Intensive care management of patients with left ventricular assist device

NATAŠA SOIČIĆ, MD, STIEPAN BARISIN, MD PHD^{1,2}

¹Department of Cardiovascular Anesthesiology and Cardiac Intensive Medicine, Clinical Department of Anesthesiology, Reanimatology and Intensive Care Medicine, University Hospital Dubrava ²Faculty of Medicine, JJ Strossmayer University Osijek

Address of corresponding author: Nataša Sojčić, MD Department of Cardiovascular Anesthesiology and Cardiac Intensive Medicine University Hospital Dubrava Avenija Gojka Šuška 6 10000 Zagreb natasa.sojcic@gmail.com

ABSTRACT

Mechanical circulatory support devices, especially left ventricular assist devices (LVADs) represent an important treatment modality for patients with end-stage heart failure (HF). In a 1-year period (from January to December 2017) in our intensive care unit (ICU) we had a total of 8 patients with LVAD implantation. LVADs are devices with unique physiology which restore tissue circulation by increasing blood supply, nevertheless, they can be challenging to manage and are associated with significant complications.

Keywords: Critical Care, Heart-Assist Devices, Heart Failure, Hemodynamics, Hemodynamic Monitoring, Cardiac surgery, Postoperative Complications

INTRODUCTION

Mechanical circulatory support devices, especially left ventricular assist devices (LVADs) represent an important treatment modality for patients with end-stage heart failure (HF). Considering the shortage of donor organs, improvement in LVAD's technology and intensive care treatment modalities, the number of patients with LVAD implantation in intensive care units is increasing. Intensive care management of these patients requires an understanding of the principles, indications, and limitations of this unique technology, as well as a multidisciplinary approach (intensivists, cardiac surgeons, anesthesiologists, cardiologists etc.) (1).

Indications for LVAD implantation include: a) bridge to transplantation (BTT), b) bridge to decision (until a determination can be made regarding a patient's eligibility for cardiac transplantation), c) destination therapy (DT) to support cardiac function for the remainder of a patient's life and d) bridge to recovery (temporary support for patients whose cardiac function is expected to recover) (2).

Older models of LVADs with pulsatile flow have been replaced with a newer generation of continuous-flow (CF) pumps which are smaller in size, more reliable, durable and subsequently lead to improvements in survival (3). Each LVAD consists of an inflow cannula positioned into the left ventricular (LV) apex, a rotating element that imparts energy to the blood to increase arterial blood flow and pressure, an outflow cannula which directs blood into the ascending aorta and a controller with battery pack.

PATIENTS AND PREOPERATIVE ICU MANAGEMENT

In a 1-year period (from January to December 2017) in our intensive care unit (ICU) we had a total of eight patients with LVAD implantation. Four patients had dilative ischemic cardiomyopathy with LVEF ranging from 15 to 25 % and were planned for LVAD implantation as DT. One patient had dilatative cardiomyopathy secondary to congenitally corrected transposition of the great arteries (dextrocardia was also present) who was on the transplant list but had NT (non-transplantable) status. LVAD exchange was planned in three patients due to microthrombosis of the LVAD in one case and infection of driveline in two

All patients planned for LVAD implantation were admitted to our ICU the day before surgery for preoperative assessment and preparation. Arterial cannula for invasive blood pressure monitoring, central venous catheter and pulmonary artery catheter with continuous cardiac output (CCO) and continuous mixed venous saturation (Sv02) monitoring were placed. Thereafter, we recorded basic hemodynamic parameters and their indexed values (IBP, CO, SV, SVR, PVR, PAP, PCWP, LVSW, RVSW, Sv02 and CVP) in all cases. There are indications that preoperative use of levosimendan (calcium sensitizer, inodilator) in patients eligible for LVAD implantation might improve clinical outcome and sur-

Our protocol in this group of patients included administration of a bolus dose of levosimendan (6 µg/kg i.v.) during 20 minutes and then as a continuous infusion (0.1 μg/kg/h) during 24 hours. In all patients administration of levosimendan was safe and no clinically relevant side effects (significant hypotension, arrhythmias) were observed. Positive effects of levosimendan include improvements in pre-implant hemodynamic performance (higher CI, lowering of PAP and CVP). There is a lack of consensus on the regimen and duration of antibiotic prophylaxis during LVAD implantation. In our ICU antibiotic prophylaxis for these cases consists of intravenous use of vancomycin, ciprofloxacin and fluconazole as well as oral (or via nasogastric tube) use of rifampicin.

POSTOPERATIVE ICU MANAGEMENT AND POTENTIAL COMPLICATIONS

In all patients, the third generation of CF LVAD devices was implanted. Three patients received HeartWare (HeartWare Inc.) and five patients received HeartMate III (Thoratec Corp.), magnetically levitated VAD with artificial pulse. In the postoperative period, a combination of inotropes, vasodilators and vasopressors were used in addition to correction of intravascular volume and speed adjustments for optimizing hemodynamic parameters. Maintenance of adequate intravascular volume is of great importance because these pumps are preload dependent and inadequate filling will result in low pump flow. LVAD variables such as pump speed (in RPMs) which is the only variable programmed by the operator and other variables which depend on the patient's underlying physiology; pump flow (L/m), pump power (W) and pulsatility index1 are recorded regularly. Cardiac ultrasonography (TTE or TEE) is very helpful for assessing hemodynamic parameters in LVAD patients, particularly in evaluation of RV size and function, septal positioning (it should be flat and neutral), LV size and function, preload, signs of pericardial effusion or tamponade, position of the cannulas and competency of the aortic valve (it should be competent and open intermittently, every second or third beat) (6). After thorough ultrasonographic assessment, optimal pump speed can be determined.

Also, these devices are sensitive to excess afterload (CF devices to a greater extent than axial flow devices) so careful monitoring of MAP and SVR should be done (7). According to the International Society of Heart and Lung Transplant (ISHLT) guidelines, MAP in patients supported by CF-LVADs should be less than or equal to 80 mm Hg (8). Also, MAP shouldn't be too low to avoid hypoperfusion of the RV, kidneys and gut. On the other hand, excessive blood pressure can lead to neurologic events, bleeding, and reduced flow of the LVAD (1). In many patients, CF-LVADs are associated with a reduced pulse pressure, and the degree of this diminished pulsatility depends on the pump speed setting, underlying LV contractility, preload, afterload pressures7 and presence and degree of aortic valve opening. Therefore, on physical examination, patients with CF devices may not have palpable pulses so it can be difficult to place an arterial cannula for IBP and may require ultrasonographic guidance.

Existing anticoagulation protocols for LVAD vary by institution, device and individual patient. Our protocol begins with starting unfractioned heparin (UHF) 12-24 hours after surgery if chest tube drainage is less than 50 ml during a 2-3 hour period and titrating it to achieve a partial thromboplastin time (PTT) of 45-50 seconds (1.2-1.4 x control). After 24-48 hours, UHF dosing needs to be increased and titrated to a PTT of 50-60 seconds (1.4-1.7 x control) and after 48-72 hours PTT values should be 55-65 seconds (1.5-1-8 x control). Aspirin is initiated on the second or third postoperative day. Once there is no evidence of bleeding and the chest tubes have been removed, warfarin can be started (overlapping with UHF). UHF can safely be removed after an acceptable, stable INR (2.0-3.0) is obtained. Anticoagulation protocols often differ from the one shown due to unexpected hemorrhage and/or different sensitivity of individual patients to administered drugs.

Postoperative complications include, but are not limited to: bleeding, RV failure, arrhythmias, infections, thrombosis, neurologic events and hemolysis. Postoperative management of LVAD patients requires a careful balance between the risks of hemorrhage and thrombosis because both procoagulant and anticoagulant pathways are activated in patients on LVAD support (9). Bleeding is the most frequent adverse event in the postoperative period and early bleeding requiring surgery is seen in 26% of patients (10,11). Like in other types of cardiac surgery, one should always try to recognize cardiac tamponade as it requires emergent surgical revision. Regular monitoring of laboratory parameters including prothrombin time, partial thromboplastin time, platelet count and fibrinogen levels guide the administration of platelets, fresh frozen plasma, and cryoprecipitate. Factor VII should be used cautiously in patients with LVADs given the potential for serious thromboembolic events, particularly at higher doses (12).

Patients with prior cardiac surgery experience longer cardiopulmonary bypass (CPB) time and more postoperative bleeding (13). One patient died in the early postoperative period (eight hours after surgery) due to a combination of excessive surgical bleeding and coagulopathy (DIC). Other forms of bleeding include epistaxis, GI bleeding (continuous blood flow may lead to formation of AV malformations) and intracranial hemorrhage (particularly with excessively high LVAD flows and MAP> 90 mmHg). Estimates of the incidence of right-sided HF after placement of an LVAD vary in literature (5 to 40%, depending on criteria of RV failure) and are associated with marked deterioration of survival prospects. Numerous predictors of post-LVAD RV failure have been identified like elevated CVP or CVP/PCWP ratio, severe renal dysfunction and ventilator

dependence.14 Specific echocardiographic measures of RV function have exhibited poor reproducibility across studies. After LVAD implantation, RV geometry changes as the septum shifts to the left with LV unloading, causing an increase in RV compliance but a decrease in contractility. Venous return is increased due to improved CO from the LVAD, but right ventricular afterload may remain high due to increased PAP.1 Maintaining the septum in its normal position can be done by carefully monitoring volume status, doses of inotropes, and device settings after echocardiography assessment. Too high of a pump speed will shift the septum leftward (causing impairment in RV function), too low of a pump speed will shift the septum rightward and cause increased LA pressure which also impairs RV function.15 In the postoperative period it is prudent to maintain a MAP >70 mmHg to preserve RV and this often requires use of one or more vasopressors (norepinephrine, vasopressin) (2). Factors which increase PVR such as hypercarbia, hypoxia, high airway pressures and levels of PEEP, also need to be avoided. One patient in our ICU presented with RV failure after LVAD implantation, presumably due to septic shock and showed no signs of recovery despite high inotropic support, antibiotics and other modalities of intensive care treatment.

Both atrial and ventricular arrhythmias are common post-LVAD implantation. Although rapid atrial arrhythmias can be tolerated initially, loss of AV synchrony results in reduced ventricular filling and decompensated RV failure and patients may therefore require rate or rhythm control (16). Ventricular arrhythmias can be triggered by contact between the inflow cannula and the ventricular septum during suction events usually caused by hypovolemia, too high of an LVAD speed, RV failure or small ventricular size (1). Therefore the speed should be set to avoid excessive ventricular unloading and volume status optimized if needed.

LVAD patients in cardiac arrest should be managed with the Advanced Cardiac Life Support (ACLS) algorithm for cardiac arrest with a few exceptions. Most importantly, chest compressions are not recommended due to potential dislodgement of the device or its outflow cannula located directly beneath the sternum, in which case massive hemorrhage can occur. In this group of patients, infection (VAD-specific, VAD-related, non-VAD infections) is the second most common cause of death after cardiac failure (17). Our three patients after LVAD implantation died of sepsis and multiple organ failure (MOF). The incidence of acute kidney injury (AKI) after LVAD implantation has been reported to range from 7 to 56 % with the large variation in range likely due to differing definitions for AKI (6). Criteria for renal replacement therapy are the same for patients with or without LVADs. Our one patient with LVAD required CVVHDF in the early postoperative period within a clinical picture of septic shock and MOF. Major thrombotic events in LVAD patients include pump thrombosis and arterial thromboembolism. Thrombi form on the impeller or areas of low flow, such as the aortic valve, atrial appendage, or a dilated LV.1 Device thrombosis can develop even when patients are fully anticoagulated and taking adequate antiplatelet therapy because the LVAD causes a chronic hypercoagulable state (6). One patient came for LVAD exchange due to late device microthrombosis (2 years after initial LVAD implantation), but we did not notice any thrombotic complications during the postoperative period in the ICU.

With the introduction of CF devices, the incidence of stroke in patients with LVADs has decreased substantially; however, patients remain at a high risk for stroke. Ischemic strokes occur in about 8-10% of LVAD patients (18). One patient in our ICU had a transient neurological disorder with disorientation after LVAD placement, but without pathology on CT scan. Hemolysis is present in about 4-18% of patients with pulsatile or CF- LVAD (18,19). Results of laboratory tests that reveal evidence of hemolysis are LDH levels greater than 3 x the upper limit of normal, elevated bilirubin and plasma free hemoglobin and low levels of haptoglobin. Hemolysis can be various in origin (sign of pump thrombosis, result of too high inlet velocities or can be transfusion related) (20).

DISCUSSION

The overall rate of LVAD implantation increases every year, especially the number of LVADs for DT. Generally, all patients planned for LVAD implantation are high risk patients with deteriorated hemodynamic status and lots of comorbidities. Several risk factors for early mortality after LVAD implantation have been identified including advanced age, female gender, obesity, INTERMACS profile 1-2, renal dysfunction, elevated bilirubin and previous cardiac surgery. Of our eight patients, seven were male with an age range from 61-72 years and one was a female and 54 years of age. All of them were IN-TERMACS 2 profile before surgery and had significant comorbidities (including hypertension, pulmonary hypertension, diabetes mellitus, renal insufficiency etc.). Our four patients had one previous cardiac surgery (CABG, valve surgery or LVAD implantation) and in one patient who underwent LVAD exchange this was their third cardiac procedure. In our patients, mortality was high due to various causes. One patient died in the operating theatre due to inability to wean from CPB (low cardiac output syndrome and vasoplegia), three patients died from septic complications (7, 10 and 11 day after surgery) and one patient died from postoperative hemorrhage eight hours after surgery. In the postoperative period LVAD patients require respiratory and hemodynamic support, broad spectrum antibiotics, regular assessment of volume status and heart function, frequent laboratory parameters

testing and meticulous attention to bleeding. Once again it should be emphasized that anticoagulation protocols are of great importance but a "one size fits all" protocol does not exist.

To conclude, LVADs are devices with unique a physiology which restores tissue circulation by increasing blood supply, nevertheless, they can be challenging to manage and are associated with significant complications.

List of abbreviations:

LVEF - left ventricular ejection fraction

IBP - invasive blood pressure

CO - cardiac output

SV - stroke volume

SVR – systemic vascular resistance

PVR – pulmonary vascular resistance

PAP – pulmonary arterial pressure

PCWP – pulmonary capillary wedge pressure

LVSW – left ventricular stroke work

RVSW - right ventricular stroke work

Sv02 - mixed venous saturation

CVP - central venous pressure

CI - cardiac index

RPM - revolutions per minute

TTE - transthoracic echocardiography

TEE- transesophageal echocardiography

MAP - mean arterial pressure

RV – right ventricle

INR - international normalized ratio

DIC – disseminated intravascular coagulopathy

LA – left atrial

PEEP – peak end expiratory pressure INTERMACS - Interagency Registry for Mechanically Assisted Circulatory Support CABG - Coronary Artery Bypass Grafting

REFERENCES

- 1. Pratt AK, Shah NS, Boyce SW. Left ventricular assist device management in the ICU. Crit Care Med. 2014; 42(1):158-68.
- 2. Koprivanac M1, Kelava M, Sirić F, Cruz VB, Moazami N, Mihaljević T. Predictors of right ventricular failure after left ventricular assist device implantation. Croat Med J. 2014; 55(6):587-95.
- 3. Cheng A, Williamitis CA, Slaughter MS. Comparison of continuous-flow and pulsatile-flow left ventricular assist devices: is there an advantage to pulsatility? Annals of Cardiothoracic Surgery. 2014;3(6):573-81.
- 4. Sponga S, Ivanitskaia E, Potapov E, Krabatsch T, Hetzer R, Lehmkuhl H. Preoperative treatment with levosimendan in candidates for mechanical circulatory support. ASAIO J. 2012;58(1):6-11.
- 5. Theiss HD1, Grabmaier U, Kreissl N, Hagl C, Steinbeck G, Sodian R, Franz WM, Kaczmarek I. Artif Organs. Preconditioning with levosimendan before implantation of left ventricular assist devices. 2014;38(3):231-4.
- 6. Sen A, Larson JS, Kashani KB, et al. Mechanical circulatory assist devices: a primer for critical care and emergency physicians. Critical Care. 2016;20:153.
- 7. Estep, Jerry D. et al. "Continuous Flow Left Ventricular Assist Devices: Shared Care Goals of Monitoring and Treating Patients." Methodist DeBakey Cardiovascular Journal 11.1 2015;33–44.
- 8. Feldman D, Pamboukian SV, Teuteberg JJ et al. The 2013 International Society for Heart and Lung Transplantation Guidelines for mechanical circulatory support: executive summary. J Heart Lung Transplant. 2013;32(2):157–87.
- 9. John R, Panch S, Hrabe J, et al: Activation of endothelial and coagulation systems in left ventricular assist device recipients. Ann

- Thorac Surg 2009;88(4):1171-9.
- 10. Slaughter MS: Hematologic effects of continuous flow left ventricular assist devices. J Cardiov Transl Res 2010;3:618-24.
- 11. Pagani FD, Miller LW, Russell SD, et al: Extended mechanical circulatory support with a continuous-flow rotary left ventricular assist device. J Am Coll Cardiol 2009; 54:312-21.
- 12. Bruckner BA, DiBardino DJ, Ning O, et al. High incidence of thromboembolic events in left ventricular assist device patients treated with recombinant activated factor VII. J Heart Lung Transplant 2009;28:785-90.
- 13. Tsiouris A, Brewer RJ, Borgi J, et al: Is resternotomy a risk for continuous- flow left ventricular assist device outcomes? J Card Surg 2013;28:82-7.
- 14. Kormos, Robert L. et al. Right ventricular failure in patients with the HeartMate II continuous-flow left ventricular assist device: Incidence, risk factors, and effect on outcomes. The Journal of Thoracic and Cardiovascular Surgery, 2010;139(5):1316 - 24.
- 15. Schlendorf K, Patel CB, Gehrig T, Kiefer TL, Felker GM, Hernandez AF, Blue LJ, Milano CA, Rogers JG. Thrombolytic therapy for thrombosis of continuous flow ventricular assist devices. J Card Fail. 2014;20(2):91-7.
- 16. Hottigoudar RU, Deam AG, Birks EJ, McCants KC, Slaughter MS, Gopinathannair R. Catheter ablation of atrial flutter in patients with left ventricular assist device improves symptoms of right heart failure. Congest Heart Fail. 2013;19(4):165-71.
- 17. Kirklin JK, Naftel DC, Pagani FD, Kormos RL, Stevenson LW, Blume ED, et al. Sixth INTERMACS annual report: a 10,000- patient database. J Heart Lung Transplant. 2014;33:555-64.
- 18. Yuan N, Arnaoutakis GJ, George TJ, et al: The spectrum of complications following left ventricular assist device placement. J Cardiac Surg 2012;27(5):630-8.
- 19. Ravichandran AK, Parker J, Novak E, Joseph SM, Schilling JD, Ewald GA, Silvestry S. Hemolysis in left ventricular assist device: a retrospective analysis of outcomes 2014;33(1):44-50.
- 20. Tchantchaleishvili, Vakhtang et al. Evaluation and Treatment of Pump Thrombosis and Hemolysis. Annals of Cardiothor Surg2014;490-5.
- 21. Morgan JA, Paone G, Nemeh HW, et al. gastrointestinal bleeding with the HeartMate II left ventricular assist device. J Heart Lung Transplant 2012;31:715-8.