

TITLE: Ventricular Assist Devices: Not Just a Last Resort

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Learning Objectives

1. To review the indications for ventricular assist devices (bridge to recovery, bridge to transplant, destination therapy)
2. To unravel the alphabet soup (LVAD, RVAD, BiVAD)
3. To present the Columbia experience with traditional devices (Abiomed I, HeartMate I, Thoractec I), including postoperative complications
4. To critically review the new generation of assist devices and the future of artificial hearts.

Indications

A ventricular assist device (VAD) is inserted to provide mechanical circulatory support. A VAD can rest the myocardium and allow it to recover from stunning or hibernation, while maintaining vital organ perfusion (*bridge to recovery*). If myocardial recovery cannot occur, the goal is to support the patient to transplantation (*bridge to transplantation*), or, if the patient is not a transplant candidate, to enhance quality of life for a limited period (*destination therapy*).

Bridge to Recovery

VAD insertion may be considered for cardiogenic shock occurring after cardiectomy or myocardial infarction, or as a consequence of acute viral myocarditis or peripartum cardiomyopathy.

Intractable cardiogenic shock may be defined as a cardiac index (CI) < 2 L/min/m², pulmonary artery occlusion pressure (PAOP) > 25 mmHg, SvO₂ $< 50\%$, oliguria and/or malignant arrhythmias despite the use of high dose inotropic therapy, tachycardia > 100 beats/min and intra-aortic balloon pump (IABP)¹.

Outcome after cardiogenic shock is very dependent on timely placement of the VAD because vital organ damage becomes more extensive with increased duration of a low perfusion state. Mortality increases from about 10% when moderate dose inotropic drugs are required to nearly 80% if insertion of VAD is delayed until inotropic agents are at three times normal doses¹. It also increases from 20% to 40% if insertion is delayed > 3 h after the first attempt to wean from CPB¹, and from 10% to 35% if cardiac arrest occurs prior to insertion³. Additional markers of poor outcome include technically unsuccessful primary surgery, and age > 70 y (13% survival). Right heart failure is a particularly ominous sign. Right atrial pressure (RAP) > 20 mmHg is associated with oliguria, bleeding, venous and hepatic congestion.

Oz et al. defined independent predictors of poor outcome as oliguria < 30 mL/hr, CVP > 16 mmHg, requirement for mechanical ventilation, prothrombin time > 16 s and prior cardiac surgery⁴.

Bridge to Transplantation

In the majority of cases, a VAD is inserted into a patient awaiting heart transplantation for chronic cardiomyopathy (ischemic, viral or toxic), who is developing signs of end organ failure (acute renal failure, pulmonary edema) or life-threatening ventricular arrhythmias.

Chronic placement of LVADs successfully bridge about 70% of transplant candidates to transplantation². About 20% die in the perioperative period, 5% during ongoing support and 5% peritransplant¹.

Destination Therapy

Destination therapy is based upon the REMATCH study^{*1}. This demonstrated that in patients with end-stage CHF who were not transplant candidates, the HeartMate LVAD provided significantly longer survival and quality of life than medical management alone.

Types of Devices

A VAD may assist the left ventricle (LVAD), right ventricle (RVAD) or both (BiVAD). Note that the intra-aortic balloon pump (IABP) is not an assist device, but provides counterpulsation that enhances myocardial oxygen balance (MVO₂). Any increase in cardiac output that occurs is a consequence of improved myocardial function. Extracorporeal membrane oxygenation (ECMO) is essentially a BiVAD with a membrane oxygenator and heat exchanger, and has been used as an assist strategy in postcardiotomy shock⁵.

Three types of VAD are currently in common use: extracorporeal centrifugal pumps (e.g. Biomedicus, Sarns)⁶; extracorporeal pulsatile devices (e.g. Abiomed, Thoratec TLC-II)³ and the first-generation long-term implantable LVADs (e.g. TCI HeartMate, Novacor)¹. Advantages and disadvantages of the various devices are summarized in Table 1.

Insertion of a long term implantable first-generation LVAD requires a median sternotomy and cardiopulmonary bypass (CPB). The inflow cannula is sited via the apex of the left ventricle and the outflow cannula in the ascending aorta. The pump itself is placed into a subfascial, extraperitoneal pocket in the upper abdominal cavity. The driveline is connected to a portable control console or a battery pack.

It is important to recognize that LVAD stroke volume is entirely dependent on the adequacy of left ventricular (LV) filling, which in turn depends on intravascular volume and right ventricular (RV) output. LVAD rate responds to fill time, and in exercise the TCI HeartMate can generate

* Randomized Evaluation of Mechanical Assist Therapy for Congestive Heart Failure

up to 9 L/min. However, in low systemic vascular resistance (SVR) states, e.g. sepsis, this may be inadequate to prevent hypotension. Increases in pulmonary vascular resistance (i.e. acute or chronic pulmonary hypertension) markedly impede RV outflow.

Anesthetic Considerations for Implantable LVAD Insertion (e.g. TCI HeartMate)

Patients are inevitably in end-stage cardiac failure with mild to severe pulmonary hypertension, and may be on chronic inodilator therapy with dobutamine and/or milrinone, and have substantial hepatic, renal and pulmonary insufficiency. Some may have an IABP in place and already be mechanically ventilated or on intermittent or continuous hemodialysis. Many of these patients are reops (prior coronary revascularization, valve surgery, AICD) and therefore require anticipation of major bleeding and/or incision of vital structures during opening, dissection and cannulation.

In anticipation of the potential for massive blood loss large bore central venous access is obtained together with pulmonary artery catheterization. A rapid infusion blood-warming device is primed to ensure the ability to give fully warmed blood and blood products at volumes of 250-1000 mL/min. Blood and blood products (e.g. 6 units of packed red blood cells, 6 units of fresh frozen plasma, 12 units of platelets) are readied in preparation for post-CPB coagulopathy. Early transfusion may reverse factor deficiency before vicious cycles (bleeding \Rightarrow DIC \Rightarrow bleeding) develop.

The anesthetic regimen should acknowledge the tenuous hemodynamic state and compromised drug elimination capacity in many of these patients; for example, cisatracurium should be used instead of vecuronium.

Aprotinin, a kallikrein and serine protease inhibitor that has antifibrinolytic and platelet sparing effects on CPB, is routinely used because it has been shown to decrease blood loss, blood requirement and perioperative mortality⁷. Some advocate priming the CPB circuit with fresh frozen plasma to decrease dilution of clotting factors in patients with preoperative coagulopathy and maintain levels of antithrombin III, thereby avoiding consumptive coagulopathy⁸.

Transesophageal echocardiography (TEE) is essential not only to monitor LV filling and RV function throughout the case, but also to exclude the presence of an atrial septal defect (ASD), patent foramen ovale (PFO), aortic regurgitation or mitral stenosis. These lesions must be repaired prior to separation from CPB; with an ASD or PFO a right to left shunt may commence as left-sided filling pressures are decreased when LVAD support begins⁸.

Adequate LVAD output during separation from CPB requires aggressive volume loading because the LVAD decompresses the LV and left atrium. RV dysfunction is treated by inodilator drugs (milrinone, dobutamine), excessive systemic vasodilatation causing systemic hypotension is treated with norepinephrine and/or vasopressin. Severe pulmonary hypertension may induce acute RV failure, and responds well to inhaled nitric oxide, 10-20 ppm, which has markedly decreased the requirement for emergency placement of an RVAD to come off CPB in the OR.

These issues are discussed in more detail below.

Postoperative Considerations

Vasodilatory Shock

Contact activation of leukocytes triggers inducible nitric oxide synthase (iNOS) to produce massive amounts of endogenous nitric oxide. Tissue acidosis opens K^+ ATP channels (resulting in K^+ efflux from cells) and closes Ca^{++} channels. These processes combine to induce peripheral vasodilation refractory to catecholamines such as norepinephrine. It has also been demonstrated that the protracted baroreceptor response to hypotension results in arginine vasopressin (AVP) deficiency.

Infusion of AVP (1-6 units/h) restores AVP to normal levels, opposes the vasodilator actions of nitric oxide, inhibits cyclic guanosine monophosphate (cGMP) formation, restores membrane polarity and closes K^+ ATP channels. Perfusion pressure is restored, catecholamine requirements are dramatically decreased⁹, and GFR is improved because AVP preferentially constricts the efferent arteriole of the glomerulus¹⁰.

Bleeding

The risk of bleeding is high because there are multiple causes of perioperative coagulopathy. These include preexisting liver congestion and dysfunction, preoperative anticoagulation, prolonged CPB, dilutional coagulopathy (thrombocytopenia) and DIC.

Postoperatively, there is a high risk of cardiac tamponade, which should be suspected when a decrease in LVAD flow is associated with an elevated CVP and declining SvO_2 . In high-risk situations, especially with incomplete hemostasis at the end of the case, the chest should be left open, or reopened in the ICU at the first sign of tamponade.

Right Ventricular Failure

Pulmonary hypertension is the most proximate cause of postoperative RV failure. It may preexist because of chronic LV failure, or acutely develop as a consequence of prolonged CPB, contact activation (LVAD), reactions to blood products or volume overload during resuscitation¹¹. It is exacerbated by hypoxemia, hypercarbia, or acidosis.

Therapeutic strategies to decrease pulmonary artery pressures and improve RV afterload, end diastolic volume and ejection fraction include intraoperative aprotinin (i.e. to decrease requirement for blood products); inodilation with milrinone and/or dobutamine; and selective pulmonary vasodilation with inhaled nitric oxide (10-20 ppm) or inhaled prostacyclin (5-50 ng/kg/min).

Acute Renal Failure

Many patients have preexisting renal insufficiency or acute renal failure (ARF) at the time of LVAD insertion. Many other factors predispose to perioperative ATN including hemorrhagic and vasodilatory shock. The early consequence is pulmonary edema and ventilator dependence because the massive amounts of sequestered fluid are unable to be eliminated once they are mobilized from the interstitial and intracellular space.

Continuous venovenous hemodialysis (CVVHD) has a number of advantages over conventional hemodialysis in that it requires single vessel venous cannulation only, and provides continuous flow that allows large volumes of fluid to be removed with relative hemodynamic stability. There is no doubt that this facilitates ventilatory weaning and tracheal extubation (decreased pulmonary edema) and possibly promotes wound healing (decreased tissue edema). Limitations of CVVHD include the requirement for anticoagulation (increased risk of bleeding) to prevent clot formation which shortens filter survival, and the inability to mobilize the patient.

Infection

Infection may be a devastating complication, resulting in septic shock, systemic inflammatory response syndrome (SIRS) or indolent, deep seated and intractable infections of the device pocket. Prophylactic care includes soaking the device in bacitracin prior to implantation, staphylococcal coverage (avoiding vancomycin because of the emergence of vancomycin resistant *Enterobacter fecalis*, VREF), and stringent drive line (sterile dressing qd) and central line care. Candidal infections are rare and routine fluconazole administration is not indicated.

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Table 1: Advantages and Limitations of Mechanical Assist Devices ¹

Device	Advantages	Limitations
<i>IABP</i>	<ul style="list-style-type: none"> • Easy insertion • Enhances coronary perfusion • Afterload reduction • 	<ul style="list-style-type: none"> • Indicated for acute ischemia only • Does not increase CO • Limited VO₂ decrease • Vascular complications
<i>ECMO</i>	<ul style="list-style-type: none"> • Peripheral cannulation • Lung support • BiVAD • Can be used in presence of intracardiac shunt 	<ul style="list-style-type: none"> • Inflammatory response (oxygenator) • Retrograde perfusion may distend LV
<i>Extracorporeal centrifugal pumps (e.g. Biomedicus, Sarns)</i>	<ul style="list-style-type: none"> • Easy setup • No size limit • Maintain perfusion 	<ul style="list-style-type: none"> • Technician in ICU • Nonpulsatile flow • Bleeding • Hemolysis
<i>Extracorporeal pulsatile devices (e.g. Abiomed BVS 5000)</i>	<ul style="list-style-type: none"> • Pulsatile flow • BiVAD • No technician • Chest closure possible • Bridge to transplant 	<ul style="list-style-type: none"> • No mobility • Anticoagulation • BSA must be > 0.7 m²
<i>Long-term Implantable Devices (e.g. TCI Heartmate, Novacor)</i>	<ul style="list-style-type: none"> • Mobility and discharge from hospital • Volume mode • Robust, long lasting (1-2 yrs) • HeartMate I: textured titanium surface (anticoagulation not required – aspirin only) • Thoratec I: BiVAD 	<ul style="list-style-type: none"> • Thoratec I BiVAD: Cannot leave hospital • BSA must be > 1.5 m² • Bleeding (insertion) • HeartMate I: textured surface (endothelialization; expression of abnormal antigens; increased risk of rejection of subsequent heart transplant) • HeartMate, Novacor: LVAD only • Infection

Table 2: Comparison of Short-term and Long-term MCADs

Device	Abiomed BVS 5000	TCI Heartmate
<i>Assist</i>	LVAD / RVAD	LVAD
<i>Use</i>	Post-cardiotomy support	Bridge to transplant
<i>Pump</i>	Pneumatic	Vented electric
<i>Inflow</i>	RA / LA	LV apex
<i>Outflow</i>	PA /Asc. Aorta	Asc. Aorta
<i>Flow (L/min)</i>	0.5 - 5.5	1.5 - 10