Management of advanced heart failure is often less evidence-based than earlier stages of the disease. By definition, these patients are typically failing evidence-based medical and electrical heart failure therapies, so there are few clinical trials to guide therapy. Professional societies have developed definitions of “advanced” heart failure, but all tend to share common data elements: objective evidence of ventricular dysfunction, marked functional limitations, evidence of volume overload and/or hypoperfusion, end-organ dysfunction, diminished responsiveness to diuretics, inability to tolerate standard heart failure therapies, and heart failure hospitalizations. The size of the population that fulfills the definition of “advanced” heart failure is unknown but may exceed 250,000 patients in the United States (see also Chapter 18). However, the morbidity and mortality associated with advanced heart failure are clear: 4-month readmission rates approximate 50% and the annualized mortality is 80% to 90%.

In this chapter, we will discuss the role of mechanical therapies designed to improve cardiac output and lower cardiac filling pressures in patients with acute and chronic advanced systolic heart failure. In the past decade, this strategy has gained wide acceptance in the treatment of advanced heart failure patients.

**ACUTE CARDIOGENIC SHOCK**

During the past decade, the incidence of acute cardiogenic shock has doubled in the United States and remains an important cause of cardiovascular morbidity and mortality. Most commonly, cardiogenic shock results from left ventricular (LV) failure after acute myocardial infarction (MI), or a mechanical complication following MI such as ventricular septal defect or mitral insufficiency (see also Chapter 19). However, other conditions may present with similarly deranged hemodynamics, such as acute viral myocarditis (see also Chapter 28), giant cell myocarditis, or acute aortic insufficiency (AI) (see also Chapter 26). Postcardiotomy shock has been reported as a complication of cardiac surgery in 0.2% to 6% of cases and is associated with high short-term mortality risk without mechanically assisted circulation.

Despite advances in coronary reperfusion, including a focus on early intervention, post-MI cardiogenic shock is associated with high short-term mortality. The SHOCK II-IABP trial examined the impact of the intra-aortic balloon pump (IABP) in patients with cardiogenic shock following acute MI. The 30-day mortality rate was 40% in both the IABP and medical therapy arms of the trial despite revascularization and contemporary medical therapy.

The approach to acute cardiogenic shock requires rapid integration of clinical information targeted at determining the etiology, the severity of hemodynamic compromise, and the therapeutic options that address the physiologic needs of the individual patient (Fig. 45.1). A directed history, physical examination, and electrocardiogram (ECG) are critical elements of the initial evaluation. If the cause or severity of the heart failure is not evident following the aforementioned, echocardiography and/or coronary angiography should be performed to evaluate ventricular and valvular function. Endomyocardial biopsy should also be considered in new-onset, nonischemic cardiomyopathy but should probably be limited to centers with expertise in the performance of the procedure and interpretation of the histology.
Initial interventions should include appropriate volume resuscitation, vasodilators in selected patients, and inotropic agents if the patient remains in shock. Placement of a pulmonary artery catheter (see also Chapter 34) has been advocated to guide volume administration and vasoactive drug therapy. Mechanical circulatory support (MCS) should be considered in patients with persistent evidence of shock despite the aforementioned interventions. Device selection should be tailored to each patient’s unique hemodynamic abnormalities and the need for respiratory support.

**Devices**

**Intra-Aortic Balloon Pump**

Over the past 50 years, the IABP has been the most commonly used MCS device. The IABP is generally inserted retrograde in the aorta via the femoral artery and positioned with the distal tip just beyond the left subclavian artery (Fig. 45.2). Balloon filling is triggered from the ECG or from the arterial pressure trace; the balloon inflates during diastole and deflates during systole. The favorable physiologic effects of diastolic augmentation include enhanced coronary blood flow and reduced left ventricular afterload.

The effectiveness of the IABP is highly dependent on proper timing of the balloon inflation and deflation (Fig. 45.3). Optimal timing results in IABP inflation just after the dicrotic notch in the aortic pressure tracing and deflation before the pressure upstroke of ventricular systole. The hemodynamic and physiologic benefits of IABP support include elevation of systemic blood pressure relative to unassisted beats and reduction of LV afterload, LV wall stress, and myocardial oxygen demand. Inappropriate timing with early inflation or late deflation results in balloon expansion during ventricular systole increasing the afterload against which the ventricle is ejecting. Late balloon inflation or early deflation limits the hemodynamic benefits of the therapy.

The hemodynamic effectiveness of the IABP may be limited by tachycardia, such as atrial fibrillation with rapid ventricular response. More than mild aortic valve insufficiency is likely to limit the hemodynamic benefits of IABP therapy and is a contraindication to therapy. Significant aortic or iliofemoral atherosclerotic disease is also a relative contraindication to IABP support and has led some to propose alternative insertion strategies, including subclavian artery or direct aortic access used in the context of cardiac surgery.

The IABP has been used as an adjunctive therapy for many cardiac conditions, including acute MI, postinfarction VSD, acute mitral insufficiency with compromised hemodynamics, and cardiogenic shock. However, improved outcomes with IABP therapy in clinical trials have been difficult to demonstrate. Perhaps the most validated use of the IABP is as adjunctive therapy for the treatment of acute MI treated with thrombolytic therapy. In this setting, the use of prophylactic IABP was associated with an 18% reduction in all-cause mortality.

However, the SHOCK II-IABP trial failed to demonstrate improved
survival in a more contemporary cohort of patients with acute MI and cardiogenic shock treated with IABP compared with those supported medically. The limitations of the IABP coupled with a lack of positive outcome studies has resulted in the proliferation of other percutaneous approaches for the treatment of cardiogenic shock and support of complex cardiac procedures, such as high-risk percutaneous coronary interventions and ventricular tachycardia ablations. These devices can be rapidly inserted and are approved for short-term (hours) support.

**TandemHeart**

The TandemHeart (CardiacAssist, Pittsburgh, PA) is an extracorporeal centrifugal continuous flow pump that receives blood from a 21-F cannula inserted in the femoral vein and passes into the left atrium via a transseptal puncture (see Fig. 45.2). The TandemHeart returns the blood to the arterial circulation via a 17-F catheter inserted in the iliofemoral system. In this configuration, the device can provide up to 5 L/min of flow and is approved for short-term support. The hemodynamic effects of the TandemHeart were compared with IABP in two small, randomized clinical trials that demonstrated superior improvements in cardiac index and the lowering of intracardiac filling pressures with the TandemHeart pump. A nonrandomized, experiential series described the potential benefits of the TandemHeart in patients with cardiogenic shock. In this series, 117 patients with clinical evidence of shock (including almost 50% who were receiving or had just received cardiopulmonary resuscitation) were treated with the device. The median cardiac index increase from 0.5 to 3.0 L/min/m² was associated with improvement in serum lactate and creatinine. The 30-day survival in this cohort was 60% and largely dependent on candidacy for another treatment such as implantable left ventricular assist device (LVAD). Limitations of the TandemHeart device include the transseptal puncture, which adds technical complexity and may require surgical closure if the patient is transitioned to surgical LVAD. In addition, the 17-F arterial cannula in the femoral artery can result in limb ischemia and often requires surgical closure. More recently, the TandemHeart pump has been used in conjunction with a novel dual-lumen catheter (Protek Duo) that allows withdrawal of blood from the right atrium and delivery of blood to the pulmonary artery, providing isolated right heart support. The TandemHeart systems for left and right heart support provide reasonable ventricular unloading and increased cardiac output without the need for major thoracic incisions that were previously necessary for temporary VAD applications. Importantly, these percutaneous systems use smaller cannulas relative to surgically placed devices, and this may result in limited flow and increased risk for hemolysis.

**Impella**

This miniaturized, microaxial flow pump is incorporated into a catheter-based technology and is available in several sizes capable of producing flows from 2.5 to 5.0 L/min (see Fig. 45.2). The smaller Impella (ABIOMED, Danvers, MA) pumps (9 F) can be inserted percutaneously via the femoral artery, whereas the larger device capable of greater blood flow requires surgical implantation techniques. Impella withdraws blood from the distal port in the LV and delivers it to the ascending aorta. This device has been demonstrated to improve cardiac output and reduce left ventricular filling pressures to a greater degree than IABP. Impella 5.0 was studied in a prospective registry that included 16 patients with postcardiotomy shock. Following implantation, the mean arterial pressure increased by 12 mm Hg and the mean cardiac index increased from 1.65 to 2.7 L/min/m². There were two primary safety events in this study, one stroke and one death, and the 30- and 180-day survival rates were 94% and 81%, respectively. The Impella EUROSHOCK Registry retrospectively examined 120 patients with cardiogenic shock following MI treated with Impella 2.5. Less than half of the patients were able to be weaned from support, with an associated 30-day mortality rate of 64%. Furthermore, 15% of the patients experienced a major cardiac or cerebrovascular adverse event. Finally, a randomized trial of Impella CP versus IABP was conducted in patients with cardiogenic shock following acute MI.

---

**Fig. 45.2 Percutaneous devices for mechanically assisted circulation.** The intra-aortic balloon pump (A) is inserted retrograde in the aorta and functions as a counterpulsation device with balloon inflation during diastole and deflation during systole. The Impella (B) is a microaxial flow device that is inserted across the aortic valve and withdraws blood from the left ventricle and delivers it in to the aortic root. The TandemHeart (C) is a paracorporeal centrifugal flow pump that withdraws blood from the left atrium via a transseptal catheter and returns blood to the iliofemoral system. (From Desai NR, Bhatt DL. Evaluating percutaneous support for cardiogenic shock: data shock and sticker shock. Eur Heart J. 2009;30[17]:2073–2075.)
Therapy for Heart Failure

No difference was observed between treatment group in either 30- or 60-day mortality rates.26

The design of Impella has been reconfigured to allow percutaneous right-sided support. The Impella RP features a 22-F pump mounted on an 11-F catheter that withdraws blood from the right atrial/inferior vena caval junction and delivers the blood to the pulmonary artery. The RECOVER RIGHT trial prospectively examined the outcomes of 30 patients with right heart failure following LVAD, cardiotomy, or an MI who were treated with Impella RP. The hemodynamic benefits of Impella RP support included clinically meaningful improvements in central venous pressure and cardiac output. The 30-day survival rate was 73% in this cohort.27

Extracorporeal Membrane Oxygenation

Extracorporeal membrane oxygenation (ECMO) is a temporary strategy to provide circulatory and/or respiratory support to critically ill patients. The ECMO circuit consists of a cannula inserted either percutaneously or centrally in the venous system for device inflow. (Fig. 45.4).

A centrifugal flow pump moves the blood through an oxygenator and returns it to the body via a cannula placed in the arterial system (venoarterial ECMO for cardiorespiratory failure) or to the venous system (venovenous ECMO for respiratory failure). Flow rates of 4 to 6 L/min are typical for most adult patients. ECMO can be initiated rapidly, and peripheral cannulation allows its use in many settings, including the cardiac catheterization laboratory, the intensive care unit, and the operating room. Overall, application of both venovenous (VV) ECMO and venoarterial (VA) ECMO has increased in the United States, related mainly to improvements in safety and durability of the oxygenators. In the setting of cardiogenic shock, establishing hemodynamic stability with ECMO allows time to assess cardiopulmonary recovery and improvement in end-organ function. ECMO is generally considered useful for short periods (days to weeks). An important complication of peripheral ECMO that limits longer-term benefit is a lack of direct LV unloading, with resultant ventricular distention and pulmonary venous hypertension. Furthermore, extended support is undesirable because the patient is typically confined to bed and the incidence of adverse events,
including bleeding, hemolysis, thrombocytopenia, limb ischemia, vascular injury, and stroke, is related to the duration of support. Thus, after stabilization for a brief period, the clinical team must decide on the next step in the patient’s care. In some cases, ECMO can be weaned and the patient separated from the system. In other cases, it serves as a bridge to another procedure such as permanent MCS or transplantation. There are limited outcomes data examining the role of ECMO for the treatment of heart failure and cardiogenic shock. Survival following ECMO support appears to be strongly related to the underlying cause of the ventricular dysfunction, as well as the timing of application, with patients placed on ECMO following cardiac arrest faring poorly. ECMO-supported patients still have a 50% in-hospital mortality, with 6-month survival rates as low as 30%. ECMO has also been used to provide hemodynamic support during high-risk procedures such as percutaneous coronary interventions and ventricular tachycardia ablations.

**INDICATIONS FOR IMPLANTABLE MECHANICAL CIRCULATORY SUPPORT DEVICES**

Decision-making regarding implantation of durable MCS devices is dependent on the clinical status of the patient and the recognized indications for the therapy. Historically, there are two recognized indications for implantable LVADs: as a means to support critically ill patients until they can receive cardiac transplantation (bridge to transplant [BTT]) or as permanent therapy in non–transplant candidates (destination therapy [DT]). This narrowly focused paradigm is not aligned with contemporary use of these devices, and the following definitions are commonly used by clinicians:

*Bridge to bridge* is a strategy in which a short-term circulatory support device is used until a more definitive procedure can be performed. This is typically used for patients in cardiogenic shock who...
require rapid hemodynamic restoration to reverse the shock state and/or improve end-organ function. Device selection depends on the severity of hemodynamic compromise, the presence or absence of biventricular heart failure, and the anticipated duration of this approach. In many cases, percutaneous devices or ECMO are used.

*Bridge to recovery* may be used in disease processes anticipated to recover with a period of hemodynamic support, such as acute myocarditis, peripartum cardiomyopathy, cardiac transplant rejection with hemodynamic compromise, or postcardiotomy shock. Selection of the most appropriate device typically involves determination of the need to provide partial or full hemodynamic support and the projected duration of therapy.

*Bridge to decision* acknowledges that transplant candidacy is frequently confounded by potentially reversible comorbidities when the decision for durable MCS is made. The favorable hemodynamic impact of LVAD support commonly improves end-organ function, lowers pulmonary artery pressures, and allows the patient to become physically and nutritionally rehabilitated before consideration of transplantation. However, if the patient does not achieve these milestones, he or she may remain on mechanically assisted circulation for prolonged periods or indefinitely.

*BTT* is reserved for device implantation in patients listed for transplant at high priority who are failing optimal therapies. DT designates LVAD implantation in a patient with advanced heart failure who is currently ineligible for transplantation. The DT criteria are aligned with the inclusion criteria from clinical trials and include an ejection fraction less than 25%, NYHA class IIIb to IV symptoms, objective functional impairment with a maximal oxygen consumption of less than 14 mL/kg/min (or <50% predicted), and treatment with either optimal medical therapy for 45 of the past 60 days, intravenous inotropic support for 14 days, or an IABP for 7 days. During deliberations for LVAD financial coverage in the United States, the Centers for Medicare and Medicaid Services was unable to agree on the definition of NYHA class IIIb symptoms and subsequently supports only payment for patients with NYHA class IV functional limitations.

More recently, a clinical trial was completed that redefined LVAD implantation into either short- or long-term support. This approach is more aligned with contemporary clinical practice because it is less dependent upon future events (such as transplantation).

### Table 45.1 INTERMACS Patient Profiles

<table>
<thead>
<tr>
<th>Adult Profiles</th>
<th>Current CMS DT Indication?</th>
<th>IV Inotropes</th>
<th>Official Parllane</th>
<th>NYHA Class</th>
<th>Modifier Option</th>
</tr>
</thead>
<tbody>
<tr>
<td>INTERMACS Level 1</td>
<td>Yes</td>
<td>Yes</td>
<td>“Crash and burn”</td>
<td>IV</td>
<td>A, TCS</td>
</tr>
<tr>
<td>INTERMACS Level 2</td>
<td>Yes</td>
<td>Yes</td>
<td>“Sliding fast” on inotropes</td>
<td>IV</td>
<td>A, TCS</td>
</tr>
<tr>
<td>INTERMACS Level 3</td>
<td>Yes</td>
<td>Yes</td>
<td>“Stable” on inotropes</td>
<td>IV</td>
<td>A, FF, TCS</td>
</tr>
<tr>
<td>INTERMACS Level 4</td>
<td>+peak VO2 ≤ 14</td>
<td>No</td>
<td>Resting symptoms on oral therapy at home</td>
<td>Ambulatory IV</td>
<td>A, FF</td>
</tr>
<tr>
<td>INTERMACS Level 5</td>
<td>+peak VO2 ≤ 14</td>
<td>No</td>
<td>“Housebound,” comfortable at rest, symptoms with minimal activity or ADLs</td>
<td>Ambulatory IV</td>
<td>A, FF</td>
</tr>
<tr>
<td>INTERMACS Level 6</td>
<td>No</td>
<td>No</td>
<td>“Walking wounded,” ADLs possible but meaningful activity limited</td>
<td>IIIb</td>
<td>A, FF</td>
</tr>
<tr>
<td>INTERMACS Level 7</td>
<td>No</td>
<td>No</td>
<td>Advanced class III</td>
<td>III</td>
<td>A, FF</td>
</tr>
</tbody>
</table>

A, Arrhythmia; ADLs, activities of daily living; CMS, Centers for Medicare and Medicaid Services; DT, destination therapy; FF, frequent flier; INTERMACS, interagency registry for mechanically assisted circulation; IV, intravenous; NYHA, New York Heart Association; TCS, temporary circulatory support; VO2, maximal oxygen consumption. From Stewart GC, Stevenson LWV. Keeping left ventricular assist device acceleration on track. *Circulation.* 2011;123(14):1559–1568.

### Patient Selection for Mechanical Circulatory Support

In general, patients considered for MCS have severely depressed ventricular function, have marked limitation in functional capacity, are treated with evidence-based medical and electrical therapies, and have a high residual mortality risk within the ensuing 1 to 2 years. Patient selection is critically important to achieving optimal postoperative outcomes. Selection criteria should identify patients with sufficient severity of illness to derive benefit from MCS while simultaneously avoiding those with a severity of illness or comorbidities that would compromise survival following implantation. Baseline characteristics of patients enrolled in LVAD trials demonstrated end-organ dysfunction with hypernatremia and elevated serum blood urea nitrogen and creatinine levels. In addition, the mean ejection fraction was less than 0.20 with elevated right- and left-sided cardiac filling pressures and mean cardiac index of 2.0 L/min/m² despite treatment with continuous infusion intravenous inotropes in 80% to 90% of patients and IABP support in 20% to 40%.

DT was originally conceived as a treatment for patients with end-stage heart failure ineligible for cardiac transplantation. As a result, many of those being referred for DT LVAD are older than 65 years. Older age has been identified as an important predictor of adverse outcomes in the VAD population. The HeartMate II risk score demonstrated an increased postimplant mortality risk of 32% per decade. Data from the Interagency Registry for Mechanically Assisted Circulation (INTERMACS) also described older age as a risk factor for early mortality following LVAD placement and highlighted the important interaction between age and other risk factors for mortality, such as severity of illness. However, carefully selected patients older than 70 years appear to derive similar benefits with VAD as a younger cohort, raising the important concept of chronologic versus physiologic age in patient selection. Chronologic age is likely an imperfect surrogate for the true predictors of adverse outcomes in this population, which are more likely measures of frailty and debilitation.

Beyond age, other contraindications to implantable VAD therapy appear to influence short- and long-term outcomes and must be considered in the overall risk assessment of the candidate. INTERMACS developed a new nomenclature for classification of advanced heart failure that has been used to understand the impact of severity of illness on outcomes. Patients with INTERMACS profile 1 and 2 have a high early mortality hazard relative to MCS patients with
lesser degrees of hemodynamic compromise, leading many centers to be highly selective in the use of durable implantable LVADs in these patient cohorts.33

Right ventricular (RV) failure, defined as the need for prolonged inotropic therapy to support the right heart or a RV assist device, remains an Achilles heel of LVAD therapy and is associated with multisystem organ failure, prolonged hospitalization, and increased morbidity and mortality following LVAD implantation.35 Unfortunately, prediction of post-LVAD RV failure is challenging despite identification of individual parameters and multivariable models that provide insights into the likelihood of RV failure in larger patient populations. Predictors of RV failure following LVAD fall into three general categories: (1) echocardiographic measurements; (2) hemodynamic parameters; and (3) clinical features before LVAD insertion. Increased RV size and severe RV systolic function are associated with post-LVAD RV failure.37 Quantitative measures of RV performance, such as a tricuspid annular plane systolic excursion (TAPSE) of less than 7.5 mm, reduced RV peak longitudinal strain, and the severity of tricuspid insufficiency have been shown to be useful markers in the prediction of RV failure after LVAD.37 Hemodynamic variables such as a central venous pressure to pulmonary capillary wedge pressure ratio of greater than 0.63 or an RV stroke work index of less than 250 to 300 mm Hg × mL/m² are linked to worse outcomes following LVAD placement.38 Finally, general clinical features such as preoperative mechanical ventilation and abnormal renal and hepatic function have been identified as risk factors for RV failure.38 A recent validation study of several published RV failure risk scores demonstrated only modest accuracy, highlighting the real clinical dilemma facing clinicians in the preimplant prediction of this important comorbidity.39

Renal failure requiring dialysis is considered a strong relative contraindication to durable MCS. Significant renal dysfunction was an exclusion criterion in the clinical trials, so the benefit and potential incremental complications of implanting an LVAD in dialysis patients are unknown. However, 1-year survival in LVAD patients requiring renal replacement therapy is approximately 50% and significantly reduced compared with nondialysis patients in the INTERMACS registry. Furthermore, support with newer-generation LVADs that provide continuous flow results in a minimal (and often imperceptible) pulse pressure, making measurement of blood pressure difficult during hemodialysis.

Active systemic infection is a strong relative contraindication to LVAD implantation. Patients with fever or unexplained leukocytosis should undergo thorough evaluation, including blood and urine cultures, chest x-ray, and other diagnostic testing directed at potential sites of infection. Hospitalized patients and those with chronic indwelling catheters should have intravenous cannulae removed. Patients with pacing systems and unexplained bacteremia may require chest wall or transesophageal echocardiography to rule out pacemaker-associated endocarditis.

An evaluation for cerebrovascular disease should be performed in at-risk patients using noninvasive imaging.40 The presence of a prior stroke does not preclude implantation of an LVAD, but consideration must be given to the potential for meaningful rehabilitation and the patient’s ability to interact with the device. For example, an individual with hemiparesis of a dominant arm may have difficulty making the electrical connections required to operate the VAD.

Other end-organ dysfunction may also limit favorable outcomes with VAD therapy and should be considered during the evaluation. Individuals with clinically significant chronic obstructive pulmonary disease whose FEV₁ is less than 1 L are likely to have residual dyspnea despite hemodynamic improvement and may have difficulty weaning from the ventilator postoperatively. A VE/MVV ratio of more than 80% on a preoperative cardiopulmonary exercise test suggests a pulmonary component to dyspnea.41 Patients with long-standing right heart failure or other conditions associated with liver injury should undergo an evaluation for hepatic insufficiency.42 Serum transaminases, albumin, and imaging studies to examine the texture and contour of the liver may provide insights about the necessity for liver biopsy. The presence of an elevated model for end-stage liver disease (MELD) score has been linked to higher post-LVAD mortality.43 Careful evaluation of the coagulation system is warranted in individuals with a history of bleeding diathesis or in those with unexplained thrombotic or thromboembolic events. Patients with a history of gastrointestinal bleeding or intolerance to systemic anticoagulation with warfarin should be carefully evaluated because of their high risk of rebleeding following LVAD implantation. Patients with a low platelet count and exposure to heparin should be screened for heparin-induced thrombocytopenia with a PF4 antibody and a serotonin release assay.44 To the extent possible, patients should have a normal coagulation profile before MCS surgery, because an elevated international normalized ratio (INR) at the time of LVAD implantation was identified as a risk factor for mortality.42 Correction of coagulopathy will reduce the likelihood of bleeding complications and associated perioperative morbidity. Malnutrition is considered an important risk factor for adverse outcomes, including infection, prolonged debilitation, and mortality. However, the ability to favorably impact nutrition in a critically ill heart failure patient is unclear. Instead, nutrition management should be a primary focus of the entire VAD team following device implantation.45 Supplemental enteral feedings may be required perioperatively, with additional support in the outpatient setting until nutritional deficits are corrected.

Disease processes with an anticipated survival of less than 3 years were an exclusion criterion in the DT clinical trials, so there are no data supporting the role for mechanically assisted circulation in the management of these patients.

Psychosocial factors also play a pivotal role in VAD outcomes. As part of the evaluation, patients should be seen by multiple health care providers, including those who focus primarily on prior history of compliance, substance use, health literacy, and the availability and abilities of family and friends who will participate in the ongoing outpatient management of the patient and the device. There is a high caregiver burden with MCS, including the need for device training, care of the percutaneous driveline, and companionship. These issues and expectations need to be clearly articulated by the team and agreed on by the patient and his or her caregivers prior to device implantation. In an attempt to integrate large numbers of predictive clinical variables, the HeartMate II Risk Model was derived from a large clinical trials database and demonstrated that age, elevated INR, increased serum creatinine, and lower serum albumin were predictive of postimplant mortality.42 Follow-up analyses in institutional datasets suggest only modest predictive accuracy (C-statistic 0.6) for short- and long-term outcomes.46

Recent successes in mechanically assisted circulation have resulted in acceptance of this approach as a useful therapy for the treatment of selected patients with advanced heart failure. The INTERMACS registry has captured almost all implants using FDA-approved MCS devices in the United States since 2006 and has carefully documented the growth of this field following the introduction of the new-generation continuous flow devices.33 The number of centers implanting long-term devices is increasing and has expanded from traditional transplant centers to programs that do not perform transplantation. The impact of center volume on outcomes was recently reported from INTERMACS and showed that both very low volume and high volume programs had higher perioperative and long-term mortality rates.47
MECHANICAL CIRCULATORY SUPPORT DEVICES

The mechanical blood pumps can be characterized in several ways: temporary versus permanent, intracorporeal versus extracorporeal, and pulsatile flow versus continuous flow. At present, the vast majority of clinically available pumps are continuous flow devices. Pulsatile flow pumps such as the ABIOMED 5000, Thoratec PVAD and IVAD, Novacor LVAD, and HeartMate XVE are of historical interest. However, their importance in supporting patients and forming the foundation of the principles of mechanically assisted circulation cannot be underestimated. For example, the HeartMate XVE (Fig. 45.5) and Novacor LVAD were the original electric, implantable LVADs that were tested in clinical trials and shown to be superior to optimal medical heart failure treatment in patients either awaiting transplantation or as DT.\textsuperscript{5,6,48}

**Temporary Continuous Flow Ventricular Assist Devices**

**CentriMag**

The CentriMag (Abbott, Abbott Park, IL) pump is an extracorporeal device approved for short-term support in the United States and can be configured to provide univentricular (either right or left) or biventricular support (Fig. 45.6). It is a magnetically levitated centrifugal flow device capable of delivering 10 L/min, although the standard clinical flows are 4 to 6 L/min. PediaMag is a smaller version of the same device capable of flows to 1.5 L/min.

**Rotaflow**

Rotaflow (Maquet, Inc, Wayne, NJ) is an extracorporeal centrifugal flow pump with specifications that are similar to those of the Centrimag device. Rotaflow features a magnetically levitated rotor and has been used as an right ventricular assist device (RVAD), LVAD, or in ECMO circuits.

**Durable Continuous Flow Pumps**

A pivotal innovation in mechanically assisted circulation came with the observation that the human body did not require a “normal” pulse pressure. This led to the development of LVAD pumps with rotary mechanisms that produced continuous rather than pulsatile blood flow. These devices are smaller nonvalved systems that draw blood from the LV apex and return the blood to the circulation via an outflow graft generally attached to the ascending aorta. The devices are electrically driven by external battery or AC power delivered to the pump via a subcutaneous driveline that exits the skin and is attached to a wearable controller that regulates and monitors pump function (Fig. 45.7). The blood-propelling mechanism in these devices rotates at a constant set speed and operates to maximally reduce LV size with minimal or no aortic valve opening. As a result, there may not be a detectable pulse in patients supported with a continuous flow device (Fig. 45.8), and most of the observed pulsatility is derived from the contribution of native ventricular systole to LVAD filling.

Cardiopulmonary bypass provided an extensive experience with short-duration nonpulsatile blood flow. The clinical trials of continuous flow LVADs provided the opportunity to explore the impact of chronic minimally pulsatile flow on end-organ function. Russell and colleagues were unable to demonstrate any decline in renal or hepatic function over a 6-month observation period.\textsuperscript{49} Similarly, neurocognitive function was examined over 24 months of continuous flow support with no evidence of decline in executive cognitive function.\textsuperscript{50} Finally, submaximal exercise performance was serially evaluated and shown to improve during the first 3 months following LVAD implantation and remain stable throughout a 24-month follow-up period, suggesting no detrimental impact on peripheral muscle function.\textsuperscript{51} Thus there is no evidence from clinical trials to suggest a decline in end-organ function resulting from chronic circulatory support with minimal (or no) pulsatility.

**HeartMate II**

HeartMate II (HMII, Abbott, Abbott Park, IL) is an axial flow LVAD that is implanted in a preperitoneal pocket beneath the left costal margin. It is small, operates in a quiet mode, and is capable of flows
However, there was a higher than anticipated stroke rate in the BTT trial (Fig. 45.9). The primary composite end point of the study, while the primary cohort completed follow-up. This resulted in the mode of circulatory support (pulsatile vs. continuous flow). Like the HeartMate II, the end point in both studies was survival without disabling stroke or the need to repair or replace the device. Both the short- and long-term trials demonstrated superiority of the HeartMate II–treated patients in this cohort demonstrated a 2-year survival of 63%.55

HeartWare HVAD
HeartWare HVAD (Medtronic, Minneapolis, MN) is a bearingless centrifugal flow pump capable of providing up to 10 L of blood flow. Its small size and design allow placement in the pericardium (Fig. 45.9). The HVAD was studied as a BTT in a noninferiority trial that used concomitantly enrolled patients in the INTERMACS registry implanted with a commercially available device as a control group.34 The primary end point was survival to 180 days on the originally implanted device, transplant, or device removal for recovery. Ninety-two percent of the HVAD population successfully achieved the primary end point compared with 90.7% of the control group (noninferiority, P < .001). On the basis of this trial, HVAD was approved as a BTT device by the FDA.

The HVAD was also evaluated in the DT application in a 446-patient randomized, noninferiority trial comparing the HVAD to the HMII. The primary end point, survival to 2 years on the originally implanted device without a disabling stroke, was not statistically different between the two groups.55 However, there was a higher than anticipated stroke rate in the HVAD cohort. This led to the ENDURANCE Supplemental trial designed to test the impact of blood pressure control on the 12-month incidence of stroke. The HVAD cohort in the supplemental trial had an absolute stroke reduction of nearly 50% compared with the primary study but failed to reach its primary noninferiority end point.56

HeartMate 3
The HeartMate 3 (Abbott, Abbott Park, IL) is another intrapericardial centrifugal flow LVAD (Fig. 45.10) that incorporated several design features to reduce adverse events. Gaps between the rotor and the pump housing were increased to reduce shear force in the pump, hemolysis, and device thrombosis. In addition, an algorithm for speed increase and decrease every 2 seconds was used to improve device washing. The HeartMate 3 recently completed clinical trials with a novel adaptive design that focused on short-term (6 months) and long-term (24 months) support rather than BTT or DT. The comparator device in these studies was the HeartMate II, and the end point in both studies was survival without disabling stroke or the need to repair or replace the device. Both the short- and long-term trials demonstrated superiority of the HeartMate 3 device with important reductions in device thrombosis leading to device replacement as the key driver of the end point.57,58

Jarvik 2000
The Jarvik 2000 is a small axial flow device with several interesting innovations, including implantation of the pump directly into the left ventricle, variable speed control that can be manipulated by the patient, and novel power cord implantation. The BTT trial with this device has completed enrollment and is in the follow-up phase.

Management Issues of a Continuous Flow Pump
Beyond the unique physiology associated with continuous flow VADs, management of patients on these devices is nuanced. The minimally pulsatile blood flow can make standard blood pressure monitoring difficult. Doppler appears to be superior to auscultation or the use of automated blood pressure cuffs to assess blood pressure.99 Hypertension is common following a period of support on a continuous flow LVAD. Careful assessment and management of hypertension may have a favorable impact on the risk of stroke and other adverse events in this patient population, particularly with the HVAD.

Systemic anticoagulation with warfarin and an antiplatelet agent is recommended with all commercially available devices. However, the
**Fig. 45.8** Pulse Pressure in Continuous Flow Left Ventricular Assist Device (LVAD). The pulse pressure in a continuous flow LVAD is dependent on the speed. At slower speeds (8000–9000) a dicrotic notch can be seen in the arterial pressure tracing. As the ventricular assist device speed is increased further, the pulse pressure narrows as the cardiac output increases. These very low pulse pressures are often clinically imperceptible. (From Frazier OH, Jacob LP. Small pumps for ventricular assistance: progress in mechanical circulatory support. *Cardiol Clin.* 2007;25[4]:553–564.)

**Fig. 45.9** HeartWare HVAD. The HeartWare HVAD (Medtronic, Minneapolis, MN) is a centrifugal flow pump with a size sufficiently small to be implanted in the pericardial space. The remainder of the implant configuration is similar to that shown in **Fig. 45.7**.

**Fig. 45.10** HeartMate 3 left ventricular assist device (Abbott, Abbott Park, IL) is a fully magnetically levitated intrapericardial centrifugal flow device designed to improve hemocompatibility. Recent clinical trials show a significantly reduced incidence of device thrombosis relative to HeartMate II. (HeartMate 3 is a trademark of St. Jude Medical, LLC or its related companies. Reproduced with permission of St. Jude Medical, © 2018. All rights reserved.)
Most adverse events following LVAD placement are common. A recent analysis demonstrated that 70% of patients have a major adverse event within 12 months of device implantation. Most adverse events occur early after device implantation. However, some complications such as infections are time dependent, with progressive risk the longer the patient has an LVAD in place. One of the important challenges in understanding the rate of device-related complications was the lack of standardized definitions. The INTERMACS registry has developed standardized definitions for common adverse events that are now being used in the registry and in clinical trials.

### Right Heart Failure

Right heart failure following LVAD implantation is associated with incremental morbidity and mortality. The need for continuous infusion inotropes to support RV performance for more than 2 weeks or an RV assist device following LVAD reduced 180-day survival from 87% to 66% in the HeartMate II BTT trial. Furthermore, many events categorized as multisystem organ failure in the clinical LVAD trials can be traced back to RV failure. The clinical presentation is typically in the first hours following LVAD implantation and is characterized by systemic hypotension, elevated right atrial pressure, and poor VAD filling. Echocardiography may demonstrate a dilated and dysfunctional RV with or without tricuspid insufficiency and a small and underfilled left ventricle (Fig. 45.13).

Prevention of RV failure by careful patient selection is desirable, but the available tools lack high predictive accuracy. Integration of clinical parameters, imaging measures of RV performance, and hemodynamic variables may assist the clinician in prognostication. Treatment of post-LVAD RV failure includes the use of pharmacologic agents that increase cardiac contractility such as dobutamine or milrinone, drugs that lower pulmonary artery pressures such as inhaled nitric oxide, prostacyclin, or oral phosphodiesterase-5 inhibitors such as sildenafil. If these agents are ineffective, an RV assist device may be required. Determination of significant right
heart failure after LVAD should prompt the clinician to consider early transplantation in eligible patients.

**Neurologic Events**

In the clinical trials of MCS devices, neurologic event reporting has ranged in severity from metabolic encephalopathy to ischemic and hemorrhagic stroke. Hemorrhagic strokes have the highest associated mortality and result from the requisite use of anticoagulants and antiplatelet agents, the presence of acquired von Willebrand factor deficiency, and systemic hypertension (see later discussion). The stroke rate appears to be device specific and has been reported as high as 29% in the first 24 months following implantation.\(^3\)

**Infection**

The diagnosis and management of infections in patients supported on an MCS device can be challenging, relating to the complexity of intracorporeal foreign materials and their anatomic position, the presence of a percutaneous driveline, the surgical implant procedure, and the poor general health of many of the heart failure patients undergoing the procedure. Standardized definitions for device-specific,
device-related, and non-VAD infections in device-supported patients have been described. During the early perioperative period, infectious complications are typically related to the surgical procedure and nosocomial infections, such as pneumonia, urinary tract infections, and wound infections. Development of a sternal infection following VAD implantation can be a devastating complication because of the proximity of the VAD components. Infection of device components is almost impossible to correct without replacement of the pump. In many cases, long-term suppressive antibiotic therapy is used, and transplant should be considered if the infection is controlled and the patient is otherwise an acceptable candidate. Late infectious complications are more likely related to the percutaneous driveline. Trauma to the exit site can result in disruption of the driveline-tissue barrier, leading to an ascending infection that tracks proximally toward the device. The diagnosis is often made clinically by the identification of purulent drainage from the exit site coupled with erythema and tenderness along the driveline (which is commonly palpable). In some cases, CT imaging can identify areas along the driveline surrounded by fluid or stranding in the subcutaneous tissues. Antimicrobial therapy should be directed against the cultured organism. However, surgical débridement is often required with fashioning of a new exit site.

**Bleeding**

Bleeding is the most common, early adverse event early following LVAD implantation. Early bleeding complications are primarily surgical and are treated with correction of operative coagulopathies, as well as identification and management of anastomotic bleeding sources. Late bleeding is more common with continuous flow LVADs than pulsatile pumps and is typically mucosal. There appear to be at least three critical components to late bleeding following LVAD. First, many patients on contemporary continuous flow devices develop acquired von Willebrand disease caused by device-related shear stress applied to the von Willebrand molecules, resulting in exposure of a cleavage site for the ADAMTS13 enzyme. Subsequent degradation of the large molecular weight von Willebrand multimers into smaller fragments that are less efficient at crosslinking platelets and clot stabilization increase bleeding risk. Second, small arteriovenous malformations (AVMs) occur primarily in the small intestine but may also be present in the large bowel or nasal mucosa. Recent studies have demonstrated that continuous flow LVAD patients have elevated levels of angiopoietin 2, a factor that promotes growth of abnormal blood vessels in the alimentary tract. Finally, the requisite use of antiplatelet agents and anticoagulation associated with MCS use contributes to bleeding complications.

**Valvular Heart Disease**

Several valvular lesions can impact the performance of an LVAD. The presence of hemodynamically significant mitral stenosis will limit LVAD filling and should be addressed at the time of LVAD implantation. A previously implanted, undersized mitral annuloplasty ring may need to be removed at the time of LVAD implantation if it is causing significant limitation of flow across the mitral annulus. Mitral regurgitation (MR) is not typically thought to be an important valvular lesion in LVAD patients. In most cases a normally functioning LVAD will reduce the residual blood volume in the LV to such an extent that secondary mitral regurgitation will be significantly reduced. Residual MR following LVAD implantation is associated with persistent pulmonary hypertension, worse RV function, and shorter times to rehospitalization leading some to advocate for surgical correction at the time of implantation. Aortic stenosis without insufficiency tends not to be a lesion that requires intervention as the LVAD circumvents this valve. De novo aortic stenosis has been reported in LVAD-supported patients and is thought to result from limited opening of the aortic valve with subsequent scarring and fusion of the aortic valve cusps. As a result, some advocate setting the pump speed to allow intermit tent opening of the aortic valve. The presence of greater than mild AI at the time of LVAD implantation should be corrected. The optimal surgical technique has not been defined, but many surgeons favor the Park stitch that consists of a central oversewing of the three valve leaflets with sutures placed in the nodules of Arantius. An alternative is replacement of the valve with a bioprosthesis. Development of clinically significant de novo AI following LVAD appears to be time dependent and may result in symptomatic heart failure if the regurgitant volume becomes sufficient. To date, correction of AI in the LVAD population has typically required redo sternotomy with placement of an aortic bioprosthesis, but eventually catheter-based approaches may prove beneficial with less comorbidity. Presence of a mechanical aortic prosthesis must be addressed at the time of LVAD implantation because of the risk of thrombus development with reduced leaflet movement. The surgical approach to these patients has been to either replace the valve with a bioprosthesis or alternatively occlude the valve with a circular felt patch.

**Hemolysis/Pump Thrombosis**

Subtle alterations in the flow characteristics in the LVAD or its inflow or outflow cannulae may result in hemolysis. This can be caused by the development of thrombus on the blood-contacting components of the pump, twisting of the pliable outflow graft, or any other change in the VAD anatomy that alters the normal rheology. The clinical presentation is often asymptomatic and detected with serologic measures of red blood cell trauma, including elevated levels of serum lactate dehydrogenase (LDH) or plasma-free hemoglobin or a low serum haptoglobin. Recently, LDH level has been validated as a predictor of hemolysis, and elevated levels predate other manifestations of device thrombosis. Patients are frequently asymptomatic, although they may complain of nausea and vomiting or abdominal pain. In addition, hemoglobinuria may be seen in cases of more significant hemolysis. Paradoxically, the LVAD flow may appear elevated on the system monitor associated with high power consumption. Imaging of the device is a critical component of the evaluation. Transthoracic echocardiography should be performed to assess LV size and valvular function. Left ventricular enlargement, frequent opening of a previously closed aortic valve, and worsening mitral insufficiency...
all suggest increased left ventricular volume and pressure and abnormal LVAD function. A ramp study (previously described) may also be useful in establishing the diagnosis. Failure of the LV end-diastolic dimension to decrease with increasing pump speed is highly correlated with VAD thrombosis.\(^5^2\) Cine CT of the chest allows determination of the LV inflow cannula position, as well as examination of the LV outflow graft. Finally, determination of invasive hemodynamics may provide useful information in some cases. Demonstration of elevated pulmonary capillary wedge pressure and a low cardiac output (that may be discrepant from the system monitor) are also suggestive of device malfunction. Treatment of hemolysis and LVAD thrombosis should be directed at the cause. If the inflow cannula is in continuity with the left ventricular myocardium, surgical repositioning may be required. If the outflow graft is twisted, surgical manipulation will be required to either untwist or replace the graft. Medical management of device thrombosis is more controversial. Some have advocated a stepped approach that includes the administration of unfractionated heparin, direct thrombin inhibitors, glycoprotein 2B/3A antagonists, or tissue plasminogen activator inhibitor.\(^8^8\) If ineffective, LVAD replacement should be considered early if the patient is a suitable candidate. Two-year survival following device exchange for thrombosis is reduced relative to primary LVAD implant (56% vs. 69%, \(P < .0001\)).\(^8^9\)

Support for Biventricular Heart Failure

Managing biventricular heart failure with MCS requires use of devices that were not intended for long-term, out-of-hospital use in the biventricular configuration, the use of continuous flow VADs implanted in both ventricles, or the total artificial heart (TAH). INTERMACS has provided important insights about the outcome of patients requiring biventricular support.\(^6^3\) One-year survival in LVAD-treated patients was 80% versus 64%, and 48% in patients treated with a continuous flow or pulsatile biventricular assist devices (BiVADs), respectively (\(P < .0001\)).

The TAH can be used to support patients with severe biventricular failure and is approved as for BTT. The surgical approach requires a cardectomy and attachment of the TAH to atrial cuffs and the great vessels. The SynCardia TAH (SynCardia Systems, Tucson, AZ) is available as both a 50-mL and 70-mL ventricle to accommodate a variety of patient sizes (Fig. 45.14). In a prospective clinical trial comparing TAH to optimal medical therapy and IABP, patients supported with TAH had a significantly improved survival to transplantation (79% vs. 46%, \(P < .001\)) than the control group.\(^9^0\) Previously the SynCardia TAH was limited to use in the hospital because of the size of the pneumatic driver used to actuate the device. A smaller version of the driver has been developed that allows enhanced patient mobility and the ability to be managed outside the hospital. The CARMAT TAH features bioprosthetic valves and a bovine pericardial blood-contacting surface and is undergoing early phase clinical evaluation.\(^9^1\)

Mechanical Circulatory Support in Children

The use of mechanical blood pumps in children poses several challenges beyond those encountered with adults. An array of devices must be available to accommodate body sizes from infant to adolescent. In addition, as body size increases, the need for higher device output may exceed the capabilities of an implanted pump. Many children with failing ventricles have structurally abnormal hearts or prior cardiac procedures that add technical limitations to MCS (see also Chapter 27). Furthermore, the daily interaction of a child with a VAD and the impact on physical and psychosocial growth is understudied. Finally, the paucity of small donor hearts for transplantation predictably results in relatively long support times.

The most commonly used mechanical device to support the circulation of children remains ECMO.\(^5^2\) The versatility of ECMO, including its ability to support both cardiac and pulmonary systems, the ease and rapidity of implantation, and limited alternatives for mechanically assisted circulation in children, has resulted in the widespread adoption of this technology. The majority of pediatric patients are supported on ECMO for short durations, although a series of patients supported for more than 30 days has been reported.\(^9^3\)\(^9^4\) Neurologic complications remain an important adverse event in ECMO-supported children. Twenty-four percent of children in the Extracorporeal Life Support Organization (ELSO) registry had a neurologic event.\(^9^5\) Low birth weight, gestational age less than 34 weeks, the need for pre-ECMO cardiopulmonary resuscitation, systemic acidosis or the use of bicarbonate, and recurrent need for ECMO were important predictors of mortality. Age-dependent survival following ECMO in children has been demonstrated with neonates having lower survival rates than pediatric patients.\(^9^6\)

An extracorporeal, pulsatile pump is also available for use in children. The Excor Pediatric VAD (Berlin Heart, Woodlands, TX) is manufactured in multiple sizes to accommodate children across a broad spectrum of body sizes (Fig. 45.15). This device was recently tested in a single-arm trial of children younger than 17 years who weighed 3 to 60 kg and had two-ventricle circulation and severe heart failure.\(^9^7\) Study participants were enrolled in one of two cohorts based on body surface area (cohort 1 < 0.7 m\(^2\); cohort 2 = 0.7–1.5 m\(^2\)) and compared with a historical control group supported with ECMO. The primary end point of the VAD-treated patients was death, withdrawal of support with an unacceptable neurologic outcome, or unsuccessful weaning from the device. The primary end point for the ECMO-treated control cohort was all-cause mortality. Both VAD-treated study cohorts had superior freedom from the primary end point compared with controls. Adverse events with the Excor device included bleeding, infection, stroke, and hypertension. In addition, pump exchange was common and most often resulted from device thrombosis. Based on the results of this clinical trial, the Excor was approved by the FDA as a BTT in children. An recent analysis of outcomes with the Excor device following FDA approval demonstrates lower rates of successful bridging to transplant or weaning the device in a “real world” cohort of patients compared with the clinical trial (77% vs. 90%, \(P = .05\)), with similar rates of bleeding and stroke.\(^9^8\)
The DeBakey Child VAD is the other FDA-approved device for supporting children to transplant. Clinical application of this device has been limited by a relatively high risk of thrombosis.99

**FUTURE DIRECTIONS**

**Partial Support Devices**

An evolving innovation in the field of mechanically assisted circulation is the development and clinical assessment of partial support devices. Currently used VADs are designed to replace the entirety of the cardiac output. However, a larger patient population exists that would benefit from cardiac output augmentation and reduction in the left-sided filling pressures. The CircuLite Synergy (HeartWare) axial flow device was designed to be implanted in a pacemaker-like pocket fashioned in the infraclavicular subcutaneous tissues with pump inflow obtained through a minithoracotomy to access the right superior pulmonary vein and cannulation of the subclavian artery for device outflow. Eventually, inflow may be obtained by placing the cannula retrograde through the subclavian vein into the left atrium via a transseptal puncture. This device has been shown to augment cardiac index by 0.5 to 1.0 L/min/m² and reduce the left atrial pressure by 8 to 10 mm Hg.100 Further development and clinical trials with this device are uncertain.

**Totally Implantable Systems**

Development of reliable totally implantable systems is anticipated to have an important impact on patient acceptance of the therapy, as well as to reduce the infection rates associated with these devices. As currently envisioned, patients would have a capacitor implanted in the soft tissue of the abdominal wall that would allow several hours of untethered use. Tethering would involve wearing a vest containing an energy transmission coil that would transfer energy from batteries to the subcutaneous capacitor. Other novel methods of battery charging are being explored, including the use of electrically charged rooms capable of charging battery-operated devices.

**Novel Patient Populations**

Approximately 80% of patients currently implanted with an LVAD have a severity of illness that requires treatment with intravenous inotropic therapy.63 In this cohort, LVAD has been shown to provide important improvements in both quality of life and survival. The Risk Assessment and Comparative Effectiveness of Left Ventricular Assist Device and Medical Management (ROADMAP) study was a nonrandomized evaluation of the HeartMate II device compared with optimal medical therapy in patients ineligible for transplantation, who met current indications for DT and were not yet treated with inotropic therapy. LVAD-treated patients had a statistically better 12- and 24-month survival with improvement in submaximal exercise performance than the medically treated patients.101,102

**Myocardial Recovery**

An important promise of MCS is the opportunity to support the circulation sufficiently to allow recovery of native heart function, either by reversal of the process causing ventricular dysfunction, such as acute myocarditis, or allowing the use of adjuvant therapies that promote myocardial functional recovery. Contemporary registry data demonstrate a recovery rate with successful LVAD removal in approximately 1% to 2% of the implanted population.103 Predictors of recovery include younger age, nonischemic cause, and shorter duration of heart failure before device implantation.104 In general, the management strategy to promote myocardial recovery has included maintaining the device speed such that the heart size is maximally reduced and the use of standard heart failure therapies. Serial assessment of intrinsic myocardial function typically includes measurement of cardiac structure and function using echocardiography, submaximal and maximal exercise testing, and evaluation of hemodynamics. The aforementioned studies are performed with the pump speed turned down to achieve a net neutral flow such that there is no backflow through the outflow graft into the pump and left ventricle.

Preliminary results from the multicenter RESTAGE HF trial demonstrate that 40% to 45% of LVAD-supported patients with nonischemic cardiomyopathy treated with high doses of neurohormonal antagonists may have sufficient improvement in ventricular function to warrant device removal.105 Stem cell therapy may also prove to be an important adjuvant to mechanically assisted circulation (see also Chapter 41). An NIH-sponsored clinical trial using allogeneic mesenchymal precursor cells was recently reported.106 This safety trial included 30 patients randomized to administration of either 25 million allogeneic stem cells or control medium directly injected into the left ventricular myocardium during LVAD implantation. There were no safety events associated with direct myocardial injection of stem cells nor was there evidence of increased immunologic sensitization. Injection of mesenchymal precursor cells did not increase the likelihood of temporary VAD weaning at 90 days or 1 year, nor did it improve the ejection fraction in this small trial. A follow-up trial focused on efficacy using injection of 150 million cells is now underway.

![Image](image.jpg)

**Fig. 45.15 The Berlin heart pediatric ventricular assist device (VAD).** The Berlin heart VAD is an extracorporeal device that is manufactured with various chamber sizes (10, 25, 30, 50, and 60 mL) to accommodate a range of pediatric patients.
The field of mechanically assisted circulation is growing and evolving rapidly with proliferation of new devices designed for short- and long-term circulatory support. Clinical trials in the past several years have clearly demonstrated reduced mortality and quality-of-life improvements in patients with advanced heart failure. However, the persistently high mortality rates associated with cardiogenic shock following acute MI demands careful evaluation and innovative solutions that may require multiple devices to improve survival. The role of mechanically assisted circulation in expanded patient populations such as children, NYHA class III, and right heart failure will require new device design and thoughtful clinical trials. Moving forward, centers invested in mechanically assisted circulation will have clinical expertise with a broad array of VADs that can be tailored to the specific needs of the individual patient. Newer-generation continuous flow pumps with smaller size, more durable design, and novel blood-contacting surfaces are likely to have favorable and incremental impact on the long-term outcomes for MCS patients. Concerns that prolonged exposure to reduced pulsatility plays a role in some of the adverse events associated with these devices are likely to result in innovative device design and management strategies to restore a higher degree of pulsatility. Finally, there will be an even greater focus on the patient and caregiver experience as more patients live for prolonged periods of time on MCS devices.

KEY REFERENCES


The full reference list for this chapter is available on ExpertConsult.
REFERENCES


References


