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VENTRICULAR ASSIST TECHNOLOGIES

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EXECUTIVE SUMMARY

Ventricular assist technologies are a valuable tool for patients with severe hemodynamic instability and cardiac dysfunction. These devices are not only important as a bridge to cardiac transplantation, but may serve as a critical therapy for patients with reversible cardiac dysfunction as a bridge to recovery. Ultimately, the greatest expanding indication for the ventricular assist device is as destination therapy in patients who are ineligible for cardiac transplantation. Full support devices such as the Thoratec® VAD, HeartMate®, Novacor®, and Lionheart™ are available for either temporary or long term support. The newer turbine technologies such as the Jarvik 2000® and HeartMate® II are also available for cardiac support and provide a smaller implantable option. Lastly, the Impella® and TandemHeart® technologies are now available for temporary hemodynamic support that can be placed percutaneously reducing the morbidity of surgical placement and explantation.

Introduction

Congestive heart failure (CHF) is a debilitating disease that currently impacts 5 million Americans. As a result of improved survival from acute myocardial infarction, the incidence of CHF is rapidly increasing, with 550,000 new cases diagnosed annually (1). Patients with CHF suffer symptoms resulting from a decreased cardiac output and have an increased risk of sudden death. In the Framingham Heart Study, the 5-year mortality rate for patients with CHF was 75% in men and 62% in women (2). In those patients with New York Heart Association (NYHA) Class IV heart failure who were not candidates for transplant and receive medical therapy alone, the annual mortality rate is 75% (3).

Patients with intractable heart failure despite optimal medical therapy may be candidates for cardiac transplantation. Transplantation is limited, however, by a shortage of donor organs and by patient ineligibility due to age and comorbidities. In addition, patients listed for heart transplantation may die while waiting for an organ. In 2004, 15% of patients waiting for transplant died prior to receiving a heart (4). The need for ventricular assist technologies that can augment cardiac output to meet systemic perfusion deficits in patients with severe cardiac dysfunction is clear. Currently, ventricular assist devices (VAD) can be used to bridge patients to transplantation or recovery, and are increasingly used as destination therapy. Based on data provided by registries from the International Society for Heart and Lung Transplantation, 655 left ventricular assist devices (LVAD) were placed worldwide from 2002-2004. Of these, 78% were placed as a bridge to transplantation, 5% were placed as a bridge to recovery, 12% were placed as destination therapy, and 5% were placed for unspecified reasons (5).

VAD as a Bridge to Transplantation or Recovery

The major application for VADs has been as a bridge to cardiac transplantation in patients with end-stage heart failure. The first implantation of a LVAD as a bridge to transplantation was performed by Phillip Oyer in 1984 (6). Subsequently, the Food and Drug Administration (FDA) approved pneumatically driven LVADs as a bridge to transplantation in 1994 and self-contained, vented electric devices in 1998. A long-term retrospective analysis reported progressive improvements in bridging to transplantation success and post-transplant survival (7). Despite being refractory to optimal medical therapy, those who receive an LVAD as a bridge to transplantation have similar post-transplant survival to those who are maintained on medical therapy alone during the pre-transplant period.

The LVAD may also be utilized as a bridge to recovery in those patients with severe hemodynamic instability from reversible etiologies. Studies have demonstrated that the LVAD can regress cellular hypertrophy, improve myocyte contractile function, and restore beta-adrenergic responsiveness (7-9). However, there are contrasting reports on the rate of sufficient cardiac recovery needed to allow weaning to explant (10).

VAD as Destination Therapy

Due to the shortage of donated organs and patient ineligibility, combined with improvements in VAD technologies, the fastest expanding application for VADs is as destination

therapy in patients with end-stage CHF. This therapeutic strategy was examined in the REMATCH (Randomized Evaluation of Mechanical Assistance in the Treatment of Congestive Heart Failure) trial, which was a randomized, multi-center, NIH-sponsored study in 129 patients with NYHA Class IV CHF, an ejection fraction < 25%, and a VO₂ max < 12 ml/kg/min or dependence on continuous intravenous inotropes (3). The patients were ineligible for cardiac transplantation and were randomized to the HeartMate® left ventricular assist system (LVAS) (Thoratec, Pleasanton, CA) or optimal medical management. The results demonstrated a 48% reduction in all-cause mortality in the LVAD group compared with the medical group (p = 0.001). The median survival was 408 days in the LVAD group and 150 days in the medical group. The LVAD was also associated with improved NYHA functional class (from IV to II) and quality of life. However, the major modes of death in the LVAD arm were complications related to infection and device failure.

To compare outcomes between LVAD devices, the RELIANT (Randomized Evaluation of the Novacor® LVAS in a Non-Transplant Population) trial is ongoing. It is a randomized equivalency trial designed to compare the HeartMate to another LVAD, Novacor (World Heart, Inc., Oakland, CA) in non-transplant eligible patients. This trial is sponsored by World Heart, Inc. and is expected to enroll 390 patients at 40 clinical centers. The primary endpoint is patient survival. Secondary endpoints include health status and neurocognitive assessments, and the incidence of certain adverse events including device failure.

VAD Designs

The VAD may directly augment ventricular function or it may “unload” the ventricle by withdrawing blood from the atrium and directing it into an arterial conduit. The VAD can be placed in an extracorporeal or intracorporeal position, and may require surgical implantation or may be implanted by a less invasive approach, such as a minimally invasive cut down or percutaneously. The VAD is in stark contrast to artificial hearts that are placed in the orthotopic position and require removal of the dysfunctional heart.

VADs are generally separated into full support devices, which can maintain physiologic levels of cardiac output, or partial support devices, which augment cardiac output to a lesser degree in patients with less severe cardiac dysfunction. The support can be pulsatile, in synchrony with the functioning cardiac cycle, or non-pulsatile (continuous). The full support pulsatile devices use a pneumatic or electrical energy source to drive the pump and require a compliance chamber. The first generation pumps used an external drive connected by a drive line that passed either compressed air or electricity through the skin. Some of the second generation devices have a power-pack placed subcutaneously that charges through the skin via an induction coil. The continuous devices are non-pulsatile and propel blood continuously to assist ventricular output. These devices are smaller in size and may be suitable for complete implantation in smaller patients.

Full Support VAD

Pulsatile

The Thoratec® VAD system (Thoratec, Pleasanton, CA) is positioned extracorporeally and connected to tubes (cannulae) inserted into the heart (Figure 1). The pump has a rigid plastic case that contains a flexible pumping sac. Blood is ejected from the pump when the pumping sac is compressed by air from the external control console. Within the inflow and outflow conduits, mechanical valves control the direction of blood flow. The Thoratec VAD has a stroke volume of 65 ml. It can be operated at up to 100 beats per minute, resulting in blood flow rates of up to 7 liters per minute. Critical issues related to the device are the need for strict anticoagulation, infection risk due to indwelling cannulae, and limited mobility. One or two Thoratec VADs can be used to provide left, right, or biventricular support.

The Novacor VAD is an abdominally implanted, electro-magnetically driven pump that collapses a polyurethane bladder, propelling blood from the left ventricle into the aorta (Figure 2). In contrast to the Thoratec VAD, the Novacor device utilizes porcine valves to maintain directional blood flow. The device has a percutaneous drive line which provides power from an external battery source. The system is completely self-regulating, automatically adjusting its beat rate and stroke volume in response to the recipient's changing circulatory requirements. The Novacor LVAD was the first VAD utilized as a bridge to transplantation and was the first mechanical circulatory support device to support a single patient for more than six years. Critical issues with this device are the strict need for anticoagulation and infection risk due to the percutaneous drive line.

The Lionheart™ (Arrow® International, Inc., Reading, PA) is unique among LVADs because it has a wireless power transmitter, allowing it to be completely contained inside the chest. The external power pack is worn on a belt and charges the internal batteries by conducting its power transcutaneously. This pulsatile VAD pumps when a metal plate pushes on a plastic blood sac, forcing the blood out of the sac. The metal plate is driven by a miniature electric motor, with a controller that varies pumping based on activity level. A theoretical benefit is a reduced risk of infection since there are no external cannulae or drive lines. The device is used strictly for destination therapy and has been in clinical trials in Europe since 1999 and in the US since 2001.

The Thoratec HeartMate® IP (implantable pneumatic) became the first commercially available, FDA approved LVAD in the US for use as a bridge to transplantation in 1994. This pneumatic (air-driven) LVAD is a titanium alloy pump that consists of a blood chamber, air chamber, drive line, and inflow and outflow conduits. Each conduit is a titanium cage that contains a 25-mm porcine valve within a woven Dacron-fabric graft. Textured surfaces within the blood chamber promote the development of a cellular lining, which helps prevent blood clots and infection. There is no need for anticoagulation, which may lead to fewer bleeding complications. With a stroke volume of 83 milliliters and a maximum pumping rate of 140 beats per minute, the IP LVAD can provide flow rates of up to 12 liters per minute.

The Thoratec HeartMate XVE (extended lead, vented electric) LVAD is an electrically powered version of the IP, which has wearable batteries allowing the patient to be mobile. It is

currently the only FDA approved LVAD available for destination therapy. The system consists of a titanium blood pump that is comprised of a blood chamber, a motor chamber, a drive line, and inflow and outflow conduits. The XVE LVAD has a maximum stroke volume of 83 milliliters. It can be operated at up to 120 beats per minute, resulting in flow rates of up to 10 liters per minute.

Continuous

The Jarvik 2000 FlowMaker® (Jarvik Heart, Inc., Manhattan, NY) is a valveless axial flow blood pump that uses electrical power to rotate a vaned impeller, which is its only moving part. Unlike the previous technologies, this device provides continuous non-pulsatile augmentation of the cardiac output. The device is 2.5 cm in diameter, 5.5 cm long, weighs 85 grams, and is positioned directly into the left ventricle (Figure 3). The impeller is a neodymium-iron-boron magnet, supported by ceramic bearings and housed inside a welded titanium shell. A small cable, which exits the body through the abdominal wall, delivers power to the impeller. The device requires strict anticoagulation and the drive line may increase the risk of infection. The normal operating range for the control system is 8,000 to 12,000 revolutions per minute (rpm), which will generate an average pump flow rate of 5 liters per minute. Patients have been sustained for more than 400 days on this device.

The Thoratec HeartMate® II is also a high-speed, axial flow, rotary blood pump that produces no pulsatile action. It is 4 cm in diameter, 6 cm long, weighs 375 grams, and is positioned in sequence between conduits from the left ventricle to the aorta. Within the pump is a rotor that contains a magnet. The rotor assembly is rotated by the electromotive force generated by the motor. The rotor propels the blood from the inflow cannula out to the natural circulation. The pump speed can vary from 6,000 rpm to 15,000 rpm, providing blood flow of up to 10 liters per minute. The device is significantly smaller than the other HeartMate systems and as such, it may be suitable for a wider range of patients, including small adults and children. Clinical trials are currently underway evaluating the safety and efficacy of the HeartMate II as both a bridge to transplantation and as destination therapy.

Partial Support VAD

The CircuLite™ MicroVAD (CircuLite, Inc., Hackensack, NJ) is a minimally invasive, partial support left ventricular assist device intended for destination therapy. The MicroVAD consists of a mixed flow pump, an inflow cannula, an outflow graft, and a controller system. The pump is designed to provide 2-3 liters per minute of blood flow to a larger, less ill population of Class III and IV CHF patients. A key advantage of the pump is its 14 mm diameter, 25 gram weight, and 1.75 ml priming volume. The MicroVAD is unique in its left atrial-to-peripheral artery flow path with the pump placed subcutaneously in a “pacemaker” pocket near the shoulder. The pump’s inflow cannula is placed in the left atrium, allowing a less invasive access to the left ventricle and preserving function of the left ventricle. The pump’s outflow graft discharges blood to the subclavian artery. The size of the pump may decrease perioperative morbidity associated with its implantation because it can be performed with a less invasive surgical procedure. The MicroVAD pre-clinical animal studies were successfully conducted using a surgical thoracotomy procedure. The FIM (First-In-Man) clinical studies will use a mini-thoracotomy approach, while the phase I IDE (investigational device exemption) clinical studies

will use a video-assisted thoracoscopic procedure. Ultimately, the pivotal IDE clinical study will be conducted using the MicroVAD endovascular system.

The Impella Recover® system (Impella CardioSystems AG, Aachen, Germany, recently acquired by Abiomed, Inc., Danvers, MA) is a miniaturized impeller pump located within a catheter (Figure 4). The device can provide support for the left side of the heart using either the Recover LD 5.0 (implanted via direct placement into the left ventricle) or the Recover LP 5.0 LVAD (placed through a small cut down in the groin and positioned in the left ventricle), or the Recover LP 2.5 (placed percutaneously). There is also a Recover RD for right ventricular support. The microaxial pump of the Recover LD/LP 5.0 can pump up to 4.5 L/min at a speed of 33,000 rpm. The pump is located at the distal end of a 9 Fr catheter. At its largest outside diameter, which contains the pump housing, the Impella measures 21 Fr. The catheter shaft contains the electrical connections for the pump motor and sensor, as well as a separate tube used for transfer of purged fluid. The Impella Recover LD/LP 5.0 system was developed to provide immediate, temporary (up to 7 days) ventricular support in patients who have heart failure following heart surgery and who are not responding to standard medical therapy. The Recover LP 2.5 is only 4mm in diameter (12F) and delivers 2.5 liters of blood per minute. It can augment circulatory support for up to 5 days, such as during recovery from myocardial infarction.

The TandemHeart® PTVA® (percutaneous transeptal ventricular assist) (CardicAssist Inc., Pittsburgh, PA) is a continuous-flow centrifugal percutaneous ventricular assist device (pVAD) positioned extracorporeally (Figure 5). Cannulae are inserted percutaneously through the femoral vein and advanced across the interatrial septum into the left atrium. The pump withdraws oxygenated blood from the left atrium, propels it by a magnetically driven, six-bladed impeller through the outflow port, and returns it to one or both femoral arteries via arterial cannulae. The pump weighs 8 ounces and is capable of delivering blood flow up to 3.5 liters per minute. The pump also has a proprietary fluid-infusion system that provides cooling and lubrication to the impeller, designed to enhance thromboresistance. In addition, the system provides localized anticoagulation to the blood inside the pump, reducing the need for systemic anticoagulation. The TandemHeart pVAD provides short-term support from a few hours up to 14 days, giving the heart time to strengthen and potentially regain native function.

Conclusions

Ventricular assist technologies are rapidly expanding to meet increasing clinical applications. The largest application of VADs remains bridge to transplantation in patients with severe hemodynamic instability. It is very reassuring that patients undergoing VAD placement have a similar post-transplant outcome to those on medical management despite their sicker status. Improvement in the technology has also led to decreased rates of complications during surgical placement and long-term use. In addition, temporary, partial support devices that can be placed with a minimally invasive surgical procedure or percutaneously are increasingly available as an adjunctive therapy for patients with severe cardiac dysfunction. Finally, VAD utilization as a bridge to recovery and as destination therapy will likely continue to expand with the development of newer generation technologies.

Figure Legends:

Figure 1. The Thoratec® VAD System

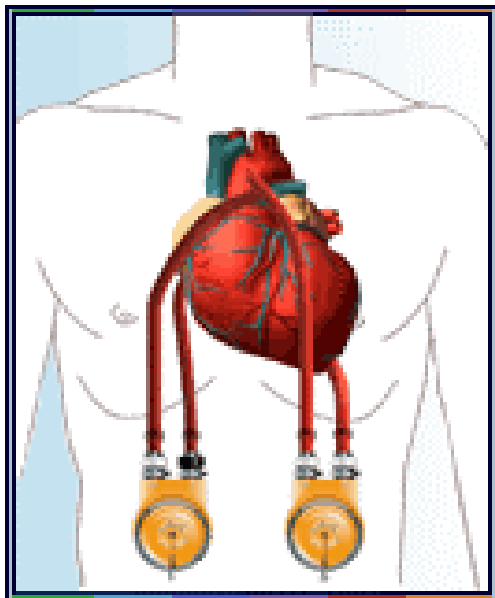


Figure 2. The Novacor® LVAS

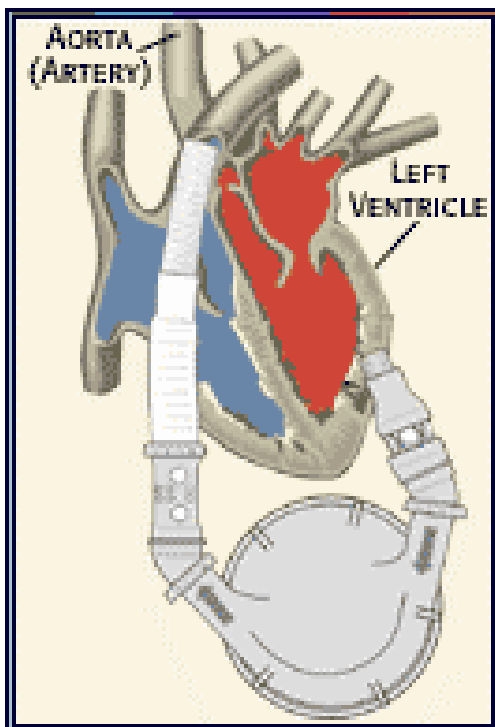


Figure 3. The Jarvik 2000 FlowMaker®

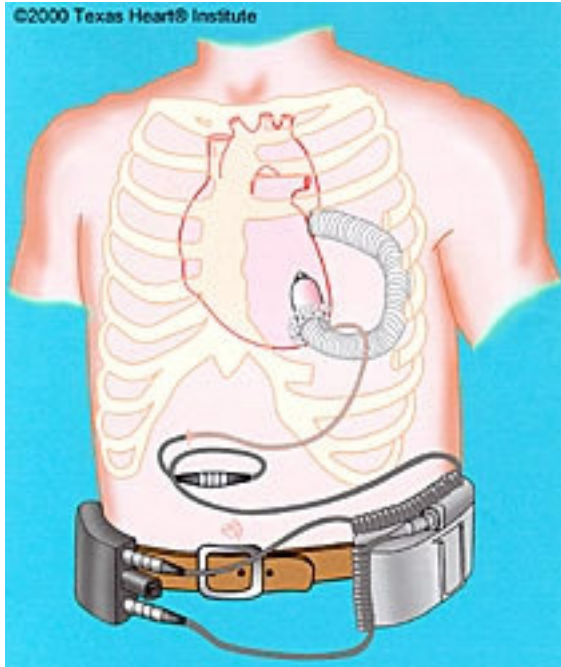


Figure 4. The Impella Recover® system

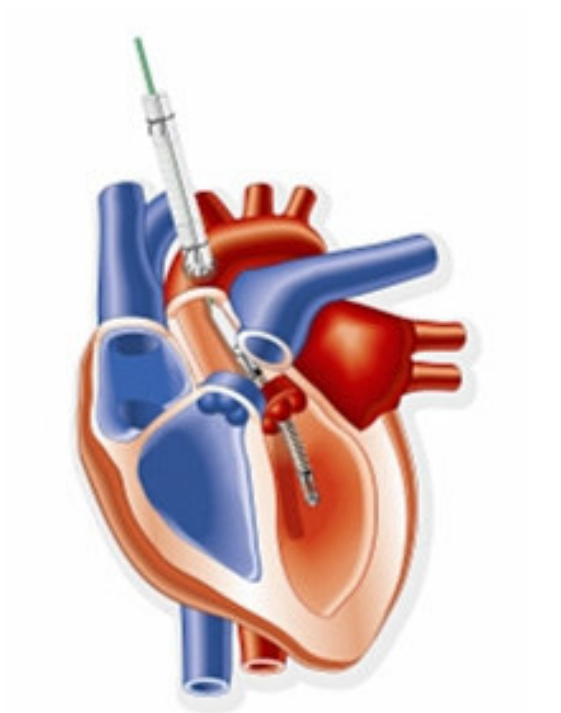
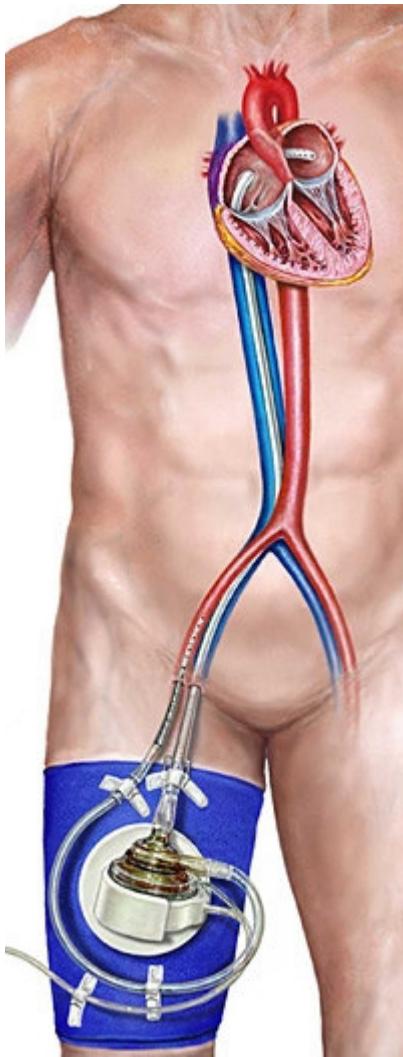


Figure 5. TandemHeart® PTVA®



References

1. Thom T, Haase N, Rosamond W, et al. Heart disease and stroke statistics--2006 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation* 2006;113(6):e85-151.
2. Ho KK, Anderson KM, Kannel WB, Grossman W, Levy D. Survival after the onset of congestive heart failure in Framingham Heart Study subjects. *Circulation* 1993;88(1):107-115.
3. Rose EA, Gelijns AC, Moskowitz AJ, et al. Long-term mechanical left ventricular assistance for end-stage heart failure. *N Engl J Med* 2001;345(20):1435-1443.
4. Orens JB, Shearon TH, Freudensurge RS, Conte RS, Bharade SM, Ardehali A. Thoracic organ transplantation in the United States, 1995-2004. *Am J of Transpl* 2006;6:1188-1197.
5. Deng MC, Edwards LB, Hertz MI, Rowe AW, Keck BM, Kormos R, Naftel DC, Kirklin JK, Taylor DO. Mechanical Circulatory Support Device Database of the International Society for Heart and Lung Transplantation: Third Annual Report—2005. *J Heart Lung Transplant* 2005;24:1182-1187.
6. Dagenais F, Portner PM, Robbins RC, Oyer PE. The Novacor left ventricular assist system: clinical experience from the Novacor registry. *J Card Surg* 2001;16(4):267-71.
7. Morgan JA, John R, Rao V, et al. Bridging to transplant with the HeartMate left ventricular assist device: The Columbia Presbyterian 12-year experience. *J Thorac Cardiovasc Surg* 2004;127(5):1309-1316.
8. Bruckner BA, Stetson SJ, Perez-Verdia A, et al. Regression of fibrosis and hypertrophy in failing myocardium following mechanical circulatory support. *J Heart Lung Transplant* 2001;20(4):457-464.
9. Heerdt PM, Holmes JW, Cai B, et al. Chronic unloading by left ventricular assist device reverses contractile dysfunction and alters gene expression in end-stage heart failure. *Circulation* 2000;102(22):2713-2719.
10. Ogletree-Hughes ML, Stull LB, Sweet WE, Smedira NG, McCarthy PM, Moravec CS. Mechanical unloading restores beta-adrenergic responsiveness and reverses receptor downregulation in the failing human heart. *Circulation* 2001;104(8):881-886.