SMGroup

Anesthesia for Patients Undergoing Ventricular Assist Devices Implantation- Review

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ABSTRACT

Heart failure is a progressive disease, and patients at the end of life have few options, given the limitations of intravenous positive inotropes and a finite number of donor organs. Ventricular Assist Devices **(VADs)** have revolutionized long-term care for patients with congestive heart failure. Multiple different VADs have been developed. Originally introduced as a temporary bridge to recovery and then, as a bridge to transplantation, permanent or destination therapy for patients with refractory heart failure. Whilst advances in both technology and medical care have reduced the morbidity and mortality related to VAD use over the past decade, VAD continues to be associated with a high incidence of complications and adverse events (bleeding, tamponade, reoperation, right ventricular failure, arrhythmias, suction events, infections, thrombosis and thromboembolism, haemolysis, respiratory failure, neurologic events, renal and hepatic failure, device failure, cannula obstruction and aortic valve degeneration). Anesthetizing these critically compromised patients requires skillful anesthetic management, extensive monitoring and expert postoperative care. This review describes the current state of anesthesia in VAD support. First, we show the importance of specific perioperative issues to patients undergoing VAD implantations. Second, we show the role of echocardiography in the perioperative management of mechanical circulatory assistance (echocardiography is an ideal modality to monitor patients undergoing VADs because it is less invasive).

Keywords: Echocardiography; Heart failure; Propofol; Sevoflurane; Ventricular assist devices

INTRODUCTION

Ventricular Assist Devices **(VADs)** are pivotal treatment options for patients with end-stage heart failure. Cardiac transplantation is the most successful treatment modality for patients with end-stage heart failure. However, VADs are increasingly used owing to the shortage of appropriate donor organs and the long waiting times for heart transplantation. These devices have also been applied for destination therapy, as a bridge to recovery, and as a bridge to decision making.

Several features distinguish VADs placement from other procedures encountered by the anesthesiologist. These include the extreme degree of heart failure, the circulatory implications of Left Ventricular Assist Device **(LVAD)** therapy and device complications. Neurological events (stroke, which can be caused by hypoperfusion) are among the most common complications after placement of VADs; therefore, the choice of an appropriate LVAD is important in patients at greater risk of neurological damage. This problem has been analyzed for our group research. Our results show that cerebral blood flow can vary with the VAD used (our results showed greater cerebral blood flow during partial support in a new pulsatile device with a compliance chamber compared to the Berlin Heart device and Bio-Medicus centrifugal pump) [1]. The main purpose of a VAD is to unload the failing heart and help maintain forward cardiac output and vital organ perfusion. To improve the clinical output of the VAD, it is necessary to optimize perioperative conditions (continuous-flow VAD, hemodynamic monitors, and anesthetic drugs). Our results show the effect of anesthetics on organ blood flow in patients with a VAD (sevoflurane could be superior to propofol with respect to blood flow in the brain, liver, and heart tissue after implantation of VADs in a preclinical study) [2].

This chapter describes these and other issues that arise during VADs placement, as well as discusses a range of scenarios that can be encountered by the anesthesiologist in an active VADs program.

ANESTHESIA: DRUGS AND MONITORING

The implantation of VAD is a complex operative procedure. Anesthetics and techniques for induction of anesthesia should be selected with consideration of the patient's cardiac pathophysiology and other comorbid conditions. Preoperative assessment of the patient should be performed to evaluate cardiac status, renal and hepatic function as well as coagulation status and current drug therapy. The anesthesiologist must manage patients who are severely limited in their cardiac performance often with diminished renal and hepatic functions [3] and should be prepared to manage cardiac decompensation and acute desaturation before institution of Cardio Pulmonary Bypass **(CPB)** as well as right ventricular failure and severe coagulopathic bleeding after CPB [4].

Anesthetic Induction

No single "recipe" can guarantee hemodynamic stability during anesthetic induction [5]. The reduction in venous return is usually well tolerated in the heart failure (flat portion of the relationship of Frank-Starling mechanism), but the reduction of left ventricular preload can induce a bad hemodynamic tolerance in patients who received high doses of diuretics preoperatively [6]. Hypotension may result from a relatively hypovolemic state and vasodilation secondary to a reduction in sympathetic tone induced by anesthetics. Hemodynamics can be disrupted by the blockage of the sympathetic system during induction of anesthesia; in that case, the use of vasoactive agents must be considered for the purpose of balancing the systemic vascular resistance. Small doses of phenylephrine (or norepinephrine) may be used to help to maintain preload and afterload at adequate levels [3]. The intention is to maintain blood pressure to ensure adequate systemic perfusion as assessed by urine output and the absence of metabolic acidosis on blood gas analysis rather than to achieve normal hemodynamic parameters [7]. Mean Arterial Blood Pressure **(MAP)** should be maintained between 70 and 80 mm Hg [7] and should not exceed 90 mm Hg [8].

Intravascular volume optimization for VAD implantation is a crucial point. Before induction of general anesthesia, the volume deficiency should be estimated and carefully be substituted. After weaning from CPB, volume management should result in a sufficient VAD performance avoiding a collapse of the left ventricle [9].

In hemodynamically unstable patients, it is important that the anesthesiologist maintains the previous rates of inotropic and vasoactive drug infusions and optimizes intra-aortic balloon pump function before induction of anesthesia, using cardiac hemodynamic monitoring with radial arterial and central venous and pulmonary artery catheters in addition to standard, noninvasive tools. Transesophageal Echocardiography **(TEE)** is used for all patients, to assess ventricular function, contractility, cannulas position, volume status, and the presence of a thrombus or air [10].

In patients with end-stage heart failure, agents with the least hemodynamic effect, such as etomidate, ketamine, fentanyl, or midazolam, should be used for induction of anesthesia [4]. Vecuronium or rocuronium may be preferred as a neuromuscular blocking agent; rocuronium has become more popular than vecuronium in cardiac surgery. The intubated patient is mechanically ventilated targeting an end-tidal CO_2 partial pressure of 32-40 mmHg, with a tidal volume of 6-8 $mL.kg^{-1}$, because hypoxia and hypercapnia cause pulmonary hypertension. In these patients, Positive End-Expiratory Pressure **(PEEP)** must be used carefully, it is best adjusted to maintain lung compliance and right ventricle function (which can be monitored carefully with TEE) without compromising surgical exposure and operating conditions [9,11].

Monitoring

Standard monitoring (5-lead Electrocardiography **(ECG)**, pulse oximetry, capnography and core and peripheral temperature probes) and an invasive arterial blood pressure monitoring are mandatory [9]. Standard cardiac hemodynamic monitoring is used: a triple-lumen central venous catheter and a pulmonary artery catheter along with an introducer sheath. The central venous route is used in the majority of patients via Internal Jugular Vein **(IJV);** the subclavian route in others, usually with ultrasound-guided placement because of high incidence of central venous thrombosis. In a VAD implantation planned as a 'bridge-to-transplantation' scenario, puncture of the left IJV is recommended so that the right IJV can be preserved to facilitate endomyocardial biopsy post-transplantation to evaluate for cardiac rejection [12].

Although the use of Pulmonary Artery Catheters **(PACs)** has not demonstrated an overall benefit in direct improvement in mortality outcomes [13,14] and therefore cannot be recommended as a matter of routine, but a definite role is suggested in selected groups of patients undergoing cardiac surgery [15]. The placement of PAC is therefore recommended in this special setting [3]. Other alternatives for hemodynamic monitoring include the use of hemodynamic transesophageal echocardiography system [16]. Usually, it is constantly monitored central venous and pulmonary arterial pressures, central and rectal body temperatures, as well as intraoperative TEE [10,17]. Continuous measurement of cerebral oxygenation with near infrared spectroscopy is strongly recommended during the perioperative period [18].

Anesthetic Maintenance: Propofol and Sevoflurane

Given the clinical and hemodynamic inclusion criteria, it is expected that patients who are considered candidates for an LVAD are often critically ill, with severe heart failure and on multiple inotropic agents [3]. In patients with end-stage heart failure, hemodynamics depends on high catecholamine levels in the circulation. Cardiac failure is often associated with disturbances in cardiac output, autonomic nervous system activity, central and systemic venous pressures, and sodium and water metabolism [19]. It is also associated with hypoperfusion to various organs including the sites of drug clearance, i.e. the liver and kidneys. It also leads to organ congestion as seen in the liver and gut. The main changes in drug pharmacokinetics are a reduction in the volume of distribution and impairment of clearance [20]. As the circulation is slower owing to low ejection fraction and the distribution volume of drugs is lower than in normal physiology, drug concentrations are higher in these patients when conventional drug doses are used [21]. Therefore, anesthesiologists must be careful about the doses and effects of anesthetic drugs and allowing time to evaluate their effects.

Anesthesia can be maintained with either sevoflurane or desflurane at concentrations about 1.0 Minimum Alveolar Concentration **(MAC)** (2% sevoflurane or 4% desflurane in 50% oxygen-50% air). Since midazolam is absorbed completely and subsequently metabolized in the liver, the reduced plasma clearance in the congestive heart failure patients reflects reduced

hepatic blood flow and/or metabolic activity in such patients. In those patients, midazolam clearance is decreased by 30%. Nevertheless, the drug is well tolerated and does not cause any adverse effects [22]. Propofol and benzodiazepines given during surgery can be administered to prevent recall [11,23,24].

The main purpose of a VAD is to maintain perfusion of vital organs. It is known the beneficial effects of volatile anesthetics (sevoflurane) compared with intravenous anesthesia (propofol) on organ blood flow during cardiovascular surgery [25,26]. Sevoflurane tends to cause cerebral vasodilatation, increases cerebral blood flow **(CBF),** and decreases cerebrovascular resistance [27]. However, propofol produce cerebral vasoconstriction indirectly by reducing cerebral metabolism and causes a decrease in CBF that is well matched to cerebral metabolism [28]. CBF is lower with propofol than with sevoflurane [29]. Sevoflurane also induces preconditioning and attenuates myocardial ischemia/reperfusion [30] and provides cardio protection in patients undergoing Coronary Artery Bypass Graft **(CABG)** [31]. Compared with propofol, sevoflurane increases blood flow in the brain, liver, and heart after implantation of an LVAD under conditions of partial support [2].

Anesthetic Maintenance: Inotropes and Vasoactives Drugs

In patients with end-stage heart failure undergoing LVAD implantation, inotropic and vasoactive agents may be needed owing to the deep vasodilatation occurring especially during separation from CPB despite a smoothly functioning device (Figure 1). This period may become further complicated with right ventricular failure. Therefore, inotropic support is important for the purpose of improving right ventricle function and pulmonary vascular resistance.

• **Levosimendan** is a calcium sensitizing agent which can exert its inotropic effect by increasing the sensitivity of cardiomyocyte to intracellular calcium [32]. Short-term use of levosimendan has been shown to cause rapid dose-dependent improvement in hemodynamics and symptoms in patients with decompensated heart failure [33]. In the Levosimendan Infusion versus Dobutamine **(LIDO)** study, intravenous levosimendan was compared with dobutamine in severe low-output heart failure patients: a hemodynamic improvement (increase in cardiac output and decrease in pulmonary capillary wedge pressure) was associated with a lower mortality at one- and six-months with levosimendan compared to dobutamine [34]. Compared to dobutamine, levosimendan increases the incidence of postoperative atrial fibrillation [35] and it decreases myocardial infarction, ICU length of stay [36], acute renal dysfunction, ventricular arrhythmias, and mortality in the treatment of postoperative left ventricular dysfunction [37]. As an inotropic agent, levosimendan can be started either alone as pretreatment in patients with right heart insufficiency prior to LVAD implantation [38] or in combination with an agent from another class (multimodal approach) in myocardial depression.

• **Milrinone** is a widely used positive inotropic agent in patients with end-stage heart failure and cardiogenic shock [39]. Milrinone is a bipyridine and inhibits the phosphodiesterase-3

intracellular enzyme, thus preventing the degradation of cyclic adenosine monophosphate within the cell. Milrinone has inotropic properties and also causes peripheral vasodilation [40] and reduces left ventricular filling pressure in chronic heart failure patients.

Pulmonary hypertension in patients with Congestive Heart Failure **(CHF)** is a risk factor for increased mortality after orthotropic cardiac transplantation. Reversibility of elevated Pulmonary Vascular Resistance **(PVR)** by pharmacologic agents predicts improved outcomes. Milrinone lowes PVR by decreasing mean pulmonary artery pressure and increasing cardiac output significantly [41]. Milrinone also provides right ventricle afterload reduction, and patients treated with prolonged milrinone therapy for right ventricle failure have similar survivals compared with patients without right ventricle failure [42].

Milrinone is cleared renally and has a longer half-life of a few hours, so it should be avoided in patients with severe renal dysfunction [43]. Milrinone can induce cardiac arrhythmias and hypotension that can persist for a few hours even after its infusion is switched off. Considering the concern for cardiac arrhythmias and higher mortality with milrinone and dobutamine, these inotropic agents should be used in selective groups of patients [32]: in cardiogenic shock and decompensated heart failure patients who are not able to be adequately diuresed secondary to worsening end-organ function [44], in chronic heart failure patients as a bridge to recovery from an acute hemodynamically compromised state and in advanced stage heart failure patients awaiting advanced heart failure therapies, such as mechanical circulatory support and heart transplant [32]. As Home-Based Milrinone Therapy **(HMT)** is used as a bridge to cardiac transplant, acute hemodynamic response to milrinone predicts success of HMT as a bridge to cardiac transplant [45].

- **Inhaled Nitric Oxide (iNO)** therapy as a selective pulmonary vasodilator in cardiac surgery has been one of the most significant pharmacological advances in managing pulmonary hemodynamics and life threatening right ventricle dysfunction and failure [46]. iNO may be efficient in pulmonary hypertension, RV dysfunction and severe hypoxemia [47]. There are only weak clinical practice guidelines on the field and only European expert opinion for the use of iNO in routine and more specialized cardiac surgery such as heart and lung transplantation and LVAD insertion [46].

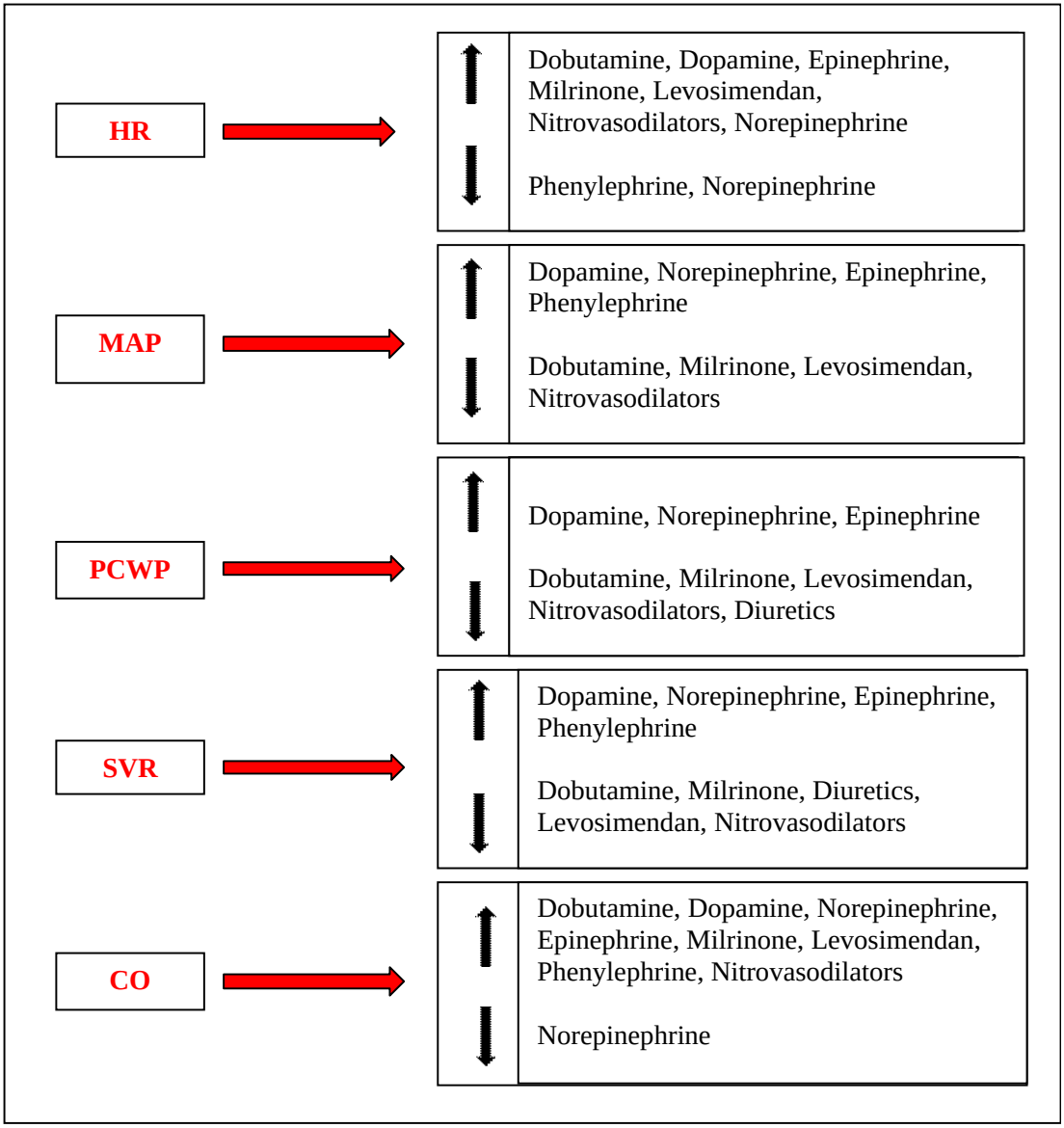

Figure 1: Hemodynamic effects of intravenous drugs for treatment of heart failure.

HR = Heart Rate; MAP = Mean Arterial Pressure; PCWP (preload) = Pulmonary Capillary Wedge Pressure; SVR (afterload) = Systemic Vascular Resistance; CO = Cardiac Output.

POSTOPERATIVE CARE AND COMPLICATIONS AFTER VAD IMPLANTATION

The operative period imparts the greatest risk for death following LVAD implantation. In the sixth annual report of the Interagency Registry for Mechanical Circulatory Support **(INTERMACS),** the risk of multi-system organ failure mortality persists out to about 4 months before it merges with a constant hazard. After the first 3 months, neurologic causes of death have the greatest risk during the remainder of the first year. When extended out to 4 to 5 years, the gradually increasing late hazard for death from infection and multi-system organ failure is apparent [48]. Although Biventricular Assist Devices **(BiVAD)** support is an established treatment modality for biventricular failure, it is associated with worse outcomes as compared to LVAD therapy [49].

Despite there have been advances in the perioperative and long-term results associated with VAD implantation in recent years, this operative procedure may still cause serious morbidity and mortality. Important complications include infection, stroke, device thrombosis, gastrointestinal bleeding, and recurrent heart failure symptomatology with or without multisystem organ failure [50]. It has been reported that complications such as infection, bleeding, renal failure, respiratory failure, neurologic dysfunction, or right heart failure were seen in 10-30% of patients undergoing VAD implantation [51]. Strategies to reduce right ventricular failure, bleeding, and infection risks are the focus of perioperative LVAD and patient management [52]. A best knowledge of pathophysiology of these complications is necessary to an optimal management of patients with VAD [6].

Early Postoperative Management

After the operation, patients are transferred to the cardiac surgical ICU and mechanically ventilated. In addition to a vigilant intraoperative hemostatic technique [53], preemptive preoperative assessment of bleeding and right ventricle failure risk is important [54,55]. In patients with end-stage heart failure undergoing LVAD implantation, all organ systems are either insufficient or are close to being insufficient. In these patients, diminishing the inflammatory processes on the lungs and kidneys improves right ventricle and renal functions [56].

When possible, glycoprotein IIb IIIa inhibitors and vitamin K antagonists should be discontinued well in advance of surgery and International Normalized Ratios **(INRs)** should be normalized. Measures to reduce hepatic congestion (diuresis, inotropes, right ventricle afterload reduction) and improve nutritional status should be undertaken. At the time of LVAD initiation, optimization of speeds/flows should be done with transesophageal echocardiography guidance to minimize septal shift and, thereby, right ventricle wall stress. Early postoperative inotrope administration with close monitoring of cardiopulmonary hemodynamics is often beneficial for right ventricle support and to assist with management of mobilized intraoperative fluids [52].

Kocabas et al. [10] started heparin within 24 hours after VAD implantation as an anticoagulant with dipyridamole added as an antiadhesive on day 3. In the following days, warfarin sodium

was added to the therapy with a target of the INR of 2.5-3.0. Acetylsalicylic acid (100 mg) was started at 1 week after implantation when all of the drains had been removed. In some patients, clopidogrel was added as an anti-aggregant according to platelet aggregation test results. Platelet functions were analyzed using the multiplate method [10].

Early and Late Postoperative Complications

The early complications are mainly represented by bleeding complications (tamponade, abdominal hemorrhage) and right ventricular failure (Table 1). Late complications generally occur a few weeks after LVAD implantation: systemic infections and thromboembolic complications [6] (Table 2).

VAD and coagulation disorders

Perioperative bleeding is multifactorial but is often a combination of impaired hepatic synthetic function, preoperative anticoagulation therapy, and excessive fibrinolysis, thrombogenesis, and platelet activation related to the assist device [57]. Additional complications of pump thrombosis include neurologic events such as transient ischemic attack, ischemic stroke with or without hemorrhagic conversion, and arterial thrombosis [58].

Since continuous-flow LVADs came into wide use, there have been increased reports of pump thrombosis (clot formation in the LVAD system that can lead to pump dysfunction and clinical complications) [58]. Anticoagulation and antiplatelet therapies are important for preventing pump thrombosis, although the optimal antithrombotic regimen remains unclear. INR goals should be determined according to specific device characteristics and patient risk factors. Medication therapy for pump thrombosis provides a less invasive option than surgical pump exchange or heart transplantation but is associated with high risks of bleeding events, recurrent pump thrombosis, and mortality. Decisions regarding medical versus surgical management should be based on clinical status and surgical candidacy. Management of pump thrombosis may include intensified i.v. anticoagulation, i.v. or intraventricular thrombolytics, or glycoprotein IIb/IIIa inhibitors. Optimization and close monitoring of anticoagulation and antiplatelet therapy can help reduce the risk of pump thrombosis [58]. Goldstein et al. [59] have proposed an algorithm to aid clinicians in appropriate evaluation and treatment when pump thrombosis is suspected.

Surgical pump exchange is a known high-risk surgery with a high perioperative mortality rate. But as Systemic Thrombolysis **(STL)** can be associated with high risk of bleeding complications and device exchange is currently considered as the gold standard. Recent data indicate that STL is a feasible treatment alternative for selected LVAD patients with pump thrombosis [60,61].

VAD and right ventricle failure

Right ventricle failure is not an infrequent complication of LVAD implantation and has an important influence on morbidity and mortality. Hemodynamic instability can still occur secondary to vasodilatory shock and cardiac arrhythmias. Hypothermia must be avoided by using

warmed fluids, airway humidifiers, and forced air warming blankets. Judicious application of inotropes and pulmonary vasodilators as milrinone, and timely right VAD insertion, if necessary, should be maintained.

Table 1: Main postoperative early complications**.**

Type and Incidence	Predisposing factors	Detection	Treatment
Bleeding (15-30 %)	• Prolonged heart failure • Hepatic failure • Heparin • Thrombopenia • Preoperative hypothermia • Chronic anemia • Increase in nonsurgical GI bleeding incidence (arteriovenous malformations) in continuous flow LVADs	• Hemodynamics • Analysis • Echo-cardiography • Upper and lower endoscopy (GI bleeding)	• Surgery • Blood transfusion • Intravenous fluids • For GI bleeding: endoscopic guided therapy with or without intravenous proton pump inhibitor therapy.
RV Failure (20-50%)	• Before LVAD implantation, evaluate the RV function for adequate function by imaging and hemodynamics. • Worse preoperative renal and hepatic function • Higher preoperative CVPs and PCWPs • MCS and inotropes at LVAD implantation • Mechanical ventilation • must achieve normoxaemia and normocarbia • More blood trasnfusions • Longer times CPB	• Ensure RV perfusion • Echocardiography	• Treatment of atrial and ventricular arrhythmias. • To improve RV perfusion (RV afterload reduction) and function: milrinone. • If systemic hypotension: dobutamine and/or dopamine. • If increased right atrial pressure (>15 mmHg): furosemide, ultrafiltration, or renal replacement therapy, or decreasing the LVAD flow • If low right atrial pressure (<10 mmHg): intravenous saline • If low systemic vascular resistance (<800 dyn/s/cm^5): inotropic support and vasopressor agent. • To reduce reactive pulmonary hypertension: iNO (20 ppm inhaled) or iloprost after cessation of CPB and for 24-48 h postoperatively. • Surgical intervention.

GI = Gastrointestinal; RV = Right Ventricle; LVAD = Left Ventricular Assist Device; CVP = Central Venous Pressure; PCWP = Pulmonary Capillary Wedge Pressure; MCS= Mechanical Circulatory Support; CPB = Cardiopulmonary Bypass; iNO = inhaled Nitric Oxide.

Table 2: Main postoperative late complications.

Type and Incidence	Predisposing factors	Detection	Treatment
Infection (5-33%)	• Suboptimal perioperative antibiotic prophylaxis • Longer times ventilation support • Second surgery	• Determination of mechanical circulatory support device infections: microbiologic, pathologic, echocardiographic, or clinical criteria to achieve a firm diagnosis. • Pocket infections: abdominal wall or close to the pericardium and the diaphragm. • Percutaneous driveline infections. • Echocardiography (transthoracic and transesophageal), US, and CT.	• Standard sepsis treatments with antibiotics and vasopressors. • Antimicrobial therapy. • Antifungicals
Thrombosis (10%)	• Patient-related factors: noncompliance to anticoagulation therapy, hypercoagulable state, atrial fibrillation, and infection. • Pump-related factors: pump heating and inflow cannula malposition. • Management-related factors: subtherapeutic INR, inadequate antiplatelet therapy, inflow cannula malposition, and low pump flow.	• Clinical signs of congestion and poor perfusion (pulmonary edema, decreased CO, organ hypoperfusion, lactic acidosis). • Hemolysis: hemoglobinuria, increased LDH (>3 times the upper limit of normal) and plasma free hemoglobin levels (>40 mg/dL). • Echocardiography (Increase in LVEDD, dilated ventricle, New or worsened mitral valve regurgitation, and frequent aortic valve opening).	• Intravenous heparin. • Supportive care. • Increase aspirin dosage to 325 mg/d, INR target level to 2.5, or add second antiplatelet therapy. • Intravenous direct thrombin inhibitors and glycoprotein IIb/IIIa inhibitors. • Surgical intervention - heart transplantation.

US = Ultrasound; CT = Computerized Axial Tomography Scan; CO = Cardiac Output; INR = International Normalized Ratio; LDH = Lactate Dehydrogenase; LVEDD = Left Ventricular End-Diastolic Diameter.

ROLE OF ECHOCARDIOGRAPHY IN THE PERIOPERATIVE MANAGEMENT OF VAD

Echocardiography is the main diagnostic tool used in the management of patients with LVAD, essential for the successful completion of the whole process. Guidelines of the American Society of Echocardiography for the echocardiographic management of patients with LVAD recommend that the exam must be performed either by a cardiologist experienced in LVAD and perioperative TEE either by a cardiothoracic anesthesiologist with advanced TEE expertise [62].

We will provide an overview of the role of TEE monitoring during the operative period for LVAD implantation. The pre-implant assessment should confirm previous findings and rule out the presence of intracardiac shunts, Aortic Regurgitation **(AR)** or thrombi, and perform a detailed study of the function of the right ventricle. The post-implantation examination will focus on proper de-airing of the heart and the correct position and adequate flow of the cannulas. In addition, its use in the immediate postoperative period will allow the identification of possible complications.

Pre-Implantation Evaluation

The pre-implantation LVAD assessment should include evaluation of the left ventricle morphology and function, investigate the presence of thrombi or intracardiac communications, evaluate the function of the right ventricle and the tricuspid valve, and rule out AR (Table 3).

Table 3: Parameters pre-implantation VADs.

Pre-Implantation Parameters	
1.	Left ventricle assesment Function Dimensions
2.	Intracardiac thrombi
3.	Intracardiac shunts
4.	Aortic regurgitation
5.	Right ventricle assesment Function Dimensions
6.	Tricuspid regurgitation

The beginning of the pre-implantation assessment should confirm the diagnosis of end-stage left ventricular failure, since the signs of improvement could make unnecessary the placement of the device. The anatomy and cardiac function can significantly influence the surgical approach in selecting the device and placement of the cannulas [63]. The evaluation of the left ventricle before implantation should show a depressed function (left ventricle ejection fraction <25%). Although the ejection fraction of the Left Ventricle **(LVEF)** is not the only clinical parameter used for the determination of ventricular function, its determination is of great importance for the decision on the implantation, being the biplane method of disks (modified Simpson's rule) the most used. Other echocardiographic signs of end-stage left ventricular failure are the presence of a spherical shaped and severely dilated ventricular chamber, serious segmental wall-motion abnormalities and spontaneous echo contrast. The presence of a restrictive ventricular diastolic physiology also supports the implantation of the device. It is also crucial to perform a baseline measurement of Left Ventricular End-Diastolic Diameter **(LVEDD)**, as its difference with the post-implant diameter is the most important clinical measure of an adequate ventricular unloading. Displacements of both atrial and ventricular septum will indicate an increase in pressure in the left atrium or left ventricle respectively.

The echocardiography should rule out the presence of thrombi in the heart chambers, since their presence increases the risk of devastating embolic phenomena during cannulation, especially if the trombi are in the left side of the heart. The main places of presence of thrombi are the left atrial appendage and the ventricular apex. One should keep in mind the limitations of TEE compared with transthoracic echocardiography on visualization of the ventricular apex. In patients with increased risk, as are those with a very depressed LVEF and / or ventricular aneurysm, a microbubble contrast agent should be used.

The presence of a Patent Foramen Ovale **(PFO)**, present in up to 30% of the general population, or an Atrial Septal Defect **(ASD)** increases the risk of hypoxemia [64] and paradoxical embolism once initiated the LVAD, due to pressure drop in the left atrium as a result of the unloading of the left ventricle, while the pressure in the right atrium is maintained or increased due to increased venous return through increase systemic flow. In the evaluation of these patients for the detection of PFO or ASD using agitated saline combined with performing adequate Valsalva maneuver is necessary, as the high pressure in the left atrium can interfere with detection using only the color-flow Doppler and agitated saline (even more complicated if there is also right ventricular dysfunction and high pressure in the right atrium). The presence of a ventricular septal defect must also be systematically excluded. These defects must be closed before the implementation of assistance.

Diagnosis of aortic regurgitation and its severity is also crucial before and after implantation of the device. After initiation of the pump, the antegrade flow will be reduced by the regurgitant volume through the incompetent aortic valve, generating an increase in left ventricular preload that causes up-regulation of pump flow. This generates a "futile cycle", with high pump flow, low systemic antegrade flow and increased pressures in left ventricle and left atrium. The severity of AR can be determined by measures such as the vena contracta width, the pulse-wave Doppler diastolic blood flow in the descending aorta, the ratio of the AR jet width to the left ventricular outflow tract width, and calculation of the regurgitant volume [65].

Right ventricular failure after implantation of a left ventricular assist device is associated with increased morbidity and mortality, but identification of patients at risk for right ventricular failure after implantation is challenging [66,67]. In a study evaluating the risk of right ventricular dysfunction, they found that the only echocardiographic parameter predictor of right ventricular failure was "severe" dysfunction (as defined by the echocardiographer) prior to implantation of the LVAD [68]. Echocardiographic signs of right ventricular dysfunction include systolic dysfunction and / or dilatation of the right ventricle, increased right atrial pressure (established by the size and collapsibility of the inferior vena cava) and moderate or greater degree of Tricuspid Regurgitation **(TR).** The best views for the evaluation of the right ventricle include mid-esophageal four-chamber and right ventricle inflow-outflow views, and trans-gastric short axis view. Systolic right ventricular function can be measured using different alternatives: global fractional area change, Tricuspid Annular Plane Systolic Excursion **(TAPSE),** tissue Doppler-derived lateral annular systolic velocity (s'), isovolumic acceleration, RV outflow tract fractional shortening using M-mode echocardiography, and longitudinal strain and strain rate.

The presence of moderate or greater tricuspid regurgitation is an ominous finding that may indicate severe right ventricular dysfunction, as mentioned above. Both the severity and mechanism (organic or functional) of tricuspid regurgitation should be examined.

Implantation and Post-Implantation Evaluation

Evaluation with transesophageal echocardiography is essential to evaluate the placement and function after implantation of LVAD. The main considerations to be evaluated are: proper de-airing of the left ventricle and the device, adequate position of input and output cannulas, Doppler velocities of input and output cannulas, structure and function of left and right heart chambers, presence of AR, presence of TR, and presence of intracardiac shunts or thrombi not detected in the pre-implantation assessment (Table 4).

Table 4: Parameters implantation and post-implantation VADs.

Implantation and Post-Implantation Parameters
1. De-airing
2. Adequate position of input and output cannulas
3. Structure and function of left ventricle (unloading)
4. Mitral regrugitation
5. Structure and function of right ventricle
6. Tricuspid regurgitation
7. Aortic regurgitation
8. Intracardiac shunts
9. Intracardiac trombi

In the immediate post-implantation period and before activation of the device, the echocardiographer must carefully inspect for signs of air in left atrium, left ventricle (including the apex and the inflow cannula), aortic root, ascending aorta, anastomosis of the graft outlet cannula to the ascending aorta (outflow graft-to-ascending aorta), and transverse and descending aorta. A dysfunction or acute right ventricle dilation and / or increased TR may result from air embolization to the right coronary artery.

The inflow cannula is usually placed in the left ventricle apex. The cannula must be aligned with the opening of the mitral valve without impinging the septum or the side wall of the left ventricle. The best visualization of the input cannula is acquired in the 4-chamber and 2-chamber views. The ecocardiographer should check for laminar flow from the ventricle into the device (velocity <1.5 $m.s^{-1}$). Upon finding of turbulent flow or high Doppler velocities, obstruction of the cannula should be suspected. The combination of a small ventricular chamber and an angled cannula may result in direct contact between the cannula and septum, which can lead to ventricular arrhythmias and obstruction of flow in the inflow cannula.

The outflow cannula anastomosis to the ascending aorta can be observed at approximately the level of the right pulmonary artery. The best views for visualization are at mid-esophageal level the short axis of the ascending aorta or the long axis of the aortic valve. As with the inflow

cannula, visualized Doppler flow should be low speed, laminar and unidirectional, with a variable amount of systolic augmentation. Upon a flow velocity >2 $m.s^{-1}$ some kind of obstruction should be suspected and requires detailed examination. It is important to note that the sternal closure can change the orientation of the cannula with respect to their position with the chest open, so a reassessment should be performed.

After initiation of the device, the most reproducible measure of a successful unloading of the left ventricle is the LVEDD. Pre-implantation mitral regurgitation usually disappears after activation of the pump, mainly by the continuous flow generated by the device and by the proper left ventricle unloading. The presence of mitral regurgitation after LVAD implantation may be secondary to increased filling pressures of the left ventricle, indicating an improper unloading of the left ventricle. Mitral regurgitation could also be caused by an interference of the inflow cannula with mitral subvalvular apparatus.

After implantation of the device, both the function of the right ventricle and the presence of TR must be re-evaluated, in a similar way to that performed before implantation. Inadequate left ventricular preload from the right ventricular outflow can produce a low-output state and device failure.

Another major complication that must be evaluated is the presence of a "suction event". If the speed of the pump is set too high, the left ventricle can be over-unloaded, producing an abnormal movement of the interventricular septum into the left ventricle, causing distortion of the geometry of the right ventricle, which can impair the function of the right ventricle and worsen TR. This can ultimately produce a suction event, because a myocardial segment partially occludes the inlet cannula and reduces pump flow. It is important to know that a suction event that happens with low pump flows may reflect a severe right ventricle failure, and may indicate the need of restore CPB or implant a biventricular support.

As previously mentioned, it is mandatory the evaluation of AR, which can generate a futile cycle and ineffective function of the LVAD.

Postoperative hemodynamic instability forces the echocardiographer to evaluate for the presence of hypovolaemia (small right ventricle and left ventricle), acute right ventricle dysfunction (dilated and hypocontractile right ventricle, with functional TR, small left ventricle, and intermittent obstruction of the inflow cannula into the collapsed left ventricle), cardiac tamponade (difficult diagnosis after LVAD implantation, as may occur with small amounts of blood), pulmonary embolism and LVAD dysfunction.

CONCLUSION

Anesthesia and peri-operative management of patients undergoing implantation of VADs are challenging aspects of cardiac anesthesia. There special need for teamwork with all involved professional group (anesthesiology, cardiology and cardiac surgery). The purpose of this chapter

is to present anesthesiologists with the advances in the VADs management and we show our experience in an active VADs program (clinical and experimental animal).

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