

Right ventricular dysfunction is best managed with a total artificial heart



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Patients with both acute and chronic right ventricular (RV) failure can be extremely challenging for heart failure teams to manage both medically and surgically. Defined as any structural or functional process decreasing the ability of the RV to pump blood into the pulmonary circulation, RV failure can be caused by myriad processes that either directly or indirectly compromise RV function. The RV is plagued by very complex pathophysiology that renders it very susceptible to changes in inflammatory cytokines, endothelial function, changes in oxygenation and ventilation, ischemia, and arrhythmias (Figure 1).¹ As a result, medical treatment of right heart failure is often targeted at volume optimization, inotropy, afterload reduction, and targeted interventions aimed at the underlying cause.

The most common cause of RV failure is left ventricular (LV) dysfunction, and indeed RV failure secondary to LV dysfunction may be treated with durable LV assist devices (LVAD). Whereas patients with refractory isolated LV failure are excellent candidates for LVADs, those patients with biventricular failure are less likely to benefit from durable LVAD support. As many as 25% to 35% of patients with implanted LVADs either have or develop RV failure.² Patients with RV failure after LVAD implantation have a high likelihood of needing temporary RV support that is associated with a significant reduction in overall survival.³ Further, patients with RV failure while being supported by an LVAD as a bridge to transplant have an increased risk of primary graft dysfunction and resulting decreased survival after heart transplant.⁴ Management of RV failure before and after LVAD is further complicated by imprecise medical interventions fraught with deleterious side effects, and there are no Food and Drug Administration (FDA)-approved implantable devices designed for the RV. We believe that LVAD therapy alone for patients with or at risk for RV failure is unacceptably high. We therefore propose a more proactive approach: The total artificial heart (TAH).

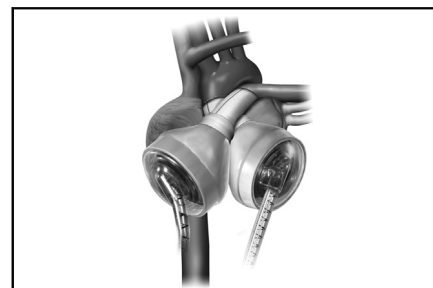
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SynCardia total artificial heart.

CENTRAL MESSAGE

In patients with end-stage biventricular heart failure, the most optimal management is accomplished by a total artificial heart that allows for precise physiologic control of both ventricles.

TAH DEVICES

The only commercially available TAH in the United States is the SynCardia TAH (SynCardia Systems, Inc, Tucson, Ariz), and it is currently approved by the FDA as a bridge to heart transplantation. The TAH is a pneumatically driven, pulsatile system that consists of 2 polyurethane ventricles each equipped with 2 tilting disc, Syn-Hall (Medtronic, Minneapolis, Minn) mechanical valves (Figure 2).⁵ With 50 cc and 70 cc sizes approved by the FDA, there have been >1700 implants worldwide. It is lined with polyurethane and has a displacement volume of 400 mL with the capability of producing a stroke volume of 70 mL and cardiac output of 9.5 L/min.⁵ There are also 2 drivers: the C2 driver for inpatient control and the Freedom Driver for outpatient control. The device is also currently under clinical trial to explore its use as a destination therapy in patients who are not transplant candidates.⁶

A newer device that is much less proven and was implanted in the first US patient on July 12, 2021, is the Aeson Total Artificial Heart (Carmat, Velizy-Villacoublay, France).⁷ This device is composed of a biventricular hydraulic pump housed in a single unit designed to mimic the shape of the natural heart in the pericardial sac (Figure 3).⁸ The pump consists of 2 compartments separated by a hybrid membrane—1 that contains rotary pumps

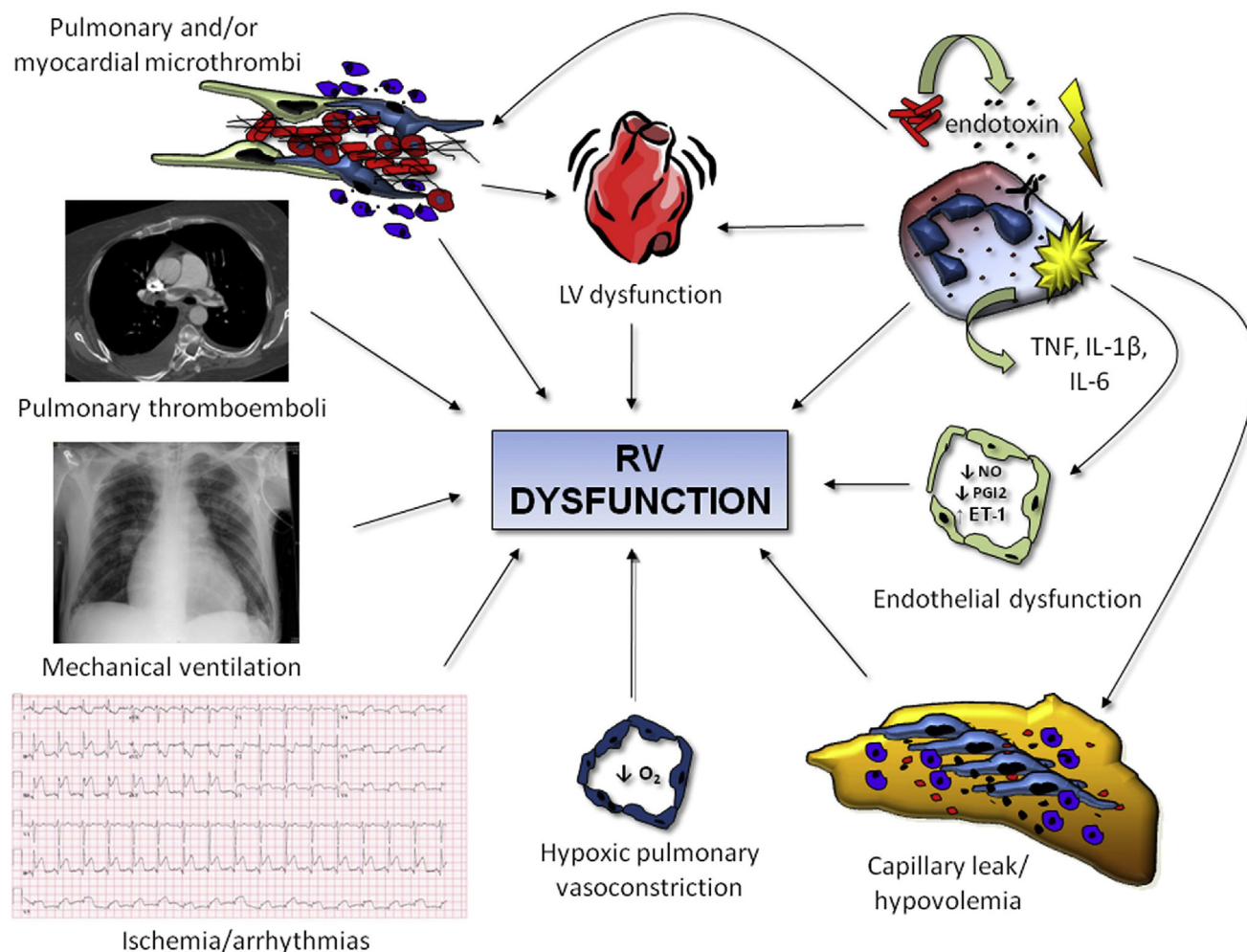


FIGURE 1. Causes of right ventricular (RV) dysfunction. LV, Left ventricle; TNF, tumor necrosis factor alpha; IL, interleukin; NO, nitric oxide; PGI2, prostaglandin-12; ET-1, endothelin-1. Reprinted with Permission from Lahm and colleagues.¹

in silicone oil; the other contains blood. The hybrid membrane has bovine pericardium lining the blood compartment and the rotary pump side is lined with polytetrafluoroethylene. The rotary pump moves the hybrid membrane back and forth mimicking systole and diastole and Carpentier-Edwards bioprosthetic valves (Edwards Lifesciences, Irvine, Calif) are positioned at the inflow and outflow of each side (Figure 3).⁸ The Aeson TAH is capable of producing cardiac output at 2 to 9 L/min and currently is available for commercial implant in Europe, having achieved the Conformité Européenne Mark in 2020.

TAH PATIENT SELECTION

The selection of patients for TAH implantation is of critical importance, and in addition to routine preoperative tests, including echocardiograph, left and right heart catheterization, cardiopulmonary exercise testing, chest computed tomography, and pulmonary function testing,

one must have a complete psychosocial evaluation and transplant eligibility determined. The preoperative assessment of RV function is essential when deciding on a support strategy because patients with biventricular failure are most likely to benefit from TAH. The right heart is assessed by a combination of physical exam, laboratory data assessing hepatic and renal function, right heart catheterization, hemodynamic data, and echocardiograph. After collection of these data, the candidacy of each patient is determined by a multidisciplinary team capable of offering TAH, LVAD, biventricular VAD, or palliation. Engagement of the patient and patient’s support network is also essential when deciding a treatment strategy.

In addition to biventricular failure, which is the most common indication for TAH, there are other clinical scenarios in which patients might benefit from a TAH device. Patients with cardiogenic shock; malignant arrhythmias; mechanical complications of myocardial infarction,

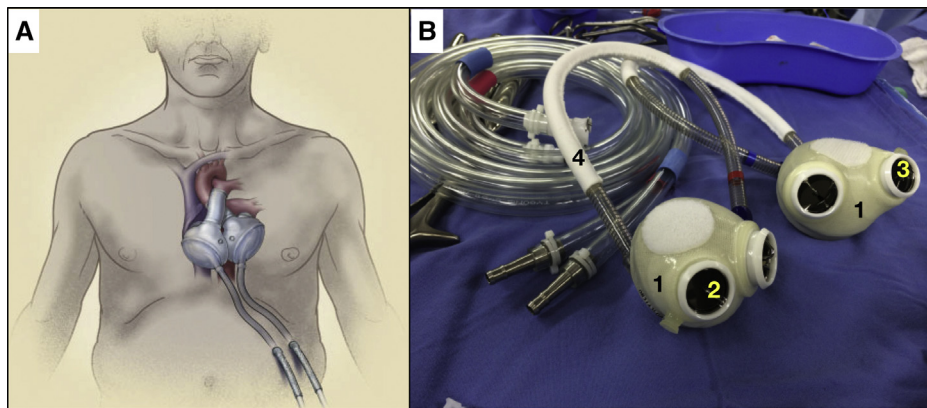


FIGURE 2. SynCardia Total Artificial Heart. (SynCardia Systems Inc, Tucson, Ariz). A, Positioning of total artificial heart and components in vivo. B, Picture of the SynCardia total artificial heart on back table before implantation. 1 = ventricle chamber; 2 = inflow mechanical valve; 3 = outflow mechanical valve; 4 = pneumatic driveline. Reprinted with permission from Noly and colleagues.⁵

including ventriculoseptal defect, ventricular thrombosis, primary graft dysfunction, or rejection following transplant; LVAD thrombosis or failure; isolated cardiac malignancy; or congenital heart disease may all benefit from a TAH device.

Particularly close attention is required to patient size; a minimum anteroposterior dimension from the posterior sternum to the vertebral body is 10 cm to accommodate the 70-cc device size. In patients with borderline anatomy, 3-dimensional imaging of the chest may assist in decision making. Smaller adult patients and even pediatric patients can be candidates for the 50-cc version of the TAH device as well.

The technical aspects of the SynCardia TAH implantation have been described in detail by our group.⁹ Briefly, after a standard sternotomy, a patient undergoes bicaval and distal ascending or proximal aortic arch cannulation. The aorta is crossclamped and divided at the sinotubular junction without the delivery of cardioplegia. The pulmonary artery is divided at the valve and the ventricles are resected at the atrioventricular groove with 3 to 5 mm of ventricular tissue preserved at the tricuspid valve and mitral valve annuli. The coronary sinus is oversewn and the presence of a patent foramen ovale is evaluated and oversewn if present. The quick-connect atrial attachments are then sewn to the tricuspid and mitral annuli

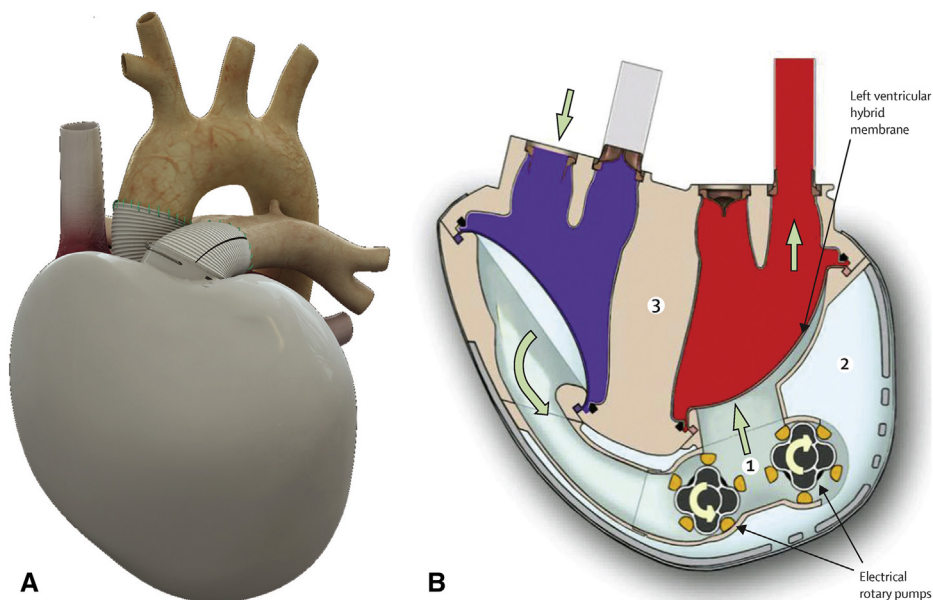


FIGURE 3. Aeson Total Artificial Heart (Carmat, Vélizy-Villacoublay, France). A, Shape of the Aeson total artificial heart after implant. B, Cross-sectional view demonstrating the components of the device. Electrical rotary pumps (1) in silicone oil (2) move the hybrid membranes back and forth to simulate systole and diastole. The new mechanical interventricular septum is where the electrical components are stored (3). Reprinted with permission from Carpentier and colleagues.⁸

incorporating epicardium using 2 separate running 4–0 Prolene stitches on each annulus.

The pulmonary artery and aortic quick-connect grafts are then trimmed and sewn to the pulmonary artery and aorta, respectively. The LV followed by the RV are attached and the drivelines tunneled out 5 cm apart. To facilitate future transplantation, polytetrafluoroethylene pericardial membranes are sutured from the superior vena cava to inferior vena cava laterally, used to wrap the aortic and pulmonary artery grafts and anastomoses, and cover the TAH anteriorly.

TAH RESULTS

The SynCardia device is by far the most studied TAH, starting with the first landmark study that enrolled 130 heart transplant candidates who were at risk for death on the list between 1993 to 2002.¹⁰ These patients were at risk for imminent death due to irreversible biventricular failure and were not candidates for LVAD. When compared with historical controls, the rate of survival to transplantation was significantly higher in those who underwent TAH (79% vs 46%; $P < .001$). Further, the 1-year and 5-year survival rates after transplantation were 86% and 64%. This is the main study that led to FDA approval in 2004 of the SynCardia TAH as a bridge to transplant.

In a follow-up analysis of 101 patients implanted with the SynCardia TAH by Copeland and colleagues¹¹ survival to transplantation was 68% with survival after transplantation at 1, 5, and 10 years of 76.8%, 60.5%, and 41.2%, respectively. Further, these results are coupled with an impressively low stroke rate of 7.9%. However, among the Achilles' heels of the TAH is the risk of hemorrhage and in this series 24.7% of patients were taken back to the operating room for bleeding.¹¹

In the largest compilation of data on TAH, Arabia and colleagues¹² reported on 450 patients who received TAHs between June 2006 and April 2017 from the Interagency Registry for Mechanically Assisted Circulatory Support database. Overall actuarial survival at 3, 6, and 12 months were 73%, 62%, and 53%, respectively. When broken down by experience, centers with >10 total implants had 73% of patient either alive or transplanted. These results are particularly impressive when one considers that 43% of patients were on temporary mechanical support at the time of TAH implantation.

In contrast to LVADs in which the settings can control pump speed, with a TAH we are able to control a wide range of parameters. In a TAH device, we are able to adjust heart rate, the amount of time the ventricles spend in systole and diastole, the pressures on the right and left side independently of each other to deal with systemic or pulmonary vascular resistance, and the vacuum on either side to adjust preload. With the ability to adjust for these parameters, the

TAH device allows patient-specific adjustments to deal with any acute change in a patient's physiology.

COMPARISON TO ALTERNATIVE SURGICAL APPROACHES TO RV FAILURE

As many as 30% of patients with end-stage heart failure experience biventricular failure that requires biventricular support, and strategies to address the RV include medical therapy, temporary RV assist device (RVAD), implantable LVAD device in the right side of the heart, transplant, and TAH.¹³ Whereas improvements have been made in the use of temporary RVAD support, including percutaneous applications,¹⁴ the obvious drawback is that it is not only temporary, but it also renders the patient permanently in the intensive care unit until recovery or transplant. Although this is the case, the benefit of this approach is that these patients can be listed for transplant as a status 1, whereas those with TAH are status 3.

There are no studies that directly compare TAH versus durable LVAD with temporary RVAD support, but there are several that report isolated outcomes of LVAD with temporary RVAD support. In a retrospective review evaluating this patient population, out of 57 patients 6-month survival was 46%,¹⁵ whereas another retrospective review found a 6-month survival rate of 54% in 46 patients.¹⁶ These outcomes compare unfavorably to TAH device survival in the same patient population of 73% at 1 year in experienced centers.

Another strategy for RV support that been described with reasonable success is implantation of 2 centrifugal LVADs in a biventricular configuration. However, the LVAD devices on the market have certain drawbacks when employed on the right side, including requiring a noncollapsible chamber to ensure preload, the H–Q curves are optimized for systemic afterload, and they have not been studied in a prospective fashion in the RV. Further, the only controllable parameter of the left-sided devices is speed, which makes it difficult to account for the dynamic clinical variables in RV failure.

All efforts to compare TAH with these treatment strategies and others are fraught with selection bias that makes accurate comparison nearly impossible. However, perhaps the most robust evaluation comparing TAH with biventricular assist device support is from Cheng and colleagues¹⁷ who utilized the United Network for Organ Sharing Registry to compare patients with TAH support versus biventricular assist device support at the time of heart transplant. In this study, 366 patients had biventricular assist device support and 212 patients had TAH and the waitlist survival was higher in TAH patients at 1 year, but did not reach significance (77% vs 69%; $P = .8$). Those patients supported with a TAH device had higher incidences of renal failure, but had comparable 30-day, 1-year, and 3-year posttransplant survival.¹⁷

CONCLUSIONS

The etiology of RV failure is diverse and the treatment of it is complex—particularly in the setting of concomitant LV dysfunction. In this setting, isolated LVAD implantation is inappropriate and a TAH device should be considered. RV failure after LVAD implantation is unacceptably high, and perhaps these patients would be better served by a TAH, which is the only durable mechanical device approved for RV failure. By replacing both ventricles with a TAH device, we can apply precise physiologic control of both ventricles independent of each other. Although heart transplant remains the best option for patients with advanced biventricular failure, donors can be scarce and for patients who are not otherwise able to wait for a donor, the best way to manage their biventricular failure is simply to replace the both ventricles with a TAH. Excellent outcomes can be achieved with a TAH device with proper preoperative evaluation, patient selection, and at experienced centers.

Conflicts of Interest Statement

Dr Mokadam is a consultant and investigator for Abbott, Medtronic, and SynCardia, as well as a consultant for Carmat. The other author reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: total artificial heart, right ventricular failure, heart transplant, left ventricular assist device