EMERGING TECHNOLOGY REVIEW

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Development, Current Status, and Anesthetic Management of the Implanted Artificial Heart

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CARDIOVASCULAR DISEASE (CVD) is now the leading cause of death worldwide, and heart failure accounts for a significant portion of this mortality.[1] In the United States, the prevalence of heart failure is estimated at 5.8 million, about 670,000 new cases are diagnosed annually, and the current estimated direct and indirect cost for heart failure care is $39.2 billion.[2] In the United States, the "baby boom" generation is now entering the age range when heart failure becomes much more common, and, worldwide, dietary and lifestyle changes have increased dramatically the prevalence of CVD. With these population prevalence changes, the proportion of CVD mortality attributable to end-stage heart failure will only continue to increase because the prospect for definitive therapies are absent.

Replacement of the failed heart with a donor organ or artificial heart has been researched actively for more than 6 decades. A heart transplant is a very effective therapy for the few patients who are fortunate to receive this therapy, but the number of suitable donors remains at approximately 2,000 per year and there are as many as 150,000 candidates.[3] Xenotransplantation or genetically engineered donor hearts are not likely to become a suitable treatment in the foreseeable future. The goal of ongoing gene therapy research is targeted at the regeneration of myocytes or revascularization and holds some promise to become a treatment alternative for advanced heart failure. Because biologic replacement of the heart and medical therapy remain inadequate for treating the growing heart failure population, mechanical circulatory support increasingly is being used worldwide.

Presently, mechanical circulatory support with a ventricular assist device (VAD) or replacement with a total artificial heart (TAH) is the best treatment option for many patients. Circulatory support with VADs has become common in many medical centers for supporting patients with both acute and chronic heart failure.[4] Implantable left ventricular assist devices (LVADs) are now being implanted for long-term support either as a bridge to heart transplant or for destination therapy.[5,6] However, some patients require biventricular support for long-term survival, and, currently, an implantable long-term right VAD is not available. Biventricular assist device systems are extracorporeal, require multiple percutaneous cannulae and a large external pneumatic power source, and are not suitable for long-term support. Therefore, the best option for long-term survival for patients with biventricular failure and fixed pulmonary hypertension is an implantable TAH as a bridge to transplantation (heart or double lung and heart).[7,8]

HISTORY

The concept of mechanically supporting the failing heart can be traced back to the early 19th century when LeGallois[9] proposed the development of a device to restore perfusion to tissue when heart function was inadequate. In the 1920s, inventor Charles Lindbergh designed an artificial heart and with surgeon Alexis Carrel experimented with various models and designs of pumps.[10,11] In 1937, the Russian scientist Vladimir Demikhov reported development of a TAH device consisting of 2 side-by-side pumps powered by an external motor with a transcutaneous drive shaft and transplantation of this device into a dog that lived 5.5 hours postoperatively.[12]

Sustained research in this field, however, began after World War II, when the availability of funding and advances in surgical techniques, antibiotics, and other physiologic support systems made human transplant surgery a realistic goal. In 1958, Akutsu and Kolff[13] at the Cleveland Clinic reported implantation of a TAH into a dog that lived for 90 minutes; and in 1961, Domingo Liotta of the University of Cordoba, Argentina, reported survivals of up to 13 hours with his own models.[14] On the basis of this work, Liotta was recruited by Michael DeBakey of the Baylor University College of Medicine, and at

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Baylor, Liotta began collaborating with Denton Cooley. Their joint modifications to his prototype eventually led to the Liotta heart, and, in 1969, this became the first TAH used in a human being[15,16] as a bridge to cardiac transplantation. Kolff left the Cleveland Clinic in 1967 for the University of Utah,[17] and Akutsu joined Cooley and Liotta at the Texas Heart Institute (THI) in 1974.[15] The movement of these key researchers to the respective institutions established the core teams that ultimately produced the only 2 devices currently approved for human use: the AbioCor Implantable Replacement Heart (IRH, Abiomed, Inc, Danvers, MA) and the SynCardia Temporary Total Artificial Heart (TAH-t, Syncardia Systems, Inc, Tucson, AZ).

The Utah Experience: From the Jarvik Heart (New York, NY) to the SynCardia TAH

The Syncardia TAH descends from the investigational design that was in use at the University of Utah in the early 1980s. The success of the Utah group was in large measure because of the breadth and depth of bench research at that institution. Kolff took with him from the Cleveland Clinic the physician-engineer Clifford Kwan-Gett, the designer of the prototype TAH on which Kolff had centered his research. Kolff was concerned about the fit of the heart into the chest because they had observed a rise in venous pressure likely caused by improper fit and asked then-premedical student Robert Jarvik to make a "pancake heart," which emerged as the Jarvik II.[17] Several prototypes later and after the incorporation of Kwan-Gett's innovation of a seamless polyurethane membrane heart, this had evolved to the Jarvik-7, which has gone on to become the most widely implanted TAH design in the world. These researchers also advanced knowledge on driving systems, biomaterials, surgical implantation, and animal anesthesia techniques for various models of the TAH[18-22] and, in these models, also were able to work out the separate actions of various pharmaceutic agents on the peripheral vasculature versus on the native heart.[23-26]

In September 1981, the Food and Drug Administration (FDA) approved the investigational use of the Utah heart (Jarvik-7) in up to 7 patients unable to be weaned from cardiopulmonary bypass although this stipulation was extended to include those with irreversible congestive heart failure refractory to all treatment.[27] The investigational use of the TAH was for "destination therapy" as opposed to "bridge to transplantation." (This distinguishes the Utah experience from that of the THI's 2 prior implantations of the Liotta and Akutsu III hearts, the distinction implying potential differences both in the patients and the technologies involved at that time. The THI implantations were both salvage operations intended to temporize until a donor heart was available.) Selection procedures for candidates for the TAH were similar to current practices for transplantation and destination therapy; a committee reviewed the case and unanimously agreed that the patient was a candidate based on medical status, psychological status, and postsurgical social support.[28] In 1982, Dr William DeVries implanted the first Jarvik-7. This patient lived for 112 days with the artificial heart, and, although his postoperative course was complicated, the experience established the TAH in the modern therapeutic armamentarium.

In the mid-1980s, although manufacture of the heart and the drive system continued in Utah, DeVries and the Jarvik-7 program relocated to Humana Hospital in Louisville, KY, where 3 more implants for destination therapy were performed[15,29] in 1984 and 1985. The utility of the Jarvik-7 for bridge to transplantation was shown by Copeland et al[30] in 1985 at the University of Arizona. Within 2 months, Griffith at the University of Pittsburgh repeated this in a patient who survived to transplantation and then lived an additional 11 years with his transplanted heart.[31,32] However, in January 1990, the FDA withdrew permission for continued production of the Jarvik-7 from Symbion, Inc (Salt Lake City, UT) after repeat inspections disclosed multiple quality assurance and reporting failures.[33] However, work continued abroad and contributed to the overall momentum of development.[34-36] In 1992, CardioWest Technologies in Tucson, AZ, obtained FDA approval for limited manufacture for clinical trials of a bridge-to-transplantation device based on the Jarvik-7, having acquired the assets and technologies from Symbion.[37] In 2001, SynCardia Systems was incorporated to manufacture the CardioWest TAH, now again renamed the SynCardia temporary TAH (TAH-t). The TAH-t is the only device to have FDA, Health Canada, and European Union approval for bridge to transplantation, and more than 900 implants have been performed worldwide to date (R Sheets; SynCardia Systems, Inc).

The Texas Experience: THI and the Birth of AbioCor

What eventually emerged as the Abiomed/THI IRH was a collaboration between engineers at Abiomed in Massachusetts, the University of Louisville, and the THI. A succession of animal models and refinements in design and implantation operative techniques led to FDA approval for the investigational use of the IRH in a multicenter trial that began in 2001.[38-41] The first few AbioCor IRHs were implanted by Gray and Dowling in Louisville with 2 patients living for longer than one year.[39,40] In September 2006, the FDA approved the AbioCor for use under a Humanitarian Device Exemption (HDE).[42] Although the THI is not one of the implant centers for the AbioCor,[43] its TAH program is still active, and in 2008 THI received a National Institutes of Health grant to develop a new TAH using the continuous-flow technology of second-generation LVADs.[44] Abiomed is currently working on its next generation of IRH, the AbioCor II, using technology from the Pennsylvania State University TAH design.[45]

DEVICES

SynCardia Temporary TAH-t

The TAH-t consists of 2 separate blood pumps that are pneumatically driven and generate pulsatile blood flow (Fig 1). Each pump is constructed from a rigid plastic shell and contains 2 Medtronic-Hall (Minneapolis, MN) mechanical valves (27-mm inflow and 25-mm outflow). A seamless polyurethane diaphragm separates the blood sac from the air sac.[46] The maximum volume of the blood sac, which is equal to maximum stroke volume, is 70 mL. Each pump is connected to an external source of compressed air by a wire-reinforced conduit (driveline) that exits the body through a subcostal incision.[47]