Thoracic and Cardiovascular Surgery

Total Artificial Heart—Concepts and Clinical Use

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End-stage congestive heart failure remains the leading cause of death in the United States. Despite advances in medical treatment, it also remains the most common reason for admission to the hospital. The gold standard of treatment for the failing heart, orthotopic heart transplantation, is limited by a shortage of donor hearts. There are also a significant number of patients who are not transplant candidates due to comorbid conditions and/or inability to tolerate immunosuppressive therapy. To meet the need for this latter group, the medical field has embraced ventricular assist device (VAD) therapy to extend survival and improve quality-of-life for the end-stage cardiac patient. This therapy, however, has been currently limited to the failing left ventricle and is still fraught with complications that limit long-term and widespread use. The total artificial heart, as currently available with two devices, is rapidly becoming the treatment of choice for biventricular failure.
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Total replacement of the failing heart with a mechanical pump has been the Holy Grail for cardiac surgeons for decades. The U.S. Artificial Heart Program was begun in 1964 under President Johnson. This was at the behest of surgeons such as William DeBakey and Willem Kolff who, with others, visualized and pioneered early work to create a total artificial heart (TAH).[1] A number of iterations of complete replacement of the failing heart have been developed and tested clinically. These include the Liotta heart,[2] the Akutsu TAH,[3] and the trailblazing Jarvik-7.[4]

In the 21st century, this goal is on the horizon, as the total artificial heart (TAH), in two differing conceptualizations, has been tested in feasibility trials. The two devices that are now commercially available are the CardioWest TAH (Syncardia Systems, Inc., Tucson, AZ), and the AbioCor TAH (Abiomed, Inc., Danvers, MA). The CardioWest TAH (hereinafter referred to as the TAH-t) has reached significant clinical use and, thus, full FDA approval in 2004 as a bridge to transplant. The AbioCor implantable replacement heart (referred to as the TAH-irh) received FDA approval in 2006, under the Humanitarian Use Device (HUD) provision of the Food, Drug, and Cosmetic Act, for destination therapy. Their concepts of design, indications for their use, methods of implantation, patient management regimens, and clinical experiences are presented below.

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Devices—Concept of Design

CardioWest TAH

The CardioWest TAH is an iteration of the original Jarvik-7. A pair of prosthetic ventricles, made of polyurethane, is pneumatically driven and provides pulsatile flow (Fig. 1).

The prosthetic ventricles, made of biocompatible polyurethane, have a capacity of 70 mL. The ventricles are pneumatically driven and there are four flexible polyurethane diaphragms between the blood surface and the air sac. When compressed air is forced into the air sacs simultaneously, compression is effected onto the blood sac and ejection occurs in simulation of cardiac systole. Cardiac ejection in the TAH-t thus occurs in parallel from the left and right side. As the air sac is deflated, the blood sac is filled passively from the atrial connection. This can be altered slightly by adding a small amount of vacuum to the prosthetic ventricle. Two mechanical valves are situated along the prosthetic ventricle to provide unidirectional inflow and outflow. These are single-leaflet Medtronic-Hall valves, respectively sized 27 mm (for inflow to the ventricle) and 25 mm (for outflow from the ventricle). The large valves and short outflow blood path are advantageous in decreasing stasis and thrombosis (Fig. 2).

The ventricles are also configured slightly differently. The left-sided ventricle has inflow and outflow valves slightly closer together to match the proximity of the mi-

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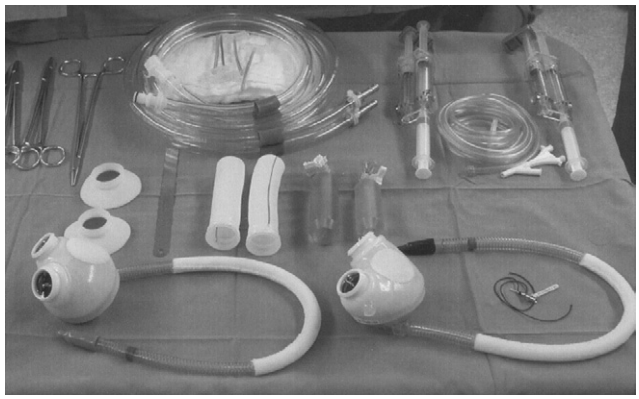

Figure 1 TAH-t components. (Courtesy of Syncardia Systems, Inc.)

tral annulus to the aorta. The right-sided ventricle is farther apart to not only reflect the slightly greater distance between the tricuspid annulus and the pulmonary artery but also to allow the pulmonary outflow graft to override the aortic outflow graft.

The prosthetic ventricles are connected via quick-connect silicone cuffs to two atrial connectors on the cuffs and two connectors on the end of the grafts sewn to the aorta and pulmonary artery. Of high importance, in the process of cardiectomy, great care must be maintained to preserve the atrial annuli. This not only gives needed strength to the connection but is a hemostatic boon to suturing to atrial tissue. The device atrial cuffs are trimmed to approximately 3 to 5 mm to minimize thrombotic surface area.

The compressed air is delivered via an external console through two separate air tubes connected to the right and left prosthetic ventricles. The console has two independent controllers that allow redundancy for emergency backup. Compressed air cylinders inside the console can be used to mobilize the patient. Maximum stroke volume is 70 mL but, ideally, partial fill and full ejection is the goal. Generally this is about 50 to 55 mL. Partial fill allows for stroke volume alteration as the patient's volume status changes. Full ejection

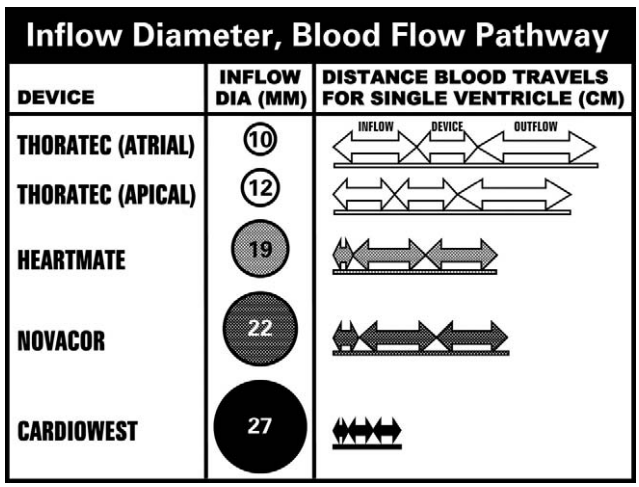

Figure 2 Inflow comparison of VAD/TAH. (Courtesy of Richard Smith, MSEE, CCE.)

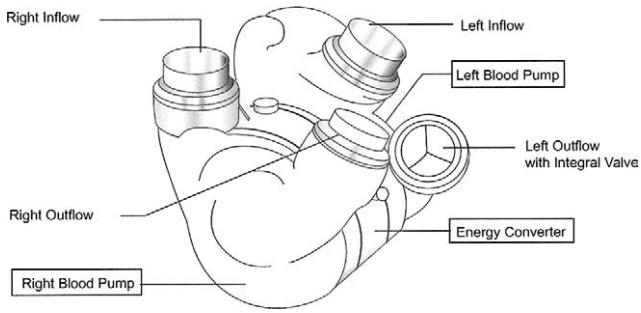

Figure 3 TAH-t design. (Courtesy of Abiomed, Inc.)

maximizes cardiac output and ventricular washing with minimal changes to the controller settings. A diagnostic unit (laptop on the console) from the console presents parameters of the TAH-t, stores data, and configures the system. Pressure waveforms are displayed beat-to-beat for each cardiac cycle, as well as for the continuum of support. Of note, if the laptop unit malfunctions or loses power, the TAH-t will continue to function. The pressure waveforms displayed confirm full ejection of the ventricles. The drive flow waveforms, also displayed concurrently, mark the beginning and end of diastole and calculate fill volumes. These drive flow waveforms help determine the partial fill and volume status.

The large console, although mobile, does not allow for discharge from the hospital. Newer portable drivers, which have been tested in Europe, are undergoing trial currently in the United States.

AbioCor TAH

The AbioCor TAH (Fig. 3) consists mainly of a thoracic unit, which houses two blood pumps in one housing, separated by an energy converter. Each blood pump is a hard-shelled chamber containing a blood sac, which has inflow and outflow valves. The inner lining of this chamber, including the trileaflet valves, are made and lined seamlessly from a proprietary membrane termed Angioflex. Hydraulic fluid fills the space between the blood sacs and the energy converter. When the hydraulic fluid is moved from one side to the other, the blood is squeezed in one chamber, thus effecting systole. During this part of the cycle, blood is actively drawn into the other pump, filling it for the next cycle, thus effecting systole. The left and right blood pumps alternately eject blood. A true innovation, this engenders that the left and right "hearts" are ejecting in series, and not in parallel (Fig. 4). Furthermore, the thoracic unit is an actively filled device, rather than allowing passive filling. Low atrial, or filling, pressures can therefore limit inflow and decreased pump output.

The energy converter consists of a unidirectional hydraulic pump that spins at 3,000 to 10,000 rpm to pressurize the hydraulic fluid. A bidirectional switching flow control valve directs flow of the hydraulic fluid toward either side of the energy converter, or simply toward each of the ventricles. These components, including pressure transducers that measure the hydraulic fluid pressure on each side, are mounted in a metal artificial septum.

The pumping chambers contain one-way inflow and out-

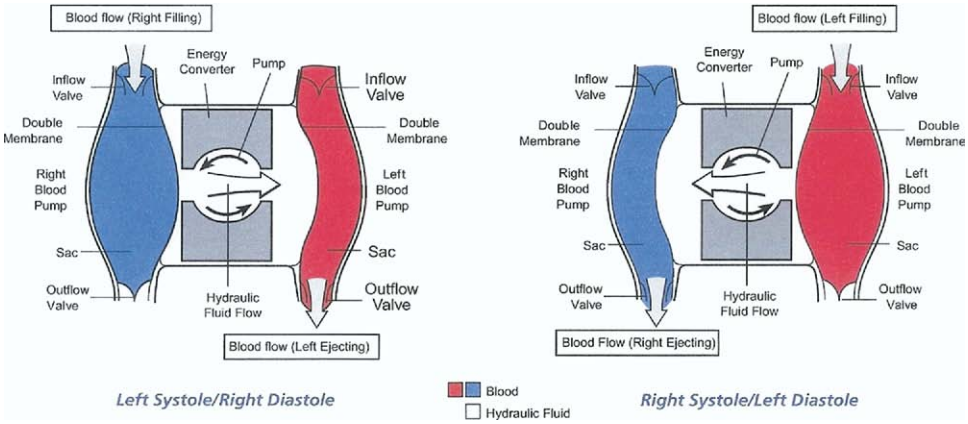

Figure 4 TAH-t flow schematic. (Courtesy of Abiomed, Inc.) (Color version of figure is available online at http://www.semthorcardiovascsurg.com.)

flow valves. They are seamlessly joined with the pump sac, the inner face of which is flexible. This inner flexible double membrane allows hydraulic pressure from the converter to cause ejection but prevents any mixing of blood and hydraulic fluid. The thoracic unit is connected to the circulatory system using two cuffs and grafts. The thoracic unit has four key settings. Beat rate and balance are set manually and left and right motor speeds are automatic in nature. By controlling the beat rate, the user can increase cardiac output and decrease right atrial pressure.

Of particular note in the AbioCor design is a balance system that produces lower flow from the right blood pump than the left blood pump. This is to compensate for the left side of the heart receiving flow from the bronchial arteries and is idealized to keep the left atrial pressure (LAP) within an appropriate range of 10 to 15 mm Hg. The left/right flow balance is set manually on the console, from a range of 0 (occluder valve fully open, low LAP) to 400 (occluder valve fully closed, high LAP).

A controller is implanted in the abdomen, preperitoneally, which switches the bidirectional flow control valve according to the beat rate setting. It opens and closes the occluder valve according to the balance setting and sets the hydraulic pump motor speeds for the left and right strokes.

A battery is also implanted preperitoneally that allows the patient freedom from external power sources for 25 to 30 minutes. The power is transmitted from an external source between an external and internally implanted unique energy transfer system. This is termed transcutaneous energy transmission (TET) and is achieved by electromagnetic coils that receive radio waves and convert it into DC power. The implanted TET coil is usually placed in a subclavicular position and improper placement or positioning can cause thermal injury and/or patient discomfort (Fig. 5).

Clinical Indications for Use

Summary of Clinical Studies for FDA Approval

The CardioWest temporary Total Artificial Heart (hereinafter referred to as the TAH-t) underwent a multi-center (five) clinical study with the intent to bridge transplant eligible patients at risk of imminent death from biventricular failure. Of the total 95 patients implanted with the TAH-t, 81 (70 males) were designated the core implant group. All patients were in NYHA class IV at time of enrollment. There were 35 patients that met the inclusion criteria but did not receive a TAH and therefore served as controls. Of note, 15 patients were on heart-lung machine/ECMO support, 25 patients had refractory malignant arrhythmias, 13 patients had aortic regurgitation, stenosis, or prosthesis and three patients had ventricular septal defects.

Trial success, defined at 30 days of being (1) alive, (2) NYHA class I or II, (3) ambulatory, (4) not ventilator dependent, and (5) not on dialysis, was achieved in 56 (69%) of the 81 core patients. Sixty-four of the 81 core patients (79%) reached transplant after a mean time of 79 days. In comparison, the control group of 35 patients survived a mean of 8.5 days. Fifty-eight (72%) survived to 30 days post-transplant and the 1 year survival post-transplant was 85%. Device failure occurred in only one patient, where a tear in the diaphragm after 4 months resulted in the patient's demise.[6]

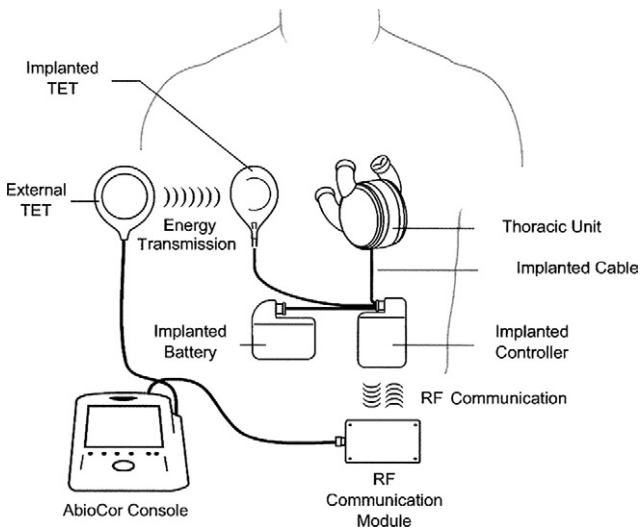

Figure 5 AbioCor component design. (Courtesy of Abiomed, Inc.)

Table 1 TAH Inclusion/Exclusion Criteria

Inclusion criteria
Age > 18 years
Ineligibility for heart transplantation
Acceptable device fitting evaluation
Biventricular failure
Optimized medical management
Inability to be weaned if on a temporary mechanical circulatory support system
Exclusion criteria
<70% probability of death within 30 days
Significant potential for reversibility of heart failure
Chronic dialysis
Recent cerebrovascular accident
Irreversible liver failure
Blood dyscrasia
Suspected or active systemic infection
Positive serum pregnancy test results
Severe peripheral vascular disease
No adequate social support system

The CardoWest TAH-t is FDA approved and indicated for use as a bridge to transplant in cardiac transplant-eligible candidates at risk of imminent death from biventricular failure. It is currently intended for use inside the hospital, although U.S. trials are underway for discharge with a portable driver. Contraindication of use of the TAH-t include patients who are not cardiac transplant eligible, who cannot be adequately anticoagulated while on the device, and patients who are not anatomically suitable for implantation in the chest cavity. This generally includes patients with body surface areas $< 1.7\ m^2$ or who have a distance between the sternum and the tent anterior vertebral body measure <10 cm.

The AbioCor TAH has obtained conditional FDA approval as a destination device with humanitarian device exemption. Inclusion and exclusion criteria from the AbioCor multicenter initial feasibility trial are listed in Table 1.

Biventricular failure is the sine qua non for which the TAH was designed. As right ventricular (RV) failure is most commonly due to primary left ventricular (LV) and the ensuing pulmonary hypertension, efforts over the past decade have emphasized left ventricular assist devices (LVAD) for mechanical support. However 10% to 20% of LVADs will require RV support, either at the time of the implant or soon thereafter.[9] Survival of patients placed on BiVADs, whether done preemptively or in a sequentially divided manner after initial LVAD placement, has a worse prognosis.[10] There is also a restriction for chronic RVAD support, as only LVADs have been designed for chronic long-term support. Most patients who are identified preoperatively with severe biventricular failure are relegated to short-term, paracorporeal devices. Historically, the most common of these are the Thoratec pVAD, iVAD, the Abiomed BVS 5000, and ABS 5000. Our group and others have also employed a hybrid approach in which long-term, intracorporeal devices are used for LV support and a short-term device is placed for right-sided support. This is done with the intention of recovering the RV, as pulmonary hypertension decreases with chronic LV unloading. Regardless, when comparing TAH to BiVAD support, survival is markedly improved. BiVADs have generally shown survival in multiple publications to be in the 40% to 50% range.[11,12] This is in contrast to the 79% reported by Copeland and coworkers in the trial study.[5]

At the University of Pennsylvania, we employ the guidelines found in Table 2 for use of the TAH.

Method of Implantation

CardioWest TAH-t

Implantation of the TAH-t involves three major components after ventriculectomies are performed.[7] They include the atrial cuffs, the outflow grafts, and the ventricles with attached drivelines. Before surgery is initiated, the atrial cuffs are trimmed to leave a 3 to 5 mm edge to which the reinforced mitral and tricuspid annuli are sewn. The outflow grafts are stretched and preclotted. In the early experience, this was done with the patient's blood but has now been replaced by spraying with Coseal to coat the interstices of the graft. Finally, the drivelines are brought through two subcostal incisions. This was also initially described as being done before heparinization but can be done after the atrial cuffs and outflow grafts are sewn in as well.

The partial cardiectomy, i.e., left and right ventriculectomies, are key to a successful implantation. Standard cannulation of the aorta and both superior and inferior vena cavae are performed. Caval snares are used to isolate venous drainage and the aorta and pulmonary artery are freed proximally, leaving full length for subsequent transplantation. After bypass is initiated, aortic crossclamp is applied, the cavae are snared and excision of the heart is begun. Of paramount importance, and significantly different from orthotopic heart transplantation, is the preservation of the annuli of the tricuspid and mitral valves. Thus, an incision is begun on the ventricular side of the AV groove. Anteriorly, it is extended across the right ventricular outflow tract, and posteriorly, across the interventricular septum. The leaflets and chordae of the tricuspid and mitral valves are excised, leaving a safety rim of 2 to 3 mm valve tissue to ensure annular integrity. The aorta and pulmonary artery (PA) are incised circumferentially just above their respective valves. Finally, the excess muscle remaining on the ventricular side of each annuli is trimmed away (Fig. 6).

At this time, the coronary sinus is first oversewn to prevent backflow of blood through the sinus to the cut vessels along the AV groove. The left atrial appendage is tied off. The annuli are then buttressed with Teflon felt strips along the entire

Table 2 TAH Clinical Indications

1. Biventricular failure
2. LV failure with intractable malignant arrhythmias
3. LV failure with prior mechanical heart valve replacement
4. LV failure with severe anatomical damage (e.g., ventricular septal defect, ventricular rupture)

LV, left ventricular.

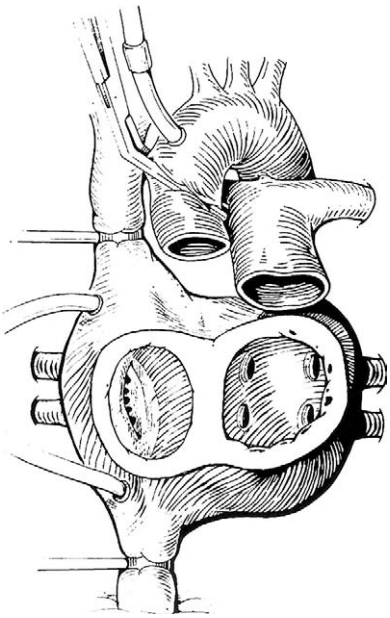

Figure 6 Excisional view for TAH. (Courtesy of Jack Copeland, MD.)

outer walls of the right and left atrial cuffs. The strips are cut to a width of approximately 10 to 12 mm and sewn into place with 3-0 polypropylene (Fig. 7).

The atrial cuffs, after being inverted and inserted into the atria, are then sewn to these buttressed suture lines with a second layer of 3-0 polypropylene. The cuffs are everted and connected to quick-fit testers to test the suture line. Any gaps or leaks should be repaired at this time as access to the suture line is highly limited once the prosthetic ventricles are connected.

The outflow grafts are then anastomosed to the great vessels. One of the outflow grafts is measured to approximately 6 cm (for the PA) and 1 to 3 cm (for the aorta). This is to compensate for the shortened distance between the left-sided ventricle outflow valve and the aorta and for the PA outflow that will override the aortic outflow graft. The pulmonary artery anastomosis is constructed first for purposes of access and is constructed with running 4-0 polypropylene in an end-to-end fashion. The aortic outflow graft is anastomosed in a similar manner. Specific testers for the outflow grafts are then connected and the suture lines tested for any leaks.

When surgical hemostasis of all suture lines is achieved, the ventricles are brought into the wound. The left-sided driveline is exited through the left midclavicular line, 5 to 10 cm below the costal margin. The right-sided driveline is exited 4 to 5 cm medial to the left drive line. The ventricles are finally connected, first to the atrial cuff and then to the respective outflow graft. The left side, lying posteriorly, is connected first and then the right side is connected sequentially. During the time of connection, the ventricles should be filled with saline through the outflow valve to minimize large pockets of air. Care must be taken to orient the inflow connection so that twisting of the outflow grafts does not occur. A de-airing vent should be placed in the ascending aorta and the patient placed in steep Trendelenburg, before taking the crossclamp off. After adequate positioning and de-airing, the patient is weaned from CPB and pumping is begun with the device.

AbioCor TAH

Due to the multiple components of the totally implantable TAH, some components should be placed and/or their pockets created before heparinization and cannulation.[8] First, an infraclavicular incision is made and the internal TET coil is placed anterior to the pectoral muscle fascia. The cable from this coil is passed to the lower part of the sternotomy incision. Preperitoneal, or subrectus, pockets are created for the internal battery and controller.

Cannulation is then performed in a similar manner as above. After the crossclamp is applied, biventriculectomy is performed in a careful fashion to maintain good annular tissue. Both atrial cuffs are trimmed to size and anastomosed with two running layers of polypropylene. This is reinforced with felt strips and leak testing is performed in a similar manner. A cast model of the AbioCor thoracic unit is positioned in the chest to determine appropriate length and orientation of the outflow grafts. The outflow grafts are then anastomosed in an end-to-end fashion to the great vessels. Of particular note with this device, the aortic outflow graft is positioned anterior to the pulmonary artery graft because of the configuration of the thoracic unit.

The AbioCor thoracic unit is brought into the field and the appropriate electrical connections are made. After connecting to the atrial cuffs and outflow grafts, caval tapes are released. The device is filled and air is evacuated by unique side ports arising from the outflow grafts. The device is actuated to flow with the crossclamp on until all demonstrable air is ejected from the side ports. After the crossclamp is released, the patient is weaned from cardiopulmonary bypass and the

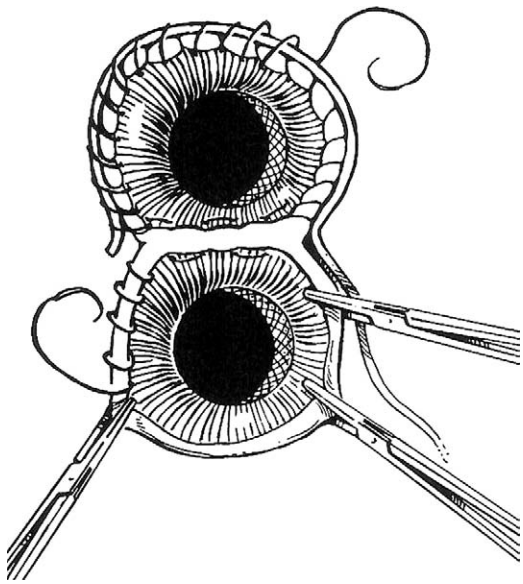

Figure 7 Atrial cuff technique for TAH. (Courtesy of Jack Copeland, MD.)

device rate is increased to fully supply an adequate cardiac output.

Patient Management of the TAH

Three major facets of management deserve special consideration for patients with a TAH. These include patient monitoring, volume/hemodynamic management, and anticoagulation. This is in addition to the routine "care" that these end-stage heart failure patients demand: supporting and recovering end-organ function, respiratory and ventilator management, infection control, maintenance of nutrition, pain control, and gradual mobilization.

Patient Monitoring

Of note, there is no need for ECG monitoring and leads or pacemakers are not necessary. There is no need for cardiotropic medications. Extensive attention must be paid to central line placement and positioning. Migration of central lines into the TAH can markedly interfere with the function, and in the case of the TAH-t, can cause marked valvular dysfunction. For the TAH-t, care must be maintained to keep the drivelines from kinking or tearing. In the case of the TAH-irh, although there are no external drivelines, area of coverage between the external and internal TET coils must be cared for meticulously.

Both systems require specialized personnel trained in and understanding of system parameters. This point must be emphasized, as multiple personnel who come in contact with the TAH patient must have an on-site referral for monitoring and trouble-shooting (Table 3).

Normal parameters for each device are delineated in device clinical regimens and are maintained by the VAD coordinators in conjunction with the bedside caretakers. For each device, care must be maintained that power from the battery and external sources is routinely examined.

In addition, normal parameters for postop cardiac surgical patients should be followed. These include arterial blood pressure (ABP), central venous pressure (CVP), pulse oximetry, and left atrial pressure (LAP) if desired. Of note, there is no ability to measure with a Swan-Ganz catheter and central lines must be closely monitored to keep from migrating into the devices.

Volume/Hemodynamics

Hypovolemia in both TAH systems manifest as inflow limitations. This can be right sided, left sided, or bilateral but all result in decreased output. The usual causes of hypovolemia in these patients are blood loss, diuretic therapy, and "third space" fluid losses. Diagnosis is usually made by low filling pressures, manifested by low CVP or LAP.

A second type of "TAH" hypovolemia can occur from inflow limitation secondary to tamponade or mechanical causes. Tamponade, and even localized clots, can impair filling of the atria and result in decreased filling of the chambers. Mechanical obstruction, i.e., device malpositioning, kinking of the cavae, may also cause a similar scenario. Diagnosis is made by increased CVP or LAP in the face of decreased filling. Although CXR or echocardiograms are helpful, a high index of suspicion is necessary for early diagnosis.

The aim of blood pressure management is to maintain standard physiologic ranges, with the thought of increasing end-organ perfusion. Standard medications used to control blood pressure fall into the categories of vasoconstrictors and vasodilators. In the former category, the most common drugs use are Vasopressin, Levophed (norepinephrine), and Neo-Synephrine (phenylephrine). Commonly used vasodilators include Nipride (sodium nitroprusside), nitroglycerin, and nitric oxide. At our institution, inhaled prostacyclin is also used for patients with underlying pulmonary hypertension.

Table 3 Postoperative TAH Parameters

AbioCor Parameters	CardioWest Parameters
Left and right hydraulic pressures	Beat rate
Beat rate	Systolic duration (% systole)
Balance	Right and left drive pressures
Left and right motor speeds	Vacuum
AbioCor estimated cardiac output	

Anticoagulation

Both versions of the TAH require a strong adherence to full anticoagulation and must be monitored closely. The goal is to achieve and maintain normal hemostasis so that appropriate clot formation occurs without inappropriate thrombosis. The balance is to maintain this hematological state without causing excessive bleeding.

CardioWest TAH-t

Management of the CardioWest TAH-t mandates multidrug therapy for anticoagulation. This consists of (1) an anticoagulant (usually intravenously administered heparin postoperatively and conversion to warfarin when tolerated), (2) a platelet antiaggregant (aspirin), (3) a "platelet-stabilizing" agent (dipyridamole), and (4) an "antiinflammatory" agent (pentoxifylline).

Heparin is begun when chest tube output is sufficiently diminished, indicating surgical hemostasis. It is continued till adequate recovery of renal and hepatic function occurs. Warfarin is begun at this time, with the caveat that the patient's nutritional status is improving and an anabolic state is achieved. Dosing of warfarin and down-titration of heparin is guided by thromboelastography (TEG). The TEG testing is critical to maintaining normocoagulability, while minimizing thrombosis. They are conducted daily in the first 2 to 3 weeks and then twice weekly as necessary. Aspirin is used as the principal antiaggregant. It is generally started at an 81 mg/d dose when chest tube drainage is satisfactorily diminished and the platelet count is adequate ($>$50,000). The effectiveness is monitored by measuring platelet counts, platelet aggregation studies (to ADP, collagen, epinephrine, and arachidonic acid), and bleeding times. The level of inhibition of aggregation is targeted to a value at least 50% to 75% below

the lower limit of the normal range of platelet aggregation for the individual institutions laboratory. Dipyridamole is administered concomitantly with aspirin to stabilize the platelets, allowing greater resistance to activation by the components of the TAH-t. Dosing begins at 75 to 100 mg every 6 to 8 hours and is empirically increased for every 100,000 increase in platelet count. The same monitoring measures are used as for aspirin. Patients should be clinically watched for headache, flushing, and dropping blood pressure, as a reflection of the vasodilating properties of dipyridamole. Pentoxifylline, which possesses nonselective phosphodiesterase isozyme-inhibiting properties, is a significant antiinflammatory agent that allows stabilization of red blood cells. It is started immediately after surgery in doses of 200 to 400 mg every 8 hours. Using this regimen, the group at the University of Arizona achieved a linearized yearly stroke rate of 0.068 for patient-year of implantation.[6]

AbioCor TAH

Management of the AbioCor TAH also demands a similar anticoagulation regimen. Anticoagulation is effected by heparin, followed by warfarin therapy. Platelet aggregation and stabilization is regulated by the use of aspirin and dipyridamole. For patients that cannot tolerate aspirin, Ticlid (ticlopidine) or Plavix (clopidogrel) is recommended. For attenuating inflammation and fibrinolysis, Amicar (aminocaproic acid) or Trasylol (aprotinin) is recommended.

Similarly, tests to monitor coagulation systems include the partial thromboplastin time (PTT), international normalized ratio (INR), thromboelastography (TEG), and platelet aggregation studies.

Clinical Experience

CardioWest TAH

More than 700 TAH-t have been implanted worldwide. In the U.S., the feasibility study was conducted in five centers from 1993 to 2002.[5] Mean support time was 79.1 days and 79% of the implanted patients survived to transplantation. As a corollary to the maintenance of end-organ function while on TAH support, the survival to 1 year after transplantation was 85.9%. A number of studies have verified the safety and efficacy of the TAH-t as a bridge-to-transplant.[13-15] Leprince and a group of European investigators reported on 127 patients over a 15 year experience. Their longest implantation was to 602 days and 6 patients were longer than 4 months. Still, there was only one device malfunction. The largest users of this device have attained survival to transplant in excess of 80%. A number of patients in the Bad Oeynhausen experience have also been discharged from the hospital (personal communication). This has been the impetus for the newer U.S. trial with the portable device. A multiinstitutional risk factor analysis of the TAH-t was recently reported.[16] Of note from previous studies, patients who received extracorporeal BiVAD support exhibited increase risk with increased age, previous mediastinal operation, elevated blood urea nitrogen, elevated bilirubin, and mechanical ventilation before implantation. Furthermore, elevated risk factor profiles for LVAD patients alone have included right heart failure, high CVP and other markers of end-organ damage, such as elevated liver enzymes, respiratory failure, etc. In this multivariate analysis, none of the above-mentioned factors influenced survival of patients bridged with the TAH-t. A major factor for this can be ascribed to the markedly increased flow that the TAH provides, as opposed to standard single VADs (Fig. 8).

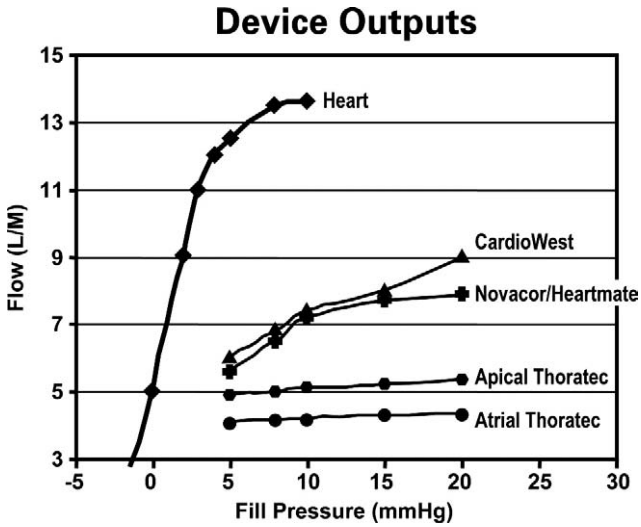

Figure 8 Flow comparison of VAD/TAH. (Courtesy of Richard Smith, MSEE, CCE.)

AbioCor TAH-irh

The AbioCor TAH was first implanted in a human in 2001 as part of a destination therapy trial for end-stage heart failure patients.[17] Fourteen patients received the device before FDA review. Patients were only offered the device if their life expectancy was <30 days. The 30-day survival rate in these patients was 71% as opposed to the predicted survival rate of 13%. Although all 14 patients in the initial group have died, the longest survival was >1 year and a number of patients were able to be discharged home. There was increased incidence of thromboembolism, found on autopsy to be due to thrombus on the support struts, in the early group. Thus, during the remainder of the feasibility trial, this necessitated changes in the design of inflow sewing cuff of the device and in the postimplantation anticoagulation protocol.[18] Of particular importance is that no serious device malfunction was reported in this trial. Most encouraging has been the success of the TET system, with little to no interruption in power supplied to the device. This was a crucial factor in the design of the AbioCor TAH from its onset, to allow full implantation without interruption of skin barriers.

Conclusion

The improvement in survival for the TAH is causally multifactorial. Primarily, the offending organ is removed. With the removal of the heart, thrombus formation and propagation,

arrhythmias, bleeding points, and such become a moot point. Although the device itself can form thrombus as well, presumably the nonthrombogenic materials and anticoagulation can mitigate this circumstance. Without doubt, future studies for device support will have to regard the thorn of thrombosis as a key element to ensuring long-term survival. Secondarily, the devices produce massive flow from the onset of operation, engendering rapid end-organ recovery. The REMATCH trial has taught us that multisystem organ failure, whether on medication or device, is the end result of diminished cardiac output.[19] Preserving end-organs, from preoperative management to immediate postoperative watchfulness, is paramount in increasing meaningful survival. Finally, the dearth of medication to support the failing heart is a boon to the postoperative management of these patients. The mechanical ability to increase flow with just volume and beat rate minimized the physiologic side effects of many cardiac drugs on other organ systems.

The AbioCor TAH, with its full implantability, has a marked advantage. In the REMATCH trial, 40% of patients on device support died of infectious causes.[20] Continued massive efforts by many groups point to the importance of this complication in VAD and TAH therapy.[21]

The clinical application for the TAH, either as a bridge to transplant or destination therapy, is on our horizon. After decades of research, trials, experimentation, and testing, the early pioneers have been validated for their vision of replacing the human heart. The mechanical performances of these two devices have been "validated" clinically in human implants. The ingenuity of radically different designs points to possible multiple pathways toward cardiac replacement. Improvements in materials, drug support, electronics, and energy sources will ensure a continuing viability for this therapy.

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