Assessment and Management of Heart Failure After Left Ventricular Assist Device Implantation

Michael A. Burke, MD; Michael M. Givertz, MD

Case Presentation: A 56-year-old man with a history of ischemic cardiomyopathy and New York Heart Association functional class IV heart failure (HF) requiring intravenous inotropic therapy underwent uncomplicated implantation of a continuous-flow left ventricular assist device (LVAD) as bridge to heart transplantation (HT). The patient was weaned off inotropic support during the first week after surgery and had progressive improvement in functional status. He was discharged home on maintenance antithrombotic therapy with aspirin 325 mg once daily and warfarin targeted to an international normalized ratio of 2.0 to 3.0. Eight weeks after LVAD implantation, he developed progressive dyspnea on exertion, recurrent pedal edema, and a 7-pound weight gain. Physical examination revealed conjunctival pallor, a palpable carotid pulse, jugular venous pressure of 14 cm H2O, and 2+ pitting edema bilaterally. A rapid and targeted assessment of recurrent HF is essential in this LVAD patient because of multiple, potentially life-threatening causes that necessitate divergent treatments.

LVAD Therapy in Advanced HF

The US Food and Drug Administration first approved implantable LVADs as a bridge to transplantation in 1994.1 Although HT remains the gold standard therapy for selected patients with end-stage HF, the stable donor base of <2500 hearts per year in North America limits its widespread applicability.2 The landmark Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) trial established the first-generation, pulsatile-flow HeartMate (HM) XVE LVAD as a viable, life-prolonging treatment in patients who were not candidates for HT, a strategy known as destination therapy (DT). However, survival 2 years after implantation was still only 23%, in part because of the high rates of mechanical pump failure.

The advent of continuous-flow LVADs has provided a more durable long-term treatment that improves quality of life and survival.3 The continuous-flow HM II LVAD has a markedly lower rate of device failure (0.06 versus 0.51 events per patient-year) and overall lower complication rates than the pulsatile HM XVE. Furthermore, survival at 2 years was 58% with the HM II compared with 24% with the HM XVE. Continued improvements have come with increasing experience, and 2-year actuarial survival for continuous-flow LVADs is now 70%.4 This has made DT a viable option for a much larger number of patients and accommodated longer waiting times for bridge-to-transplantation patients. Consequently, there has been a significant increase in both the number of LVADs implanted for DT and the use of continuous-flow LVADs, which now account for virtually 100% of DT implants in the United States.

A shift in use to less critically ill patients has occurred as a result of these improvements in survival and durability, again expanding the eligible patient population. The Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) database classifies a patient’s clinical profile on a scale from 1 to 7, with 1 being the most...
critically ill.4 The majority of patients in the REMATCH and HM II DT trials were classified as INTERMACS profile 1 (critical cardiogenic shock) or 2 (progressive decline), whereas the more recent Evaluation of the HeartWare Left Ventricular Assist Device for the Treatment of Advanced Heart Failure (ADVANCE) trial using the continuous-flow HeartWare ventricular assist device enrolled a majority of INTERMACS profile 3 (stable but inotrope-dependent) patients.5 The currently enrolling Randomized Evaluation of V AD Intervention Before Inotropic Therapy (REVIVE-IT)1 and Risk Assessment and Comparative Effectiveness of Left Ventricular Assist Device and Medical Management (ROADMAP; NCT01452802) trials aim to enroll even less sick patients with INTERMACS profiles of 4 to 7.

Various new, smaller, and more durable devices are in development. They no longer require an externalized driveline and are implantable intrapericardially or intraventricularly. These advances promise further expansion of the population of patients eligible for this technology. Not surprisingly, the number of centers implanting LVADs is also expanding, including non-HT programs.4 Although encouraging, these changes have resulted in a burgeoning population of patients presenting with post-LVAD complications. Knowledge of how to triage and manage these patients is increasingly important for emergency medicine physicians, general cardiologists, and internists as the population of LVAD patients continues to expand.

### Recurrent HF After LVAD Implantation

Persistent HF early after LVAD implantation is common, occurring in at least 20% to 25% of patients.6 Right ventricular (RV) dysfunction is the most common cause of early postoperative HF and can be attributable to preexisting RV disease, perioperative RV injury, or excessive volume resuscitation. Early postoperative RV failure is defined as the requirement for a RV assist device or continued use of inotropes >14 days after implantation and is associated with increased length of stay, bleeding, reoperation, worsening renal function, impaired quality of life, and increased mortality.7 Additional causes of early post-LVAD HF include inappropriate LVAD pump speed, misalignment of the LVAD inflow cannula, and LVAD thrombosis. Because providers specializing in mechanical circulatory support will manage most of these causes during the surgical admission, their workup and treatment are not covered further in this update. Readers are referred to comprehensive management guidelines.6

Recurrent HF late after successful LVAD implantation is also common, although the incidence is uncertain. For the purposes of this update, we define late HF as HF occurring >4 weeks after LVAD implantation in a patient with resolution of early postoperative RV dysfunction and other acute perioperative issues. HF late after LVAD implantation can be attributable to either LV or RV failure, each in turn resulting from LVAD-related or non–LVAD-related causes (Table 1).

Recurrent left-sided HF can occur with LVAD thrombosis, obstruction of the LVAD inflow or outflow cannula (as a result of kinking or, rarely, thrombosis), motor dysfunction, or fracture of the percutaneous driveline, which connects the implanted LVAD motor to the external system controller (see Figure 1 in Reference 8).6 Each of these malfunctions reduces LVAD pump output, which, if significant, can lead to HF attributable to inadequate forward flow. An inappropriately low LVAD pump speed can also cause HF as a result of inadequate LV unloading or worsening mitral regurgitation. Non–LVAD-related causes of late, left-sided HF include aortic valve insufficiency (AI) and severe anemia caused by gastrointestinal bleeding.

New or recurrent right-sided HF can be caused by inappropriately high LVAD pump speed. This results in shift of the septum toward the LV that distorts RV geometry, which in turn reduces RV systolic function and causes worsening tricuspid regurgitation (TR). Inappropriately high pump speed can also result in excessive cardiac output, increasing venous return to an already impaired RV. Recurrent primary RV failure can also be attributable to new or worsening primary RV myocardial dysfunction or tricuspid valve disease, ventricular arrhythmias, persistent pulmonary hypertension, pulmonary embolism, or rarely late cardiac tamponade. A systematic evaluation for differentiating potential causes of recurrent HF in the patient with an LVAD can lead to timely and appropriate treatment (Figure 1).

### Specific Causes and Treatment of Recurrent HF After LVAD

#### LVAD Pump Thrombosis

Thrombosis of the LVAD pump is the most concerning cause of recurrent HF because it can cause death if not identified and managed promptly. Pump thrombosis occurred in 2% of patients in the HM II bridge-to-transplantation

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**Table 1. Causes of Late Heart Failure After LVAD Implantation**

<table>
<thead>
<tr>
<th>LVAD related</th>
<th>RV Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pump thrombosis</td>
<td>Cardiac tamponade</td>
</tr>
<tr>
<td>Inflow or outflow cannula obstruction</td>
<td>Pump speed too high</td>
</tr>
<tr>
<td>Percutaneous lead or motor failure</td>
<td></td>
</tr>
<tr>
<td>Pump speed too low</td>
<td></td>
</tr>
<tr>
<td>Non–LVAD related</td>
<td>Intrinsic RV dysfunction</td>
</tr>
<tr>
<td>New/worsening aortic insufficiency</td>
<td>Persistent pulmonary hypertension</td>
</tr>
<tr>
<td>Gastrointestinal bleeding with</td>
<td>Pulmonary embolism</td>
</tr>
<tr>
<td>severe anemia</td>
<td>New/worsening tricuspid regurgitation</td>
</tr>
<tr>
<td></td>
<td>Ventricular arrhythmias</td>
</tr>
</tbody>
</table>

LV indicates left ventricle; LVAD, left ventricular assist device; and RV, right ventricle.
trial and 4% in the HM II DT trial, but recent series indicate the frequency is likely closer to 8%.

Pump thrombosis is suggested clinically by a variable combination of HF symptoms, a palpable pulse, increased pulse pressure (caused by an increase in the portion of cardiac output from native LV contraction), and laboratory evidence of hemolysis secondary to shearing of blood cells from nonlaminar blood flow through the clotted pump. With severe thrombosis, hemodynamic instability and acute kidney injury can occur, posing a life-threatening situation necessitating rapid workup. In this setting, echocardiography and LVAD interrogation can help confirm the diagnosis. Echocardiography will show LV dilation and increased aortic valve opening, and Doppler examination of the inflow and outflow cannulas may show reduced flow through the LVAD with increased pulsatility. LVAD pump parameters will demonstrate increased pump power (or intermittent power spikes) and inappropriately high estimated pump flow with a concomitant decrease in the pulsatility index resulting from a reduction in flow through the LVAD.

Rarely, thrombosis can occur in the LVAD cannulas. This can be assessed by cardiac computed tomography angiography, a standard part of the workup that may require assessment by a cardiovascular imager with LVAD experience.

Management includes prompt recognition, an increase in systemic anticoagulation, and consultation with cardiac surgery. Mild pump thrombosis in the hemodynamically stable patient may resolve with increased anticoagulation alone, as evidenced by reduced hemolysis, improved HF symptoms, and normalized LVAD pump parameters and echocardiographic findings. Successful resolution of pump thrombosis with the use of glycoprotein IIb/IIIa inhibitors has been reported in individual patients and small case series, although success rates may be only ≈50%. Case reports have demonstrated efficacy with directed thrombolysis; however, this is not always successful, especially when therapy is delayed, and the hemorrhagic risks may outweigh the benefits. Ultimately, most patients with significant thrombosis will require pump replacement. Thrombosis remains the most common reason for replacement of a continuous-flow LVAD and is associated with perioperative mortality of ≈5%.

Gastrointestinal Bleeding and Anemia

Bleeding, in particular gastrointestinal bleeding, remains one of the most common complications after implantation of an LVAD as a result of shearing of von Willebrand multimers and a predisposition to the formation of arteriovenous malformations. The incidence of gastrointestinal bleeding is typically 20% to 25% but has been reported to be as high as 40%. Gastrointestinal bleeding is higher with continuous-flow LVADs than with the older-generation pulsatile-flow devices. The bleeding source can be the upper or lower gastrointestinal tract but often is not identified. The majority of gastrointestinal bleeding in LVAD patients is not life threatening, but if anemia is severe, HF can result.

Management consists of hemodynamic support and blood transfusion as needed, along with temporary cessation of anticoagulation. Importantly, a high threshold for transfusion in bridge-to-transplantation patients is necessary to avoid pre-HT allosensitization. In general, an attempt to identify the source of bleeding and to treat it should be made because of the need for long-term anticoagulation. A stepwise approach including upper, lower,
and video endoscopy, followed by push or balloon enteroscopy and tagged red blood cell scanning, is necessary. HF is typically mild and self-limited, resolving with restoration of an adequate hematocrit. Some have advocated the use of the somatostatin analog octreotide, although data in LVAD patients are mixed and extremely limited. Once bleeding has resolved, anticoagulation should be reinstated with a lower target international normalized ratio. Gastrointestinal bleeding can be recurrent, and in rare cases, patients have been managed off anticoagulation.

**Primary RV Dysfunction**

Failure of the RV is the most common cause of late HF after LVAD implantation. In the HM II DT trial, late RV failure, defined as reinstitution of inotropes >14 days after implantation, occurred in 7% of patients. Late RV failure can be due primarily to intrinsic RV disease or can be secondary to a number of causes, including ventricular arrhythmias, progressive TR, pulmonary hypertension, or pulmonary embolism. Initial workup should focus on ruling out other causes of HF, in particular ventricular assist device malfunction or thrombosis.

With LVAD support, ventricular arrhythmias are generally not life-threatening but, when sustained or repetitive, can cause RV dysfunction and recurrent HF. Antiarrhythmic or ablative therapies are usually warranted. Rarely, refractory arrhythmias may require the addition of RV assist device support. Pulmonary hypertension, which is nearly ubiquitous in the advanced HF population, improves significantly with LVAD therapy, even when defined as “fixed” before ventricular assist device implantation. However, the time to reversal varies from days to months. Therefore, patients with persistent pulmonary hypertension after LVAD implantation are at risk for early or late RV failure resulting from sustained RV afterload in the setting of increased RV preload and preexisting RV dysfunction. Treatment with phosphodiesterase type 5 inhibitors can improve pulmonary hemodynamics in those with persistent pulmonary hypertension after LVAD, but it is unclear whether there is any clinical benefit. Standard HF therapies, including diuresis and, in severe cases, inotropes, are used as supportive therapy when overt HF is present.

Primary RV myocardial dysfunction in the absence of a secondary cause poses a greater challenge. Initial treatment with diuresis is warranted, but for those with progressive myocardial dysfunction, reinstitution of inotropic therapy may be necessary. The use of inotropic therapy is associated with reduced survival and worse quality of life and should be avoided if possible. In those eligible for HT, RV support with a durable RV assist device is indicated for refractory HF, but this option is not approved for DT. Therefore, a major goal of the pre-LVAD workup is to identify patients at risk for RV failure. Despite the availability of several different risk scores, RV failure after LVAD implantation has proved difficult to predict.

**Valvular Heart Disease**

New or worsening AI can also result in late-onset HF. AI after LVAD implantation is common, occurring in up to 38% of patients, and is associated with a worse prognosis. As a result, preexisting AI greater than mild in severity should be corrected at the time of LVAD implantation. Despite this, AI frequently occurs de novo after LVAD surgery and is progressive with continued LVAD support as a result of changes in hemodynamics across the aortic valve and in the aortic root. Significant AI increases LV preload and LVAD flow while paradoxically reducing forward cardiac output and thus can cause LV failure despite adequate LVAD function. Changes in medical therapy and device speed are usually ineffective, and refractory AI causing HF must be treated invasively.

First-line treatment is surgical, either with oversizing of the aortic valve or valve replacement. Percutaneous aortic valve closure or replacement can also be performed successfully in those who are at excessive risk for surgery.

Severe TR resulting in RV failure is typically attributable to worsening of preexisting TR in the setting of either progressive primary RV dysfunction and dilation or high LVAD pump speed that causes septal shift and altered RV geometry. Preexisting TR is associated with worse outcomes after LVAD surgery. As with preexisting AI, the best treatment is prevention by performing tricuspid valve surgery at the time of LVAD implantation. Tricuspid valve annuloplasty may reduce the incidence of post-LVAD HF. Management of worsening TR post-LVAD implantation begins with

### Table 2. Pertinent Laboratory Values at Baseline, Admission, and Follow-Up

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline</th>
<th>Admission</th>
<th>Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium, mmol/L</td>
<td>136</td>
<td>136</td>
<td>139</td>
</tr>
<tr>
<td>HCO₃, mmol/L</td>
<td>22</td>
<td>22</td>
<td>25</td>
</tr>
<tr>
<td>BUN, mg/dL</td>
<td>14</td>
<td>26</td>
<td>21</td>
</tr>
<tr>
<td>Creatinine, mg/dL</td>
<td>0.91</td>
<td>2.15</td>
<td>1.49</td>
</tr>
<tr>
<td>ALT, U/L</td>
<td>30</td>
<td>30</td>
<td>21</td>
</tr>
<tr>
<td>Total bilirubin, mg/dL</td>
<td>0.3</td>
<td>1.6</td>
<td>0.3</td>
</tr>
<tr>
<td>LDH, U/L</td>
<td>470</td>
<td>5230</td>
<td>416</td>
</tr>
<tr>
<td>Hemoglobin, g/dL</td>
<td>10.5</td>
<td>6.9</td>
<td>11.2</td>
</tr>
<tr>
<td>Free hemoglobin, mg/dL</td>
<td>3.3</td>
<td>26.5</td>
<td>5.5</td>
</tr>
<tr>
<td>Hematocrit, %</td>
<td>33.3</td>
<td>21.5</td>
<td>34.9</td>
</tr>
<tr>
<td>Haptoglobin, mg/dL</td>
<td>&lt;8</td>
<td>&lt;8</td>
<td>&lt;8</td>
</tr>
<tr>
<td>INR (Target) 2.0-3.0</td>
<td>1.8</td>
<td>2.9</td>
<td></td>
</tr>
</tbody>
</table>

ALT indicates alanine aminotransferase; BUN, blood urea nitrogen; HCO₃, bicarbonate; INR, international normalized ratio; and LDH, lactate dehydrogenase.
conservative therapies that target a poorly functioning RV or a reduction in LVAD pump speed to mitigate septal shift. If this is not successful, surgical valve repair may need to be considered.

Clinical Follow-Up
On admission, the patient was found to have dark urine, and laboratories demonstrated significant intravascular hemolysis and pigment-induced nephropathy (Table 2). Urgent echocardiography showed LV dilation (LV end-diastolic diameter, 55 mm, increased from 46 mm 4 weeks postoperatively) and aortic valve opening with each beat (Figure 2). LVAD parameters showed increased basal power with intermittent power spikes and a reduction in the pulsatility index. These findings were consistent with inadequate LV unloading, suggestive of LVAD malfunction. Cardiac computed tomography angiography did not demonstrate kinking or thrombosis of the LVAD inflow or outflow cannula (Movie I in the online-only Data Supplement). These data, taken together with recurrent HF and severe hemolysis, were highly suggestive of pump thrombosis. Intravenous heparin was initiated, but the patient developed worsening hemolysis and progressive HF. He underwent successful LVAD replacement. After surgery, his target international normalized ratio was increased to 2.5 to 3.0, and he was discharged home in good condition with improved laboratory values (Table 2).

Acknowledgments
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Disclosures
None.

References


Supplemental Video

Cardiac computed tomography angiography demonstrating no obstruction to flow in either the LVAD inflow or outflow cannula.
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