# PRO AND CON

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## Pro: The Total Artificial Heart: Is It an Appropriate Replacement for Existing Biventricular Assist Devices?

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CONGESTIVE HEART FAILURE (CHF) defines the endpoint of cardiac dysfunction in most cardiac diseases, and while advancements in medical therapy have been promising, the incidence of CHF is approximately 500,000 per year, and it is estimated that nearly 5 million patients in the U.S. suffer from some degree of heart failure. In fact, annual healthcare costs are up to $38.1 billion; and in the United States, $500 million per year, is spent on medical drug treatment for heart failure.[1] Despite the best efforts of medical and surgical care, nearly 300,000 patients die of heart failure as a primary or contributory cause each year.[1] Patients continue to decline in health, have a decline in quality of life, require increased hospitalizations, and ultimately succumb prematurely to their illness. While heart transplantation remains a viable solution for these patients, shortages in donor supply have limited transplants to fewer than 2,500 per year. Since 2005, the number of active new adult candidates on the heart transplant waiting list increased by 19.2%. Currently, it is estimated that up to 50,000 people per year die while waiting for a transplant. Of patients on the heart transplant list in 2008, 11.6% died after 36 months while still waiting for an available transplantation.[2]

Although medical algorithms have proved useful for the treatment of class I to class III CHF, patients with class III and, especially, class IV require more aggressive management for survival.[3] For appropriate patients with isolated left ventricular failure, left ventricular assist devices (LVAD) have been shown to increase survival to transplantation, increase survival after transplantation, and improve quality of life.[4] Patients with more severe disease prove to be much more difficult to manage. As left heart failure progresses to biventricular failure, replacement of total heart pump function is needed. Heart transplantation is currently the best treatment for patients with end-stage biventricular heart failure. The International Society of Heart and Lung transplant registry shows that more than half the patients who undergo transplantation have a survival rate of 11 years, with a much more dramatic improvement in quality of life than they would have had if they remained in medical therapy.[5] Yet, heart transplantation has its limitations. Contraindications to heart transplantation include existence of recipient antibodies, high pulmonary vascular resistance, and adverse events related to immunosuppression, and these are just some of the relative contraindications to heart transplantation. The scarcity of donor hearts coupled with the progressive nature of heart failure lead patients to deteriorate while on the transplant waiting list, and some patients will die before a suitable donor becomes available.

The use of mechanical circulatory support (MCS) has been the mainstay of non-surgical approaches to the failing heart. There exists a spectrum of MCS devices that address the varying degrees of cardiac dysfunction encountered in heart failure patients. These devices have a wide range of capabilities ranging from partial support to ventricular assist to full replacement. The total artificial heart (TAH) system has several unique features that are advantageous relative to ventricular assist devices (VAD). In the United States, 2 artificial heart systems have been used since the 1960s.

### ABIOCOR TAH

The AbioCor TAH by Abiomed, Inc. is a single-body, pulsatile device that uses an electrohydraulic actuator system rather than pneumatic drives. An implanted internal coil is coupled with an external coil that receives power from an external source. An oscillator in the external coil generates a magnetic field, which then gets converted into electrical energy by the internal coil. The external power source is a portable battery pack that can last for 2 hours. There is also a built-in internal battery that provides 20 to 30 minutes of power for limited disconnections from external sources. The AbioCor is capable of producing cardiac outputs of 8 L/min with a stroke volume of 60 mL. Its size and mass (900 gm) limit its usefulness; it will only fit in approximately 50% of men, 20% of women, and 0% of children.

Initial testing of the AbioCor TAH began in 2001 at the University of Louisville. The preliminary trial, which included 14 patients, revealed that thromboembolism was a recurring complication.[6] The most common causes of death were stroke (4 patients) and multiple system organ failure (3 patients). Intraoperative death occurred twice. Six patients survived between 53 and 151 days, 1 patient survived 293 days, and the longest surviving patient survived 512 days. The 30-day

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survival rate was 71% compared to the predicted survival rate of 13% with only medical intervention. At 60 days, 43% were still alive. There were no reports of device-related malfunctions or infections. Several patients were able to become ambulatory, and 1 patient was discharged from the hospital for 9 months.[7] In September 2006, the FDA approved the AbioCor for use under a Humanitarian Device Exemption (HDE), which limited the use of the AbioCor to patients with severe biventricular heart failure who were not candidates for transplantation and who had an expected 30-day survival less than 30%. To date, the AbioCor only has been used as destination therapy in patients with end-stage CHF, and the number of transplants is limited compared to the CardioWest TAH. Only 1 patient had received an AbioCor TAH since the HDE was granted. Although the AbioCor is no longer in production, a second generation AbioCor II is in development that will circumvent size limitations and potentially reduce the complications of thromboembolism and atrial suck-down events that have occurred with the AbioCor.[8]

## SYNCARDIA TAH

In 2004, The SynCardia Total Artificial Heart (TAH-t) (CardioWest) became the first and only TAH to receive FDA approval, and in 2008 the Centers for Medicare and Medicaid Services also approved the TAH-t. It remains the only fully approved TAH system in use today. More than 11,000 TAH-t units have been implanted. While only approved for bridge-to-transplant therapy in the United States, centers in Europe and Australia currently are performing destination implants. The current design is a pulsatile, pneumatically driven pump with 3 components: A prosthetic pair of ventricles made of polyurethane, drivelines, and an external pneumatic driver. Each prosthetic ventricle contains an air chamber and a blood chamber and is separated by a diaphragm. Ventricular systole occurs when air is driven into the chambers displacing the diaphragms causing ejection of blood from the blood chamber. During diastole, the diaphragm relaxes, allowing passive filling of blood into the prosthetic ventricles. Compressed air is delivered by an external driver console attached to the ventricles by PVC and polyurethane tubing. Parameters that can be adjusted include driving pressures for the left and right ventricles, beat rate, systolic duration, and vacuum pressure, all done through the external console. The ability to adjust systolic duration indirectly can adjust diastolic filling time, allowing cardiac output to increase with increased venous return. The TAH-t is able to deliver stroke volumes of up to 70 mL and can deliver cardiac outputs of up to 9.5 L/min. The first-generation external consoles were large 180-kg devices that restricted patient mobility and prevented hospital discharge. Advances in driver technology have led to the production of the Freedom driver, a 6-kg console that allows for patient discharge and mobility.[9] Current guidelines from SynCardia recommend that implantation be limited to patients with a body surface area $\geq$ 1.7 $m^2$ or an anteroposterior distance of $\geq$ 10 cm as measured by CT. In the near future, with the release of the next generation of TAH-t, a 50 mL heart will be available in addition to the present 70 mL version, extending the therapeutic window of TAH support to smaller adults and children.[10]

The capabilities of the TAH-t allow for rapid and full hemodynamic restoration in both ventricles for patients in severe biventricular heart failure. Organ perfusion is enhanced and backward failure is reduced to a degree superior to that of an LVAD or biventricular assist device (BiVAD).[10] The TAH-t allows for much higher flows than possible with univentricular devices. TAH-t also has shown to have limited hemolysis and coagulation activation relative to the rotary VAD systems that exist today.[11-14]

While studies have shown that LVADs lead to recovery and return of function, there is a frequent unmasking of right heart failure. If right heart function is not augmented with an additional VAD, the increases in morbidity and mortality are significant. Placement of a right ventricular assist device and the unmasking of right heart failure following LVAD placement are associated with up to 50% mortality. If the patient requires a conversion to a dual-system BiVAD, they face a reduction in bridge-to-transplantation survival.[12]

The TAH-t's pulsatile flow also may confer some advantages over traditional non-pulsatile, continous-flow VAD support. The pros and cons of pulsatile flow have been debated for years, but it offers practical and theoretical advantages. From a practical standpoint, the pulsatile TAH-t is not as pressure- and volume-sensitive as traditional VADs. When presented with hypertension and increased afterload, VAD flow and systemic perfusion may be compromised due to the impedance to forward flow. With reduced volume status, VADs will have a decrement in cardiac output. In contrast, the pulsatile nature in the TAH-t can sustain its ejection force even in the face of afterload increase as its blood chamber reservoir allows full filling of ventricles per beat. This system appears to be less volume- and pressure-sensitive, allowing the maintenance of full flows in a wide range of hemodynamic conditions.[13]

From a theoretical standpoint, pulsatility will decrease the likelihood of turbulent flow.[11] This translates into less platelet activation and reduced risk for thrombosis. Pulsatile flow systems also have been shown to be associated with reduced inflammation, enhanced endothelial function, and maintenance of arterial integrity compared to continous-flow systems.[13,14] Lastly, the characteristics of flow dynamics in MCS can affect the occurrence of post-implant bleeding and hemorrhagic stroke. Studies have shown that bleeding events after LVAD implantation are related to an acquired von Willebrand syndrome (AVWS), possibly stemming from the turbulent flow encountered in LVADs. The high shear can lead to denaturation of von Willebrand multimers, reducing the effect of platelet function and hemostasis.[15] AVWS is not seen in TAH-t, as pulsatile flow coupled with flow through large orifices is free of protein denaturation. Spontaneous GI bleeding has been reported to be less than 4% with the TAH-t compared to continous-flow non-pulsatile devices that show GI bleeding rates between 20% and 50% in the first implant year.[16]

The embolic risk has been shown to be consistently higher in LVAD patients due to occult thrombi present in the native sluggish ventricles found in severe heart failure. Often, intraventricular thrombi are missed with conventional imaging modalities and only are found after direct visual inspection. In contrast, TAH-t implantation involves excision of the native