Evolving understanding of total artificial heart support of young infants and children

Ronald K. Woods, MD, PhD, Steven Kindel, MD, Michael E. Mitchell, MD, Viktor Hraska, MD, PhD, and Robert A. Niebler, MD

ABSTRACT

Background: We have developed a new method of total artificial heart (TAH) support for young patients, and here share our preliminary results and evolving understanding.

Methods: This report is a retrospective chart review of all patients <10 kg who received a TAH at our institution from May 2017 to the time of this report.

Results: Our cohort includes 5 patients. Two had single-ventricle circulation, 1 of whom had undergone a Glenn procedure and was revised back to a Sano shunt. Four were on extracorporeal life support for longer than 10 days, 3 with an open chest. In these 3 patients, the TAH was a salvage operation. Centrifugal pumps were used for 2 patients and pulsatile pumps for 3 patients. Three patients survived to transplantation and discharge, with support times of 79, 44, and 96 days; in these patients, the duration of follow-up from discharge to the time of this report was 687, 19, and 8 days, respectively, and all patients were well. For the pulsatile pumps, in the first patient we placed valved conduits for inflow connections. For the second patient, we omitted the valved conduits and oversized the pumps to avoid full fill; yet, despite our best efforts, full fill occurred frequently, and thus we converted to a systemic centrifugal pump.

Conclusions: Our method of TAH support can be tailored to provide effective support of carefully selected young children with single or biventricular physiology. In our opinion, for pulsatile pumps, oversizing the pump and using valved inflow conduits may be important adjuncts to achieve effective support. (J Thorac Cardiovasc Surg 2020;159:1075-82)

For certain smaller patients with heart failure, standard methods of biventricular assist device (BiVAD) support may be exceptionally challenging. Although total artificial heart (TAH) support is theoretically possible in small children, up to now, the majority of reports of TAH implants have included the Syncardia TAH (Syncardia Systems, Tucson, Ariz) or modifications using various ventricular assist devices (VADs) in adults or teenagers. TAH support of patients in the neonate to toddler age range is distinctly unusual. We have developed a method of TAH support that can be implemented in patients across this age range. As our experience continues to evolve, we considered that it might be useful to share some lessons we have learned.
PATIENTS AND METHODS

Patients

We reviewed records of all patients weighing <10 kg who had received TAH support at the Children’s Hospital of Wisconsin between May 2017 and December 2018. The hospital’s Institutional Review Board authorized the collection of data from existing medical records and a waiver of consent for this retrospective study.

Data Collection

Study participants were identified from the Herma Heart Institute cardiology and cardiothoracic surgery database. Patient information was obtained from medical records and was deidentified before analysis.

Outcomes

The primary outcome was survival to transplantation and discharge. Secondary outcomes included observations about the quality of the support and major complications, including pump thrombus, pump malfunction, stroke, new-onset organ failure, and reoperation for bleeding.

Statistical Methods

Descriptive methods were used to summarize case vignettes, which required no formal statistical analysis.

Abbreviations and Acronyms

BiVAD = biventricular assist device
ECLS = extracorporeal life support
LVAD = left ventricular assist device
PTFE = polytetrafluoroethylene
TAH = total artificial heart
VAD = ventricular assist device

Surgical Technique: Biventricular Anatomy

Our technique has been described in a previous report. After establishing mildly hypothermic cardiopulmonary bypass with bicaval cannulation, the aorta was clamped, and the ventricular mass excised to the tricuspid and mitral annuli. Connections to the annuli were established with either porcine-valved Dacron conduits (Hancock-valved conduit; Medtronic, Minneapolis, Minn), or ringed reinforced polytetrafluoroethylene (PTFE) conduits with the annostomosis reinforced with bovine pericardial strips. For the valved conduits, the conduit was trimmed to place the base of the valve at the annulus (Figure 1). The tip of the EXCOR inflow cannula (Berlin Heart, The Woodlands, Tex) was placed approximately 2 to 2.5 cm from the commissural pillars of the valve. Appropriate-sized Dacron conduits were sewn to the pulmonary artery and aorta into which the EXCOR outflow cannulas were inserted. For all cases, the inflow cannulas were deliberately brought out more leftward than would typically be done for a left ventricular assist device (LVAD) to effectively pull the atrial mass away from the systemic and pulmonary veins.

Surgical Technique: Single-Ventricle Anatomy

The technique for single-ventricle anatomy also has been described previously, albeit for an adult using a Syncardia TAH. The only major difference for single-ventricle patients—and the critical enabling step—is that the cardiac mass is resected just above the plane of the atrioventricular annulus to allow expansion of the atrial cuff. The atrium is then septated with a PTFE patch to create neo-right and neo-left atria for drainage of the systemic and pulmonary venous flow, respectively (Figures 2 and 3). Inflow conduits are anastomosed to the atrial mass with a mild offset of the suture lines at the PTFE patch to permit a more hemostatic connection.

For both types of anatomy, the remainder of the technique is identical to that of standard left or right VAD using either centrifugal pumps or EXCOR pumps. Hemostatic packing is left in place after TAH implantation. The packing is removed and the chest closed on postoperative day 1. To prepare for later reentry and transplantation, we place a small saline prosthesis to the left of the inflow cannulas, place sterile strips of PTFE around the cavae and great arteries, and line the posterior and anterior pericardial spaces with thin-wall PTFE.

FIGURE 1. Method of total artificial heart implantation in a young patient with a biventricular circulation. Appearance after resecting the ventricular mass, leaving the inflow annuli (A), and completing the inflow and outflow connections (B). Porcine valved Dacron conduits were used for the left and right inflows. Inflow and outflow cannulas were EXCOR cannulas. Note the saline implant placed leftward and inferior, to maintain sufficient pericardial space for subsequent transplantation. Either pulsatile or centrifugal pumps can be used with this arrangement. MV, Mitral valve; TV, tricuspid valve; PA, pulmonary artery; Ao, aorta; RA, right atrium. (Reproduced with permission.)

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mass just above the plane of the atrioventricular annuli, allowing expansion of the atrial cuff (B); and septation of the atrial mass with 0.4-mm-thick polytetrafluoroethylene to create neo-right and neo-left atria.

FIGURE 2. Method of total artificial heart implantation in a young patient with single ventricle and hypoplastic left heart syndrome who had previously undergone a Norwood with Sano procedure. Appearance after resection of the ventricular mass, leaving the Sano in place (A); further resection of the atrial mass just above the plane of the atrioventricular annuli, allowing expansion of the atrial cuff (B); and septation of the atrial mass with 0.4-mm-thick polytetrafluoroethylene to create neo-right and neo-left atria.

Patient and Pump Selection
Currently in our practice, for biventricular patients who clearly need biventricular support, we prefer TAH support for patients weighing ≤5 to 7 kg and patients with anatomic features that would complicate BiVAD support regardless of atrial or ventricular cannulation for inflow, and consider it more selectively for patients weighing 7 to 10 kg. These size criteria are based simply on ease of establishing good inflow and readily accommodating early chest closure. For single-ventricle patients, we currently consider TAH support for patients who are either not candidates for or have failed stage I palliation. However, our experience with both groups of patients is early, and we continue to refine our patient selection criteria.

We have modified our platform for centrifugal pumps to address 2 issues: thermal loss and risk of air embolism. We use an adjustable bed frame mount that positions the pumps immediately adjacent to the patient (within 2 to 3 feet). Also, we no longer use any stopcocks or pressure transducers in the circuit, to reduce the risk of air entry. This platform is very effective but does entail certain limitations for patient mobility; therefore, we prefer pulsatile pumps for patients whom we expect to mobilize.

Anticoagulation
Anticoagulation is initiated following resolution of surgical bleeding (typically 12 to 24 hours postoperatively). An argatroban infusion is titrated to a goal activated partial thromboplastin time of 2 to 3 times the baseline level. Antiplatelet agents, including aspirin and clopidogrel, are used in patients with EXCOR pumps. The dosage is increased to 30 mg/kg of aspirin and 5 mg/kg of clopidogrel over the first 2 weeks of therapy.

Pump Management
Regardless of the type of pump used, we adhere to management principles that would apply to standard BiVAD support: achieve good systemic perfusion without systemic or pulmonary venous congestion and place even more emphasis on avoiding overflowing the right pump to minimize the risk of pulmonary edema. For example, if the left (systemic) flow target were 800 mL/minute, then flow for the right would be approximately 650 to 700 mL/min. We also adhere to the principle of partial fill and full eject for the pulsatile pumps. For centrifugal pumps, we use flow probes on both outlet lines to measure output. For pulsatile pumps, we estimate flow based on percent fill and rate. In all cases, we also use cerebral and somatic noninvasive regional saturations as well as mixed venous oxygen saturation from a central venous line to assess the adequacy of oxygen delivery. We maintain central venous pressure monitoring in all patients and left atrial pressure monitoring more selectively. We acknowledge the importance of the data provided by left atrial pressure monitoring, particularly in the context of a pulsatile TAH, but also are concerned about the risk of air in the event of human error. For pulsatile pumps, we set the diastolic pressure to ~20 mm Hg while the chest is open and decrease it to ~40 mm Hg after chest closure. Systolic pressure and percent systole are adjusted to ensure full empty and minimize the systolic time.

In general, we have achieved support goals with flows ranging from 150 to 200 mL/kg/minute. We have not had to make substantial changes in pulsatile pump settings based on positive or negative pressure ventilation; however, for centrifugal pumps during positive-pressure inhalation, we have occasionally noted decreases in cone pressure and flow in the right pump that required changes in pump revolutions per minute or volume administration. Such issues resolved with negative-pressure inhalation after extubation.

RESULTS
Case Vignettes in Temporal Sequence
Case 1. Our first case was a 448-day-old, 8-kg child born with Swiss cheese apical ventricular septal defects and a pulmonary artery band placed early in life who presented with biventricular dysfunction (case report published previously). The patient was placed on extracorporeal life support (ECLS) after both device and surgical closure. After 2 weeks of ECLS and open sternum with no sign of myocardial recovery, and with a concern for residual ventricular septal defect, we offered the parents a salvage procedure consisting of a TAH using EXCOR pumps and valved conduits (20 mm for left, 18 mm for right). The chest was closed on postoperative day 1. Owing to mild thrombus deposition on the left pump, we placed the patient on ECLS via the neck and changed both pumps, upsizing to 25-mL pumps, with ECLS decannulation and vessel repair done immediately thereafter. The patient was extubated 9 days after TAH implantation. Support was excellent and resulted in successful bridge to transplantation after 3 months of...
support with no need for interval cardiac studies. During support, the child was breathing spontaneously on room air, fully fed enterally, and had good end-organ function. At the time of this report, the patient was alive and well as an outpatient.

**Case 2.** The second case was a 72-day-old, 4.5-kg patient with hypoplastic left heart syndrome who had failed an early Glenn and was revised back to a Sano shunt and ultimately placed on ECLS a second time for ventricular dysfunction. The patient developed renal and hepatic insufficiency and severe anasarca. With a second round of ECLS support and the chest open for over 40 days, we offered the parents a salvage TAH. We used centrifugal pumps with a 12-mm valved conduit for the neo-left atrial connection and a ringed 10-mm Gore-Tex conduit for the right side. Even though we used centrifugal pumps, we used the valved conduit on the left based on the supporting metal ring and resistance to collapse. Despite good bilateral support with superior vena cava saturation >80% for 30 days, liver failure and anasarca persisted, and support was withdrawn.

**Case 3.** The third case was a 37-day-old, 3.4-kg patient with a massive intracardiac (ventricular septal) tumor obliterating the ventricular cavities and leading to cardiogenic shock. An LVAD was placed using EXCOR cannulas and a centrifugal pump. For inflow, we cannulated the left atrium by creating a PTFE tunnel from the low right atrial free wall to a newly created atrial septal defect. Echocardiography demonstrated no impediment to inflow from the inferior vena cava or from the atrium through the tricuspid valve. ECLS was implemented to support the right ventricle and lungs (central venous pressure 25 mm Hg with 2 attempts at staying on LVAD support alone and visibly poor right ventricular function). Lung function improved moderately, but right ventricular failure persisted. After 12 days of bilateral support and an open chest, we offered the parents a salvage TAH, as achieving biatrial cannulation, good drainage, and adequate room for chest closure seemed improbable. At reexploration, a portion of the right lung was necrotic (necrotizing pneumonia) and was wedge-resected (confirmed by pathology/culture).
Despite the grim prognosis, the parents requested that we do everything possible. A TAH was implanted using ringed PTFE inflow conduits and centrifugal pumps. We achieved excellent support, but the necrotizing pneumonia progressed to bilateral disease with inability to wean from extracorporeal gas exchange. Support was withdrawn 14 days after TAH implantation.

Case 4. The fourth case was a 42-day-old, 3.4-kg patient with heterotaxy, single ventricle with balanced circulation, and congenital heart block who underwent early placement of a temporary pacemaker that was subsequently converted to a permanent pacemaker. During the fifth week of life, the patient required escalating inotropic support (had remained intubated and mechanically ventilated since shortly after birth). Owing to evolving cardiogenic shock, we implanted a TAH using ringed PTFE for inflow connections and oversized EXCOR pumps (15 mL) in an effort to avoid full-fill cycles and high left atrial pressure. The chest was closed on postoperative day 2. We achieved excellent cardiac output based on regional oximetry and mixed venous blood gases; however, the preexisting respiratory failure thought to be secondary to pulmonary edema did not resolve. Therefore, on postoperative day 22, we converted the left pump to a centrifugal pump. Despite continued good measures of cardiac output, respiratory failure persisted. The patient had abnormal movements concerning for a seizure and was found to have an ischemic cerebral infarction on brain computed tomography scan performed on postoperative day 34. The patient was supported well with full enteral nutrition and end-organ function until transplantation following 44 days of support (normal neurologic exam). Pulmonary failure, which ultimately resolved, persisted for weeks after transplantation despite low left atrial pressures. At the time of this report, the child continues to do well as an outpatient.

Case 5. The most recent case is an 8-month-old, 8-kg child with ECLS initiated during cardiopulmonary resuscitation. A left ventricular vent was placed via sternotomy. Inspection revealed thrombosed, massively diluted coronaries and a noncontractile heart (presumed end-stage Kawasaki’s disease), with visible evidence of infarction of both ventricles. Eleven days later, we implanted a TAH using valved inflow conduits (16 mm for left, 14 mm for right) and 25-mL EXCOR pumps. The chest was closed on postoperative day 1, and the patient was extubated on postoperative day 7. The patient was well-supported, engaged in regular therapy with our child-life and play specialists, breathed spontaneously on room air, received full enteral nutrition, and underwent transplantation after 96 days of support. At explant, the leaflets of the left porcine valve were thin, mobile, and free of thrombus (Video 1). At the time of this report, the child continues to do well as an outpatient.

Table 1 summarizes preoperative characteristics and details of the support platforms, and Table 2 summarizes outcomes. Morbidity included 1 EXCOR pump exchange for thrombus, 1 conversion from EXCOR to a centrifugal pump, 1 patient with 2 reoperations for bleeding, and 1 patient with ischemic stroke.

DISCUSSION

We have described a fairly simple and robust method of achieving TAH support in young patients. Our method also enables the creation of an in-series, fully septated circulation for single-ventricle patients, thereby eliminating cyanosis. The limited number of patients precludes meaningful comparison to outcomes achieved with more standard methods of biventricular support. Nevertheless, it is noteworthy that in Conway and colleagues’ cohort of 97 patients weighing <10 kg, those undergoing BiVAD support with congenital heart disease on ECLS had a survival of only 24%. In contrast, Miller and colleagues reported excellent survival in a cohort of 31 patients aged 1.3 to 9.3 years. In their cohort, only 10% of the patients had congenital heart disease, and 65% of patients weighed >10 kg. One of 3 patients weighing <5 kg died, and 2 of 8 patients weighing 5 to 10 kg died.

We respectfully acknowledge Ziegler and colleagues, who first reported TAH support in a 6-month-old patient with primary graft nonfunction. They described using unsupported PTFE conduits for inflow and ultimately 10-mL EXCOR pumps. We credit them for their creative work and success in bridging their patient to retransplantation. We do not refute the possibility that a Gore-Tex conduit could provide some degree of capacitance. We have not taken this approach with our
subsequent patients, based on the concern that unsupported conduits might be prone to kinking or partial collapse.

Others have described success with various forms of BiVAD support using either paracorporeal or intracorporeal devices (for older children). Likewise, for single-ventricle patients, others have reported success with a single VAD and either using a systemic-to-pulmonary artery shunt or using the ductus arteriosus for pulmonary blood flow and pulmonary artery branch bands. We do not claim superiority of our approach; rather, we are simply more inclined to create a fully septated heart and a fully saturated systemic circulation that is not dependent on a shunt or ductal stent.

We believe that we have learned a couple of important lessons in our early experience with this technique. First, we do not advocate for an aggressive approach to resecting ventricles and recognize the implications of acute pump failure and the probable need for ECLS for elective pump changeouts. However, if a small patient is clearly going to need more than temporary BiVAD support, or there are anatomic factors that might complicate standard BiVAD support, making the difficult decision to remove the

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LA, Left atrial pressure or measurement of oxygen gas exchange; CVP, central venous pressure; CI, cardiac index, L/min/m²; N/A, data not available; SpO₂, pulse oximetry estimation of oxygen saturation; PaO₂, partial pressure of oxygen in arterial blood. *CI estimated as 70% of maximal flow on the EXCOR pump assuming full fill (pump size × rate), as all pumps were intentionally set for partial fill.
ventricles earlier in the course may be associated with better outcomes. In the 2 patients who died, we likely waited too long.

Second, to an extent greater than we anticipated, removal of the ventricular mass dramatically simplified creation of widely patent inflow and outflow connections and allowed for early chest closure even in the smallest patient without untoward effects on the systemic or pulmonary veins. While not novel to our technique, in the 3 patients who underwent transplantation, the tissue expander nicely maintained the space and allowed implantation of an appropriate-sized donor heart.

Finally, our experience has prompted us to critically think about the implications of the absence of the ventricular mass in a pulsatile TAH arrangement in a small child. Before our first patient, we were aware of the report by VanderPluym and colleagues demonstrating pulmonary vein flow reversal in pump systole in a patient with a Fontan circulation and the ventricular mass removed. Conversion from an EXCOR pump (size not specified) to a continuous-flow pump resolved these findings and associated pulmonary edema. In the usual LVAD arrangement, in pump systole, the pump inlet valve closes, and any additional volume entering the left heart is accommodated by the atrial and ventricular mass (along with closure of the native atrioventricular valve), without a substantial rise in left atrial pressure. However, it is also possible that in pump systole, any pressure wave transmitted up the inflow cannula could be "absorbed" by the ventricular mass and closure of the native atrioventricular valve. Full fill before pump systole might further exacerbate the latter. In the absence of further data, we do not know the true explanation. However, we speculated that the addition of a valve near the atrial mass might mitigate potential negative consequences of either mechanism. Therefore, in our first case, we placed valved conduits with the valves positioned at the annuli. We observed no problems with pulmonary edema, despite occasional full fill cycles. At TAH explant, the valve cusps of the inflow conduits were soft, pliable, and mobile with no visible thrombi (findings very similar to those of patient 5 shown in Video 1). This suggests that the leaflets were likely closing intermittently in response to the rise in pressure in the cannula from either a forward flow capacitance issue and/or retrograde pulse wave reflection.

After further consideration, we reasoned that it should be possible to avoid a valve by simply upsizing the pump to always maintain a state of partial fill. Theoretically, this would prevent, or at least reduce, the previously described effects. However, more than once, we have done the exercise of standing at the bedside and staring at the systemic pump for an extended period versus the usual protocolled pump inspection times. For case 4 (3.4 kg, 15-mL pumps, no valved conduits), extended inspection revealed brief periods of full fill cycles despite our best efforts and multiple readjustments of the pump settings. The important lesson that we have learned is that the real-world dynamic state of the patient can make it extremely difficult, if not impossible, to avoid full fill cycles. Therefore, with pulsatile pumps, we believe use of a valved inflow conduit may (albeit speculatively at this point) be a useful adjunct, despite the theoretical incremental risk of thrombus and/or valve dysfunction. Unfortunately, we have no objective imaging or catheterization data to substantiate our opinion.

To be clear, we are not stating that a full fill cycle is always going to create problems; this would depend on multiple variables. We are simply stating full fill is more likely than partial fill to be associated with problems. In addition, we acknowledge a strong counterargument based on the experience with the Syncardia TAH. Considering pump volume–to–patient weight ratio, values in our patients are much higher than those in a standard adult-sized patient with a 70-mL pump. In our cohort, we either estimated or measured flows at approximately 200 mL/kg/minute; it would be exceedingly uncommon to flow 14 L/minute in an adult. With the Syncardia, flow pathways are much shorter and likely more efficient, and during the first 1 to 2 weeks of inpatient support, the continuous monitoring of pump volume and the alarm system simplify adherence to the principle of allowing no full fill. We suspect this is an incomplete explanation. Perhaps we simply lack understanding of the relationship between age, atrial size, pump size, and capacitance of the atrial and venous vasculature that would better inform decisions about pump size for a small child and this particular TAH arrangement.

Limitations
This is a very preliminary and descriptive report. We have shared certain notions and lessons learned, but regard these as merely opinions at this point. We also acknowledge the importance of the lack of left atrial pressure monitoring with pulsatile pumps.

CONCLUSIONS
Our method of TAH support can be tailored to provide effective support of carefully selected young children with single or biventricular physiology and may offer a salvage option when no other options exist. The optimal method of inflow cannulation and pump sizing for pulsatile pumps remain to be determined. It is our current opinion that pump upsizing and valved inflow conduits may be important adjuncts.

Conflict of Interest Statement
Dr Woods is a cofounder of OperVu. Dr Mitchell is a cofounder of Ariosa Diagnostics and TAI Diagnostics.
Dr Niebler has received travel funds from Abbott to attend learning network conferences that have no relationship to the content of this manuscript. All other authors have nothing to disclose with regard to commercial support.

References


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