Use of left-ventricular assist devices in treatment of advanced heart failure

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Left-ventricular assist devices (LVAD) are totally implantable pumps able to support circulation in patients with advanced heart failure by draining blood from the ventricular chamber into the aorta, thereby replacing function of the left-ventricle. Due to the totally implantable and compact LVAD design, device ability to sustain normal cardiac output for few years and patients' ability to exercise, rehabilitate and be discharged home soon after surgery, LVAD therapy has become increasingly popular in 1990s, primarily used as a "bridge" to heart transplantation in patients with profound circulatory failure. Currently, nearly two hundred centers worldwide perform routine LVAD implantations in the sickest heart failure patients, and in large volume centers 20 to 30% of all heart transplant candidates are supported with LVADs [1, 2].

Over the last three decades, the field of mechanical circulatory support has made a tremendous progress. The design and safety profile of various new LVADs evolved a great deal. There are currently several types of circulatory assist devices, including those which support one- and/or both ventricles [3, 4].

This article will focus on the experiences with the most widely used LVAD system in the United States, HeartMate Left-Ventricular Assist Systems, produced by the market leader Thoratec Incorporation, Pleasanton, California, which has accounted for more than 4,500 of the LVAD implantations worldwide.

Long-Term Implantable Left-Ventricular Assist Devices

The two most popular long-term left-ventricular assist devices are HeartMate XVE pump (Thoratec Laboratories Corp., Pleasanton, CA) and Novacor (WorldHeart, Ottawa, Canada). In the United States HeartMate XVE is the only approved device to be used as "bridge" to transplant or "destination therapy". In Europe, the Novacor LVAD has unrestricted approval for use as an alternative to transplantation.

Both LVAD models are a totally implantable pusher plate pumps that can fully sustain systemic circulation and adapt to increased cardiac output needs with exercise. They can generate stroke volume up to 80 mL, pulsatile flow up to 10L/min and pulse rate up to 120 beats per minute, Figure 1.

One of the major advantages of the HeartMate pump over Novacor is its textured internal reservoir surface which encourages adherence of circulating endothelial cells and formation of a pseudointima, thus obviating the need for anticoagulation. The thromboembolism rate in Novacor recipients is 10% and the use of these devices require chronic anticoagulation.

The only obstacle in using either of the pusher plate devices is their relatively large size, which limits their use to patients with a body surface area > 1.5 m^2. Therefore, in children and smaller adults, axial flow devices may be a preferred choice. Axial flow devices are the newest generation of mechanical pumps. These are very small devices, which employ an electromagnetically actuated impeller drive shaft which rotates at a controllable speed of 9-11,000 rpm, Figure 3. The pump speed varies depending on the needs of the individual patient and can provide up to 10 liters of non-pulsatile flow. There are several pumps of this type, including the Micromed, DeBakey and HeartMate II. Because of relatively high thromboembolic rate, patients supported with axial flow devices require full anticoagulation. The use of these pumps remains to be approved only for investigational use.

Indications for LVAD Implantation

There are three main indications for LVAD implantation. The most common is "bridge" to heart transplantation in patients with cardiogenic shock or those who are too unstable to remain on the waiting list. In patients ineligible to transplantation, LVAD implantation may be performed as a permanent alternative to heart transplantation, or "destination therapy". LVAD implantations can also be used as a "bridge to recovery" in a small percentage of patients

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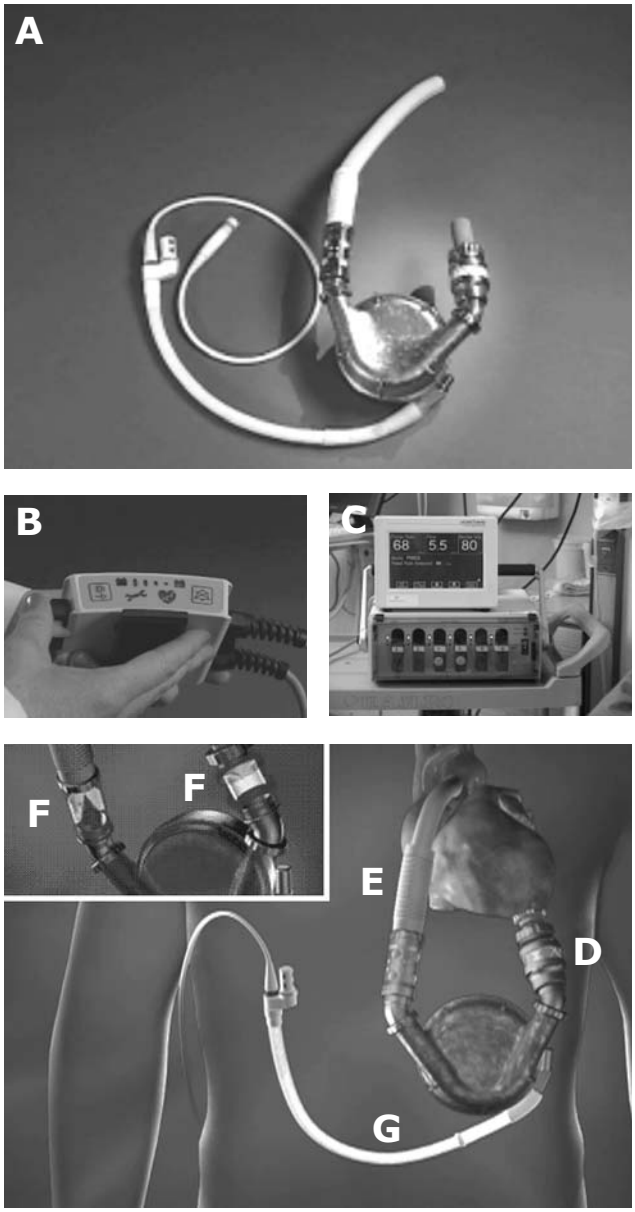


Fig. 1. The HeartMate XVE Left Ventricular Assist Device. The HeartMate XVE LVAD consists of an implantable titanium blood pump (A), an external system controller (B), a system monitor and display module (C) and external power supply component (C) and a pair of wearable rechargeable batteries. The inflow valve conduit of the LVAD (D) is attached to the apex of the left ventricle and the outflow graft (E) is attached to the ascending aorta. This device is equipped with porcine tissue inflow and outflow valves providing unidirectional, pulsatile blood flow based on preload and filling pressures (F). A percutaneous drive line carries the electrical cable and air vent to the battery packs and electronic controls, which are worn on a shoulder holster and belt (G). The patient can be fully mobile while wearing the portable controller and two rechargeable batteries. The batteries can provide periods of stored power of up to six hours before change out. (Adapted from HeartMate XVE Left Ventricular Assist System, Professional Education Program, Thoratec Corporation, 2004)

with potentially reversible etiology of heart failure, such as acute myocarditis or postpartum cardiomyopathy, to obviate the need for heart transplantation. According to the most recent Report of the Mechanical Circulatory Support Database, the vast majority of LVAD recipients between years 2000-2003 were bridged to transplantation, and of the remaining patients, 12% received LVAD as "destination therapy" and 5.3% as "bridge to recovery" [3].

Patient Selection for LVAD Implantation

Although there are no fixed hemodynamic criteria for device implantation, mechanical support should be considered only in patients with profound circulatory failure refractory to medical therapy. The two most common clinical scenarios, which would prompt consideration of patients for LVAD implantation, include either acute cardiogenic shock (most commonly due to acute myocardial infarction or post-cardiotomy) or decompensated end-stage heart failure. Most candidates for LVAD therapy have low cardiac index < 2 L/min/m^2, persistent hypotension or impaired function of end-organs (mental status changes, renal or hepatic dysfunction) despite inotropic support or intra-aortic balloon counterpulsation [5].

All patients considered for long-term LVAD support as "bridge to transplantation" should fulfill the criteria for transplant recipient selection [6]. Typical contraindications for LVAD implantation include fixed pulmonary hypertension, irreversible end-organ failure, active infection, unresolved malignancy, recent pulmonary infarction or advanced age. In patients who are not eligible to heart transplantation due to advanced age or co-morbidities, LVAD implantation may be considered as "destination therapy". In these patients LVAD implantation should be performed as an elective procedure after optimization of risk factors.

Since LVAD filling pressures rely on preserved right ventricular function, in patients with suboptimal right ventricular function, single left ventricular support may lead to worsening of right sided pressures, poor renal function and poor post-implant survival [7]. In these patients strategies to reduce pulmonary hypertension prior to LVAD insertion, such as intraaortic balloon pump support [8], treatment with nitric oxide or sidenafil, nesiritide or ultrafiltration, should be considered [9, 10]. In 15-20% patients with the evidence of chronic severe biventricular failure the implantation of short-term biventricular support device [11] or total artificial heart [12] may be necessary.

All patients undergoing LVAD implantation should have a competent aortic valve to ascertain generation of effective cardiac output. Metallic prosthetic aortic or mitral valve usually require the use of warfarin or conversion to a bioprosthesis at the time of LVAD implant. Atrial septal defects and PFO are usually closed at the time of surgery. Challenging heart anatomy, such as hypertropic cardiomyopathies, large ventricular septal defects or congenital cardiac disease [12] may often preclude LVAD use.

Appropriate timing of LVAD implantation is key to the success of mechanical circulatory support. As illustrated in Figure 2, LVAD implantation should be considered before left-ventricular failure impairs end-organ function, right ventricular function and patient's general medical condition deteriorates [12, 13]. Abnormal renal, hepatic and pulmonary dysfunction, nutritional deficiency and/or cachexia, abnormal coagulation profile, active infection, all contribute to increased morbidity and mortality after LVAD implantation [14]. High composite risk scores assigned to critically ill patients, such as APACHE II score (Acute Physiology and Chronic Health Evaluation), or the Heart Failure Survival Score have shown to correlate closely with poorer outcomes after LVAD implantation [14]. In the highest risk patients the perioperative survival after LVAD implantation is very low and such implantation may be considered futile [15].

Urgent LVAD implantations in patients with cardiogenic shock are usually associated with poorer perioperative outcomes. Whenever possible, it is recommended that before LVAD is implanted, patients should be aggressively treated with maximal conventional therapies, such as inotropes, insertion of intraaortic balloon pump, dialysis or mechanical ventilation. In patients who suffered massive myocardial infarction with > 40% loss of functional left-ventricular mass, temporary support may allow normalization of patient condition until myocardial revascularization can be undertaken. In some patients, however, especially those at risk for multiorgan failure, the surgery cannot be delayed.

In patients with acute cardiogenic shock and uncertain neurologic status or multiorgan failure who require immediate device placement, short-term support with a less expensive temporary device can be utilized, as "bridge-to--bridge" [15]. After few days of temporary support, neurologic and end-organ function can be reassessed to determine the need for long-term LVAD support.

Survival after LVAD Implantation

The REMATCH Trial (Randomized Evaluation of Mechanical Support for the Treatment of Congestive Heart Failure) was the first and only randomized trial which compared the use of mechanical circulatory support as "destination therapy" to optimal medical management in patients with end-stage heart failure ineligible to transplantation [16]. Entry criteria included NYHA class IV heart failure, left ventricular ejection fraction < 25% and either peak oxygen consumption <12 to 14 mL/kg/min or dependence on intravenous inotropic infusion. The projected life expectancy of enrolled patients was less than two years. The trial demonstrated nearly a two fold improvement in survival at one and two years follow up and better quality of life in the LVAD group (52% one-year survival) as compared to patients treated medically (25% one-year survival), as illustrated in Figure 3. The longest living survivor of LVAD implantation is still alive six years after device placement.

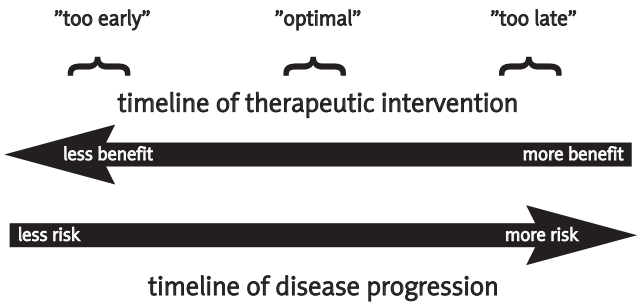


Fig. 2. Severity of heart failure and timing of LVAD implantation.

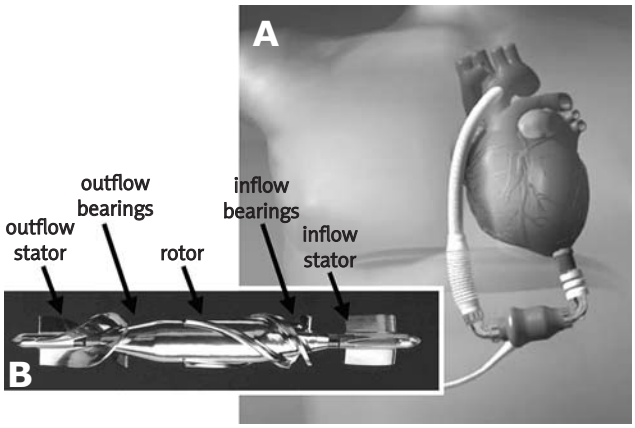
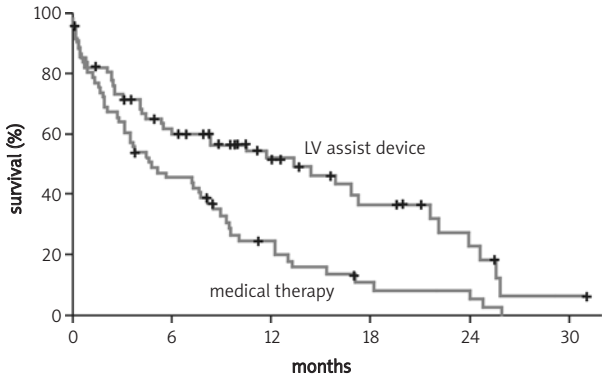


Fig. 3. The axial flow pumps are much smaller than the conventional pusher-plate pumps. The HeartMate II is one of the axial flow pumps (A), which can produce high-flows using electromagnetically actuated impeller housed within a very small titanium pump (B).



No. at risk						
LV assist device	68	38	22	11	5	1
medical therapy	61	27	11	4	3	0

Fig. 4. Kaplan-Meier analysis of survival in the group that received LVAD (n=68) and the group that received optimal medical therapy (n=61) who were enrolled in the REMATCH trial between July 1998 and July 2001. The one-year survival in device therapy group was superior to medical management regardless of treatment crossover; p= 0.002.

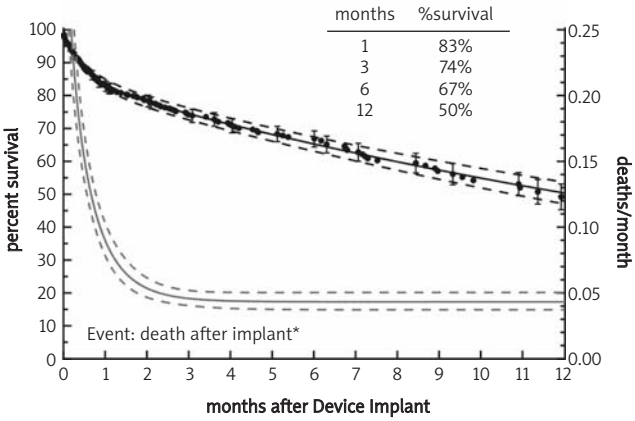


Fig. 5. Actuarial survival after LVAD Implantation "Mechanical" Circulatory Support Database Analysis: January 2002 – December 2004, n=655. (Adapted from the Deng MC, Edwards LB, Hertz MI, et al. International Society for Heart and Lung Transplantation. Mechanical circulatory support device database of the International Society for Heart and Lung Transplantation: third annual report-2005. J Heart Lung Transplant. 2005; 24 (9):1182-7)

Complications after LVAD Therapy

The highest risk of complications and mortality after LVAD implantation occurs within the first postoperative month, as shown in Figure 5. The most common complications as well as causes of death include sepsis, multiorgan failure, right ventricular failure and bleeding [13, 3], Tables I and II. Neurological complications are common, although only a small percentage involving an actual stroke [17].

LVAD Durability

Device failure can be a life-threatening event. In the REMATCH trial 17% of deaths were caused by the device failure and all of these deaths occurred after the first post-implant year. The relatively high device failure rate leading to either patient death or replacement of device, led to several modifications of the older model of HeartMate VE pump. The new and improved model of HeartMate XVE showed much better longevity and less than 1% risk of fatal device malfunction at one year. The reported median mechanical support time of HeartMate XVE is approximately 18 months with only 2% reported device failures beyond the first posttransplant year [13].

Table I. Major causes of death after LVAD implantation (n=655). (Adapted from the Deng MC, Edwards LB, Hertz MI, et al. International Society for Heart and Lung Transplantation. Mechanical circulatory support device database of the International Society for Heart and Lung Transplantation: third annual report-2005. J Heart Lung Transplant 2005; 24 (9): 1182-7.

Major Causes of Death	% of 178 Deaths
Multiple organ failure	34.8%
Hemorrhage	15.2%
Cardiovascular	12.4%
Stroke	10.1%
Infection	7.9%
Pulmonary	5.1%
Other	13.5%
Unspecified	1.1%

Heart Transplantation after LVAD

Under current guidelines, patients who received LVAD as "bridge to transplantation", can be listed as status 1A only for up to 30 days. After this time the patients become listed as status 1B even if still hospitalized, unless significant complications develop requiring immediate transplantation [6]. Seventy percent of LVAD recipients can be successfully bridged to transplantation, compared to 36% of patients managed on inotropic agents (with or without intra-aortic balloon pump support) [3]. Eighty percent of the transplanted patients will survive to hospital discharge. The long-term survival after heart transplantation in patients previously supported with VAD is similar to those supported with inotropes and nearly identical to those not supported by LVAD. If transplantation is delayed, patients

Table II. Major causes of death after LVAD implantation (n=655). (Adapted from the Deng MC, Edwards LB, Hertz MI, et al. International Society for Heart and Lung Transplantation. Mechanical circulatory support device database of the International Society for Heart and Lung Transplantation: third annual report-2005. J Heart Lung Transplant 2005; 24 (9): 1182-7.

Event	% of all Patients
Infection	32.5%
Bleeding	27.8%
Arrhythmia	24.2%
Renal dysfunction	20.6%
Respiratory dysfunction	16.0%
Neurological dysfunction	14.0%
Right ventricular dysfunction	10.7%
Hepatic dysfunction	7.2%
Cardiac tamponade	5.3%
Thrombotic vascular complication	4.4%
Hematoma	2.4%
Pleural effusion	2.2%
Internal organ compromise	1.2%
Pacemaker implanted	0.5%

supported with LVAD as "bridge to transplantation" will demonstrate similar 50% one-year survival as LVAD recipients enrolled in the "destination therapy" arm of the REMATCH trial, Figure 5.

Conclusion

Technology of artificial heart replacement therapies has made a tremendous progress during the last three decades in LVAD design and implementation. New devices can provide life-saving treatment and good quality of life in terminally ill patients with heart failure. More than two hundred centers worldwide perform routine LVAD implantations in patients with advanced heart failure. New generation, small and relatively simple axial flow pumps are currently undergoing clinical trials. They show promise to open up new clinical applications such as treatment of small adults and children.

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