




Troubleshooting Left Ventricular Assist Devices: Modern Technology and Its Limitations

Alfredo L. Toll, MD¹

Luis Hernandez Mejia, MD^{2, *} 

Amandeep Sidhu, MS³

Andres Carmona-Rubio, MD, FACC⁴

Address

¹Universidad Iberoamericana, Santo Domingo, Dominican Republic

^{*,2}Cleveland Clinic Florida, Weston, FL, USA

Email: lahm2011@gmail.com

³Midwestern University, Glendale, AZ, USA

⁴Cleveland Clinic Foundation, Cleveland, OH, USA

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Abstract

Purpose of review As the incidence of heart failure continues to rise, modern generation left ventricular assist devices (LVADs) have become the primary therapeutic modality used as both bridge to transplant (BTT) and destination therapy (DT) in patients with acute and chronic heart failure. This review aims to highlight the progression of LVAD technology, outline LVAD complications and manifestations, and provide evidence-based therapeutic methods to troubleshoot such adverse events.

Recent findings Despite modern innovation, LVAD adverse events continue to hinder the progress of HF paradigms and are associated with a rise in morbidity and mortality. Complications such as bleeding, pump thrombosis, right heart failure, infections, stroke, valvular insufficiency, and arrhythmias are among the most described.

Summary While the management of LVAD complications is described, standardized guidelines are needed to properly identify and troubleshoot all the complications faced by this patient population to decrease morbidity and mortality further.

Introduction

With an aging population, heart failure (HF) prevalence continues to rise across the world. An estimated 6.2 million American patients >20 years old had HF between 2013 and 2016, compared with an estimated 5.7 million between 2009 and 2012 [1]. The incidence of HF is 650,000 patients per year, with 50% reaching end-stage HF and over 300,000 succumbing to the disease [2]. While heart transplantation (HT) continues to be the gold standard intervention for patients with end-stage HF, nationwide HT rates do not meet the demand.

Left ventricular assist devices (LVADs) have formed the foundation in mechanical circulatory support (MCS) for patients with severe acute and chronic HF [3]. While its initial use was isolated as a bridge to transplant (BTT) in patients awaiting HT, LVAD implantation has become a new therapeutic modality used as destination therapy (DT) in patients that are poor surgical candidates for transplantation [3]. Notably, a recent analysis of the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) demonstrated that specific subsets of DT-LVAD had comparable 2-year survival rates compared to HT recipients [4].

LVAD progression through time

Left ventricular assist devices are implantable MCS devices whose role is to pump blood from the left ventricle (LV) into the aorta to maintain hemodynamic stability. An inlet cannula is placed in the LV apex; blood subsequently enters a pump and is transferred through the outflow graft into the ascending or descending aorta [5]. Since its FDA approval in 1994, improvements in LVAD technology and outcomes have led to a rise in its implementation as BTT and DT. The first-generation LVADs, Berlin Heart EXCOR, Thoratec PVAD, and XVE, consisted of either pneumatically or electronically driven membrane pumps generating a unidirectional pulsatile flow with artificial heart valves. These LVADs had several disadvantages: large size, significant surgical dissection, noise emission, infection of cannulas, malfunction induced by tears in the membrane or degradation of valves, and limited durability (\approx 18–30 months) [3, 5]. Independent of these limitations, they were shown to increase patients' quality of life with end-stage HF compared to optimal medical therapy [6].

Second-generation LVADs were introduced in the 1990s and consisted of continuous flow (CF) devices with axial and centrifugal mechanisms. This variation

improved patient outcomes by reducing infection susceptibility and a significant reduction in size and noise. The first CF LVAD approved by the FDA as BTT and DT was the HeartMate II (Fig. 1B). Due to its new structural and functional modifications, these devices' durability increased to a minimum of 5 years. This enhanced the overall quality of life, led to the restoration of end-organ function, and was associated with improved survival compared to first-generation pulsatile flow devices [3, 6].

Third-generation LVADs include HeartWare (Fig. 1A1/A2) and HeartMate III (Fig. 1C1/C2); both examples have incorporated modern-day innovation to optimize device size and functionality. The main characteristics include a radial pump with magnetic and hydraulic positioning, reduced size allowing for biventricular implantation, durability of \approx 10 years, and can maintain complete circulatory support with a flow of up to 10 L/min. They can also be implanted using a bilateral thoracotomy surgical approach compared to a full sternotomy required for prior generations. The HeartWare HVAD device is fitted with a periodic speed modulation system (Lavare cycle), allowing alterations of flow patterns every 60 s to prevent blood stasis [7]. Similarly, the HeartMate III is a CF device that generates a pulsatile flow pattern by modifying rotor speed, thereby decreasing the incidence of blood stasis in the LV and limiting the risk of hemorrhagic and thrombotic complications [3].

Multiple studies have compared the HM2 vs. HM3 or HVAD. The ADVANCE trial showed that the HVAD device was noninferior to the HeartMate II device as BTT with a 1-year survival of 86% and enhanced quality of life and functional capacity [4]. Additionally, the ENDURANCE trial demonstrated noninferiority of the HVAD compared to the HeartMate II as DT in survival at 2 years free from disabling stroke and alive on the initially implanted device [8, 9]. Lastly, in the MOMENTUM 3 trial, the HeartMate III demonstrated superiority over the HeartMate II in its composite outcome of survival without disabling stroke and reoperation secondary to device malfunction (79.5% vs. 60.2%) [3].

Left ventricular assist device indications and contraindications

According to the American College of Cardiology and the American Heart Association, LVAD implantation is indicated in patients with NYHA class IV that is refractory to optimal medical therapy, left ventricular ejection

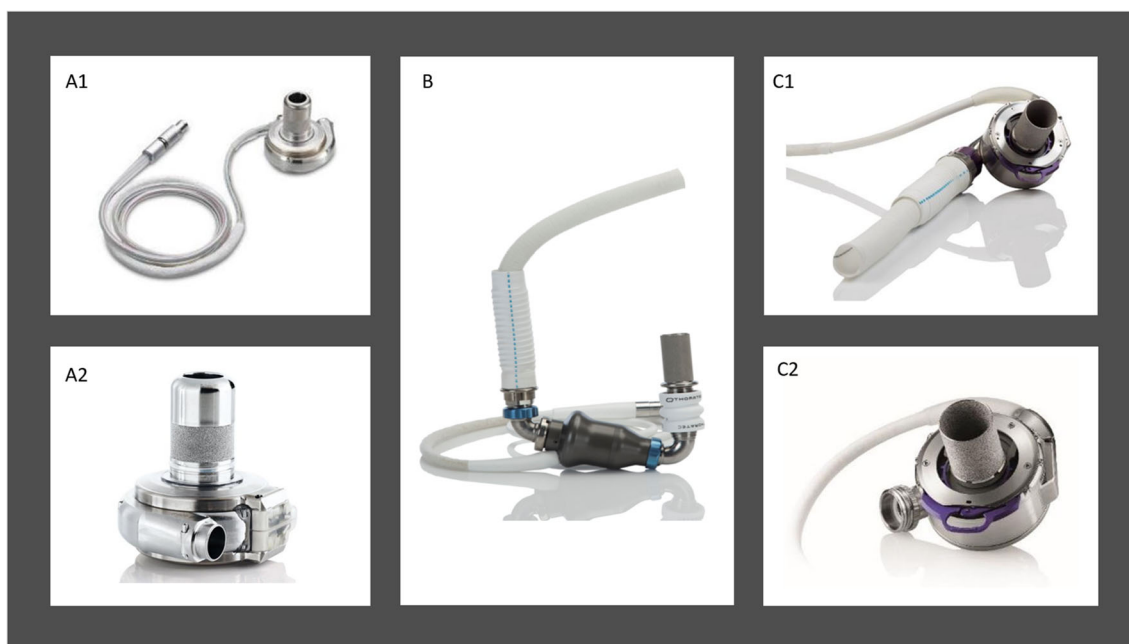


Fig. 1. **A1/A2** HeartWare HVAD, **B** HeartMate II LVAD, and **C1/C2** HeartMate III LVAD. HeartMate II™ LVAD and HeartMate 3™ LVAD images, reproduced with permission of Abbott Laboratories. Medtronic HeartWare HVAD images, reproduced with permission of Medtronic.

fraction (LVEF) <25%, systolic blood pressure (SBP) <90 mmHg, pulmonary capillary wedge pressure (PCWP) >20mmHg, and cardiac index <2.0 L/min/m² despite continuous IV inotropic therapy or intra-aortic counterpulsation. Malignant arrhythmias and patients on the heart transplant waiting list can also receive LVADs [3, 5]. LVAD contraindications include diverse comorbidities and socioeconomic considerations that must be addressed before implantation. Implantation contraindications are right ventricular dysfunction, coexisting terminal comorbidities such as end-stage renal disease (GFR <30 or creatinine clearance <30 mL/min), pulmonary disease (obstructive/restrictive lung pattern, O₂ requirement, pulmonary infarction within the past 6 weeks), liver disease (bilirubin >2.5 or an international normalized ratio (INR) >2.0 with cirrhosis or portal hypertension), neurological disease, and evidence of advanced metastatic cancer [8]. Hematologic complications such as active bleeding, thrombocytopenia, and confirmed heparin-induced thrombocytopenia can also be limiting factors, not only because of the risk of bleeding but the inability to have proper anticoagulation. Anatomic factors such as hypertrophic cardiomyopathy and ventricular septal defects can also be contraindicated for device placement and function.

Social considerations are of high importance since LVAD management requires a high degree of patient compliance and adequate psychosocial support to comply with medication and device maintenance [5].

Left ventricular assist device complications

Complications related to LVAD implantation can be divided into those that are LVAD-associated and LVAD-specific. LVAD-specific complications consist of device malfunction/failure 2–3% and pump thrombosis (PT) 1.1–12.2%. LVAD-associated complications include gastrointestinal (GI) bleeding 15–30%, cerebrovascular accident (CVA) 13–30%, device-related infections 15–24%, right HF 15–25%, dysrhythmias <1%, and valvular regurgitation 30% at 2 years (Table 1) [8–10].

LVAD complications can also be subdivided based on time frame (early vs. late). Surgical bleeding (intra-thoracic and/or mediastinal hemorrhage), PT, driveline infections (DLI), and right HF are among the most common early postoperative complications. On the other hand, device failure, GI bleeding, valvular regurgitation, and CVA's typically develop as late complications [11]. However, it is important to note that according to the AHA, right HF, PT, device-related infections, and CVA's can have a varied time of presentation and require

Table 1. Complications related to LVAD implantation

Complications	Incidence rate	Diagnostic modality	Intervention strategy
Early complications			
Early bleeding requiring RBC transfusion	Kilic et al. 50–85%	Hemodynamic parameters, Hgb levels	<ul style="list-style-type: none"> •Correction of coagulopathy •Red blood cell transfusion may be necessary •Re-exploration if chest tube output is >200 mL/h following correction of coagulopathy
Early bleeding requiring reoperation	Kilic et al. 30%	Chest tube outputs of >200 mL/h	
Pump thrombosis	Han et al.	1.1–12.2% Kilic et al. 2–9% Thiha et al. 2%	Hemolytic biomarkers, echocardiogram
<ul style="list-style-type: none"> •Assess LVAD parameters and patient hemodynamic stability •Assess biomarkers for hemolysis (LDH, Hgb, and bilirubin) •Augment anticoagulation and antiplatelet therapy •If the patient is unresponsive, pump exchange should be evaluated 			
LVAD infections	Han et al. 15–24% Kilic et al. 50% Thiha et al. 16–24%	Clinical	<ul style="list-style-type: none"> •Obtain local wound and blood cultures •Imaging if suspicious for driveline infection or if bacteremia is present •Broad-spectrum antibiotics and possible surgical debridement •LVAD removal may be required in the case of sepsis, septic emboli, or end-organ dysfunction
Right heart failure	Han et al. 15–25% Kilic et al. 15–25% Thiha et al. 14%	Echocardiogram, right heart catheterization	<ul style="list-style-type: none"> •Assess for right-sided vs. left-sided heart failure •Optimize LVAD speed and diuresis •Medical therapy to improve RV contractility and dilate the pulmonary vasculature •Consider RVAD implantation
Late complications			
Stroke	Han et al. 13–30% Kilic et al. 10–15% Thiha et al. 8–16%	CT or MRI	<ul style="list-style-type: none"> •Activate stroke team •Hold anticoagulation until imaging is performed •Obtain NC-CT, INR, platelet count and Glasgow coma scale

Table 1. (Continued)

Complications	Incidence rate	Diagnostic modality	Intervention strategy
Device		malfunction/failure	<ul style="list-style-type: none"> •Ischemic stroke - CT angiogram and potential endovascular therapy should be considered. Poor surgical candidates should receive anti-platelet and anticoagulation in consultation with the stroke team and LVAD specialist •Hemorrhagic stroke - Neurosurgical consultation and reversal of anticoagulation <p>Han et al. 2–3% Kilic et al. <5% Thiha et al. 2–3%</p>
Clinical, LVAD alarms	<ul style="list-style-type: none"> •Ensure device 	connections are secure <ul style="list-style-type: none"> •Review LVAD alarms •Evaluate LVAD parameters (flow, power, PI) and patients’ clinical stability •If device malfunction is not amenable, pump exchange may be required 	
Arrhythmia	Han et al. <1% Thiha et al. <1%	EKG	<ul style="list-style-type: none"> •Consider rate control and anti-arrhythmic medications •Cardioversion if hemodynamically unstable •Ablation therapy for unstable patients with AFL and segmental pulmonary vein isolation for unstable patients with AF can be considered •Optimize fluid status
Valvular regurgitation	Han et al. 30% at 2 years	Echocardiogram	<ul style="list-style-type: none"> •Optimize LVAD speed and pulsatility •Diuretics for symptomatic relief •Surgical or transcatheter valve repair or closure
Late bleeding (GI)	Han et al. 15–30% Thiha et al. 19–20%	Endoscopy, colonoscopy If (-): Balloon enteroscopy, diagnostic mesenteric angiography, tagged RBC scan, or capsule endoscopy	<ul style="list-style-type: none"> •Hold aspirin and anticoagulants •Initiate PPI’s and administer blood products as necessary •Monitor hematologic parameters •Perform upper and lower endoscopy to isolate source •For severe bleeding, consider reversal of anticoagulation after consulting with an LVAD specialist •Endoscopic control can be successful; however, surgical exploration may be required

significant vigilance to prevent an elevated morbidity and mortality [8].

Pump thrombosis

Pump thrombosis (PT) occurs when a blood clot is lodged within the inflow/outflow cannula, pump rotor, or conduit; this can lead to pump failure and subsequent circulatory collapse. A multi-institutional review of ≈ 900 HeartMate II patients demonstrated an abrupt increase in PT rate 3 months post-implant from 2.2% in 2011 to 8.4% in 2013 [4]. The HeartWare device also reported an 8.1% incidence of PT; however, the incidence has remained stable since 2008 [4]. Comparatively, in the MOMENTUM 3 trial, the HeartMate 3 was associated with a 1.1% rate of PT vs. 15.7% with the HeartMate 2 (HR, 0.06; 95% CI, 0.01 to 0.26; $P < 0.001$) [12].

Though device hemocompatibility is improving, high awareness is essential for early diagnosis and medical intervention. Early thrombus detection is critical in all LVAD platforms since early medical intervention for moderately elevated LDH levels (2.5–3.2 \times the upper limit) may increase the likelihood of successful medical management without the need for surgical intervention. Uriel et al. reported that an LDH 5 \times the upper limit of normal was 100% sensitive and 92% specific for diagnosing PT [4]. Patients will typically present asymptomatic, with worsening HF, a new thromboembolic event, or pump parameters changes. The biomarkers for hemolysis (LDH, plasma free hemoglobin, and indirect bilirubin) and device parameters (flow, power, and pulsatility index (PI)) should be assessed in conjunction with clinical symptoms to increase the diagnostic sensitivity and specificity [13].

Risk factors for PT can be categorized as patient-related, device-related, and management-related. Patient-related factors include prothrombotic conditions such as HF, infections, malignancy, and hypercoagulable states. Device-related factors include the pump's regional heat, outflow graft kinking, extrinsic compression, and slow pump speed. An important risk factor for PT is inadequate anticoagulation; this can occur secondary to medical noncompliance and reduction/discontinuation of anticoagulation secondary to bleeding events [4].

Pump thrombosis prevention is imperative and includes the administration of aspirin 81–325 mg for 2–5

days post-implantation. The patient should be properly anticoagulated with a heparin bridge as the chest tube output decreases. During the first 2 days post-op, the goal for aPTT is 40–45; this should be increased to 60–80 if no bleeding is evident. The INR goal is 2.0–2.5 with Coumadin 5–7 days post-op [13].

Therapeutic intervention of PT varies depending on the LVAD platform. The International Society for Heart and Lung Transplantation (ISHLT) published an algorithm for managing suspected pump thrombosis in the HeartMate II device. In the case of malposition or kinked inflow cannula or outflow grafts, surgical intervention is required. In cases where imaging demonstrates good positioning, no obstruction, and poor LV unloading, admission to the ICU for medical management with inotropes, diuretics, and intravenous heparin may be needed. Unfractionated heparin as a means of anticoagulation typically provides temporary improvement but is associated with a high recurrence rate and increased stroke risk [4]. If there is no resolution of decreased ventricular unloading, power elevations, and hemolysis, then antiplatelet agents such as glycoprotein IIIb/IIa inhibitors or direct thrombin inhibitors should be added. If the patient is unresponsive to the aforementioned, pump exchange, urgent transplantation, or explantation should be evaluated, with thrombolytics considered for poor surgical candidates [4].

Bleeding

Bleeding is the most common complication following LVAD implantation, occurring in both the perioperative and postoperative period. In the HeartMate II BTT trial, the rate of bleeding requiring reoperation was 31%, with 53% of patients requiring at least two units of transfused red blood cells (4). Perioperative bleeding is generally suspected with chest tube outputs of >200 mL/h in patients with normal coagulation parameters. Increasing central venous pressures (CVP), increasing pressor requirements, and decreasing LVAD flows can also raise clinical suspicion for surgical bleeding. Early rather than delayed re-exploration is generally advised as massive transfusions can result in right heart failure [4].

Gastrointestinal bleeding occurs in approximately 20% of LVAD patients. Firstly, LVAD rotors generate high shearing forces that lead to the Von Willebrand factor's degradation and subsequent acquired Von Willebrand syndrome. CF devices generate low pulse

pressure, which causes GI hypoperfusion leading to mucosal ischemia and angiodyplastic lesions. Arteriovenous malformations (AVM) may also be induced via the stimulation of pro-angiogenic factors secondary to the non-pulsatile blood flow [10]. Most LVAD patients are also treated with anticoagulation and antiplatelet regimens, further increasing the risk of bleeding events [4, 6]. In a recent observational study, the use of angiotensin receptor blockers or angiotensin-converting enzyme inhibitors was associated with reduced AVM-related GI bleeding. Alternative retrospective studies have shown beneficial effects using digoxin, omega 3, LVAD speed adjustments, thalidomide, and estrogen therapy [13, 14].

It is essential to distinguish between GI bleeding, diffuse coagulopathy, and surgical bleeding. Monitoring hematologic parameters, including prothrombin time, partial thromboplastin time, platelet count, and fibrinogen levels, helps guide therapeutic interventions with platelets, fresh frozen plasma, and/or cryoprecipitate. Management involves immediate discontinuation of anticoagulation and antiplatelet agents, initiating intravenous proton pump inhibitor therapy, and administering blood products as necessary. Upper and lower endoscopy can be performed to localize the bleeding source. If negative, balloon enteroscopy, diagnostic mesenteric angiography, a tagged red blood cell scan, or capsule endoscopy can be pursued. Endoscopic control of bleeding can be successful in some cases; however, surgical exploration is sometimes indicated in ongoing or massive bleeding not amenable to endoscopic management [4].

Cerebrovascular events

A cerebrovascular accident (CVA) is the most dreaded complication of LVAD implantation, occurring in 13 to 30% of patients [8]. Both ischemic and hemorrhagic variants occur either immediately post-operatively or several months later, with ischemic etiologies being more common than hemorrhagic (5.5% vs. 3.1% annual incidence). Ischemic CVA's (ICVA) have been attributed to embolic sources, such as thrombus deposition, partial obstruction of the inflow cannula, deformation of blood in the pump apparatus, outflow graft obstruction, subtherapeutic anticoagulation, or infection. On the other hand, hemorrhagic CVA's (HVCA) are predominantly associated with anticoagulation therapy,

hypertension, endocarditis, and hemorrhagic conversion of ischemic strokes [5, 8].

The INTERMACS registry found an estimated stroke rate of 3%, 5%, and 11% at 1 month, 3 months, and 1 year with the use of CF-LVADs [4]. The ENDURANCE Supplemental Trial failed to demonstrate the HVAD vs. HeartMate II noninferiority concerning stroke outcome. However, the trial confirmed that BP management was associated with a reduced risk for stroke in HVAD subjects. This study supports the ISHLT recommendations regarding BP management in patients with durable MCS, confirming the importance of BP monitoring twice daily for at least the first 3 months post-implantation. The MOMENTUM 3 trial demonstrated a lower incidence of stroke with the HeartMate III device than the HeartMate II (10.1% versus 19.2%) at 2 years [8].

According to Teuteberg et al., the major risk factor for a HCVA was an elevated mean arterial pressure (MAP). The prevalence of ICVA and HCVA was 6.8% and 8.4%. The 6-month survival for those with an ICVA was similar to patients that did not have a CVA (91% vs. 93%; $p = 0.51$). However, HCVA were associated with significantly worse survival (72% vs. 93%; $p < 0.0001$). Multivariable predictors of ICVA were aspirin ≤ 81 mg and atrial fibrillation (AF); predictors of HCVA were MAP > 90 mm Hg, aspirin ≤ 81 mg, and an INR > 3.0 . Sites with improved BP management protocols showed a significant reduction in the prevalence of HCVAs (8.4% vs. 2.6%; $p = 0.037$). Standard practices among these sites included targeted MAP of ≤ 90 mmHg, utilizing a pressure-driven drug therapy protocol, and close BP surveillance until the MAP was under control [15].

In LVAD patients who present with a new focal neurologic deficit, it is imperative to immediately evaluate the INR, platelet count, Glasgow Coma Scale, and a non-contrast CT. In patients on antiplatelet therapy who present with a hemorrhagic stroke on CT and an INR > 1.4 , prothrombin complex concentrates or fresh frozen plasma in addition to vitamin K, desmopressin acetate, and platelets should be administered immediately. However, if the INR < 1.4 , then only desmopressin acetate and platelets should be administered. In the case of ischemic stroke, a CT angiogram and potential endovascular therapy should be considered if the infarction site is less than 1/3 of the cerebral hemisphere, the onset was within 8 h, the National Institute of Health Stroke Scale is > 6 , and there are cortical or brainstem symptoms [4].

Device-related infections In addition to common postoperative infections, there are device-related infections that specifically affect patients with an implanted LVAD. Up to 50% of LVAD patients will experience some form of infection; thus, this constitutes the third leading cause for LVAD readmission and is associated with a higher mortality rate [13]. Although the prevalence of VAD-associated infections are improving with second- and third-generation devices, it continues to be a worrisome complication since 20% of VAD deaths are attributed to infections [6].

Elevated BMI is the most cited independent predictor of infection followed by history of trauma to the driveline site, young age (increased risk of trauma to the driveline), and duration of VAD therapy [16]. The ISHLT identified three primary categories of infection in LVAD recipients: (1) VAD-specific infections such as driveline or pump pocket infections (PPI), (2) VAD-related infections such as sternal-wound infections or bloodstream infections, and (3) non-VAD infections such as cholecystitis or urinary tract infections [6].

Although perioperative antibiotics are standard practice, alternative means of prevention have been described. One of the most important factors in preventing the morbidity of infections is the use of various anchoring devices to help stabilize the driveline; this minimizes trauma and tension at the exit site. Patients are also educated on routine driveline site care such as cleaning the exit site daily with chlorhexidine [17]. Chlorhexidine is preferred due to lower rates of DLI as compared with povidone-iodine solution (10.3% vs. 60.0%) [16]. Surgical techniques such as increasing intrafascial tunneling of the driveline and externalization of the silicone portion of the driveline can decrease infections [17]. A recent study found that increased tunneling of the driveline decreased LVAD infections by up to 86%, while complete implantation of the driveline velour reduced DLI by up to 50% [16].

Driveline infections are the most prevalent type of VAD-related infections, developing in 15.4–23.8% of CF-LVADs and typically occurring >30 days post-implantation [8, 16]. The percutaneous driveline is an ideal focus for pathogens, particularly in this patient population that is often critically ill, immune-compromised, or malnourished. DLI can also reflect the presence of a deeper infection of the device hardware (pump, cannula) or the pocket space. PPI occur in 2–10% of patients, those occurring in the first 30 days are likely caused by direct inoculation during surgery,

whereas later PPI are usually an extension of underlying DLI [16]. Due to the marked variability in the clinical presentation, vigilance is required for early recognition and aggressive intervention. LVAD-related infections typically occur within 3 months of implantation and can manifest with fever, leukocytosis, purulent drainage, tenderness, lethargy, and fatigue [4, 13]. Among the most common pathogens responsible for PPI and DLI are *Staphylococcus aureus*, *Staphylococcus epidermidis*, and *Enterococcus* [4].

Alternative LVAD infections are also described; internal component and bloodstream infections are less frequent but most commonly occur in the immediate postoperative period (<30 days post-implantation). Mediastinitis affects 2% of LVAD patients, typically in the immediate postoperative period, with mortality rates as high as 53%. Cardiovascular implantable electronic devices (CIED) commonly left in place following LVAD implantation can also serve as infectious foci with a reported incidence of 2.8% [16, 18].

In 2017, the ISHLT published a report detailing the medical and surgical management of LVAD infections; this should be thoroughly analyzed for accurate implementation [16]. Superficial and localized DLI may be treated with IV/PO broad-spectrum systemic antibiotics for 2 weeks alone, although in some cases (fluid collection), surgical debridement with driveline revision may be needed. Antibiotic regimens typically include a beta-lactam and/or vancomycin for gram positive organisms, a cephalosporin, and/or quinolone for gram negative organisms and fluconazole for fungal prophylaxis [16]. Deep DLI/ PPI require IV antibiotics for 6–8 weeks followed by long-term PO suppression. Surgical debridement and new driveline exit site may be required. Pump/cannula infections require IV antibiotics until after heart transplant in patients with BTT or an extended course followed by PO suppression in patients with DT. Surgical drainage, debridement, or explant may be required. Urgent device replacement should be considered in BTT to prevent end-organ damage that may prevent heart transplant. Antibiotic regimen/duration for bacteremia is highly dependent on the source, organism, and clearance. The antibiotics should be continued for at least 2 weeks from the first negative blood culture [16]. In the case of bacterial mediastinitis, antibiotics should be continued for 6–8 weeks following the last surgical debridement. Muscle or omental flaps or vacuum-assisted closure therapy may be utilized in

severe cases. CIED pocket infections can be managed by device removal, implantation in the contralateral side once blood cultures are negative, and a limited course of systemic antibiotics for 10–14 days [18]. However, CEID removal is generally recommended in cases of primary CEID infection due to the high mortality rate [16]. In some cases, LVAD removal may be required if they are associated with sepsis, septic emboli, or end-organ dysfunction [4].

Right ventricular failure Right ventricular failure (RVF) after LVAD implantation generally affects up to 40% of LVAD patients [4]. A commonly utilized definition is the need for postoperative inotropes for >14 days, inhaled nitric oxide (INO) for >48 h, the need for right-sided MCS, or hospital discharge on an inotrope after LVAD implantation. The presence of at least two of the following hemodynamic parameters in the absence of tamponade can also signal right heart dysfunction post-LVAD implant: a cardiac index <2.0 L/min/m², mixed venous oxygen saturation <55%, CVP >16 mmHg, and MAP <55 mmHg [4].

Prevention of RVF relies upon optimization of preload, contractility, and afterload in the perioperative period. Aggressive diuresis to maintain CVP <15 mmHg is essential. Pulmonary vasodilators may be needed to reduce elevated pulmonary artery pressures and reduce right ventricular afterload. Correction of coagulopathy and meticulous hemostasis are also important components of right HF prevention as these can decrease the utilization of blood products and reduce volume overloading [4].

If RVF occurs after LVAD implantation, medical therapy with agents such as dobutamine, milrinone, inhaled NO, and epoprostenol may improve contractility and dilate the pulmonary vasculature. Beta-blockers and ACEi are not ideal in the management of RV dysfunction post-LVAD and should be avoided. The heart rate must be maintained between 80 and 100 bpm; this can be achieved via cardioversion, MgSO₄ or digoxin if >100 bpm and DDD pacing, adrenaline or isoproterenol if the HR is <80 bpm. Normal sinus rhythm can be maintained/restored by using MgSO₄, amiodarone, or lidocaine [19].

Patients who are considered high risk for RVF preoperatively may be selected for upfront mechanical biventricular support using designated risk scores [4, 20, 21]. However, the application of scoring systems has proven difficult since the predictive capacity has been limited outside of their respective cohorts.

Echocardiographic and hemodynamic markers for RVF include severe TV regurgitation, RV ejection fraction <30%, right atrial diameter >50mm, decreased right ventricular stroke work index, and elevated serum bilirubin, creatine, pulmonary artery pressure, or central venous pressure [22]. In these circumstances, a temporary right VAD may be inserted at the time of LVAD implantation [22]. Patients who required early RVAD were statistically more likely to have a more advanced INTERMACS profile, higher BUN, higher mean RA pressure, lower pulmonary artery pulsatility index (PAPi), and higher CVP/PCWP ratio [23]. Peripheral venoarterial extracorporeal membrane oxygenation (ECMO) can also be used to support the RV as it recovers after LVAD implantation. However, it is less effective at unloading the ventricle and can be associated with thromboembolism, major bleeding, and extremity hypoperfusion [4].

Arrhythmias Ventricular arrhythmias (VA) are common following LVAD implantation. Ischemia, fibrosis, inotropic/pressor therapies, mechanical induction from the inflow cannula, and suction events are attributed etiologies. The strongest predictor of post-LVAD VAs has VA before LVAD implantation. Early observational studies have noted good tolerance to VAs, with symptoms of weakness or palpitations and substantial protection from sudden cardiac death. Atrial arrhythmias (AA), particularly AF, atrial flutter (AFL), and other atrial tachycardia's, have also been reported. Although the strongest predictor for post-LVAD AF is pre-implant AF, ~20 to 30% of patients can develop de novo AF after LVAD implantation [24].

An observational study reported the occurrence of VAs in LVAD recipients to range from 20 to 50%, with ICD shocks in 16 to 42% [24]. A systematic review with 393 patients on CF-LVAD with VAs demonstrated that 37% experienced a new onset VA after LVAD implantation. Multivariable analysis identified six independent predictors of late VA: VAs before LVAD implantation, atrial fibrillation before LVAD implantation, idiopathic etiology of the cardiomyopathy, HF duration >12 months, VA <30 days post-LVAD, and no ACE inhibitors during follow-up. A "VT-LVAD score" identified four risk groups: low (score 0 to 1), intermediate (score 2 to 4), high (score 5 to 6), and very high (score 7 to 10). The rates of VA's at 1 year were 0.0%, 8.0%, 31.0%, and 55.0%, respectively [25, 26].

Ventricular arrhythmias can often be corrected with alterations in device settings, including reducing LVAD

speed to allow adequate ventricular filling. VT ablation should be considered in a patient with recurrent drug-resistant VA's resulting in hemodynamic compromise or recurrent ICD shocks [24].

Due to the lack of conclusive evidence regarding the efficacy of specific anti-arrhythmic medications in the LVAD population, further investigation is warranted to establish safe therapeutic practices with beneficiary effects on mortality and morbidity. As a result, current guidelines for treating AA's and VA's in the non-LVAD population can be used. Beta-blockers with/without digoxin are commonly used to achieve rate control in patients with a LVAD and AF [24]. Atrial arrhythmias with rapid ventricular response compromising LVAD performance should undergo electric or chemical cardioversion for rhythm control. Ablation therapy should be considered the first-line therapy for AFL in LVAD patients with hemodynamic compromise. Segmental pulmonary vein isolation has similarly been reported for poorly controlled AF [24]. Refractory cases require endocardial catheter ablation or device exchange [5, 27]. Although data on amiodarone's efficacy as a rhythm control strategy for either AA or VA patients with an LVAD is limited, 40% of patients with an LVAD are prescribed amiodarone 3 to 6 months following implantation [24].

Valvular regurgitation De novo aortic insufficiency (AI) post-LVAD is a significant barrier to long-term MCS, with >30% of the patients reaching moderate or severe insufficiency after 2 years. The underlying mechanisms are likely multifactorial, including changes in the aortic valve leaflets, altered root biomechanics, and excessive left ventricular unloading. Aortic insufficiency is also believed to be caused by the VAD generating a pressure gradient across the aortic valve; this leads to AV closure and eventual commissural fusion, resulting in blood volume recirculation, increased pump work, and HF exacerbation [8]. Early postoperative de novo AI can also be influenced by preoperative leaflet trauma from temporary percutaneous LVADs [13]. Risk factors for AI development include advanced age, lower body surface area, systemic hypertension, large aortic diameter, permanently closed AV, and support duration [28].

Speed optimization or maintenance of pulsatility can ensure AV opening and appears to preserve AV structure and function. Patients can be treated with diuretics for symptomatic relief and systemic vasodilators to reduce the gradients and enhance forward flow [29]. Alternative therapeutic modalities include AV closure

with occluder devices, replacement with a bioprosthetic valve, leaflet stitching (Park stitch or modified Park stitch technique), aortic patch closure, or cardiac transplantation [8, 29, 30]. TAVR has also been described as an alternative treatment modality for symptomatic AI in patients on CF-LVAD support [29].

Device malfunction Device malfunctions can be caused by technical problems related to the physical hardware. Algorithms and alarms have been designed to detect threatening device malfunctions and are incorporated into the device controller units [31]. In a recent study, controller-related malfunctions accounted for 30% of all malfunctions, premature battery failure 19%, patient cable failure 14%, pump failure 13%, and miscellaneous peripheral component failure (cables and monitors) 24% [32]. The ADVANCE trial reported 26 device malfunctions from 20 patients, and 6 of these malfunctions led to device replacement [31]. [CRA1]

Various parameters, including pump rotor speed, power, PI, and flow, must be monitored in conjunction with the patient's clinical status for early recognition of potential malfunctions [4]. The combination of high power, low PI and fluctuating pump speed can be an indication of underlying pump thrombosis or hypotension. On the other hand, low power, low PI and unchanged speed can indicate hypertension or inflow/outflow obstruction [4, 33]. As previously described, inflow/outflow obstruction can manifest with parameter alterations in conjunction with HF signs and symptoms. Management includes ensuring adequate hydration, supporting the RV, and evaluating for tamponade or a need to adjust pump positioning (34).

LVAD alarms vary by generation and type of VAD; thus detailed information regarding the specific VAD alarms is necessary for adequate management. The following are examples of HeartMate III alarms: "Connect power" indicates that one of the two power cables is disconnected, so the patient should promptly connect the disconnected power cable to the power source. "Replace power + low battery" indicates a low power input with < 15 min remaining, so the patient should promptly connect to a working or different power source. "Call hospital contact" indicates a system controller hardware fault, so the patient should contact the hospital. "Connect driveline" indicates that the driveline is disconnected. Immediately reconnect the driveline to the system controller and move the driveline safety tab on the system controller to the locked position. If the alarm persists after reconnecting the driveline, press any button

on the system controller to potentially resolve. If the driveline is connected and the alarm persists, replace the system controller with a programmed backup controller [34].

Percutaneous lead or motor failure manifests with pump vibration, not maintaining a set speed, and a high PI in association with HF symptoms, a decreased BP, and increased pulse pressure. If the controllers are defective, the pump should be run on batteries. If the lead is damaged, repair should be attempted; however, if not amenable, pump exchange may be required [4, 35].

Lastly, inflow valve regurgitation (IVR) can lead to ineffective decompression of the LV. This can lead to a volume overloaded state and the inability of the LVAD to empty the LV. Inflow valve regurgitation can be caused by a torn cusp or commissure dehiscence of a prosthetic valve; this results in high pump chamber pressures and can be secondary to significant hypertension and outflow graft twisting/distortion. Patients with IVR have significantly lower cardiac output, higher LVAD flows/rates, and a greater difference between the cardiac output and pump flow ($p < 0.001$) [36].

Conclusion

Left ventricular assist devices have become a therapeutic marvel as BTT and DT in patients with end-stage HF. Functional improvements have already resulted in size reduction, performance optimization, and enhanced clinical applicability. With the emergence of new generation devices, LVADs will continue to provide quality circulatory support and potentially replace heart transplantation as the therapeutic gold standard in the future. As their design continues to evolve, it is imperative to identify and isolate methods to troubleshoot device-related complications and establish a synergistic approach between a medical intervention and innovative engineering.

Compliance with Ethical Standards

Conflict of Interest

Alfredo L. Toll declares that he has no conflict of interest. Luis Hernandez-Mejia declares that he has no conflict of interest. Amandeep Sidhu declares that she has no conflict of interest. Andres Carmona-Rubio declares that he has no conflict of interest.

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