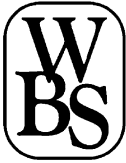

CARDIOLOGY
CLINICS

Cardiol Clin 21 (2003) 51–55

Indications for long-term assist device placement as bridge to transplantation

Benjamin C. Sun*

Ohio State University Medical Center, Columbus, OH, USA

The use of mechanical support as a bridge to cardiac transplantation has evolved to become the standard of care in most cardiac transplant programs throughout the world. Approximately 30,000 patients are listed worldwide for cardiac transplantation every year, and only around 3500 cardiac transplantations are performed [1]. Cardiac transplantation rates have reached a plateau since 1989 [1,2], and unless society's attitude toward organ donation radically changes, cardiac transplantation will remain an epidemiologic triviality. Assist devices as a bridge to transplantation currently exacerbate this discrepancy, as the destination is still transplantation. Cardiac assist devices, total artificial hearts, xenotransplantation, and others will likely play important complementary roles in the future treatment of heart failure. These therapies need to be developed not only to prolong life but also to provide good quality of life, so the paradigm shift can occur and these alternative therapies become destination. Only then will we be able to make an impact on this epidemic.

As of July 2002, 3302 patients have received the Heartmate® LVAD systems (both pneumatic and vented electric). There have been 1341 patients supported with the Thoratec® system, more than half of these patients received bi-VADs (n = 751). There were 495 isolated LVAD implants, 89 isolated RVADs, and 6 patients not accounted for. Most of these implants were used as a bridge to transplantation (Greg Robinson, personal communication).

* Division of Cardiothoracic Surgery, Ohio State University Medical Center, Columbus, OH.

E-mail address: sun03@medctr.osu.edu

Indications for ventricular assist devices

All of the commercially available VADs are designed to address three specific, though overlapping, indications. When a patient is in severe cardiogenic shock from a potentially reversible cardiac insult, an assist system may be used as a bridge to myocardial recovery. As the heart recovers and is able to sustain the circulation, the assist device may be weaned and subsequently explanted. Cardiac transplant candidates who continue to deteriorate despite aggressive pharmacologic support can become candidates for long-term assist support. The assist device is used as a bridge to cardiac transplantation and is explanted at the time of transplantation. This article focuses on this indication. The third indication for assist systems is as an alternative to cardiac transplantation, though this use is currently investigational, pending FDA approval. This indication will likely be the most important use of mechanical support in the coming decade. Bridge to transplantation will be the focus of this chapter.

Institutional criteria for device placement

The algorithm often used to select therapy determines what the survival to transplant will be with a "medical bridge," as compared with a "mechanical bridge." The anticipated length of support relative to patient stability and rate of decompensation is the factor that most directly influences the timing of device implantation. This becomes an institutional as well as regional factor. Many regions have quite long wait times for cardiac transplant, and individual risks can exacerbate this. Large patient, blood group O, and high panel reactive antibodies contribute to prolonged waiting times for cardiac transplantion. These patients

0733-8651/03/$ - see front matter © 2003, Elsevier Science (USA). All rights reserved.
doi:10.1016/S0733-8651(03)00004-3

often benefit from earlier device implant when their operative risks are lower. These issues are astronomically more complex in the current listing criteria defined for status 1a and 1b, especially with regard to mechanical support.

Listing and status criteria for mechanical support can influence device implantation. Under current guidelines, a patient who receives an LVAD or Bi-VAD can be listed as a status 1a (most acute status) for up to 30 days (provided the patient remains in the hospital). After 30 days, the patient becomes listed as a status 1b, even if the patient remains in the hospital. Unfortunately, in many regions, status 1b patients are infrequently transplanted as more patients reach 1a criteria before transplant due to the long wait times and the inevitable clinical decompensation of other patients. More than 90% of the patients receiving heart transplants in the United Network of Organ Sharing (UNOS) region 2 are transplanted as status 1a in blood groups A or O (Gift of Life Region 2 Thoracic Committee, unpublished data). The wait times of patients in blood group O who are status 1a exceeds 100 days (Greg Robinson, personal communication). This relegates patients in these blood groups to long-term, almost destination therapy, until a device-related complication occurs. When a device-related complication develops, the patient can be up-listed to status 1a.

There are still regions in the nation where status 2 patients are routinely transplanted. The threshold for device implantation in these areas tends to be higher, as the "borderline" patient can often be successfully supported for a short time on higher dose inotropes and a balloon pump.

The decision of which device to use in a given clinical situation often rests not only on what is available in an institution but also on the experience, comfort, and biases of the physicians with the devices available to them. Device selection almost approaches an art form when trying to match device to patient and vice versa in a given clinical situation. Though there are trends and anecdotes, there is insufficient experience to unequivocally declare that a certain device, or combination of devices, is the perfect treatment for a given clinical scenario. Indeed there are few studies to date that attempt to compare outcomes between two long-term assist devices in a single institution [3–5].

Institutional resources may limit mechanical support programs to a single system. The system that exists may only be able to support the left ventricle but has the ability for outpatient therapy. However, a patient requiring biventricular support may not be adequately treated with this device. The system that allows both univentricular as well as biventricular support, however, has not been FDA approved for outpatient therapy yet. The consequences of these issues from a patient quality of life as well as cost perspective can be substantial.

Patient eligibility for long-term device implantation

Patient selection and timing are crucial for good outcomes in this critically ill population. Attempts have been made to stratify risk by hemodynamic, physiologic, and laboratory parameters [6]. These parameters tend to reflect the level of end-organ function or dysfunction and are useful in general risk assessment; however, end-organ injury can rapidly change during periods of instability, and the patient is a moving target. The challenge is to identify the patient who will not survive to cardiac transplantation on medical management alone, yet has not decompensated so far to be unable to tolerate the device implant.

These long-term devices should not be used for cardiac arrest–type resuscitation. For the patient who has significant organ dysfunction, it can still be very difficult to deny them treatment because of high surgical risk, because denying them mechanical support often condemns them to death. Nevertheless, attempting to resuscitate a cadaver generally results in the same outcome, only after consuming significant physical, psychological, emotional, and financial resources. A poor outcome often leads to a delay in implementing support on the next candidate, which again leads to a poor outcome. This scenario can become a vicious cycle to where placement of a device is perceived by the patients and staff as a testimony of failure. Conversely, appropriately treated patients become a testimony of success. Turning down a patient request for a device implant because they are too healthy is a relatively desirable situation.

Existing valve prosthesis/intracardiac shunts

The flow patterns of left ventricular assist mandate a competent aortic valve. Patients with incompetent aortic valves can have that surgically addressed at the time of device implant. Having prosthetic valve in the aortic position has been an area of historical concern. During support with an LVAD, the prosthesis remains shut. The subvalvular region is thus at risk for thrombus formation. If the prosthesis were to open during a native ventricular ejection, the thrombus could be

dislodged. The bioprosthetic in the aortic position can often be left alone, though anticoagulation may be beneficial to minimize thromboembolic events [7]. A mechanical prosthesis in the aortic position can easily be closed with a patch at the time of device implant. This prevents the valve from opening, and anticoagulation may not be required.

Mitral valve prostheses are generally not considered a contraindication for device support, because the valve will continue to open and close provided the apex of the left ventricle is cannulated for device inflow. Anticoagulation is recommended for any kind of mitral prosthesis [8].

Quiescent intracardiac shunts may become clinically apparent and significant with changes in chamber pressures when these devices are initiated. A patent foramen ovale (PFO) is present in up to 20% of the population but is clinically quiescent in the vast majority of these patients. With unloading of the left ventricle and left atrium with LVAD support, right atrial pressure will be higher than left atrial pressure. Even a small PFO in these circumstances can produce a large right-to-left shunt manifested by arterial desaturation and potential air embolism. These shunts should be closed when identified and should be assessed for both before and after initiation of device support by transesophageal echo flow studies. If identified preoperatively, cannulation techniques for cardiopulmonary bypass (CPB) may be altered to facilitate repair.

Right-sided circulatory failure

Preoperative assessment of the right-sided circulation is critical in determining the type of support that may be needed. It can be surprisingly difficult to assess. Right-sided circulatory failure can involve either or both the right ventricular stroke work (RVSW) as well as the pulmonary vascular resistance (PVR). The central venous pressure (CVP) and the presence of tricuspid insufficiency are also important data points in this assessment.

If the RVSW is low and the CVP and the PVR are also low, the patient can often do well with only left-sided support. Right-sided support may still be required in the immediate postoperative course (as the PVR rises from inflammatory-mediated events related to CPB). As the inflammatory response resolves and PVR returns to normal, right-sided support can be withdrawn. The use of inhaled nitric oxide is often the only treatment required to treat the PVR, and RVAD support subsequently is not needed. If the RVSW is low and the CVP is high, the patient will likely benefit from an RVAD regardless of the PVR.

Though the two electrically actuated LVAD systems approved for outpatient management are costlier than the pneumatically driven devices, outpatient management may offset their cost difference. Placing a paracorporeal RVAD in the patient with an implantable LVAD would require a return back to the operating room for RVAD explant to take advantage of the discharge potential of the implantable LVAD. For the patient who may have a long wait time, and discharge desirable, the extra initial hospital costs could be recovered with prolonged outpatient therapy (compared with a prolonged in-hospital course). The improved mobility of the patient, better quality of life with the implantable systems, and anticipated cost savings with outpatient therapy could justify this approach. The paracorporeal Thoratec® system has a portable drive system that is approved in Europe for outpatient therapy and is undergoing FDA trials in the United States for this indication as well. Implanting a Thoratec® system on both right and left sides is certainly an excellent option for patients with biventricular failure, because a trip back to the operating room for RVAD removal is rarely necessary. Unfortunately, it currently relegates patients to in-hospital support until transplant. If the portable drive system is approved for outpatient therapy, the Thoratec® system will likely become the Bi-VAD configuration of choice.

The concept of "fixed PVR" needs to be revisited in this heart failure population. Many of us have observed fixed PVR of 7 or 8 Woods units decrease to 2 to 3 Woods units when on chronic mechanical support. If a patient is placed on chronic LVAD or Bi-VAD support and the PVR does not improve to acceptable levels, the patient should be assessed for options other than isolated orthotopic heart transplant.

Device size and magnitude

The current implantable systems are somewhat bulky and do require a certain body size ($> 1.5\ m^2$ BSA) as well as an appropriate body habitus to comfortably implant these devices. The size issue is not only related to the technical ability to implant the device, but the lowest rate the device will flow before increased thrombus risk develops. Patients as small as $0.8\ m^2$ BSA have been successfully supported by the Thoratec®

system, which would be the preferred device in the smaller patient population (< 1.5 m^2). Large patients often have longer wait times and may benefit from early implant with an electrically actuated pump.

Blood type and preformed antibodies

Patients' blood types, as well as the presence of preformed antibodies, affect their wait times. The controversies surrounding preformed antibodies will not be addressed here. Nevertheless, if high preformed antibodies mandate cross-matching at an institution, it will likely increase the wait time. This would influence the type of support, and the placement of an implantable device would be advantageous especially if discharge is an option.

Etiologic diagnosis of heart failure

There are many types of disease processes that lead to heart failure. The more common ones include idiopathic/dilated cardiomyopathies and ischemic cardiomyopathies. Mechanical support is commonly used in the support of patients who have class IV heart failure with these diagnoses. Other disease-specific diagnoses can be challenging to support with the current devices. These include hypertropic cardiomyopathies, acute myocardial infarction with a large ventricular septal defect, endocarditis with heart failure, tachyarrhythmia-induced heart failure, and heart failure in patients with congenital cardiac anomalies.

Some of these anatomic challenges could be addressed by excising the heart and implanting a total artificial heart (TAH). The CardioWest TAH is a pneumatic, implantable system and is currently the only TAH in clinical use for bridge to transplantation. It is the current iteration of the widely publicized Jarvik-7-100 heart used in the patient Barney Clark. It has been used worldwide as a bridge to heart transplantation in 79 patients. A total of 55 patients (70%) were transplanted of whom 50 survived (91% of patients transplanted) to discharge [9].

In most centers, a TAH is unavailable, and creative surgical techniques are used to address individual anatomic challenges. The Thoratec® BiVAD system can be used as a "TAH" if the ventricles are excised and large vascular grafts attached to the atria, facilitating cannula attachment to the atria. A subsequent end-to-end attachment of the outflow graft of the pump to the aorta/pulmonary artery completes the vascular circuit. This technique was described and has been used successfully by Latif Arusoglu from Bad Oeynhausen, Germany [10].

Social and emotional support structure

The patients' support system includes social, emotional, as well as financial components. These issues are often overlooked in the decision process of device selection. If there is limited support for discharge, the additional cost for an implantable system that allows for such may not be justified. Current reimbursement rates are beyond the scope of this article. Hospital and professional reimbursements are lagging behind the development and clinical application of this technology, and this certainly could influence device selection in any given institution.

Though many patients are eager to be discharged on support, many require the comfort of hospital-based care given the nature of "life support" that they are requiring. Appropriate support networks need to be established before discharge. The possibility of outpatient management must be considered with device selection. This hinges on the patient's support network as well as the region's anticipated support time for that patient.

Summary

The current indications for long-term mechanical support as bridge to transplantation first require the patient to be a transplant candidate. Often times a patient presents with limited history and refractory cardiogenic shock, where a full transplant work-up for contraindications cannot be safely performed. The use of short-term mechanical support can be used to help filter out many patients who have easily identifiable contraindications to heart transplant. Nevertheless, patients need to be listed for a heart transplant before the implantation of some of these devices. This paradigm needs to be altered, because there are many instances where mechanical support can be used to support a patient for an intervention to "make" them a transplant candidate where they otherwise would not have been. Long-term mechanical support can overcome the cardiac contraindication to the surgical-/interventional therapy to "cure" them of the process that would have prevented them from being a good cardiac transplant candidate in the first place. Noncardiac surgical procedures are well tolerated in these patients [11].

The FDA is currently evaluating the Vented Electric Heartmate® system for use as destination

therapy for patients who are not transplant candidates. Approval for this indication (with a device that is already approved for bridge to transplantation) will allow this paradigm shift. This system could be used in the group who may be good candidates, but not determined. If they were subsequently determined to not be a good surgical candidate, they would be chronically supported with the LVAD as destination therapy.

References

[1] Hosenpud JD, Bennett LE, Keck BM, et al. The registry of the International Society for Heart and Lung Transplantation fifteenth official report–1998. J Heart Lung Transpl 1998;17:656–68.

[2] United Network for Organ Sharing (UNOS). Annual report. 1996.

[3] Mehta S, Souza D, Boehmer J, et al. Comparison of Pierce-Donachy (PD) and TCI left ventricular assist systems as bridge to transplant—an institutional experience [abstract]. ASAIO 1999.

[4] El-Banayosy A, Arusoglu L, Kizner L, Tenderich G, Minami K, Inoue K, Korfer R. Novacor LVAS versus Heartmate as a long-term mechanical circulatory support device in bridging patients: a prospective study. J Thorac Cardiovasc Surg 2000; 119(3):581–7.

[5] Minami K, El-Banayosy A, Sezai A, Arusoglu L, Sarnowsky P, Fey O, Koerfer R. Morbidity and outcome after mechanical ventricular support using Thoratec, Novacor, and HeartMate for bridging to heart transplantation. Artif Organs 2000;24(6): 421–6.

[6] Oz MC, Goldstein DJ, Pepino P, et al. Selection scale predicts patients successfully receiving long-term, implantable left ventricular assist devices. Circulation 1995;92(Suppl II):II-169–73.

[7] Rao V, Slater JP, Edwards NM, Naka Y, Oz MC. Surgical management of valvular disease in patients requiring left ventricular assist device support. Ann Thorac Surg 2001;71(5):1448–53.

[8] Barbone A, Rao V, Oz MC, Naka Y. LVAD support in patients with bioprosthetic valves. Ann Thorac Surg 2002;74(1):232–4.

[9] Arabia FA, Copeland JG, Smith RG, Sethi GK, Arzouman DA, Pavie A, Duveau D, Keon WJ, Masters R, Foy B, Carrier M, Dembitsky W, Long J, Kormos R. International experience with the CardioWest total artificial heart as a bridge to heart transplantation. Eur J Cardiothorac Surg 1997; 11(Suppl):S5–10.

[10] Arusoglu L. Thoratec Bi-VAD as a total artificial heart. Thoratec users meeting, Phoenix, AZ, May 2002.

[11] Goldstein DJ, Mullis SL, Delphin ES, el-Amir N, Ashton RC Jr, Gardocki M, Jordan DA, Catanese KA, Levin HR, Rose EA. Noncardiac surgery in long-term implantable left ventricular assist-device recipients. Ann Surg 1995;222(2): 203–7.