

TOTAL HEART TRANSPLANT: A MODERN OVERVIEW

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More than 5 million people are diagnosed with congestive heart failure (CHF) every year, and this number rises by about 500,000 more every year. CHF is a multifaceted problem that is becoming increasingly prevalent in our society and is associated with end-stage heart disease (Norman, 2006). This final stage of heart failure is usually characterized by a myocardial infarction, a heart attack. Cardiac transplants are the only option for the long-term treatment of severe cases that lead to irreparable biventricular failure, which is a failure of both ventricles of the heart. This condition effectively handicaps the heart's ability to pump blood through the body (Copeland, 2004). Since there are many complications associated with existing procedures, there is a constant push to improve the success of treatment for congestive heart failure.

the most effective treatment for heart failure as they involve only natural human tissue, and the process of getting onto a waitlist is tightly restricted. Placement on the waitlist still does not guarantee treatment because 25% of patients on a waitlist die before they are able to receive a donor heart (Dunning, 1997).

This lag in receiving a donor heart is due to the process by which the donors are selected. The donor heart is procured from an individual that has been declared brain dead. Their organ can be used only if they have previously given consent, or their family has provided the consent on their behalf, for their heart to be donated. Before the organ can be donated, two surgeons that are not affiliated with the patient must declare it suitable for transplant, and only then does the heart qualify for transplantation. The heart is then kept

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Since a cardiac transplant is currently the only option available for patients in the final stages of heart failure, multiple devices have been developed to replace all the components of the heart (valves, chambers, and the pacemaker) before total failure. The three types of procedures currently available are a donor transplant, left ventricle assist devices (LVAD), and total artificial heart implantation (TAH) (Dunning, 1997).

In the case of donor transplant, the heart of a donor is isolated and placed into the patient's body after most of their original heart is removed. The process of obtaining a donor heart and having transplant surgery is very long and complicated due to the many criteria that must be met before the surgery can proceed. To be considered for a donor transplant, the patient must go through extensive tests proctored by cardiologists, nurses, and health workers to ensure that they will be able to survive the procedure and abide by the restrictive post-operative requirements. Once a patient is determined to be a suitable candidate, they are placed on a waiting list with thousands of other similar patients. Then begins the waiting game, as the patient must now wait until it is finally their turn to receive a donor heart. Although donor heart transplants are

beating through dopamine support and mechanical ventilation. Information regarding the blood type and health of the heart is entered into the waiting list database. The database then uses an algorithm that takes into account blood type, body size, and length of waiting period to select the most suitable candidate for the organ. Interestingly, race and gender are kept out of the consideration, although gender may affect the size requirement of the donor heart required. Once a suitable candidate has been identified, surgery itself proceeds very quickly because the donor heart is only capable of a successful transplant a few hours after harvesting (Cleveland Clinic).

Given that the donor heart has a certain blood type, there is a chance of immunosuppression or rejection by the patient's body. Although every effort is made to ensure that the donor and patient blood types are as similar as possible, there are a multitude of genes that affect blood type and composition and it is impossible to control for all blood factors. Therefore, even though a donor and patient are classified as having the same blood type, the composition of their blood may vary enough to cause immune rejection. Immunosuppression is the process by which the

body's immune system, the biological network in place to protect the body from disease, recognizes the heart as harmful foreign tissue and attempts to destroy it as it would another pathogen. The patient is given immunosuppressant drugs post-operatively to prevent this response. However, by repressing the immune system, the patient becomes more susceptible to infections and diseases. As a result, the patient's health has to be closely safeguarded after the procedure since their body is too weak to fight external infections. If the immunosuppressant drugs are not effective, or not given in certain cases where they can aggravate other conditions that the patient has, then the body's immune system will succeed in destroying the newly implanted heart in a reaction known as rejection. This is very dangerous and must be addressed immediately to prevent significant damage to the new heart, otherwise it will be rendered useless (Cleveland Clinic).

Given that organic donor hearts are difficult and time-consuming to obtain, the next best alternative is to fabricate an artificial human heart that can then be transplanted into a patient and function as a normal heart. Hence, the focus shifted to developing total artificial heart (TAH) devices whose use is permitted when an individual needs to be kept alive until a donor heart transplant or when an individual is not eligible for a donor transplant but still has final-stage heart failure in both ventricles. Currently, only a select number of people are eligible for these devices due to the complexity of their implementation. This restricted eligibility for TAH devices is due to their artificially constructed parameters such as size, weight, and pump capacity that are suitable only for certain body types. However, researchers are conducting clinical research trials to make them more efficient and much more widely available (What is a total artificial heart?, 2012).

The first instance of a successful human TAH implantation was reported in 1984. The patient was a 61-year old man who had congestive heart failure and the implanted device extended his life for an additional 112 days after the operation. The TAH transplant failure was mainly preceded by

hemorrhagic complications of anticoagulation – meaning that excessive internal bleeding due to a lack of coagulation (clotting) agents caused TAH failure, and ultimate death. Acute renal failure, the kidneys failure to remove wastes and balance body fluids, was also observed although the source was unidentified, and this also contributed to transplant failure. However, an extensive autopsy after death revealed that the artificial heart device itself had been unaffected by thrombosis, blood clots, or any infectious diseases, indicating that the device itself had successfully integrated into the body's local system but triggered external hemorrhagic responses. (DeVries, 1984).

There are multiple TAH devices currently available in the market. The two most commonly used are the CardioWest Total Artificial Heart and AbioCor Artificial Heart. The CardioWest Total Artificial Heart is a device that has been developed to replace the patient's ventricles as well as all four cardiac valves. It functions by running power tubes from the patient's abdomen through the heart and then to an outside power source. The mobility of this device is impaired by its reliance on an external power source. The battery's large, unwieldy nature requires that the patient remain in the hospital after the transplant as they must be connected to the power source at all times. The power source is available portably only in Europe, allowing the patient to leave the hospital and not be confined to inpatient care (Copeland, 2004). The AbioCor device does not have an external power source. Instead, a specially developed magnetic charger is able to fuel the battery within by simple contact with the skin, which in turn increases patient mobility (What is a total artificial heart?, 2012). The AbioCor transplant device performed well in tests of circulatory support and life expectancy extension. The device is totally implantable, and requires no penetration of the skin, minimizing the chance of infection as external pathogens have a decreased chance of penetrating the body and infecting the device surface. Its major drawback is thromboembolism due to a lack of anticoagulation protocol, meaning that the device increases the risk of developing a deep vein blood clot, as it is unable to properly form blood clots during post-operative healing. Another factor that limits the device's use is its large size, meaning that it can only be used in large male patients. This is because their bodies are equipped with the blood and respiratory vessels of the necessary size and strength to support the device's large cardiac output. It cannot be used in smaller patients such as women and children, and thus has limited application in terms of the usage by the entire population (Frazier 2004).



Normal Heart and CardioWest Total Artificial Heart

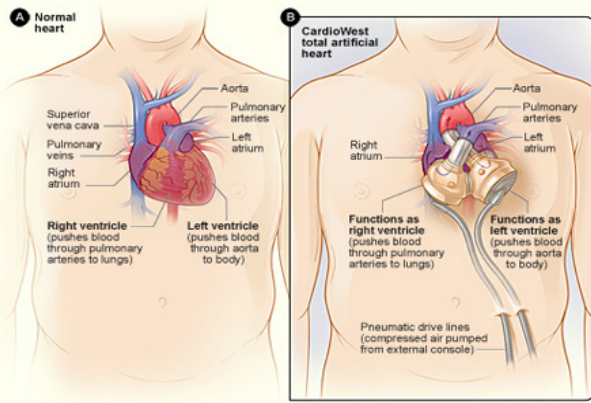


Figure A shows the normal structure and location of the heart. Figure B shows a CardioWest TAH. Tubes exit the body and connect to a machine that powers the TAH and controls how it works.

Normal Heart and AbioCor Total Artificial Heart

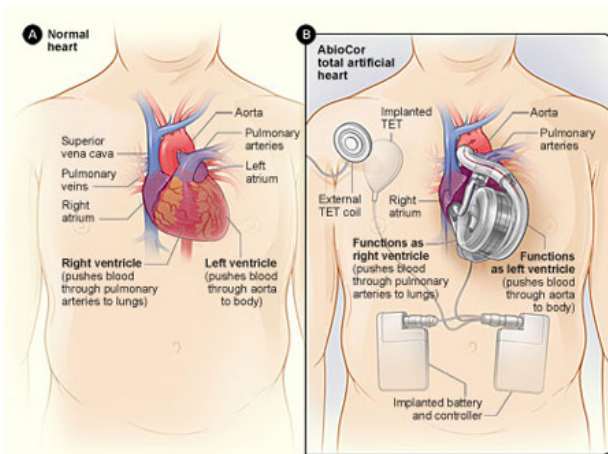


Figure A shows the normal structure and location of the heart. Figure B shows an AbioCor TAH and the internal devices that control how it works.

The latest development in TAH devices comes from the work of Alain Carpentier who claims to have made the first purely artificial, self-regulating heart whose functionality looks promising after clinical test transplantation in a 75 year-old patient. He claims that this TAH device is different from the existing models as it is self-regulating and completely mimics an actual heart. This means that rather than maintaining a consistently regulated heartbeat, it would, when you were feeling excited, speed up just like a natural heart (Seamons, 2013). The surface area of the device that is exposed to human blood is partly made from cow tissue, as opposed to synthetic material like other existing heart devices, allowing for the formation of blood clots and minimizing the chance of rejection by the host body's immune system. This is a major improvement over the currently existing devices whose main problem was thromboembolism due to anticoagulation processes. The device has greater flexibility and clotting ability, two of the most pressing problems that previous TAH devices struggled with.

Perhaps the device's most impressive claim is that it can keep the patient alive for five years after the time of transplantation, an estimate that is leaps and bounds ahead of the other devices that currently exist (Seamons, 2013). It is expected that the TAH device transplantation procedure will cost around \$190,000 when it is made available to the public, a price that is on par with the current market value of a TAH transplant procedure (Allen, 2013).

The direction of future research for the development of TAH devices has to address their clinical applicability in terms of being able to account for variation in patient body types and integrate seamlessly with the body's systems. One avenue of research focuses on positive displacement pumps and specifically their size and complications. Researchers predict that application of continuous-flow technology can help in solving some of these issues. The culmination of these research avenues is currently being applied to find a new generation of smaller, and more effective, TAH devices (Sale, 2012).

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