Evaluation and Management of LVAD Complications

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Clinical Vignette

A 67-years-old man with a long history of ischemic cardiopathy type II diabetes mellitus and carotid artery disease underwent HeartWare HVAD (HeartWare Boston MA) implantation as destination therapy via sternotomy. Surgery and postoperative recovery were uneventful and the patient was discharged home on standard antithrombotic therapy (warfarin with INR range 2–3 and aspirin 325 mg daily). He remained stable until over a year later he presented with hematuria prompting admission to the hospital. There were no signs of pulmonary or abdominal congestion or signs of cardiogenic shock. HVAD parameters showed a progressive increase in power (2.8 Watts → 3.6 Watts) and flow (3.9 L/min → 6 L/min) with an unchanged speed of 2360 rpm. How should this patient be managed?

Introduction

Mechanical circulatory support with ventricular assist devices (VADs) is an important treatment strategy for patients with end-stage heart failure (HF) that is refractory to medical therapy. The use of left ventricular assist devices (LVADs) has increased significantly over the past few years with more than 22,000 devices implanted by 2019 in the United States and more than 2,500 new implants occurring annually [1]. These patients have a 1-year and 2-year survival of 81% and 70%, respectively; however, almost 80% of LVAD patients will be hospitalized

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within the first year after implantation for some complication. The management of these devices is complex, and these patients still experience high rates of VAD-related adverse events. The most common of these directly related to the LVAD are gastrointestinal bleeding, infection, and neurologic events. However, other LVAD associated complications such as arrhythmias and aortic insufficiency are as important in the care of LVAD patients. Thus, clinicians must be familiar with common and serious complications. This chapter will give an overview of complications to assist clinicians in evaluation and management. This will focus largely on complications in HeartMate II (HMII), HeartMate 3 (HM3) and Heartware (HVAD) devices, which are those most commonly used in the United States.

Basic LVAD Physiology

The LVAD provides an alternate parallel path for blood flow from the left ventricle (LV) to the aorta [2, 3]. Contemporary continuous-flow LVADs consist of a blood pump, percutaneous lead, external power source, and system controller. The blood pump consists of an inflow cannula (inserted into and draining from the apex of the LV), an impeller, and an outflow cannula, which by means of a graft delivers the blood into the aorta. The impeller rotates at a high speed inside its housing, which accelerates the fluid forward along the axis of the impeller in axial-flow pumps (HMII) or outwardly in centrifugal pumps (HVAD and HM 3) (Fig. 1). General characteristics of contemporary devices are shown in Table 1.

Pump Parameters

Contemporary continuous-flow LVADs display the following parameters on the controller or the monitor, and Table 2 gives a brief overview of clinical scenarios causing abnormal pump parameters. (Tables 1 and 2):

Pump Flow is defined as: Flow = Rotor Speed/(P outflow − P inflow)

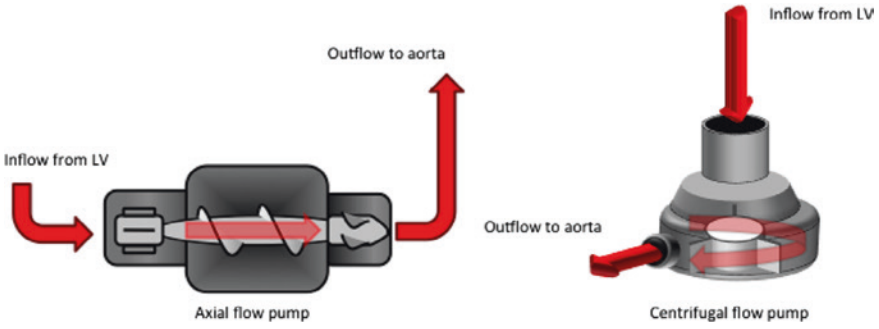

Fig. 1 The two types of impellers most commonly used clinically

Table 1 General characteristics of the three devices

Device	HeartMate II	HeartMate 3	HeartWare
Flow	Axial	Centrifugal	Centrifugal
Placement	Preperitoneal	Intrapericardial	Intrapericardial
Bearing	Ball and cup (blood immersed)	Magnetic levitation	Hydrodynamic
Speed range (rpm)	6000–15000	3000–9000	2400–3200
Maximum flow	10 L/min	10 L/min	10 L/min
Blood flow gaps, mm	0.08	0.12	0.05
Artificial pulsatility	No	Yes	No
FDA approved indications	BTT (2008) DT (2010)	BTT (2017) DT (2017)	BTT (2012) DT (2017)

Table 2 Alterations of pump parameters may suggest different clinical scenarios

Pump parameters	High pulsatility	Low pulsatility
High power/flow	Normal physiology, Improvement in cardiac function, exercise	Hypotension, high pump speed, pump thrombus (affecting rotor/bearings)
Low power/flow	Hypertension, low pump speed, inflow/outflow graft obstruction	Hypovolemia, tamponade, right heart failure, arrhythmias, inflow/outflow graft obstruction

The Flow is derived from pump power consumption and correlates:

- Directly with the speed of the rotor
- Indirectly with the pressure differential between LV and the aorta

Power ("the energy consumed to spin the impeller at the speed we have set"), is a function of:

- Patient status (volume status, degree of afterload, activity)
- Pump status (kinked outflow graft, obstructive inflow cannula, rotor and bearing thrombus)

Pulsatility Index (only reported for HMII and 3 but can be derived from HVAD screen) is defined as: PI = (maximum flow − minimum flow)/average flow × 10. PI has been used as a surrogate for the degree of LVAD support: the lower the PI, the greater the amount of support provided by the pump.

Evaluation of Abnormal LVAD Parameters

Approach

LVAD parameters are an additional vital sign. Like any vital sign, when a parameter is out of the normal range for a patient, assessment for a possible cause should

occur. The prior section provided differentials for some causes of abnormal parameters. Further assessment to narrow this differential is similar to any HF patient with a thorough history, physical exam, and selective laboratory and diagnostic testing (Tables 3, 4, 5 and 6). Early invasive hemodynamic monitoring should be considered for many LVAD complications, but especially in situations of recurrent HF to optimize patient hemodynamics and LVAD function. Clues from these evaluations can direct the clinician to the appropriate issue and management as outlined in following sections.

Table 3 History findings and differential

Symptoms	Clinical condition	Differential
Dyspnea, orthopnea, edema, abdominal bloating	Recurrent HF	Non-compliance, RHF, arrhythmia, pump malfunction
Fatigue, dyspnea, epistaxis, melena, hematochezia	Blood loss	Gastrointestinal bleeding, hemolysis
Fevers, chills, malaise, driveline drainage	Infection	Community acquired infection, driveline infection, pump/pocket infection, endocarditis
Focal weakness, slurred speech, sensation disturbances	Neurologic event	Stroke (ischemic or hemorrhagic)

Table 4 Physical exam findings and differential

Findings	Clinical considerations
Low MAP	Increased LVAD flow, hypovolemia, infection
High MAP	Low LVAD flow, hypertension
Abnormal temperature	Infection
Abnormal heart rate	Arrhythmia
Abnormal LVAD sound	Pump thrombosis, inflow/outflow obstruction
Jugular venous distension	HF, arrhythmia, tamponade
Pallor	Blood loss
Driveline erythema/discharge	Driveline infection
Lung crackles	Heart failure, pneumonia
New weakness, loss of sensation	Stroke

Table 5 Laboratory testing

Test	Clinical considerations
Complete blood count	Leukocytosis—infection Anemia—blood loss
Renal function	Acute kidney injury
Liver function	Abnormalities with congestion, infection, hemolysis
INR	Within therapeutic range?
LDH/plasma free hemoglobin	Markers of hemolysis

Table 6 Diagnostic testing

Test	Clinical considerations
Electrocardiography	Arrhythmia detection
Echocardiography	Assessment of left ventricular size—inadequate unloading? Right ventricular size/function—RHF Valvular heart disease—regurgitant lesions Thrombus
Chest X-ray	Pulmonary edema Infiltrate
Computed tomography	Head—signs of ischemic or hemorrhagic stroke Chest—infection, effusion, fluid collections Abdomen—assessment of driveline, fluid collections

Pump Thrombosis

Background

Pump thrombosis (PT) is defined as an obstruction that limits blood entering or exiting the pump or otherwise impinges the impeller from properly rotating. Recently, the MOMENTUM 3 trial showed 0.12 events per patient-year (EPPY) of PT in the HMII arm with very few events in the HM3 arm [4]. The ADVANCE trial reported an incidence of 0.04 to 0.09 EPPY in the HVAD population [5]. Notably there has been a drastic reduction in the incidence of PT since 2015 with the progressive growth in the number of HM 3 implants. Though an uncommon complication, its clinical implications are substantial as they can lead to catastrophic pump failure or other complications such as stroke.

When clot does form, the location and histology of the clot formation can differ depending on VAD type (Fig. 2). Globular clot formations have been reported on

Fig. 2 Pump Thrombosis

the inflow bearings and in regions of sharp angulation of the HMII inflow/outflow grafts. In contrast laminar fibrin formations may develop on the impeller of HVAD pumps if a thrombus event occurs. The HM 3 was designed to prevent pump thrombosis by employing three innovations:

- Use of wider blood flow passages to reduce shear stress and minimize disruption of red blood cells as they pass through the pump
- Magnetic levitation technology to create a frictionless pump with no mechanical bearings
- Incorporation of an artificial fixed pulse that speeds up and slows every two seconds to minimize blood stasis and facilitate pump surface washing.

Presentation of Pump Thrombosis

Patients experiencing PT may present with four possible scenarios:

(1) Asymptomatic sustained power elevations (defined as power $\geq$ 10 watts or power > 2 watts above baseline for > 24 h)
(2) Isolated elevation of LDH levels (>3 times the upper limit of normal) or plasma free hemoglobin (pfHb) (>40 mg/dL)
(3) Clinical signs of hemolysis (hemoglobinuria)
(4) Symptoms of HF (with or without hemodynamic abnormalities including shock)

Diagnostic Evaluation

In addition to the assessment of abnormal device parameters, the following tests are commonly used for diagnosing PT (Table 7):

Serial recording of LV end-diastolic diameter with increasing VAD speeds (known as a ramp study) may diagnose pump thrombus or other obstructions to blood flow within the rotatory pump and cannula system.

Management

At present, the ideal strategy for treating PT in contemporary devices has yet to be defined. Surgical device exchange or urgent heart transplantation represent the most definitive treatment modalities, in particular for HMII patients because clots are generally detected after they are no longer amenable to medical therapy.

Table 7 Diagnostic testing for pump thrombosis

Laboratory findings	Chest X-ray	Echocardiography	Chest computed tomography
High LDH	Malposition of inflow	Dilated ventricle	Malpositioned inflow cannula
Low hemoglobin/ hematocrit	Misaligned outflow graft protector	Severe mitral regurgitation	Kinked outflow graft
Low haptoglobin	Pulmonary congestion	Frequent aortic valve opening	If contrast used, thrombus within inflow or outflow
High plasma free hemoglobin		Elevated right ventricular systolic pressure	
Hemoglobinuria			
Elevated bilirubin			

The use of medical therapy can be considered for patients:

- With asymptomatic hemolysis
- Who are poor candidates for surgical management
- In whom it would be advantageous to avoid surgery and instead expedite transplantation

The up-titration of anti-thrombotic therapy includes

- Addition of a second anti-platelet agent (clopidogrel, dipyridamole)
- Intravenous heparin (targeting PTT two to three times upper limit) or intravenous bivalirudin
- Fibrinolytics with intraventricular or systemic administration.

Right Heart Failure

Presentation of Right Heart Failure

Right heart failure (RHF) can present at any time after LVAD placement and frequently presents in the immediate post-operative period. It can be a temporary state that resolves with therapy or a chronic problem requiring regular management and recurrent hospitalizations after LVAD implantation. Approximately one third of LVAD patients will experience RHF.

Signs and symptoms of RHF are predominately those of recurrent HF and multiple laboratory abnormalities can develop (Table 8):

Table 8 Signs, symptoms and lab abnormalities with right heart failure

Fatigue	Dyspnea on exertion
Edema	Bloating
Early satiety	Decreased urine output
Ascites	Elevated jugular venous pressure
Elevated natriuretic peptide levels	Elevated creatinine and BUN
Elevated liver function tests	Elevated prothrombin time
Low albumin	

Prediction and Diagnostic Criteria

Numerous echocardiographic and hemodynamic (Table 9) variables have been associated with an increased risk of post-operative RHF and are also used in diagnosing RHF (Fig. 3) [6, 7].

Other non-echocardiographic and hemodynamic risk factors include:

- Female gender
- Non-ischemic cardiomyopathy
- Liver dysfunction
- Kidney dysfunction

Most criteria are derived from studies with small patient populations. No one criterion is sensitive or specific enough to predict or diagnose RHF, thus one should consider and incorporate multiple criteria for predicting and diagnosing RHF. Multiple risk scores for RHF have been developed that include many of the variables above but have not shown strong predictive performance outside of the population they have been derived in (Fig. 4).

Formal criteria suggested for defining RHF are listed in Table 10 [8].

Table 9 Features associated with post-operative right heart failure

Echocardiographic features	Hemodynamic features
Enlarged RV (ratio RV/LV > 0.75, but especially when RV is larger than LV)	Elevated CVP (>15 mmHg)
Bowing of the interventricular septum towards the LV	Elevated CVP to wedge pressure ratio (>0.63)
Low tricuspid annular planar systolic excursion (TAPSE) (<8 mm)	Low pulmonary artery pulsatility index (PAPi = PA systolic pressure—PA diastolic pressure/CVP; PAPi < 2.0 indicates increased risk)
Reduced RV fractional area change (<35%)	Elevated pulmonary vascular resistance (>4 woods units
Reduced RV strain (>−15.5%)	Low RV stroke work index (<300 mmHg ml/m^2)
Severe tricuspid regurgitation	

CVP—central venous pressure; LV—left ventricle; PA—pulmonary artery; RV—right ventricle

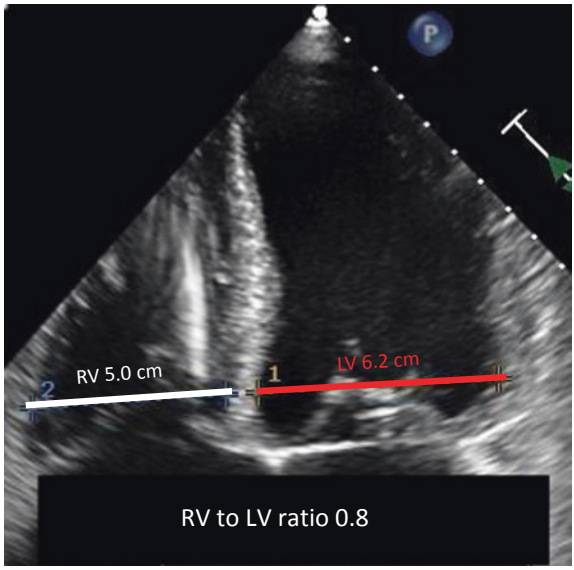

Fig. 3 Example of an echocardiogram from the apical four chamber view with substantial right ventricle (RV) dilation compared to left ventricle (LV) at a ratio > 0.75. Patient later experienced post-operative RHF after LVAD placement

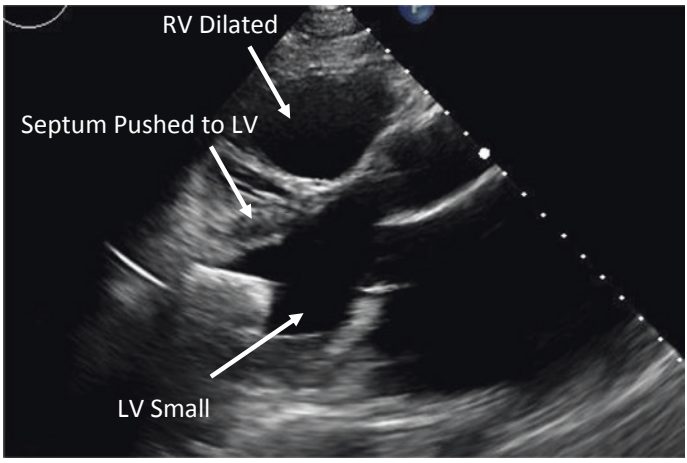

Fig. 4 Echocardiogram from parasternal long-axis view showing RHF after LVAD placement with a dilated right ventricle (RV) shifting the septum towards the left ventricle (LV) resulting in a small LV cavity. Patient's LVAD had to be run at low speed to prevent suction and RHF needed support with intravenous milrinone

Table 10 Criteria for defining right heart failure and severity

Elevated CVP reflected as either: • CVP > 16 mmHg • Dilated inferior vena cava without collapse on echocardiography • Elevated jugular venous pressure **And** signs of RHF reflected as either: • Edema • Ascites/hepatomegaly • Worsening liver or kidney function on labs
Grading
Mild • Prolonged post-implantation inotropes, inhaled pulmonary vasodilators, or intravenous vasodilators but not continued beyond post-operative day 7 after LVAD
Moderate • Post-implantation inotropes, inhaled pulmonary vasodilators, or intravenous vasodilators continued beyond post-operative day 7 but not beyond post-operative day 14 after LVAD
Severe • CVP greater than 16 mmHg **AND** • Prolonged post-implantation inotropes, inhaled pulmonary vasodilators, or intravenous vasodilators continued beyond post-operative day 14 after LVAD
Severe-acute • CVP greater than 16 mmHg **AND** • Need for mechanical right ventricular support **OR** death

CVP—central venous pressure

Differential

Mimics or causes of RHF both acutely and/or chronically include:

- Tamponade
- Inadequate LV support
- Pulmonary embolism
- Right ventricular (RV) myocardial infarction
- Arrhythmias

Management

Management of RHF is largely based on optimization of RV hemodynamics. Every effort should be made to optimize hemodynamics prior to LVAD implantation to reduce the risk of RHF. Pre-operative administration of oral phosphodiesterase-5 inhibitors has been associated with an increase in RHF post-LVAD [9]. There are no large randomized studies at this time for specific treatments or therapies to improve outcomes of RHF after LVAD. Management of RHF may vary in the acute post-operative setting and with chronic management. Therapies commonly used for both acute and chronic RHF include:

- Aggressive volume removal with diuretics and ultrafiltration if diuretics are inadequate
- Inotropic support with dobutamine, dopamine, milrinone, or levosimendan
- Inhaled pulmonary vasodilators including inhaled nitric oxide or epoprostenol
- For acute RHF after LVAD, early and planned use of mechanical RV support has better outcomes than late or emergent support [10].
- For chronic RHF, off-label use of oral phosphodiesterase-5 inhibitors are frequently administered with weak data of possible benefit, especially if hemodynamics suggest pulmonary hypertension. Digoxin can be empirically given for inotropic support.
- The ultimate therapy for chronic RHF is heart transplantation.

Bleeding

Presentation and Assessment

Bleeding is one of the most frequent LVAD complications occurring in one to two thirds of patients [1]. The most common cause is gastrointestinal, but other causes include epistaxis, bruising, and trauma related bleeding. Presenting symptoms and features of evaluation include:

- Active cutaneous bleeding, melena, hematemesis, epistaxis, fatigue, dizziness, syncope, HF
- Low mean arterial pressure (MAP), orthostatic symptoms, pallor
- Low hemoglobin, INR at goal or elevated, LDH may be elevated, elevated BUN
- Low flow on LVAD, low flow alarms, hematocrit is entered to calculate flow on HVAD and HM 3 so reprograming hematocrit will increase flow

Gastrointestinal bleeding frequently occurs from sites found in non-LVAD patients such ulcers, polyps, and hemorrhoids. Somewhat unique to LVAD patients is an increased frequency of bleeding from angiodysplasia. Arteriovenous malformations (AVMs) are thought to form from lack of pulsatile flow and an acquired von Willebrand disease (Figs. 5 and 6) [11]. Multiple risk factors have been identified for bleeding complications (Table 11).

Management

In the acute setting, therapy involves both pharmacologic and procedural interventions. Chronic management is determined by cause of bleeding, risk of recurrence and frequency of recurrence.

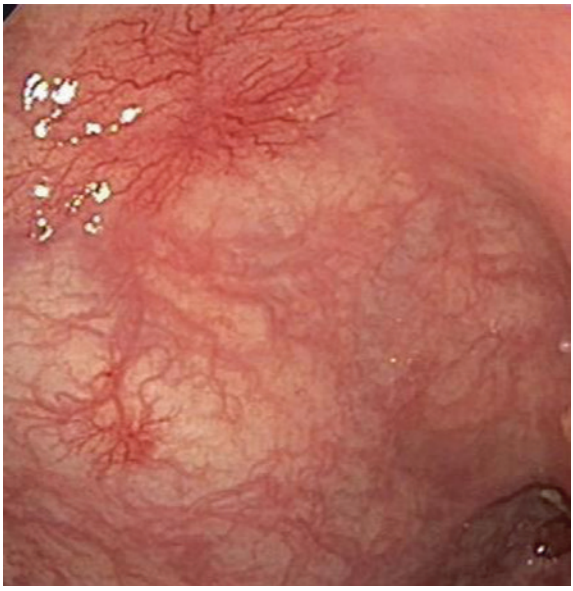

Fig. 5 AVMs in the colon of a patient with a HMII LVAD and recurrent blood loss

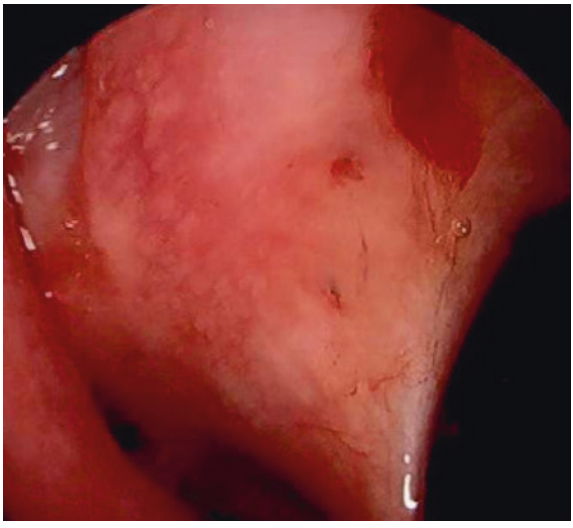

Fig. 6 Nasal AVM (top right of photo) in HVAD patient. Patient had profound epistaxis with repeated drops in hemoglobin until operative intervention where diffuse nasal AVMs were found requiring electrocautery

Table 11 Risk factors for bleeding in LVAD patients

Older patient age	Low pulsatility
History of gastrointestinal bleeding	Post-LVAD ejection fraction > 30%
Preceding coagulopathy	Post-implantation infection
Elevated creatinine	Low platelet count
RV dysfunction	

Potential interventions in the acute setting include:

- Hemodynamic stabilization with intravenous fluids and blood transfusions
- Withholding of antiplatelets and anticoagulants
- INR value and severity of bleeding should be carefully weighed against the risks of reversing anticoagulation. Administration of fresh frozen plasma could be considered with active life-threatening bleeding. Vitamin K is generally avoided as it does not acutely correct and may over-correct anticoagulation. Prothrombin complex concentrate should be given cautiously given its increased risk of thrombosis.
- Intravenous proton pump inhibitor
- Intravenous octreotide [12].
- Esophagogastroduodenoscopy and/or colonoscopy
- Capsule endoscopy (for diagnosis and identification of source)
- For severe uncontrolled or recurrent bleeding, surgical resection of bleeding bowel segment could be performed

Potential chronic therapies and measures after an episode of gastrointestinal bleeding or recurrent bleeding include:

- Adjusting LVAD speed to increase pulsatility and reduce sheer stress
- Lowering INR goal
- Stopping antiplatelets
- Chronic oral proton pump inhibitors
- Chronic octreotide (often administered in depot form) in the setting of AVMs [13].
- Studies suggest angiotensin blockade with angiotensin converting enzyme inhibitors or angiotensin receptor blockers reduces risk of gastrointestinal bleeding
- Thalidomide [14].
- Hormonal therapy with estrogen

Stroke

Background and Presentation

As with mechanical prosthetic valves, LVAD patients are at increased risk for both ischemic and hemorrhagic stroke given the thrombogenicity of the mechanical pump and necessity of anticoagulation. Almost 20% of LVAD patients will suffer a stroke within the first year after implantation, with slightly more than half being ischemic [1, 15]. Compounding risk is the presence of concomitant medical conditions that increase the risk of stroke such as atrial fibrillation, peripheral arterial disease, diabetes and hypertension. Additionally, it is believed that non-pulsatile flow alters cerebral vasculature potentially predisposing to stroke [16].

Table 12 Risk factors for stroke in LVAD patients

Systemic infection	Hypertension
Atrial fibrillation	Female gender
Anticoagulation levels	Duration of LVAD support
Low pulsatility	Prior stroke

Stroke symptoms in LVAD patients are the same as other patients. Neurologic deficits can vary and include focal weakness, sensory deficits, speech difficulties, vision loss, or loss of coordination. Symptoms may be less focal and include headache, confusion, or altered mental status. Thus, physicians should maintain a low threshold to evaluate for stroke in LVAD patients presenting with non-specific symptoms even if a neurologic deficit is not noticeable.

Risk factors for stroke are listed in Table 12. Two important risk factors are infection and hypertension. A concomitant systemic infection is one of the most common risk factors for stroke [15, 17]. Infections may promote a prothrombotic environment or become endocarditis with embolization. Hypertension has been repeatedly found to be a risk factor for stroke in LVAD patients, especially in HVAD patients [18]. Risk significantly increases when MAP is > 90 mmHg.

Assessment

Patient's with possible stroke symptoms should be rapidly assessed given the limited time available for possible intervention. Patients and their caregivers should be taught the F.A.S.T. acronym (Face drooping, Arm weakness, Speech difficulty, Time to call 911) for warning signs of stroke. Anytime stroke is a concern, neurology consultation should be immediately sought.

The preferred imaging modality for stroke is magnetic resonance imaging; however, this is prohibitive in LVAD patients [17]. Thus, diagnosis is based on history, physical exam, CT imaging, and vascular imaging. A CT scan should be obtained within 10 min of initial concern for stroke to differentiate hemorrhagic from ischemic stroke. In early ischemic strokes, CT head imaging will often be normal. Imaging is frequently repeated to assess for changes consistent with ischemic stroke, expansion of a hemorrhagic stroke, or to monitor for hemorrhagic conversion. CT angiography can evaluate for large vessel occlusions that might be intervenable upon. Digital subtraction angiography is usually only performed if endovascular intervention is performed; however, it may be necessary if there is concern for a mycotic aneurysm [17].

Evaluation for risk factors and sources of stroke should be sought. Given the association with concomitant infection, blood cultures should be drawn. This may lead to further evaluation for endocarditis. An echocardiogram should be obtained as this may visualize a thrombus or a vegetation of endocarditis (Fig. 7). Further testing may include carotid ultrasounds or transesophageal echocardiography based on evaluation.

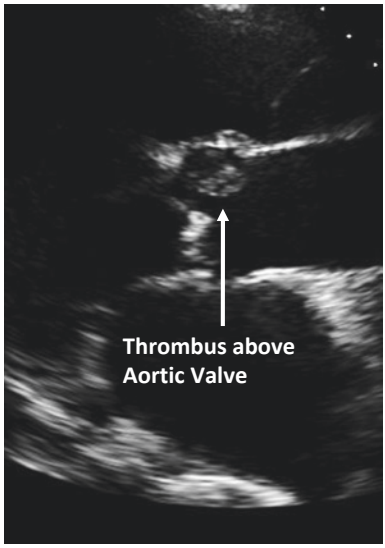

Fig. 7 Transthoracic echocardiogram showing a thrombus above the aortic valve and lack of aortic valve opening in an LVAD patient presenting with a stroke

Management of Ischemic Stroke

In non-LVAD patients, thrombolytic therapy with recombinant tissue plasminogen activator (rtTPA) is the treatment of choice if an ischemic stroke is detected early enough. However, rtTPA is frequently contraindicated in LVAD patients given the use of anticoagulation (contraindicated if INR > 1.7) and antiplatelet therapy that increase the risk of hemorrhagic complications. Additionally, there is a heightened risk of hemorrhagic conversion given the association of stroke and systemic infection in LVAD patients as well as other potential defects in the coagulation system of LVAD patients. Thus, use of rtTPA must be carefully weighed against these risks.

Mechanical thrombectomy offers an alternative for large vessel occlusion. This therapy has not been systematically studied in LVAD patients and case reports have reported variable outcomes. By avoiding systemic rtTPA, this could potentially minimize systemic bleeding risks; however, hemorrhagic conversion risk is similar and possibly higher than rtTPA [17]. The window for potential therapeutic benefit of mechanical thrombectomy is longer than rtTPA. Careful consideration and discussion with neurology should be performed when considering this treatment option.

Separate from these therapies, care is focused on supportive measures. Since most strokes in LVAD patients are presumed to be device related, risks of reversing or withholding anticoagulation should be weighed against risk for device thrombosis and possible recurrent ischemic stroke. Generally, anticoagulation should be held for the first 24 h to monitor for hemorrhagic conversion [17]. Anticoagulation may then be restarted 1 to 7 days after initial presentation based

on INR and clinical course. This decision should be individualized to a patient's risk for hemorrhage and clinical status.

Volume status should be optimized to avoid volume depletion, but also avoid fluid overload. Both hyper- and hypoglycemia should be corrected as necessary with goal of maintaining glucose in range of 80 to 180 mg/dL. In normal stroke management, permissive hypertension is allowed because of the loss of cerebral autoregulation; however, with continuous non-pulsatile LVAD flow, blood pressure often does not reach levels that would prompt treatment in normal stroke patients. Hypotension should be avoided and vasoactive agents may be needed to maintain cerebral perfusion.

Management of Hemorrhagic Stroke

An important initial distinction for management is determining if a hemorrhage is a primary process or the result of hemorrhagic conversion. Anticoagulation should often be reversed in hemorrhagic stroke; however, this must be weighed against the risk of device thrombosis. Also, if the initial stroke was ischemic with hemorrhagic conversion, reversal of anticoagulation may potentially lead to propagation of a device related thrombus. The decision to reverse anticoagulation needs to be individualized based on mechanism of hemorrhage, history of stroke or device thrombosis, current level of anticoagulation, and size of hemorrhage. Aggressive blood pressure reduction is usually pursued in hemorrhagic stroke, but because of continuous blood flow and altered blood pressure, the optimal blood pressure in an LVAD patient is unknown, but generally MAP is maintained at <90 mmHg.

For large hemorrhagic strokes with substantial vasogenic edema, there may be neurologic deficits from compression prompting neurosurgical evaluation for decompressive therapies. Studies are varied on benefits of decompressive surgeries and these procedures are even more challenging in LVAD patients given the bleeding risks from anticoagulation and need to minimize anticoagulation therapy for prolonged periods after performing such an operation. Requiring such therapies often portends a poor prognosis.

Long-Term Management

Following initial acute hospital management of stroke, care should focus on aggressive rehabilitation. For both ischemic and hemorrhagic stroke, goals of antiplatelet and anticoagulation therapy should be reassessed, and the target range of INR may need to be redefined. Blood pressure should be controlled to maintain MAP < 90 mmHg. Secondary prevention measures of lipid and glucose control have not been studied in LVAD patients but may improve outcomes depending on mechanism of stroke.

Arrhythmias

Presentation

Arrhythmias are a frequent complication in LVAD patients [19, 20]. Atrial arrhythmias and ventricular arrhythmias are estimated to occur in 20 to 50% of LVAD patients. Because of continuous flow with near full circulatory support provided, LVAD patients can be very tolerant to arrhythmias including ventricular arrhythmias (Fig. 8). Patients frequently present without symptoms or only vague and non-specific symptoms (Table 13). This requires clinicians to remain vigilant for arrhythmia detection before potential adverse consequences occur.

Risk Factors and Outcomes

Atrial arrhythmias are not well studied in LVAD patients, but the most frequent atrial arrhythmia is atrial fibrillation [19, 20]. Risk factors and outcomes are not well described for atrial arrhythmias, but the largest concern is thromboembolic risk with atrial fibrillation. The initial INR goal for LVAD patients is same for

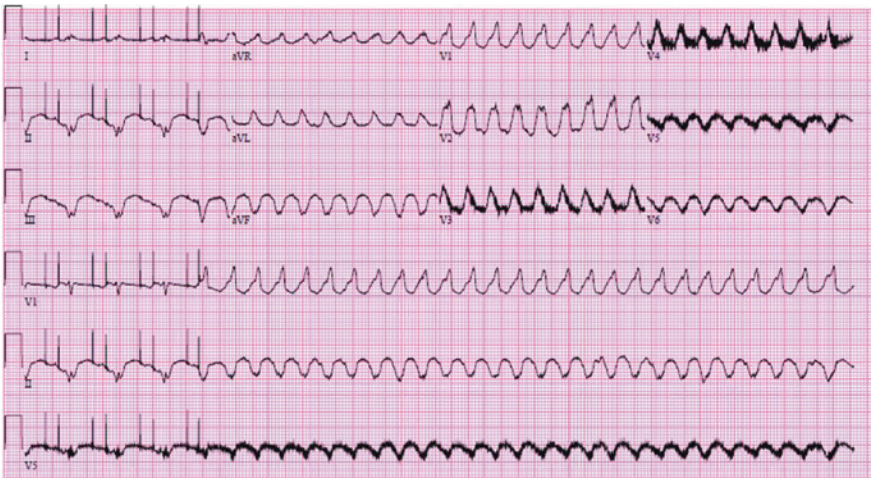

Fig. 8 Patient supported by LVAD is paced then goes into monomorphic ventricular tachycardia without loss of consciousness

Table 13 Symptoms from arrhythmias on LVAD support

Fatigue	Weakness
Palpitations	RHF
Pre-syncope	Syncope (rare)

atrial fibrillation, but a bleeding event may change the INR goal and thromboembolic risk may increase.

Ventricular arrhythmias most often occur early after LVAD implantation [20]. Risk factors include prior history of ventricular arrhythmias, lack of beta-blocker use, and potentially ischemic cardiomyopathy, though some studies report higher incidences with non-ischemic cardiomyopathy. One potential risk and source of early post-operative ventricular arrhythmias is scar from placement of the inflow cannula. Early post-operative ventricular arrhythmias have been variably associated with an increased morbidity and mortality, which likely depends on the status of the patient, RV, hemodynamic support, and clinical context.

Management

For any hemodynamically unstable arrhythmia, immediate cardioversion/defibrillation should be performed.

Management of atrial arrhythmias, mainly atrial fibrillation, focuses on rate or rhythm control and thromboembolic risk reduction. LVAD patients are usually anticoagulated to the same INR goal as atrial fibrillation. However, if a bleeding event occurs, INR goals may be lowered and the thromboembolic risk from atrial fibrillation may increase. Whether to pursue a rate or rhythm control strategy or any medical therapy at all depends on a patient's tolerance of the arrhythmia. Rhythm control should be sought for symptomatic patients with amiodarone, sotalol or dofetilide as preferred agents. Rate control with either carvedilol, metoprolol succinate, bisoprolol and/or digoxin can be used. For symptomatic patients unable to tolerate any medical therapy, AV node ablation may be necessary.

Ventricular arrhythmias are often initially managed with medical therapy including beta-blockers, amiodarone, mexiletine, sotalol or dofetilide. Early perioperative ventricular arrhythmias may resolve with sufficient time and healing. For medically refractory ventricular arrhythmias or those with significant hemodynamic impact, catheter ablation may be necessary [20]. Catheter ablation therapy has only been studied in case reports and series at specific centers. While results show efficacy in the short-term, long-term follow up studies are lacking.

Aortic Insufficiency

Presentation

Aortic insufficiency (AI) is a common complication after LVAD implantation. It is estimated that 1 in 4 patients will develop at least mild to moderate AI within one year of implantation [21]. With LVAD therapy, the heart is subjected to AI that is pancyclic, occurring throughout systole and diastole, in response to the constant positive transaortic pressure gradient. Risk factors for AI while under support are listed in Table 14 [21].

Table 14 Risk factors for aortic insufficiency

Persistently closed aortic valve	Excessive LV unloading
Prolonged duration of support	Small body surface area
Systemic hypertension	Female gender
Moderate mitral regurgitation	Older age
Larger aortic dimension at implantation	Cannulation site (at least 2 cm above the sino-tubular junction)
Anastomotic angle (≥ 90° transversally and between 60° and 120° in the coronal plane)	

Diagnosis

Transthoracic echocardiography (TTE) parameters (i.e. vena contracta, jet width/LVOT diameter, PISA) largely underestimate AI severity, because regurgitant flow occurs during the whole cardiac cycle (Fig. 9). However, TTE remains the gold-standard to detect AI.

Two novel echocardiographic parameters have been proposed for grading severity of AI [22]:

- *The outflow LVAD cannula systolic-to-diastolic peak velocity ratio (S/D ratio):* this value is inversely proportional to AR severity (significant AI is likely when S/D ratio is <5.0)
- *LVAD outflow cannula diastolic acceleration*, obtained by measuring the diastolic slope from the onset of diastolic to end-diastole (significant AI is when diastolic acceleration is >49.0 cm/s^2)

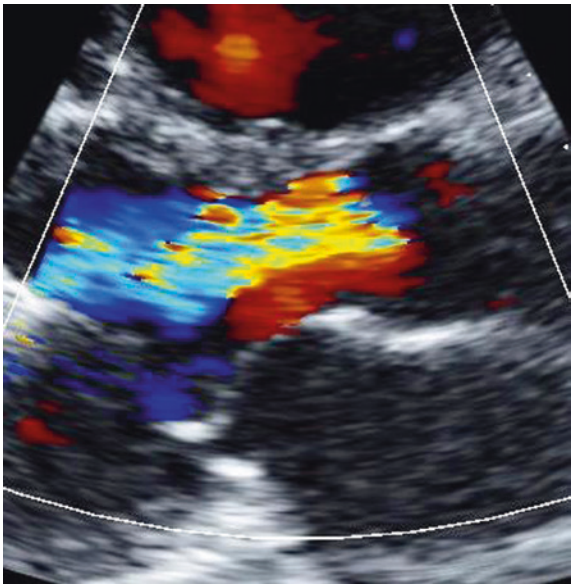

Fig. 9 Patient supported by HM3 LVAD with progressive heart failure symptoms found to have severe aortic insufficiency

Clinical Presentation

Patients may be asymptomatic or symptomatic [21]. Symptomatic patients frequently presents with recurrent HF and impaired end-organ perfusion. Asymptomatic patients may found:

- During routine TTE
- After addition of vasodilators which reduce afterload prompting less opening of aortic valve
- When diuretic therapy is given for hypervolemia leading to a decreased preload and native heart ejection and subsequently less aortic valve opening.

Management

There are no studies managing AI in asymptomatic LVAD patients; however, general recommendations include reducing LVAD speed to allow intermittent aortic valve opening and serial echocardiograms to monitor for progression [21]. For progressive AI that becomes symptomatic or hemodynamically significant management can be either medical, which only temporarily stabilizes the patient's status, or surgical with both open and percutaneous options available (Table 15) [21]. The benefits and risks of different surgical options are outlined in Table 16.

Tamponade

Presentation

Cardiac tamponade is a life-threatening complication following LVAD implantation that usually only occurs in the post-operative period [23]. Symptoms may include fatigue, dizziness, dyspnea, and chest pain. Signs include hypotension, elevated jugular venous pressure, pallor, cool extremities and decreased urine output.

Table 15 Medical and surgical options for aortic insufficiency

Medical · Escalating diuretics · Vasodilator therapy
Surgical · Over-sewing strategy (partial or complete) · Bioprosthetic replacement · Aortic valve ring annuloplasty
Percutaneous management · Transcatheter aortic valve implantation (TAVI) · Percutaneous occluder devices (PODs)

Table 16 Benefits and risks of different invasive approaches

Strategy	Technique	PROS	CONS
Surgical management	Partial over-sewing	Residual AI	20% incidence of moderate AI in 6 months
	Complete over-sewing	No residual AI	Higher mortality
	Bioprosthetic replacement	No residual AI	Only destination therapy Long term failure due to leaflet fusion
	Aortic valve ring annuloplasty	Reduces AI Landing zone for TAVI	Residual AI
Percutaneous management	Transcatheter aortic valve implantation	No residual AI	Risk of device migration Access site-related bleeding Vascular complication
	Percutaneous occluder device (PODs)	No residual AI	OFF label

LVAD parameters often show reduced flow, power and pulsatility. TTE is the diagnostic test of choice for diagnosing tamponade (Fig. 10).

Differential and Diagnosis

Few other conditions can mimic tamponade (Table 17) [23]. Given this narrow differential, chest radiography, TTE and invasive hemodynamic assessment should be performed rapidly. If initial tests are unrevealing, computed tomography for pulmonary embolus and assessment of inflow and outflow grafts should be considered. Usually TTE is adequate for diagnosing cardiac tamponade; however, in post-surgical patients, isolated effusions can occur (i.e. behind and compressing the left atrium) and transesophageal echocardiography (TEE) may be needed to identify the effusion and cause of tamponade.

Management

Tamponade is a surgical emergency and should prompt immediate return to the operating room for evacuation and determining the cause of tamponade. Pericardiocentesis can be performed as a temporizing measure for hemodynamic deterioration but is not definitive management.

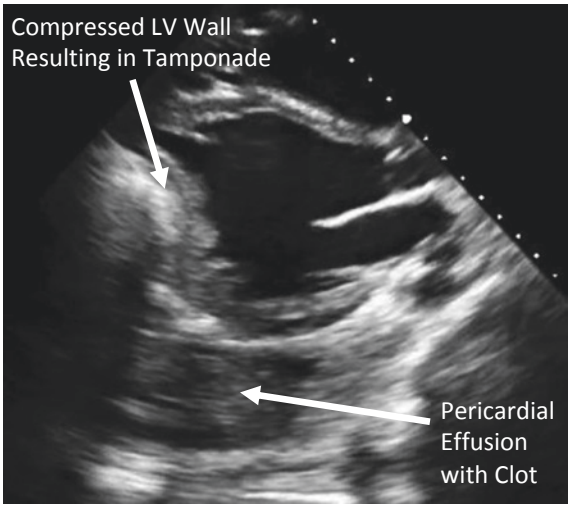

Fig. 10 Blood in pericardial space after LVAD implantation leads to LV compression and tamponade physiology requiring surgical evacuation

Table 17 Differential for cardiac tamponade

RHF	Cardiac tamponade
Pneumothorax	Pulmonary embolus
Inflow obstruction	Outflow obstruction

Infection

Presentation

LVAD patients are susceptible to community acquired infections but also have the unique risks of implanted hardware that can develop a chronic infection and externalization of the driveline that allows an entry point for infection. The International Society of Heart and Lung Transplantation (ISHLT) has divided infections into those specific to the VAD, VAD related, and non-VAD related (Table 18) [24]. LVAD related infections occur in 20–30% of patients within the first year after implantation. The most common VAD specific infections are driveline (Fig. 11) occurring in up to 50% of patients followed by bloodstream infections that may or may not be VAD related [24–26].

Presenting symptoms may be similar to a community acquired infection (i.e. fever and productive cough with pneumonia) or more indolent such as a change in odor or drainage from driveline, low-grade fever, malaise, or anorexia. Infection should be closely monitored for with routine evaluation of the driveline, and there should a low threshold to evaluate for infection in any patient presenting with symptoms concerning for infection or non-specific symptoms. Risk factors for LVAD specific infections are listed in Table 19 [25–27].

Table 18 Infection classification in VAD patients

VAD specific · Pump related · Pocket related · Driveline related
VAD related · Infective endocarditis · Bloodstream infections (may or may not be directly related to LVAD) · Mediastinitis
Non-VAD related · Pneumonia · Cholecystitis · Urinary tract infections

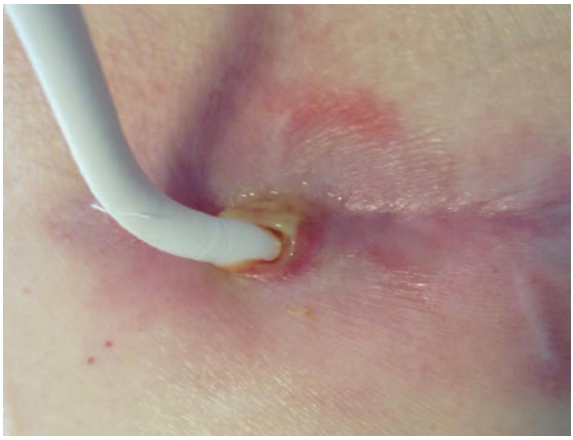

Fig. 11 Infected Driveline with Erythema and Purulent Discharge

Table 19 Risk factors for LVAD specific infections

Younger age
Higher BMI
Diabetes mellitus
Driveline site trauma
Exposed velour at driveline

Infectious Etiologies

Most VAD infections are bacterial in nature; however, fungal infections can occur in critically ill or immunosuppressed patients. The most common bacterial cause is gram-positive cocci including *Staphylococcus aureus* and coagulase-negative *Staphylococci*. Nosocomial gram-negative infections are the next most common bacteria and include *Pseudomonas, Enterobacter,* and *Serratia* [24, 26, 27]

Evaluation

A high index of suspicion should be maintained for a VAD related infection as symptoms and signs can be non-specific and patients are equally at risk for non-VAD infections as VAD related. A complete history and review of systems should be performed to find possible clues to an infection and/or cause. Physical examination should pay specific attention to surgical sites, the driveline exit site, and LVAD parameters. LVAD parameters may be abnormal from a non-VAD systemic infection causing vasodilation. All patients with suspected infection should have a white blood cell count, inflammatory markers (CRP, ESR, procalcitonin), and blood cultures sent. Blood cultures should be sent as 3 sets with a set at least 12 h separated similar to Duke Criteria for endocarditis, which have been adapted for determining a VAD-specific infection [24]. Additionally, urinalysis with culture, chest x-ray and possibly stool studies should be performed. Further testing and management are driven by the presumed cause of infection and results of cultures.

For patients with suspected driveline infection and negative blood cultures, testing is directed at evaluating the extent of driveline infection. The exit site should be thoroughly inspected for erythema, fluctuance and purulence. If pus is coming from the site, a sample should be sent for culture and examined for bacteria and fungus. Ultrasound imaging should be performed to evaluate for fluid collections around the driveline exit site and pump pockets, if accessible. CT imaging may also be used to evaluate possible fluid collections or abscesses. Based on culture and imaging findings, treatment approaches may vary [24].

When blood cultures are positive in a VAD patient, evaluation focuses on determining if this is a VAD specific infection. TTE, often followed by TEE, is performed to assess for vegetations related to the VAD or potentially other implanted devices (i.e. defibrillator). CT imaging is often performed to assess sources of infection that may or may not be VAD related (i.e. pneumonia, sternal wound infection, pump pocket fluid collection). Tagged white blood cell scans may be needed to help locate sources of infection but can return non-specific findings.

Treatment

Non-VAD related infections should be treated according to standard practice. Treatment of VAD related and specific infections should often be determined in conjunction with infectious disease consultation. General treatment recommendations are outlined in Table 20 [24, 26]. Of note, for many VAD related/specific infections, chronic suppressive antibiotic therapy may be needed.

Table 20 General treatment algorithms For VAD related/specific infections

Infection	Findings	Treatment
Localized driveline infection	Expanding erythema around driveline exit site, potentially purulent discharge	Two to four weeks of antimicrobial therapy. Chronic suppressive therapy NOT needed
Deep infection	Erythema at exit site, purulent discharge, possible fluctuance, ultrasound or CT findings of fluid/possible abscess	Two to four weeks of antimicrobial therapy Likely to need chronic suppressive therapy Surgical debridement may be needed
Pump/pocket infection	Sepsis, fluid collection/ abscess on imaging studies	Surgical debridement recommended Two to four weeks antimicrobial therapy followed by chronic suppressive therapy
Device infection or Bacteremia with presumed device infection	Sepsis, cultures meeting modified Duke's criteria for VAD infection per ISHLT guidelines	Treat as endocarditis, ≥6 weeks antibiotic therapy followed by chronic suppressive therapy Discuss surgical options, if any

Clinical Vignette: Conclusion

The patient was deemed too high surgical risk excluding option of device replacement. A continuous infusion of intravenous heparin was started and a second anti-platelet agent (dipyridamole 800 mg per day) was administered. Nevertheless, HVAD parameters continued to worsen (Flow > 10 L/min) and after 24 hours, the patient showed signs of cardiogenic shock (peripheral hypoperfusion, central venous pressure > 19 mmHg). Thus, the decision to perform fibrinolysis was made: fluoroscopy guided intraventricular thrombolysis was performed and Alteplase was administered (10 mg over 10 min every 15–20 min three times repeated a total of three times). After the third infusion, there was a complete resolution of adverse parameters with stable flows and power consumption. The patient was discharged on hospital day 15.

Key Points

- With an increasing number of LVADs implanted and prolonged use, complications are becoming increasingly prevalent.
- Pump thrombosis, although an uncommon complication, has substantial clinical implications and can lead to catastrophic pump failure or other complications such a stroke.

- Right heart failure can present anytime after LVAD implantation, but frequently presents in the immediate post-operative period.
- Bleeding can be quite frequent and occur up to two thirds of patients on LVAD support.
- LVAD patients are at increased risk for both ischemic and hemorrahgic stroke. Almost 20% of LVAD patients will suffer a stroke within the first year after implantation, although with new generation devices, this is less prevelant.
- Arrhythmias can occur in half of LVAD patients, ranging from atrial fibrillation to persistent ventricular tachycardia.
- Although LVAD patients are susceptible to community acquired infections, they are at unique risk of developing infection with implanted hardware and also infection at the exit site of driveline externalization.

Future Directions

While the newer generation of LVADs improve the hemocompatibility experienced with chronic hemodynamic support, complications continue to be of chief concern when managing patients and these devices. One of the exciting development in the next generation of devices may be eliminating the driveline exit site entirely. Both Abbott and Medtronic have dedicated enumerable resources to percutaneous battery charging, thereby eliminating the driveline all together. This development would improve the risk for infection and allow more mobility for LVAD patients.

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