Total Artificial Heart Freedom Driver in a Patient With End-Stage Biventricular Heart Failure

Kristin Friedline, CRNA, MSNA
Pamela Hassinger, CRNA, MSNA

Approximately 5.7 million people in the United States have a diagnosis of heart failure, and more than 3,100 patients are awaiting a heart transplant. A temporary total artificial heart (TAH-t,SynCardia Systems Inc, Tucson, Arizona) is approved by the US Food and Drug Administration (FDA) as a bridge to transplant in patients at risk of dying of biventricular heart failure. Currently, TAH-t recipients awaiting transplant are hospital-bound and attached to a large pneumatic driver. In 2010, the FDA gave conditional approval for an Investigational Device Exemption clinical study of the portable Freedom driver (SynCardia).

This case report describes a 61-year-old man admitted with acute decompensated heart failure, which progressively worsened, eventually requiring implantation of a TAH-t. Following stabilization, the patient was switched to the Freedom driver. After the patient and his wife proved competence in managing the device, they were able to take several daylong excursions outside the hospital. The patient considered discharge from the hospital while awaiting a transplant but ultimately received a heart transplant while still an inpatient.

Higher rates of survival to transplant have already been proved with the TAH-t. Potential benefits for the portable Freedom driver include increased mobility, decreased cost, and improved quality of life.

Keywords: Cardiomyopathy, Freedom driver, heart failure, total artificial heart.

More than 3,100 patients are awaiting a heart transplant in the United States, according to statistics from the Organ Procurement and Transplantation Network, as of December 8, 2011,1 and 20% to 30% of these people will die while waiting. Efforts to replace the failing human heart have received much attention since the 1960s.2 The temporary Total Artificial Heart (TAH-t) from SynCardia Systems Inc (Tucson, Arizona) is the only US Food and Drug Administration (FDA)–approved total artificial heart. This device has been used in several earlier forms since the 1980s, receiving FDA approval for the current design in 2004. Until now, TAH-t recipients must be hospital-bound and attached to a large pneumatic driver while they wait for a suitable donor.

However, in March 2010, SynCardia received conditional approval from the FDA to conduct an Investigational Device Exemption clinical study of the portable Freedom driver. The study allows for 60 patients at 30 institutions nationwide to be changed over (“transitioned”) to the Freedom driver, a 6-kg (13.5-lb) portable driver that may allow discharge from the hospital. Study endpoints include transplant, death, or 90 days from hospital discharge. Study success will be determined by 90% of the Freedom driver recipients maintaining an average cardiac index greater than 2.0 L/min per square meter throughout the study and a comparable adverse event rate between in-hospital recipients of the Freedom driver and patients who would have been candidates for the Freedom driver from the premarket approval study for the TAH-t.3 To date, 33 TAH-t recipients in the United States have been supported by the Freedom driver; of those, 22 have been discharged from the hospital. Nineteen Freedom driver recipients have received a heart transplant, and 5 other recipients have surpassed the study endpoint of 90 days of Freedom driver support at home.

This case report describes the successful transition to a Freedom driver in a TAH-t recipient.

Case Summary
A 61-year-old, 82-kg, and 175-cm ASA physical status class IV patient presented with a history of atrial fibrillation, nonobstructive coronary artery disease, idiopathic cardiomyopathy, noninsulin-dependent diabetes mellitus, and severe left ventricular systolic dysfunction. The patient had received a biventricular pacemaker with internal cardiac defibrillator following a cardiac arrest in 2009. In late 2010, he was admitted to an outside hospital with complaints of worsening fatigue, shortness of breath, and dyspnea on exertion with severely decreased exercise tolerance. He was found to be in atrial flutter with a left ventricular ejection fraction (LVEF) of 20%, a substantial decrease from a 40% LVEF documented in 2009. The patient was successfully treated with direct-current cardioversion and dobutamine, which decreased his symptoms of fatigue and shortness of breath. He experienced a recurrence of atrial flutter with a ventricular...
rate of 200/min to 220/min. He also received amiodarone treatment, which was later discontinued because of elevated liver enzyme levels.

The patient was transferred to our institution for further evaluation. Treatment options considered for his heart failure included medical optimization, destination left ventricular assist device (LVAD), definitive transplant, and TAH-t as a bridge to transplant.

On hospital day 1, the patient was evaluated by cardiology and electrophysiology. Dofetilide therapy was started. The patient had a successful direct-current cardioversion on hospital day 3, but the next day the patient had an episode of ventricular tachycardia, which was terminated by his internal cardiac defibrillator. The electrocardiogram (ECG) showed prolonged QTc (QT interval corrected for heart rate), a well-documented side effect of dofetilide, and the drug was discontinued. On hospital day 8, a right-sided heart catheterization showed severe right ventricular heart failure, a contraindication for LVAD. During the evaluation for the TAH-t, he was found to have prostate cancer. However, no metastasis was found, and he was determined by expert consultation to have a good likelihood of survival from the cancer; therefore, TAH-t evaluation continued. On hospital day 23, his heart failure progressed to cardiogenic shock with symptoms of increased shortness of breath, nausea, diaphoresis, and hypotension. An intra-aortic balloon pump (IABP) was inserted.

Because his severe right ventricular heart failure was a contraindication for LVAD and medical management was insufficient, treatment focused on approval for a heart transplant, with TAH-t as a bridge to transplant. He was approved by the cardiac surgery, social work, and psychology departments to be an appropriate candidate for a heart transplant. Because of his continued biventricular heart failure, no availability of an organ for transplant, and his meeting the appropriate TAH-t indications (Table 1), he was prepared for implantation of the TAH-t.

Before going to the operating room, the patient was in the cardiac surgery intensive care unit (ICU), awake and alert, on room air, in atrial flutter, and ventricularly paced. Dobutamine was infused at 10 µg/kg/min and the IABP was set at a 1:1 ratio. Bivalirudin therapy, which had replaced a heparin infusion 2 days earlier because of a decreasing platelet count, had been discontinued earlier that morning in preparation for surgery. The patient received 1 mg of intravenous (IV) midazolam and was transported to the operating room on a monitor with ECG tracing, pulse oximetry, and noninvasive blood pressure monitoring. A perfusionist assisted with transportation for management of the IABP.

In preparation for induction, defibrillator and cerebral oximeter pads were placed, and emergency drugs for IV push and infusion were immediately available. The cardiac surgery team and perfusionist were present in the operating room, and the cardiopulmonary bypass machine was primed and ready for immediate use. A 20-gauge right radial arterial line was inserted using local anesthesia while the patient was preoxygenated with 100% oxygen by face mask. General anesthesia was induced with the following IV medications: 2 mg of midazolam, 100 mg of lidocaine, 14 mg of etomidate, 100 µg of fentanyl, and 20 mg of vecuronium. During induction the anesthesia provider closely monitored the patient’s hemodynamic response. An 8.0-mm oral endotracheal tube was inserted, and placement was confirmed. General anesthesia was maintained with 0.4% to 0.6% isoflurane with a 60% oxygen and air mixture.

A right internal jugular 9-French multilumen introducer was placed using the Seldinger technique. Blood samples were drawn for a baseline analysis of arterial blood gas, hemoglobin, and basic chemistry panel and were sent to the blood gas laboratory. The starting hemoglobin level was 13.5 g/dL, and 2 U of autologous blood were removed for postprocedure transfusion. Baseline activated clotting time (ACT) was 128 seconds. Dextrose 10% as a drip carrier line and aminocaproic acid infusions were started. Nitric oxide (NO) was connected to the anesthesia circuit and started at 20 parts per million (ppm) to decrease pulmonary vascular resistance. A transesophageal echocardiogram (TEE) probe was inserted, and assessment showed mild mitral regurgitation, moderate tricuspid regurgitation, no evidence of atrial thrombus, and a greatly decreased LVEF of 10%.

<table>
<thead>
<tr>
<th>Indications</th>
<th>Contraindications</th>
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<tbody>
<tr>
<td>Heart transplant–eligible candidate</td>
<td>Nontransplant-eligible candidate</td>
</tr>
<tr>
<td>Risk of imminent death due to irreversible biventricular failure</td>
<td>Patient unable to be anticoagulated</td>
</tr>
<tr>
<td>Nontransplant-eligible candidate</td>
<td>Patients without sufficient space in the chest to accommodate the device</td>
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<tr>
<td>Left ventricular heart failure in the absence of right ventricular heart failure</td>
<td>Left ventricular heart failure in the absence of right ventricular heart failure</td>
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Table 1. Indications and Contraindications to Placement of Temporary Total Artificial Heart

a Defined as body surface area < 1.7 m² or as distance from sternum to 10th anterior vertebral body < 10 cm measured by computed tomography.
The patient was prepared and draped in the usual sterile fashion. Antibiotics were given as requested by the surgeon. An additional 400 µg of IV fentanyl was given in divided doses. Median sternotomy was performed by the surgeon. Cannulae were tunneled through the left upper quadrant to later connect the artificial ventricles to the pneumatic driver via drivelines. The patient then received 25,000 U of IV heparin and 570 U of IV antithrombin III, at the surgeon’s request, because of presumed antithrombin III deficiency from previous heparin infusion. The ACT after these medications was 454 seconds. The aorta and vena cavae were cannulated, and cardiopulmonary bypass (CPB) was initiated; mechanical ventilation and inhaled NO administration were stopped. Isoflurane was administered via CPB at a concentration of 0.5%, and an additional 2 mg of IV midazolam was given. Once on CPB, the patient no longer needed inotropic support, and the dobutamine infusion was discontinued.

Following aortic cross-clamping, the ventricles and all 4 valves were excised, leaving the atria, a rim of ventricle, and valvular tissue along the annulus. Both atrial and the aortic and pulmonary “quick connects” (flexible polyurethane-lined inflow connectors) were sutured to their respective orifices. Once these were in place, the 2 artificial ventricles were attached to the appropriate quick connects. The ventricles then were connected to the cannulae (Figure 1).

During CPB, the perfusionist gave incremental doses of phenylephrine to maintain a mean arterial pressure (MAP) greater than 60 mm Hg. Additional doses of heparin were also given to maintain ACT greater than 450 seconds. Arterial blood gas, hemoglobin, and basic chemistry values were checked every 40 to 60 minutes. An insulin infusion was started and was titrated to maintain blood glucose levels less than 200 mg/dL.

When nearing the end of the surgical procedure, mechanical ventilation was resumed and NO was restarted. The cannulae from the patient’s chest were connected to the drivelines of the pneumatic driver. The patient was placed in Trendelenburg position while low-pressure and low-rate pumping was initiated to facilitate de-airing before removal of the aortic cross-clamp. After cross-clamp removal, pneumatic pumping was increased and the patient was uneventfully weaned from CPB, with the TAH-t set at a heart rate of 120/min. The TAH-t heart rate is generally 90/min to 130/min and is determined by the surgeon to achieve an appropriate cardiac output based on the patient’s overall condition, age, size, and activity level. The target stroke volume is 50 to 60 mL, slightly less than the maximum TAH-t ventricular volume of 70 mL. These settings provided for a cardiac output of approximately 6.0 to 7.2 L/min. The TEE was used to rule out compression of the inferior vena cava and all 4 pulmonary veins by the artificial ventricles. Total CPB time was 154 minutes, and total aortic cross-clamp time was 141 minutes.

Figure 1. Two Ventricles and 4 Valves of Total Artificial Heart Replace the Human Ventricles and Valves
(Reprinted with permission of SynCardia Systems Inc.)
Heparin was reversed with 250 mg of IV protamine, and the repeated ACT was 132 seconds. The 2 U of autologous blood were returned to the patient. An additional 500 µg of IV fentanyl was given in incremental doses while a target MAP of 60 to 90 mm Hg was maintained. Calcium chloride and magnesium sulfate were given based on laboratory values. Norepinephrine was titrated between 0.03 µg/kg/min and 0.05 µg/kg/min for a target MAP of 60 to 90 mm Hg.

Coagulation laboratory test results and a platelet count were obtained because the patient was initially not clotting well. The platelet level was $74 \times 10^9/L$. Prothrombin time was 16 seconds, activated partial thromboplastin time (aPTT) was 37 seconds, the international normalized ratio (INR) was 1.5, and the fibrinogen level was 262 mg/dL. Two doses of platelets totaling 8 U, 2 doses of cryoprecipitate totaling 273 U, and 3 U of fresh frozen plasma were given. Clotting improved, and repeated laboratory values were as follows: prothrombin time, 12.6 seconds; activated PTT, 41 seconds; INR, 1.2; and fibrinogen, 332 mg/dL.

The patient’s chest was closed, and TEE was again used to verify adequate venous return and lack of compression of the inferior vena cava and pulmonary veins. Near the end of the case, the insulin infusion was discontinued when the blood glucose level decreased to 157 mg/dL. Propofol was infused at 15 µg/kg/min, and rocuronium (50 mg IV) was given before the patient’s transport to the cardiac surgery ICU. The MAP increased to greater than 90 mm Hg, and 100 µg of IV fentanyl was given, followed by discontinuation of the norepinephrine infusion. The MAP then returned to the range of 60 to 90 mm Hg. The patient was transported on 100% oxygen with NO at 20 ppm with manual breaths via resuscitation bag. The IABP was set at a 1:1 ratio. Although the patient no longer needed an IABP, it was determined that it would be discontinued later because of concerns related to bleeding. The patient was transported with full monitors except ECG, because patients with TAH-t no longer have native heart tissue to conduct an ECG tracing. Laboratory test results sent from the cardiac surgery ICU showed improved values, including hemoglobin of 9.8 g/dL and platelets of $95 \times 10^9/L$.

On postoperative day 1, sedation and NO were tapered off, and the patient was extubated. The IABP was also discontinued. The patient’s postoperative course was complicated by nosebleeds, an ileus, anemia, fever, pulmonary edema, renal insufficiency, and respiratory insufficiency. He also experienced a TAH-t console malfunction, but the console was replaced, with no negative patient outcome.

By postoperative day 53, his medical issues had resolved, and all hematologic values were stable. He had been hemodynamically stable for many weeks and no longer required any IV medications. Settings on his TAH-t no longer required adjustments. He was transitioned to a Freedom driver without incident. As is required, transition from the 188.1-kg (418-lb) pneumatic driver, commonly referred to as “Big Blue,” to the Freedom driver involved 2 providers, 1 for each ventricle, quickly and simultaneously disconnecting the patient’s cannulae from the “Big Blue” drivelines and reconnecting to the Freedom driver drivelines. The Freedom driver already was turned on and set with a heart rate, and it began pumping as soon as connected.

In-hospital teaching started immediately for the patient and his wife. They attended a lecture that covered the Freedom driver components, alarms, batteries and power options, and routine maintenance. They had hands-on training with a TAH-t simulator to become comfortable changing from a primary to a backup driver.

The patient and his wife proved competence by passing a written test and showing comfort with changing to a backup driver on the simulator. Starting approximately 3 weeks after transition to the Freedom driver, the patient was able to take several daylong excursions outside the hospital with his wife. Six weeks later, however, because of concerns regarding the medical and legal liability of an inpatient leaving the hospital, the risk management department requested that the patient cease taking day excursions. Several weeks after that, he received a heart transplant.

Discussion

An estimated 5.7 million US adults have a diagnosis of some form of heart failure, which is usually classified according to the criteria published by the New York Heart Association in 1928. The classification has been updated several times, and the currently used nomenclature has remained unchanged since 1994. Patients with class IV heart failure are unable to carry on any physical activity without discomfort, and symptoms of heart failure may be present even at rest.

Some hospitalized patients with class IV heart failure are eventually placed on a regimen of vasoactive medications, IABPs, mechanical ventilators, and ventricular assist devices. Based on several criteria, which can vary between institutions, some patients may become eligible for heart transplant. Total artificial hearts are used in this context as a bridge to transplant.

The first attempt at placing a total artificial heart was in 1969, with the patient surviving 64 hours to receive a heart transplant, but dying shortly thereafter. Various total artificial heart designs have been used since that time, but the SynCardia temporary Total Artificial Heart has been the most widely used. Initially called the Symbion or Jarvik 7 Total Artificial Heart, the device had its name changed to CardioWest Total Artificial Heart in 1993 and is now referred to as the SynCardia temporary Total Artificial Heart.

The TAH-t has 2 artificial ventricles, each with unidi-
rectional inflow and outflow valves that are connected to the patient’s native atria, aorta, and pulmonary arteries (see Figure 1). When implanted, the TAH-t replaces the patient’s native left and right ventricles and the tricuspid, aortic, mitral, and pulmonary valves. Because both ventricles and all valves are replaced, patients do not experience the common issues of heart failure with or without a ventricular assist device, such as valve regurgitation or stenosis, arrhythmia, and right ventricular heart failure. Each artificial ventricle is divided into 2 parts by a diaphragm, the movement of which is driven by the pneumatic driver. All motors, sensors, alarms, and computer monitoring are located outside the body in the large pneumatic driver (Figure 2). The patient is
attached to the driver with wire-reinforced air conduits and drivelines that are long enough to allow ambulation when appropriate. Generally, the console is plugged into wall outlets for electricity and air pressure, but it also has on-board batteries and air tanks for transport or ambulation. There are 2 pneumatic drivers: a primary and a backup. Ventricular filling occurs passively with normal venous return. The driver then delivers air to the diaphragm, causing it to rise to the top of the ventricle and thereby ejecting the total volume. Limiting filling to 50 to 60 mL allows room for the ventricles to accept a larger venous return (maximum is 70 mL), as would be expected during physical activity or volume administration. Systole and diastole times are adjustable to allow for appropriate filling and emptying of the ventricles. Additionally, filling time can be reduced by applying a small amount of vacuum (5-20 mm Hg) to the ventricle. This decreases the time in diastole, thereby increasing systolic time, which is necessary to achieve an acceptable cardiac output when using a higher heart rate. The average range for TAH-t drive pressures is 150 to 200 mm Hg for the left side and 55 to 90 mm Hg for the right side; however, the actual settings are patient specific, based on the after-load pressures of the aorta and pulmonary artery. The left drive pressure is typically set to exceed peak systolic pressure by 20 to 40 mm Hg, so that sudden increases in blood pressure or peripheral vascular resistance do not affect the amount of volume ejected from the ventricle. By adjusting these parameters, blood flow as high as 9.5 L/min can be achieved. The TAH-t is the only device that can achieve a cardiac output this high.3

When managing a patient with a TAH-t, the provider should remember that inotropic agents will not change hemodynamics.4 Because native heart tissue has been removed, an ECG is not needed and CPR is ineffective. Once settings are established, they rarely need to be adjusted,3 but if necessary, several parameters are adjustable, as we have discussed. At our institution, perfusionists manage and adjust TAH-t parameters when the patient is outside the cardiac surgery ICU or the device step-down unit without a trained registered nurse. It is essential that drivelines are not kinked during transport. Adequate battery life and compressed air should be verified before transporting a patient.

The TAH-t received FDA approval after a 9-year study under IDE, in which 81 transplant-eligible patients with class IV heart failure treated with TAH-t were compared with 45 control patients who underwent traditional management.12 The TAH-t recipients were shown to have significantly improved hemodynamics, evidence of improved end-organ perfusion, and increased mobility quickly after device implant as well as higher rates of survival to transplant and after transplant.12

The most up-to-date information regarding adverse events (Table 2) of the TAH-t is from the same 2004 study.12 Patient outcomes overall are quite good, with 79% of study patients surviving to transplant, vs 46% of controls (P < .001). Our institution is participating in gathering and publishing postmarketing TAH-t adverse-event data, which should be published in 2012 (Vigneswar Kasirajan, MD, written communication, April 2011).

The TAH-t is approved for use as an in-hospital bridge to heart transplant in cardiac transplant–eligible patients at risk of imminent death due to biventricular heart failure (see Table 1). More than 950 patients have now been implanted with the TAH-t worldwide. Hospitalized TAH-t recipients are listed as United Network for Organ Sharing (UNOS) status 1A, the highest category for organ transplant priority.

Recipients of TAH-t have been discharged with portable drivers in Germany since 2003, as well as from Russia, other European countries, and Australia. Until now, TAH-t recipients in the United States remained hospitalized while awaiting a suitable heart for transplant. However, since March 2010, an FDA-approved clinical study by SynCardia Systems Inc allows stable TAH-t recipients to be transitioned to the portable Freedom driver, which can be worn in a backpack or shoulder

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>No. of events</th>
<th>No. (%) of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection (respiratory tract, urinary tract, device/driveline)</td>
<td>172</td>
<td>73 (77)</td>
</tr>
<tr>
<td>Bleeding</td>
<td>102</td>
<td>59 (62)</td>
</tr>
<tr>
<td>Respiratory dysfunction</td>
<td>61</td>
<td>34 (36)</td>
</tr>
<tr>
<td>Hepatic dysfunction</td>
<td>37</td>
<td>35 (37)</td>
</tr>
<tr>
<td>Neurologic event (TIA, CVA)</td>
<td>35</td>
<td>26 (27)</td>
</tr>
<tr>
<td>Renal dysfunction</td>
<td>34</td>
<td>29 (31)</td>
</tr>
<tr>
<td>Reoperation</td>
<td>31</td>
<td>23 (24)</td>
</tr>
<tr>
<td>Device malfunction</td>
<td>19</td>
<td>16 (17)</td>
</tr>
</tbody>
</table>

Table 2. Common Adverse Events From TAH-t Placement to 30 Days After Transplant

* Sixteen of 19 events were related to driveline kinks or leaks, leading to a design change that resolved the issue.

Abbreviations: TAH-t, temporary total artificial heart; TIA, transient ischemia attack; CVA, cerebral vascular accident.
bag (Figure 3) and potentially allows these patients to be discharged from the hospital. To date, 22 patients in the United States have been discharged from the hospital with a Freedom driver while they await heart transplants. The UNOS status changes to 1B, the next highest priority status after 1A, after 30 days as an outpatient. Like the original driver, the Freedom driver provides pneumatic power to the artificial ventricles, causing the diaphragms to eject blood. It contains 2 rechargeable lithium ion batteries, each with a 2-hour battery life. It can be powered by these batteries or by external AC or DC power. The display shows left ventricle fill volume, cardiac output, and heart rate; however, only the heart rate is adjustable on the Freedom driver.

In planning for discharge to home, patients and 1 or more caregivers must attend a lecture and demonstrations and pass a written and hands-on test. They must live and travel within 2 hours of the hospital where they received the implant. The car they travel in should have a functional 12-V outlet, and they must carry extra fuses for it. They are told to never submerge in water, enter a steam bath or dry sauna (which will cause overheating of the driver), participate in contact sports, or participate in activities that could cause pulling, twisting, or kinking of their cannulae.

The implications for discharge from the hospital or increased mobility while in the hospital awaiting heart transplant are vast. Costs may decrease, and while not proved at this early phase, it is reasonable to assume that the patient’s quality of life will improve dramatically. Additionally, with as many as 16% of all hospital-acquired infections involving multidrug resistant bacteria, discharge to home may help protect a future immunosuppressed transplant recipient from difficult-to-treat infections.

The TAH-t provides the opportunity for heart transplant in patients who may not otherwise survive end-stage biventricular failure. Until now, TAH-t recipients were confined to hospitals while awaiting a donor heart, even once they were hemodynamically stable. Portability of the Freedom driver allows increased mobility and potentially discharge from the hospital. If proved safe and effective, the Freedom driver may offer improved quality of life and decreased costs while stable patients await heart transplants.

While hospitalized with the Freedom driver, our patient was able to attend daily cardiopulmonary rehabilitation and appreciated excellent mobility. He stated that he felt physically much stronger than before his hospital admission for treatment of heart failure in 2010. He also noted increased mental sharpness and clarity while on the TAH-t. On day 83 with his Freedom driver, the patient received a heart transplant. The surgery was a success, and recovery was swift. Fifteen days after his heart transplant he was discharged to home, where he remains today.

REFERENCES


**AUTHORS**
Kristin Friedline, CRNA, MSNA, is a staff nurse anesthetist at Virginia Commonwealth University Health System, Richmond, Virginia. Email: kfriedline@mcvh-vcu.edu.

Pamela Hassinger, CRNA, MSNA, is a staff nurse anesthetist at Virginia Commonwealth University Health System. Email: phassinger@mcvh-vcu.edu.

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