Update on the Total Artificial Heart: CardioWest™, ABIOCOR™ and Other Devices

Therapy of advanced cardiac failure may be divided into 3 general categories: medical, surgical and cardiac substitution or replacement. Medical therapy is primarily pharmacologic, that is using drugs to increase cardiac contractility (digitalis glycosides, intravenous inotropes), decrease myocardial oxygen consumption (vasodilators), alter filling volumes (diuretics), and treat associated diseases (diabetes, hypertension, lipid abnormalities, etc). These methods may significantly improve symptoms, but will not change patient mortality.

Interventional therapy such as percutaneous coronary angioplasty, coronary artery bypass, valvular repair or replacement may relieve symptoms but may not affect the progression of the basic process.

Replacement therapy may include cardiac transplantation, insertion of a temporary, long term or permanent left ventricular assist device (LVAD) or implantation of a total artificial heart (TAH). All of the devices may be used to resuscitate a moribund patient, as a bridge to cardiac transplantation or as “destination” therapy – intended for permanent support in those patients unsuitable for transplantation. Also, since the survival after cardiac transplant is approximately 10 years (some patients have survived more than 20 years), and the availability of transplantation is significantly limited (approximately 2000 cardiac transplants were done in 2004, as many as 40000 patients could be candidates for transplantation and 460 patients in 2004 died waiting for transplant), this is only a limited option considering the demand.

History

Circulatory support as a concept has existed for at least 200 years and a total artificial heart was proposed in the 1920s. The era of modern cardiopulmonary bypass dates to 1951 and was used successfully in 1953 by Gibbon. Use of heart lung machines at many hospitals allowed an expanding surgical assault on congenital and acquired defects. At the same time research into artificial internal organs progressed and the first artificial heart was implanted into an animal in 1957. Support for the research for humans was growing and in 1964 the National Institutes of Health established the Artificial Heart program to foster both development of a total artificial heart and other circulatory support devices such as LVADs. DeBakey, in Houston, implanted the first LVAD in a patient in 1963. It was used to support the patient post cardiotomy but unfortunately, the patient died after 4 days of therapy. DeBakey again, 4 years later, used an LVAD to support a patient after an aortic valve replacement and the patient was able to be weaned after 10 days of support and was later discharged from the hospital.

At the same time, TAH research was continuing at Baylor and on April 4, 1969, Cooley implanted an artificial heart designed by Domingo Liotta into a patient who could not be weaned from CPB after an aneurysmectomy. The device was dual chambered, pneumatically powered by an external console and used valves to maintain unidirectional flow. It was used for 64 hours until a donor had been secured permitting the first use of a TAH (or any device) as a bridge to transplantation. Unfortunately, this patient died of pneumonia only a day and a half after transplant. This implantation caused a marked controversy.
in medical circles and lead directly to the famous schism between Cooley and DeBakey which was not healed until 2007.

Cooley again in 1981 implanted a second TAH designed by Akutsu in a 26 year old patient who could not be weaned from CPB after coronary artery bypass surgery. This heart was also a pneumatically powered, 2 chambered device that employed reciprocating diaphragms. This patient was also successfully supported as a bridge to transplant for 55 hrs but succumbed 10 days after transplant to respiratory, renal and infectious causes.

Jarvik-7/CardioWest™ Total Artificial Heart

Kolff, who had originally implanted a TAH in an animal as noted above, developed, along with Robert Jarvik, the Jarvik-7 TAH in the 1970s. This device was used first clinically in 1982 by DeVries as a permanently implanted device in a patient unsuitable for transplantation. The Jarvik-7 was also a pneumatically powered, biventricular, pulsatile pump which was connected to the patient’s atria by synthetic cuffs. Air was the driving gas with the pneumatic chambers separated from blood containing ones by polyurethane diaphragms. Tilting disc valves maintained unidirectional flow. The drive lines were connected through the chest wall to an external console. 5 patients at 3 different centers were supported for from 10 to 620 days. This TAH was unfortunately associated with numerous complications. In 1985 the Jarvik-7 was entered into trials as a bridge to transplantation and was successfully used as such by Copeland in 1986. The Jarvik-7, renamed the Symbion TAH, was used in more than 170 patients between 1985 and 1991 as a transplant bridge with an overall success rate of 66%. The United States Food and Drug Administration (FDA) withdrew the investigational device exemption in 1991 because of inadequate FDA regulatory compliance. The device rights were acquired by CardioWest and the IDE restored. The CardioWest TAH was used successfully in a clinical trial which showed an 81% survival rate at 1 year when used as a transplant bridge. CardioWest (Syncardia Systems, Tucson, AZ) received approval to market the device as a bridge to transplant in 2004. Since that time the company reports that it has been used successfully in the U.S., Canada and Europe several hundred times to date as a bridge to transplant and is an accepted and commercially available choice for bridging.

ABIOCORTM Total Artificial Heart

The ABIOCOR TAH is a device that uses different concepts than previously, in that electrohydraulic energy transfer is employed to produce pulsatile flow and the pump is designed to be contained entirely within the body - it communicates to its’ external hardware without direct skin penetration through transcutaneous energy transfer for power and radiofrequency communication for transmission of data and control signals. It has a unique right-left flow balancing mechanism which allows the elimination of an external vent and a compliance chamber.

This TAH was developed by ABIOMED, Inc. (Danvers, MA) and the Texas Heart Institute with National Institutes of Health support for permanent support of patients with severe cardiac failure who are not candidates for other therapy and for whom transplantation is not appropriate either. The first ABIOCOR TAH was implanted by Dowling and Gray in Louisville, KY in 2001 as part of a Phase 1, FDA sponsored trial. A total of 14 patients were entered in this trial before it was completed with the longest surviving patient being supported for 512 days. A smaller version of the original ABIOCOR is presently undergoing preclinical testing prior to starting clinical trials.
Clinical Complications Associated with the TAH

Prior to implantation of any device of this type, size of the device versus size of the patient may create potential “fit” problems. All TAHs are relatively large and placement into patients less than 1.7 m² is usually not possible, which restricts use to larger patients and mainly to males. Smaller versions are under development by several companies.

During implantation and postoperatively, significant bleeding is encountered. Few patients have not had previous cardiac surgery, most have some degree of visceral organ dysfunction due to low cardiac output or right sided congestion producing clotting abnormalities, plus requiring preoperative anticoagulation to prevent thromboembolism. This therapy may be difficult or dangerous to withdraw or reverse. TAH implantation is certainly an extensive procedure with extensive cut surfaces and multiple suture lines. All these factors contribute to bleeding and often extensive use of blood and blood product transfusion.

Patients with TAH are often subject to infectious complications which may be life threatening both early and late in the clinical course. The extensive operation, tissue trauma, foreign surfaces, multiple monitoring catheters, potential device contamination, common need for reoperation, modulation or suppression of the immune response and lengthy hospitalizations are all potential contributing factors. Infectious complications claimed the lives of the majority of the early TAH implant patients though this seems to have improved in more recently.

Thrombosis and thromboembolism are also significant problems and have been present since the original Jarvik-7 implants, though they seem much diminished in the later CardioWest experience. The ABICOR TAH had several instances of thrombosis despite seemingly adequate anticoagulation. Multiple methods to achieve adequate anticoagulation are employed including careful monitoring, avoidance of stasis within the device or connection conduits, and use of intravenous heparin initially with eventual conversion to warfarin plus antiplatelet agents.

Device malfunction though rare, can occur, and may be catastrophic and irremediable. Also, device longevity in destination therapy can be estimated but is, in fact, unknown.

Future Developments

Presently, as noted above, common use of TAHs is restricted to centers that employ the CardioWest TAH as a transplant bridge. The newer version of the ABICOR is close to use in selected centers for a new round of clinical trials. A completely new TAH, the CARMAT heart is presently undergoing development in France by a group headed by Alain Carpentier. While there is little published on this device, what is states that it will use more modern biological materials in its’ construction. It appears to be a conventional pustile pump. Others have proposed a new approach. Encouraged by the relative simplicity of the now commonly used axial flow type LVADs such as the HeartMate II™, Jarvik 2000™, and DeBakey MicroMed™ and their improved mechanical reliability, they are proposing utilizing 2 axial flow pumps in series to function as right and left ventricles. The obvious difference with this concept is that there would be no pulsatile flow generated by the device which is seemingly counter-intuitive and physiologically questionable. However, many patients function quite well even outside the hospital with an axial flow pump and have little to no pulsitile aortic pressure. Similarly, it has been proposed that 2
centrifugal type LVAD blood pumps (HeartMate III™) be used in series to accomplish the same effect. Research with this concept is also continuing.

Selected References:


Websites:

1. [www.syncardia.com](http://www.syncardia.com) (CardioWest TAH)

2. [www.jarvikheart.com](http://www.jarvikheart.com) (Robert Jarvik, M.D. on the Jarvik-7)

3. [www.abiomed.com](http://www.abiomed.com) (ABIOCOR TAH)