and a rightward bulge of the interatrial septum is present throughout the cardiac cycle, effectively closing the “flap-like valve” of the PFO. This condition makes it difficult to detect right-to-left shunt without performing a provocative maneuver to temporarily augment right atrial pressure above left atrial pressure. In a mechanically ventilated patient, this can be accomplished by performing an airway pressure release maneuver combined with contrast injection. First, ventilation is stopped and airway pressure increased to 30 cmH2O and held. Echogenic contrast material (agitated saline or blood) is then injected into the patient’s central circulation. When contrast is seen in the right atrium, the airway pressure is abruptly released. An effective contrast injection will completely opacify the right atrium, and an effective airway pressure release maneuver will cause the interatrial septum to momentarily bulge toward the left. The study is considered positive if bubbles are seen on the left side within 5 cardiac cycles of the contrast injection. After separation from bypass after LVAD insertion, a repeat examination of the interatrial septum for missed PFO should be performed (see section on Postbypass Transesophageal Echocardiographic Examination). Other types of intracardiac shunt, such as atrial septal defect or ventricular septal defect, should also be sought out during the transesophageal echocardiographic examination.

The cardiac valves should be inspected during the prebypass transesophageal echocardiographic examination. Three valvular abnormalities deserve special attention. After LVAD insertion, aortic insufficiency can result in reduced forward pump flow because of recirculation of blood across the incompetent valve. In a heart with end-stage HF, the severity of aortic insufficiency may be underestimated because of a diminished diastolic gradient between the aorta and left ventricle. Aortic insufficiency of moderate or greater severity should be surgically corrected at the time of LVAD placement. Mitral stenosis is relevant if an LVAD with inflow cannula positioned at the ventricular apex is to be used. In this situation, the lesion will restrict LVAD filling and should be corrected while on bypass. Tricuspid regurgitation may contribute to right ventricular dysfunction (RVD) postbypass. If the severity of regurgitation is greater than moderate or RVD is anticipated postbypass, surgical correction (annuloplasty) should be done. Echocardiographic examination of right ventricular function is discussed in the section titled “Right Ventricular Dysfunction After LVAD Insertion.”

Transesophageal echocardiographic examination of the potential sites for LVAD cannulation may reveal unexpected problems. The inflow cannula is usually positioned at the apex of the left ventricle, a location where intracardiac clot and mural thrombus may form. A clot may also form in the left atrial appendage. If a clot or thrombus is detected by TEE, it is important to alert the surgeon to its presence so that the cannulation site can be adjusted (changed to left atrial cannulation) or the clot removed before starting the LVAD. Amputation of the left atrial appendage may be performed at the time of LVAD placement. The outflow cannula of the LVAD is usually anastomosed to the ascending aorta. Plaque, mobile atheroma, or aneurysm/dissection may complicate outflow cannula anastomosis. In the case of ascending aortic aneurysm, replacement of the aneurysmal segment with tube graft followed by end-to-side anastomosis of the outflow cannula can be performed.

POSTBYPASS TRANSESOPHAGEAL ECHOCARDIOGRAPHIC EXAMINATION

The chambers of the heart should be inspected for air before separation from CPB. There are 2 sources of air encountered with LVAD placement. First, there is the air that accumulates in the heart because of insertion of the inflow and outflow cannulae. It typically collects in the left ventricle, left atrium, orifices of the pulmonary veins and ascending aorta and can be indentified by TEE as echogenic “fireflies.” There may also be air in the pump itself. The surgeon minimizes air embolism by submerging the heart with fluid, using the LVAD as a left ventricular vent before attaching the outflow graft to the aorta, and placing a temporary vent in the outflow graft before device activation. Volume loading and vigorous ventilation of the lungs are additional steps to prevent air embolism. Head-down positioning during weaning is crucial to direct air bubbles away from the ostium of the right coronary artery. Transesophageal echocardiographic guidance aids the surgeon with locating and dislodging air pockets. The aortic root vent can be turned off when weaning is complete.

The second source of air is entrainment caused by negative pressure generated by the LVAD. The source of air is not always visible on TEE and can occur sporadically. When air bubbles suddenly appear on TEE, the surgeon should be alerted, the head of the bed lowered, and aortic root vent turned on. Air entrainment can occur along a suture line, but this does not always imply that the suture line is at fault. For example, if LVAD filling is inadequate because of hypovolemia, the pump will generate a pressure gradient that draws air across the inflow cannula suture lines. Volume replacement will correct air entrainment in this case. Other causes of air entrainment are RHF, inflow cannula obstruction, and excessive LVAD pump speed (continuous flow device). When RHF appears to be a determining factor in air entrainment, placement of an RVAD may be the ultimate solution (see section on Right Ventricular Dysfunction After LVAD Insertion).

The LVAD cannulation sites should be inspected before separation from CPB and again afterward to rule out obstruction or malposition (Figs 13 and 14). When LVAD support is expected to be long term (either DT or BTT), the inflow cannula anastomosis is made at the left ventricular apex. Less frequently, the inflow cannula insertion is made in the left atrium via the right or left pulmonary veins, as may be the case when ventricular function is expected to recover. Midesophageal 4-chamber, 2-chamber, and long-axis views are useful for visualizing a left ventricular inflow cannula. The orifice of the inflow cannula should be oriented toward the mitral valve. Excessive angulation toward the interventricular septum may lead to obstruction. The LVAD outflow cannula anastomosis is usually made at the ascending aorta, except for the Jarvik 2000, which can have an anastomosis at the descending aorta. For
both inflow and outflow cannulae, color-flow Doppler should reveal laminar, nonturbulent flow at the cannula orifice. A beam of continuous-wave Doppler aimed at the cannula orifice can be used to determine the peak velocity. Pulsatile devices have a peak velocity less than 2.3 m/s, whereas continuous-flow devices have a peak velocity of 1 to 2 m/s.

After separation from bypass is complete, the effects of LVAD insertion on heart filling pressures should be assessed. Compared with the prebypass examination, the left ventricle will appear less distended and the interventricular septum will be in a neutral position or, in the setting of RVD, shifted toward the left (Fig 15). A completely decompressed ventricle (“sucked down”) may cause inflow cannula obstruction, decreased LVAD output, and possibly air entrainment; under these circumstances, either rapid increase in left ventricular preload or decrease in pump speed needs to be performed to prevent further hemodynamic deterioration or systemic air embolization. In addition, placement of an RVAD might be considered, as described in a later section. The shape and position of the interatrial septum is likely to be changed by LVAD insertion. Prebypass, the interatrial septum is often bulging to the right because of elevated left atrial pressure. The activation of the LVAD will decompress the left ventricle and reduce left atrial pressure. In addition, right atrial pressure may increase in the setting of right ventricular volume or pressure overload that occurs postbypass. These factors alter the pressure gradient across the interatrial septum and may reveal a PFO that was unrecognized during the prebypass TEE examination. Consequences of PFO include systemic shunting, hypoxemia, and paradoxical embolism. The detection of a PFO during the postbypass examination warrants a return to bypass for PFO closure.

Information taken from the TEE and arterial blood pressure tracing is useful for optimizing LVAD function before leaving the operating room. For the pulsatile LVADs, the appearance of the arterial waveform depends on how much myocardial contractility is present. If myocardial contractil-
ity is absent (very poor ejection fraction), the arterial trace will consist of regularly spaced pressure waves generated by the LVAD. Conversely, a heart with preserved myocardial contractility will produce pressure waves that compete with those from the pulsatile LVAD, giving the arterial waveform an irregular shape. Echocardiographic images of the aortic valve will show intermittent valve opening that correlates to the myocardial contraction. Pump function should be adjusted to ensure that the aortic valve opens approximately every 3 beats of the heart. Less frequent ejection across the native aortic valve may promote blood stasis in the ascending aorta.

The shape of the arterial waveform of continuous-flow devices depends on intrinsic heart function, pump speed, and preload state of the left ventricle. The absence of myocardial contractility, which may occur if pump speed is very high or the ventricle is extremely hypovolemic, gives an arterial trace that is a “flat” line. The PI of the HeartMate II console will be low under those conditions. Compared with the pulsatile LVADs, the continuous-flow devices produce a smaller pulse pressure because these devices unload the ventricle throughout the cardiac cycle, whereas the pulsatile devices unload the ventricle only during pump systole. For the continuous-flow devices, the pulse pressure correlates inversely with pump

Fig 14. Transesophageal echocardiographic imaging of a HeartMate II LVAD outflow cannula. The midesophageal view of the ascending aorta in long axis with color Doppler (A) reveals laminar, nonturbulent flow at the anastomosis of the LVAD outflow cannula with ascending aorta. Pulsed-wave Doppler aimed at the orifice of the outflow cannula (B) shows that the peak velocity is 1 m/s (100 cm/s), which is within the normal range for a continuous-flow device. (Color version of figure is available online.)
speed (Fig 16). Pump speed should be optimized to produce a pulse pressure of approximately 15 to 20 mmHg in order to provide adequate aortic valve opening with each systole and to prevent blood stagnation in the aortic root.

SEPARATION FROM CPB AFTER LVAD PLACEMENT

Separation from CPB is a collaboration among the anesthesiologist, perfusionist, and surgeon to optimize the patient’s hemodynamics and maximize performance of the newly implanted LVAD. Key factors are preload, afterload, and LVAD settings such as pumping mode (for pulsatile devices) or impeller speed (for continuous-flow devices).

The pulsatile LVAD devices are extremely dependent on preload. Pulsatile LVADs are typically operated in an automatic “fill-to-empty” mode, in which a sensor detects when the pump chamber is full and triggers a pump cycle to empty the device. Because the pump cycle is triggered only when the pump chamber is full, inadequate left ventricular preload will severely compromise pump output. An alternate mode of operation for pulsatile devices, the “fixed” mode, is preferable during separation from CPB. In fixed-mode operation, the LVAD produces a specified number of ejections per minute regardless of fullness of the pump chamber. The pump stroke volume, which is displayed on the pump console, can be used by the anesthesiologist to guide fluid administration. Certain pulsatile LVADs (Thoratec PVAD/IVAD and AbioMed BV5000) allow the adjustment of the diastolic vacuum, which is negative pressure applied to the pump diaphragm during pump diastole. Diastolic vacuum should be kept above ~10 mmHg. Additional vacuum can be used to augment pump filling; however, such a maneuver should be avoided to prevent air entrainment across fresh suture catheters in a newly implanted VAD.

The performance of continuous-flow LVADs is determined by the interaction between the left ventricular preload and the speed of the pump’s rotating impeller. Impeller speed that is too low will not produce sufficient cardiac output and may cause the ventricle to distend. Conversely, impeller speed that is too high for the heart’s preload state may cause the left ventricle to become “sucked down” and result in reduced LVAD output because of an obstruction phenomenon. As discussed previously, the console of the HeartMate II displays the PI, a dimensionless parameter that reflects the magnitude of “flow pulse” transmitted through the pump caused by native myocardial function. The PI indicates the preload state of the left ventricle given the current pump speed and rate of ventricular filling. Ideally, the PI should be around 3 to 4. If the HeartMate II console displays a low PI (~2) and LVAD output is inadequate, fluid administration to augment left ventricular preload should be considered. Other causes of low PI, such as cardiac tamponade or malpositioned VAD cannula, can occur and should be investigated. The CentriMag device, a centrifugal pump, does not present PI on its console, but the apparatus tubing may exhibit “chatter” (shaking) when preload and device output are low.

The process of separating from CPB can begin after the LVAD is adequately deaired as discussed previously. The LVAD is started when the patient is still on full CPB. Initially, a pulsatile LVAD may be set to 40 beats/min in a fixed mode, whereas a continuous-flow device is started at a fixed RPM. The HeartMate II is commonly running at 8,000 to 9,000 RPM when first separating from CPB. The perfusionist decreases CPB flow and partially occludes the venous drainage line, resulting in greater preload to the right side of the heart. LVAD
output (displayed on the LVAD console in L/min) should rise and approach a level suitable for systemic support when the venous catheter is clamped and CPB is ceased. If LVAD output is low, LVAD pump speed should be raised (increased beats/min or RPM) and additional preload given. Transesophageal echocardiographic imaging should show a decompressed left ventricle with septum in a neutral position or in the setting of RHF bowed toward the left. A collapsed, slit-like left ventricle combined with low LVAD output indicates a need for additional left ventricular filling. Care should be taken to avoid overloading the right heart at this time because this may exacerbate RHF (see section on Right Ventricular Dysfunction After LVAD Insertion).

Excessive afterload is detrimental to both pulsatile and continuous-flow LVADs. Elevated systemic vascular resistance puts stress on the device that may lead to premature failure. Continuous-flow devices produce less flow when afterload is high. A mean arterial pressure between 70 and 80 mmHg is usually adequate in the postbypass period. Systemic hypertension should be treated with arterial vasodilators such as sodium nitroprusside or nicardipine. Conversely, frank systemic hypotension should be avoided because this would compromise coronary flow and perfusion of other vital organs. Vasopressin is a potent noncatecholamine vasoconstrictor that produces less pulmonary vasoconstriction than norepinephrine or phenylephrine. In LVAD recipients who develop refractory hypotension, vasopressin increases mean arterial pressure without significantly increasing PA pressure. Methylene blue also has been used to treat refractory hypotension (vasoplegic syndrome) in cardiac surgical patients.

RIGHT VENTRICULAR DYSFUNCTION AFTER LVAD INSERTION

Right ventricular dysfunction (RVD) is a common problem in LVAD recipients. Although right ventricular function could improve after LVAD placement as a result of reduced right ventricular afterload, this is not always the case for several reasons. First, PVR, which is often elevated in patients with end-stage HF, may be “fixed” and may not return to normal when the left ventricle is decompressed. Second, LVAD activation may cause a surge in preload to the right ventricle that is poorly tolerated. Third, the right ventricle depends on a loaded left ventricle to generate adequate contractile force, so decompression of the left ventricle may result in RVD. Finally, right ventricular function may be depressed by the effects of CPB and massive blood product transfusion. The presence of RVD should be identified in the prebypass period because this permits the anesthesiologist to initiate therapy to optimize right ventricular performance before separation from CPB. Alternatively, early detection of severe RVD may prompt the surgical team to place biventricular support. Despite best efforts, overt evidence of RVD may not be appreciated until after LVAD activation.

Hemodynamic and Echocardiographic Assessment of the Right Ventricle

The placement of a PA catheter facilitates a thorough hemodynamic assessment of right ventricular function in the period before the initiation of CPB. Although many patients with end-stage HF present with elevated right atrial pressure (RAP) and elevated pulmonary artery pressure (PAP), the identification of these abnormalities is not sufficient to predict which LVAD recipients will need biventricular support. The right ventricular stroke work index (RVSWI) is a hemodynamic calculation that reflects right ventricular contractility as follows:

\[ \text{RVSWI} = (\text{mPAP} - \text{PCWP}) \times \text{SVI} \]

In this equation, mRAP is the mean RAP and SVI is stroke volume index. A low RVSWI (<300 mmHg \cdot mL \cdot m^{-2}) is a significant predictor of need for RVAD insertion. The combination of high RAP with low PAP is concerning because it may indicate that the right ventricular systolic function is too weak to generate a high PAP. Furthermore, a patient with an elevated RAP prebypass could be expected to have an even higher RAP postbypass if there is an increase in preload after LVAD activation. Detrimental consequences of an elevated RAP include hepatic congestion and a low renal perfusion pressure.

Patients with end-stage HF frequently present with an elevated PVR, which can be calculated with the following equation: PVR = (mPAP - PCWP)/CO. In this equation, mPAP is the mean PA pressure, PCWP is the pulmonary capillary wedge pressure, and CO is cardiac output. When units of mmHg and L/min are used, the result is expressed in Woods units. Activation of the LVAD may cause an elevated PVR to normalize, but the degree to which this happens depends on the “reversibility” of the PVR. Reversibility can be tested by administering pulmonary vasodilators such as nitric oxide or prostaglandin. A PVR greater than 5 Woods units that is not reversible with pulmonary vasodilator therapy is considered to be “fixed” and is associated with an increased risk of early right ventricular failure post-CPB. The transpulmonary gradient (TPG), calculated as the difference between mean PA pressure and PCWP, may be easier to use than PVR because it does not require a determination of CO. A TPG greater than 14 mmHg indicates a significant elevation of PVR. A prebypass RAP ≥20 mmHg together with prebypass TPG ≥16 mmHg has a sensitivity and specificity of 82% and 88%, respectively, for predicting RVD after LVAD implantation.

Intraoperative echocardiography is a critical tool for the diagnosis and management of RVD. The transesophageal echocardiographic midesophageal 4-chamber and RV inflow-outflow views can be used to identify anatomic changes consistent with chronic RHF. The normal right ventricle has an end-diastolic cross-sectional area that is less than 60% of the left ventricular end-diastolic area. With dilation, the shape of the right ventricle changes from triangular to round. The apical angle of the right ventricle, as seen in the midesophageal 4-chamber view where the interventricular septum and right ventricular free wall intersect, increases significantly with RVD; the degree to which the angle increases correlates with the severity of RVD. In severe right ventricular dilation, the right ventricle replaces the left ventricle in forming the cardiac apex. The right atrium and inferior vena cava may be dilated, and pulsed-wave Doppler evaluation of hepatic vein blood flow...
Table 5. Intravenous Pulmonary Vasodilators

<table>
<thead>
<tr>
<th>No.</th>
<th>Medication</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Nitroglycerin, sodium nitroprusside</td>
<td>Nitric oxide (NO) donors → activate guanyl cyclase → increase cGMP → dephosphorylation of myosin light chains → relaxation of vascular smooth muscle</td>
</tr>
<tr>
<td>2.</td>
<td>Milrinone</td>
<td>Pulmonary and systemic vasodilation</td>
</tr>
<tr>
<td>3.</td>
<td>Prostacyclin (epoprostol)</td>
<td>Endogenous substance that increases cAMP levels in vascular smooth muscle</td>
</tr>
<tr>
<td>4.</td>
<td>Iloprost</td>
<td>Inhibition of platelet aggregation due to increased cAMP in platelets</td>
</tr>
<tr>
<td>5.</td>
<td>Recombinant B-type Natriuretic Peptide (nesiritide)</td>
<td>Stimulates guanyl cyclase to increase cGMP levels in vascular smooth muscle</td>
</tr>
</tbody>
</table>

Abbreviations: cGMP, cyclic guanosine monophosphate; cAMP, cyclic adenosine monophosphate.

Table 6. Inhaled Pulmonary Vasodilators

<table>
<thead>
<tr>
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<tr>
<td>1.</td>
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</tr>
<tr>
<td>2.</td>
<td>Milrinone</td>
<td>Pulmonary vasodilation</td>
</tr>
<tr>
<td>3.</td>
<td>Prostacyclin (epoprostol)</td>
<td>Same mechanism as intravenous milrinone</td>
</tr>
</tbody>
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Abbreviations: cGMP, cyclic guanosine monophosphate; ppm, parts per million; mL, milliliters; mg, milligrams; h, hours; COP, cardiopulmonary bypass.

Anesthetic Management of RVD

RVD is frequently a determining factor in inadequate LVAD filling after separation from CPB. When volume administration fails to achieve suitable LVAD preload, therapy to reduce PVR and augment right ventricular inotropy should be initiated. PVR may be elevated because of pre-existing fixed pulmonary hypertension, massive fluid administration, or as a result of CPB-mediated inflammatory-type response. The anesthesiologist should identify and treat conditions that may exacerbate pulmonary hypertension such as hypoxemia, hypercarbia, acidosis, hypothermia, and light anesthesia. Even when all of these factors are addressed, it is often necessary to initiate intravenous or inhaled therapy to reduce PVR (Tables 5 and 6).

Intravenous nitrates (such as nitroglycerin and sodium nitroprusside) are first-line agents that reduce PVR by acting as nitric oxide (NO) donors. NO stimulates guanyl cyclase to produce the second messenger cyclic guanosine monophosphate (cGMP), which promotes dephosphorylation of myosin light chains and reduces cytosolic calcium. The vasodilation resulting from nitrates is nonspecific; systemic hypotension is frequently the limiting factor with their use. Phosphodiesterase inhibitors, in particular milrinone, are widely used to treat RHF postbypass. Milrinone prevents the breakdown of cyclic adenosine monophosphate (cAMP) in cardiac myocytes and vascular smooth muscle, which may reveal attenuation or reversal of the systolic inflow wave. Thickness of the right ventricular free wall over 5 mm is abnormal and suggests elevated PVR. As discussed previously, the tricuspid valve should be inspected for incompetence. If tricuspid regurgitation greater than moderate in severity is present, annuloplasty should be considered. RVD requiring RVAD placement is significantly greater in LVAD recipients who have grade III or IV tricuspid regurgitation preoperatively.

The quantification of right ventricular ejection fraction with TEE is difficult because of the anatomy of the chamber. Systolic function can be estimated by calculating the fractional area change, which is normally greater than 30%. Tricuspid annular plane systolic excursion (TAPSE) is a simple measurement of the longitudinal shortening of the right ventricle during systole. The measurement is made in the midesophageal 4-chamber view with the M-mode cursor positioned across the lateral annulus of the tricuspid valve. A TAPSE value less than 15 mm is associated with severe RVD. Similar in concept to TAPSE is pulsed-wave tissue Doppler imaging of the lateral tricuspid annulus in which myocardial tissue velocity is measured against time. The peak annular systolic velocity (Sa) is predictive of low cardiac index and severe RVD when it is less than 10 cm/s. Unfortunately, tricuspid annular motion rarely aligns with the transesophageal echocardiographic cursor in the midesophageal 4-chamber view, making TAPSE and peak Sa difficult to measure. Isovolumic acceleration is a pulsed-wave tissue Doppler imaging assessment of tricuspid annular motion that is obtained in the transgastric long-axis view of the right ventricle, a view that allows parallel alignment of the Doppler beam with the annular motion. The measurement is made by determining the dominant slope of the isovolumic phase of tricuspid annular velocity during systole. In anesthetized patients without RVD, the IVA is 1.71 ± 0.59 m/s. In the future, strain, strain rate, and 3-dimensional TEE may play a role in the assessment of RVD.
lar smooth muscle. In myocytes, cAMP increases inotropy because of higher calcium levels in the cytosol; in vascular smooth muscle, cAMP promotes dephosphorylation of myosin and reduces cytosolic calcium. As is the case with nitrates, milrinone vasodilates both pulmonary and systemic vascular beds. Prostaglandins are potent, naturally occurring substances that increase levels of cAMP in vascular smooth muscle, resulting in pulmonary and systemic vasodilation. Available to the anesthesiologist are prostaglandin E1 (alprostadil) and prostaglandin I2 (epoprostenol, iloprost). Prostaglandin I2, also known as prostacyclin, inhibits the aggregation of platelets by raising cAMP levels. New experience in delivering milrinone and prostacyclin as nebulized drugs has shown that the systemic side effects can be avoided with inhalation administration. NO is the gold standard for the treatment of elevated PVR. Delivered via inhalation, NO selectively vasodilates the pulmonary vasculature by increasing cGMP levels. There are minimal systemic effects of NO, but cumbersome and expensive equipment is required to deliver the drug safely and with precision.

Inotropic drugs (Table 7) are often initiated to improve right ventricular systolic performance. Those with predominant β-receptor agonist activity are most useful because of their ability to increase myocardial contractility without excessive vasoconstriction. Dobutamine and isoproterenol are excellent right ventricular inotropes that raise inotropy and promote pulmonary vasodilation. Epinephrine is also a powerful right ventricular inotrope, but it is more likely to increase PA pressure and should be reserved for situations in which the correction of systemic hypotension is also a goal. As stated previously, milrinone is a positive inotrope in addition to its vasodilator effects but produces its effect independently of β-adrenergic receptors.

Nesiritide (recombinant B-type natriuretic peptide) and levosimendan are novel drugs that may have a role in treating RHF in the LVAD recipient. Nesiritide resembles the endogenous hormone released by the ventricles of the heart and promotes diuresis, natriuresis and vasodilation through the stimulation of guanyl cyclase and subsequent elevation of cGMP levels. It produces systemic and pulmonary vasodilation, reduces PCWP, and increases stoke volume without an increase in heart rate. Levosimendan is a pyridazinone-dinitrile with inotropic and vasodilatory properties. It functions as a “calcium sensitizer” by increasing the stability of the interaction between troponin-C and intracellular calcium ions. In addition, levosimendan opens adenosine triphosphate–dependent potassium channels in vascular smooth muscle, resulting in vasodilation. Levosimendan is also an inhibitor of phosphodiesterase type 3, but this action does not appear to be clinically relevant. Infusions of levosimendan decrease PCWP, PVR, and systemic vascular resistance and increase stroke volume in patients with severe HF. Levosimendan avoids certain deleterious effects of traditional inotropes; levosimendan does not raise myocardial oxygen consumption, raise intracellular calcium levels, or increase arrhythmogenicity.

In clinical practice, pulmonary vasodilators and inotropic drugs are selected based on the clinical situation. Combinations of drugs are often used. A right ventricle with preserved systolic function and only mildly elevated PVR may do well with intravenous nitrate therapy. Right ventricles with more depressed systolic function and higher levels of PVR usually require an inotrope and pulmonary vasodilator. Dobutamine plus inhaled nitric oxide or milrinone plus nitric oxide are effective combinations commonly used in clinical practice. Systemic hypotension resulting as a side effect of pulmonary vasodilator and inotrope therapy is not uncommon; vasopressin may be the preferred vasopressor in that situation.

### Table 7. Right Ventricular Inotropes

| Drug             | Effects                                                               |
|------------------|                                                                      |
| Isoproterenol    | Nonselective β-agonist → increased cAMP and cytosolic calcium       |
|                  | Chronotrope and inotrope                                             |
|                  | Pulmonary and systemic vasodilator                                   |
|                  | Dose: 0.025-0.5 μg/kg/min                                           |
| Dobutamine       | Primarily β1- > β2-agonist, minimal α1-agonist                       |
|                  | Chronotrope and inotrope                                             |
|                  | Pulmonary and systemic vasodilator (less than with isoproterenol)   |
|                  | Dose: 5-20 μg/kg/min                                                |
| Epinephrine      | Stimulates β1-, β2-, and α1-receptors                               |
|                  | Chronotrope and inotropes                                            |
|                  | Increases pulmonary and systemic pressures                         |
|                  | Dose: 0.03-0.1 μg/kg/min                                            |
| Levosimendan     | Calcium sensitizer → stabilizes calcium–troponin C interaction       |
|                  | → increases contractility                                            |
|                  | Open ATP-dependent potassium channels in vascular smooth             |
|                  | muscle → vasodilation                                               |
|                  | Does not increase O2 consumption or increase intracellular          |
|                  | calcium levels                                                      |
|                  | Dose: loading dose 12-24 μg/kg followed by 0.1-0.2 μg/kg/min        |

Abbreviations: cAMP, cyclic adenosine monophosphate; ATP, adenosine triphosphate.

**RVAD Placement**

The placement of a temporary RVAD may be indicated when right-heart function does not improve after maximal drug therapy. The prebypass transesophageal echocardiographic examination of the right heart may clearly identify those patients who require biventricular support ahead of time, but overt evidence of RHF may not be appreciated until after LVAD activation. If the placement of a biventricular support is not chosen from the start, careful attention to hemodynamic data and transesophageal echocardiographic imaging after separation from CPB is crucial. In particular, care should be taken to avoid overfilling the right heart when attempting to achieve adequate LVAD filling. An elevated RAP in the setting of low PAP may indicate imminent right ventricular failure. Low LVAD output along with transesophageal echocardiographic evidence of an underfilled left ventricle (slit-like left ventricle with interventricular septum bulging toward the left side) indicates the need for RVAD support (Fig 15).

The CentriMag device is ideal for short-term use as an RVAD when combined with pulsatile or continuous flow pumps on the left side of the heart. In a patient in whom RVD...
is expected to be temporary, the CentriMag can be implanted with standard bypass cannulae (right atrium to PA) and subsequently removed when right-heart function improves. Alternatively, in those cases in which the recovery of right ventricular function is less likely, the CentriMag can be implanted with cannulae compatible with the Thoratec PVAD, a device better suited to long-term support. The combination of CentriMag pump with PVAD-compatible cannulae allows the CentriMag to be exchanged for the PVAD if right-heart function does not improve.

Predicting which patients need long-term biventricular support is difficult. RHF caused by stunning of viable myocardium may be reversible after days or weeks of RVAD support, whereas the recovery of right-heart function is less likely in patients with fixed pulmonary hypertension or long-standing intrinsic myocardial disease involving the right ventricle. Repeat transesophageal echocardiographic examinations in the postoperative period are useful for assessing the recovery of right ventricular function.

POSTIMPLANTATION ISSUES AND OUTCOMES IN THE VAD RECIPIENT

Postoperative Anticoagulation

Systemic anticoagulation is frequently initiated after LVAD implantation (Table 8). The exception is with the HeartMate XVE, which only requires antiplatelet therapy. Postoperative anticoagulation is not started until the cessation of surgical bleeding and often varies from center to center. In general, an international normalized ratio between 2 and 3, activated partial thromboplastin time (aPTT) between 50 and 70 seconds, or an ACT around 200 seconds is the goal for systemic anticoagulation.

Anesthesia for Noncardiac Procedures

Many institutions are seeing an increased number of VAD patients presenting for noncardiac procedures. In the report by Stehlik et al., the most common type of operation performed was abdominal surgery (most often cholecystectomy) followed by orthopedic surgery, tracheostomy, and vascular surgery. Although VAD recipients experience a high rate of adverse events after device implantation (see section on LVAD Outcomes and Complications), the clinical condition of the VAD patient who presents for noncardiac surgery can vary widely.

The maintenance of anticoagulation before surgery is desirable to minimize thrombotic complications. The VAD patient receiving warfarin should continue the drug until the day before surgery. Unfortunately, certain procedures are not amenable to anticoagulation or surgeon preference may dictate a reduced level of anticoagulation. If the surgery is elective, the patient can be bridged from warfarin to intravenous heparin preoperatively. The heparin can be discontinued immediately before surgery and resumed postoperatively, but it is safer to maintain an intraoperative heparin infusion with the goal of achieving an ACT or aPTT at the lower limit recommended by the VAD manufacturer. In emergent situations, fresh frozen plasma can

Table 8. Systemic Anticoagulation for VADs

<table>
<thead>
<tr>
<th>Device</th>
<th>Anticoagulation</th>
<th>Degree of Anticoagulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thoratec PVAD and IVAD</td>
<td>Perioperative: heparin</td>
<td>Heparin: aPTT 1.5 times normal</td>
</tr>
<tr>
<td></td>
<td>Long-term: warfarin ± ASA</td>
<td>Warfarin: INR 2.5-3.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Some centers add ASA for devices &gt;30 days in</td>
</tr>
<tr>
<td></td>
<td></td>
<td>patients with platelets &gt;300,000</td>
</tr>
<tr>
<td>HeartMate I (XVE)</td>
<td>Heparin not routinely used postoperatively</td>
<td>Dextran recommended until patient can take oral medication</td>
</tr>
<tr>
<td></td>
<td>Long-term: antiplatelet drugs</td>
<td>Heparin required only for low-flow states</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dipiridamole, 75 mg 3 times a day, and ASA, 80 mg every day, long term if tolerated</td>
</tr>
<tr>
<td>Abiomed BVS5000 and AB5000</td>
<td>Heparin required for placement and weaning</td>
<td>ACT 180-200 s</td>
</tr>
<tr>
<td>Impella 2.5, 5.0, and LD</td>
<td></td>
<td>ACT 250-500 s for placement</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ACT 300-400 s for removal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Device has heparinized purge solution running continuously</td>
</tr>
<tr>
<td>CentriMag</td>
<td>Heparin</td>
<td>aPTT 1.5-2.5 times normal or ACT 180-200 s</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ACT &gt;250 s</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Device has heparinized lubrication solution</td>
</tr>
<tr>
<td></td>
<td></td>
<td>running continuously</td>
</tr>
<tr>
<td>HeartMate II</td>
<td>Perioperative: heparin</td>
<td>Heparin: aPTT 55-65 s or 1.5-1.8 times normal</td>
</tr>
<tr>
<td></td>
<td>Long-term: warfarin and antiplatelet drugs</td>
<td>Warfarin: INR 2.0-3.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ASA and dipiridamole as tolerated</td>
</tr>
<tr>
<td>Jarvik 2000</td>
<td>Perioperative: heparin</td>
<td>Heparin: aPTT 50-70 s</td>
</tr>
<tr>
<td></td>
<td>Long-term: warfarin and antiplatelet drugs</td>
<td>Warfarin: INR 2.5-3.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ASA and dipiridamole as tolerated</td>
</tr>
<tr>
<td>HeartAssist 5 (MicroMed DeBakey)</td>
<td>Perioperative: heparin</td>
<td>Heparin: aPTT 2 times normal</td>
</tr>
<tr>
<td></td>
<td>Long-term: warfarin and antiplatelet drugs</td>
<td>Warfarin: INR 2.5-3.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ASA 50-100 mg every day</td>
</tr>
</tbody>
</table>

Abbreviations: ASA, aspirin; aPTT, activated partial thromboplastin time; INR, international normalized ratio; ACT, activated clotting time.
be used to reverse the effect of warfarin, but again complete reversal should not be the goal.

Standard American Society of Anesthesiologists monitors should be used, and invasive monitors should be selected based on patient and surgical factors. It should be kept in mind that the electrocardiogram heart rate signal corresponds to the native electrical rhythm not the pump rate of a pulsatile VAD. Although pulse oximeters and oscillometric noninvasive blood pressure devices often function normally in VAD patients, it may be difficult to obtain a reading in a patient with a nonpulsatile VAD who has very little myocardial contractility. If the patient’s condition allows, pulsatility can be temporarily augmented by decreasing pump RPM; this may permit a “spot check” of oxygen saturation or blood pressure to be recorded. A hand-held Doppler probe can be used to measure systolic blood pressure by listening for the return of blood flow as the blood pressure cuff is deflated. Ultimately, ultrasound-guided arterial catheter insertion will permit blood pressure recording and blood gas analysis. The monitoring of central venous pressure is not usually necessary unless large fluid shifts are anticipated. PA catheters should be reserved for patients who require intraoperative therapy to reduce PVR or increase right ventricular inotropy. If the patient is undergoing a general anesthetic, insertion of a transesophageal echocardiographic probe can help guide fluid administration. Finally, the VAD display console reports several important parameters, such as pump flow (in L/min) and PI (pulsatility index, if the patient has a HeartMate II LVAD), that should be recorded in the anesthetic record.

The selection of drugs to induce and maintain anesthesia should match the patient’s degree of end-organ dysfunction. Spontaneous ventilation may be advantageous to positive-pressure ventilation because preload is not decreased. Intracorporeal VADs exert pressure on the stomach and impair gastric emptying, so it may be wise to consider these patients to have full stomachs. Pulsatile VADs are operated in the automatic, “full-to-empty” mode, and continuous-flow devices operated at a fixed RPM. Mean arterial pressure should be maintained between 70 and 80 mm Hg. Hypotension, low VAD output, and low PI may indicate hypovolemia, which can be corrected with fluid administration. Hypertension should be avoided and treated with arterial vasodilators. Right-heart function is frequently marginal, so it is important to avoid factors that worsen PVR (hypoxia, hypercarbia, and light anesthesia) and overfilling the right ventricle with fluid. Therapy to increase right ventricular inotropy and reduce PVR may need to be implemented. Prophylactic antibiotics may be indicated depending on the type of procedure. Intra-abdominal operations require broad-spectrum antibacterial and antifungal coverage before incision, whereas nonabdominal procedures receive vancomycin plus a cephalosporin.  

During the procedure, the VAD should be powered by an alternating current electric outlet. It is preferable to connect the system display module, as opposed to a portable controller, so that all parameters are displayed and adjustable. Finally, a clinician (perfusionist or biomedical engineer) with extensive knowledge of the VAD and its control panel should be immediately available to adjust pump settings and troubleshoot problems that may arise.

LVAD Outcomes and Complications

LVADs have been used clinically since 1966 when DeBakey successfully used an extracorporeal blood pump to support a patient for 10 days with postcardiomyotomy HF. 168 In 1978, an LVAD was successfully used as a BTT, supporting a patient for 7 days until transplantation. In the 1980s and 1990s, efforts were directed at designing intracorporeal LVADs that could provide longer-term support for patients awaiting heart transplantation. 147-149 DeRose et al 150 reported the clinical outcomes of 32 recipients of HeartMate-vented electric LVADs between 1993 and 1997. Overall survival, defined as progression to transplantation (20/32 patients), device explantation (1 patient), or ongoing LVAD support (5 patients), was 77%, with mean LVAD support duration of 122 ± 26 days. The most common complications were RHF, device-related infection, and hemorrhage. Three device malfunctions were encountered after prolonged support.

The efficacy of the long-term use of LVADs, in particular for those patients ineligible for heart transplantation (destination therapy, DT), was shown in the REMATCH study 151 conducted during 1998 to 2001. One hundred twenty-nine patients with end-stage, class IV HF were randomized to receive either insertion of an LVAD (HeartMate XVE) or optimal medical therapy. One-year survival was 52% in the device group and 25% in the medical therapy group, whereas at 2 years survival was 23% and 8%, respectively. Patients in the device group showed significant improvement in certain measures of quality of life. Device recipients were more likely to have adverse events such as bleeding (42% at 6 months) and device infection (28% at 3 months). Device failure did not occur before 12 months in any patient, but by 24 months there was a 35% probability of failure. Ten patients underwent device replacement.

In 2007, Lietz et al 158 published a follow-up to the REMATCH study describing the outcomes of 280 patients who received HeartMate XVE LVADs between 2001 and 2005. Survival at 1 year was 56%, and at 2 years it was 30.9%, a slight improvement at both time points compared with the REMATCH data. In-hospital mortality was 27% (76 patients), and 71% survived to hospital discharge (200 patients). The most common causes of in-hospital mortality were sepsis (33%), multiple organ failure (20%), and RHF (15%). The probability of device malfunction or replacement increased dramatically with time, starting at 17.9% at 1 year and growing to 72.9% at 2 years. Unlike the REMATCH study, a surprising number of LVAD recipients (47 [17%]) went on to receive heart transplantation, most often because of improvement in pulmonary hypertension.

Regardless of the device implanted, the typical LVAD recipient is a high-risk patient undergoing high-risk surgery. The spectrum and severity of complications encountered are wide ranging. Postoperative bleeding is frequently encountered and often requires re-exploration. 20 Coagulopathy results from prolonged CPB time, disseminated intravascular coagulation, pre-existing hepatic dysfunction, and activation of the coagulation and fibrinolytic cascades caused by a systemic inflammatory response. 57,151 Acute renal failure, hepatic dysfunction and failure, acute respiratory distress syndrome or pneumonia, and
multiorgan failure can complicate both the immediate postoperative course as well as long-term recovery.26 Neurologic injury in the form of ischemic, hemorrhagic, and embolic events as well as anoxic brain injury also contribute to perioperative morbidity.20 RHF can persist or worsen, and patients can often still require prolonged inotropic support despite adequate unloading of the left ventricle.20

In addition to the routine postoperative complications, patients with LVADs continue to be at risk for morbidity and mortality many months out from implantation. Device infection, including superficial infection of transcutaneous drive catheters69 and VAD endocarditis involving the device or the native valves, is a constant danger.88 Despite systemic anticoagulation, LVADs carry a significant thromboembolic burden that manifests as stroke, pulmonary embolus, mesenteric ischemia, and device thrombosis and may be underestimated by clinical evaluation.151 RVD and ventricular arrhythmias unresponsive to therapy can compromise LVAD output and present long-term management difficulties.69 Decreased or absent ejection from the native ventricle can lead to aortic valve fusion and insufficiency and thrombosis of the noncoronary sinus.54 Lastly, axial flow and centrifugal devices introduce long-term considerations, such as increased arteriovenous malformations and gastrointestinal bleeding, which may result from reduced arterial pulsatility.54

NEW VAD TECHNOLOGY

Emerging VAD technology offers the potential to safely and effectively support a broad population of HF patients for durations of many years. The most recent generation of blood pumps are primarily characterized by their small size and frictionless movement of a rotor or diaphragm.152 Being smaller than the first generation of pulsatile pumps, these third-generation devices can be implanted with less surgery and accommodate smaller patients, and their reduced surface area should result in fewer complications related to thromboembolism and infection. The most important advances of this new design are the hydrodynamic and magnetic bearings, which eliminate heat from friction and wear of components. These features optimize biocompatibility and greatly enhance durability.

The latest VAD system designs are in various stages of development (Table 4). Of the 8 devices in this group, only 2 are yet to be used clinically; the Novacor II (World Heart Inc, Salt Lake City, UT) and the HeartMate III (Levitronix LLC)153 are presently undergoing preclinical testing. The HeartWare HVAD (HeartWare, Inc, Miami Lakes, FL),154 Duratech LVAS (Terumo Heart, Inc, Ann Arbor, MI),155 Levacor LVAS (World Heart Inc),156 and HeartMate III LVAD are similar in design and are intended to provide long-term support for a range of patient size. These LVADs are implanted within the pericardial space or an abdominal pocket, and they pump blood from the left ventricle to the ascending aorta.

Each of these devices has a unique design and operational features; however, 3 differences are noteworthy. The CircuLite Synergy device (CircuLite, Inc, Saddle Brook, NJ) uses a small blood pump that is about the size of an AA battery and is placed into a chest wall pocket similar to a pacemaker. Inflow to the Synergy pump is from a cannula that is placed across the atrial septum into the left atrium. The pump outflow graft is anastomosed to the subclavian artery. The Synergy system provides up to 3 L/min of blood flow and can be used in adults or children for chronic partial circulatory support.

The PediVAS is an extracorporeal VAD system (Levitronix LLC) that can be used in children for short- or long-term support or for cardiopulmonary bypass. The PediVAS can provide univentricular or biventricular support and creates pulsatile flow. This system is designed specifically for pediatric use and is based on the CentriMag pump manufactured by Levitronix.

The Novacor II is unique by its magnetically actuated pusher-plate design, which is a pulsatile pump that does not require a compliance chamber or external venting. This is the only blood pump that can provide pulsatile blood flow without contact of moving pump components. The Novacor II is being developed for total implantation of all system components, including batteries and a control unit. This device uses transcutaneous energy transfer for a continuous power supply and to recharge implanted batteries.

For the third generation of VADs that are undergoing clinical trials, results are inconclusive because analyses of data are pending completion of studies. The preliminary and anecdotal results have been very positive for patients who have been supported for BTT, DT, or myocardial recovery. Market approval is expected in the near future for the third-generation devices that are presently being studied clinically.

FUTURE DIRECTIONS

The number of people worldwide with HF continues to grow, and there are no definitive therapies currently available or on the horizon. Heart transplantation is very limited by the fixed number of heart donors, and medical therapy remains palliative. Therefore, the present and future demand is for mechanical circulatory support to be widely available to a broad population of patients. VAD technology has advanced greatly in recent years, and its use is increasing. Clinical experience over the past 2 decades has led to important advances in patient selection and supportive care, which have resulted in markedly improved survival rates for patients with severe HF.18,21 Continued improvement in the design of VAD technology along with refinements in care should help to more effectively treat HF in the future.

The use of various VAD systems in combination is leading to new paradigms in HF care. The temporary use of a percutaneous VAD can stabilize patients with cardiogenic shock until there is recovery of myocardial function, or, in the absence of recovery, a long-term VAD can be implanted electively and more safely. Bridging to decision with a temporary VAD has the potential to save the lives of many patients who have a very high expected mortality.157-159 Also, the use of long-term VADs in combination with drug or gene therapy that improves myocardial function adequately to allow pump removal has great potential to further enhance survival.160

Most HF patients are not given the option to be treated with VAD support because of the significant cost associated with the placement of the device or because of the lack of availability of HF services.161 Expanding the use of VAD technology to treat more patients will require a greater acceptance by the public,
the medical community, government agencies, and insurance providers and a significant reduction in the financial burden associated with the placement of the device. Greater acceptance is dependent on improving outcomes and reducing the frequency of adverse events. The smaller and more reliable VAD technology, along with improvements in patient selection and care have made progress in improving outcomes, but implanting VADs in less sick patients is an important next step. Once general practitioners, internists, and cardiologists refer HF patients earlier for VAD support, the survival rate of VAD-supported patients could approach that of heart transplantation.

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