



## ORIGINAL CLINICAL SCIENCE

# Interagency registry for mechanically assisted circulatory support report on the total artificial heart

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**KEYWORDS:**

total artificial heart;  
mechanical circulatory  
support;  
INTERMACS;  
biventricular failure;  
bridge to  
transplantation

**BACKGROUND:** We sought to better understand the patient population who receive a temporary total artificial heart (TAH) as bridge to transplant or as bridge to decision by evaluating data from the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) database.

**METHODS:** We examined data related to survival, adverse events, and competing outcomes from patients who received TAHs between June 2006 and April 2017 and used hazard function analysis to explore risk factors for mortality.

**RESULTS:** Data from 450 patients (87% men; mean age, 50 years) were available in the INTERMACS database. The 2 most common diagnoses were dilated cardiomyopathy (50%) and ischemic cardiomyopathy (20%). Risk factors for right heart failure were present in 82% of patients. Most patients were INTERMACS Profile 1 (43%) or 2 (37%) at implantation. There were 266 patients who eventually underwent transplantation, and 162 died. Overall 3-, 6-, and 12-month actuarial survival rates were 73%, 62%, and 53%, respectively. Risk factors for death included older age ( $p = 0.001$ ), need for pre-implantation dialysis ( $p = 0.006$ ), higher creatinine ( $p = 0.008$ ) and lower albumin ( $p < 0.001$ ) levels, and implantation at a low-volume center ( $\leq 10$  TAHs;  $p < 0.001$ ). Competing-outcomes analysis showed 71% of patients in high-volume centers were alive on the device or had undergone transplantation at 12 months after TAH implantation vs 57% in low-volume centers ( $p = 0.003$ ).

**CONCLUSIONS:** Patients receiving TAHs have rapidly declining cardiac function and require prompt intervention. Experienced centers have better outcomes, likely related to patient selection, timing of implantation, patient care, and device management. Organized transfer of knowledge to low-volume centers could improve outcomes.

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Physicians, engineers, scientists, and even science fiction writers had long pondered the idea of replacing the human heart with an artificial pump, but it was not until 1935 that aviator Charles Lindbergh and Nobel laureate Alexis Carrel designed the first prototype<sup>1</sup> made entirely of hand-blown glass. Subsequently, numerous models of total artificial hearts (TAHs) have been designed and even implanted—many of which preceded the development of the left ventricular assist device (LVAD)—but only the pneumatic pulsatile TAH has been widely used.<sup>2–7</sup>

Throughout the world, the continuous-flow (axial or centrifugal) LVAD is the primary long-term mechanical circulatory support (MCS) for patients with severe congestive heart failure, as either a bridge (to transplant or decision) or destination therapy. However, the LVAD is not the final solution for many patients with failing myocardium. The reported incidence of right ventricular (RV) failure after LVAD placement, even with the use of newer LVAD models, ranges from 9% to 30%,<sup>8,9</sup> which results in prolonged inotrope dependence or the need for short-term or long-term MCS. RV failure has a negative effect on patient survival,<sup>10</sup> but identifying reliable predictors of which patients will develop RV failure has proven elusive.<sup>11–16</sup> No single parameter is sufficient to predict RV failure before or after LVAD implantation.<sup>17</sup>

Comparison of results from LVADs and biventricular assist devices (BiVADs) have suggested that the patient's condition at implantation rather than device technology may dominate the calculus of inferior survival with biventricular support.<sup>18,19</sup> However, TAHs and BiVADs have different profiles of survival and are associated with different adverse events (AEs). Others showed that survival rates were higher in patients who had a TAH implanted compared with patients who received support from implantable or paracorporeal BiVADs for longer than 90 days.<sup>20</sup> There has never been a TAH randomized trial.

The primary aim of this study was to determine the patient characteristics and survival outcomes of the TAH with current technology. We also sought to determine risk factors and document AEs for patients who received a TAH.

## Methods

### Intermacs

The Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) database represents a public-private partnership among the National Heart, Lung, and Blood Institute, hospitals, and industry. Before data collection began on June 23, 2006, 53 institutions received Institutional Review Board approval to participate in the INTERMACS Registry and subsequently contributed data to the registry. The Data Coordinating Center at the University of Alabama and participating institutions manage the data according to Health Insurance Portability and Accountability Act requirements.

## Patient population

We examined data from all patients aged 19 years and older who received the SynCardia temporary TAH (TAH-t) 70 mL (SynCardia Systems, LLC, Tucson, AZ; [Figure S1](#), available online at [www.jhltonline.org](http://www.jhltonline.org)) between June 23, 2006, and April 30, 2017, as a bridge to transplantation or candidacy. This device is the only of its kind approved by the United States Food and Drug Administration.

## Analytics

The Data Coordinating Center at the University of Alabama performed the data analysis. Patient condition at implant was categorized according to the INTERMACS Patient Profiles (IPP).<sup>21</sup> For descriptive purposes, categoric variables are expressed as frequencies and percentages. Continuous variables are expressed as means  $\pm$  standard deviation. Discrete variables were compared using the chi-square test. Continuous variables were compared using the *t*-test or non-parametric Wilcoxon rank sum test, as indicated. AE rates were calculated within 3 months and more than 3 months after implant. Device malfunction AEs were examined by separating the events by thrombosis and device malfunction, whether major or minor. Minor events included events (fault alarms, small air leaks, other) that did not cause the patient to have symptoms. All other events were considered major (driveline disconnection, driver failure).

Survival analyses were performed using Kaplan-Meier depictions and parametric survival analysis. Patients were censored at transplant. The mutually exclusive patient outcomes of death, transplant, or alive on a TAH were analyzed using competing outcomes methods. Risk factors for mortality were examined using multivariable analysis in the hazard function domain. Site TAH volume was investigated as cumulative TAH volume at the time of the patient's implantation and total site TAH volume in the registry. These volume indicators were evaluated as continuous variables and at various cut points (e.g., 5, 10, 15 implants). The volume indicator was selected to provide the best fit in the overall risk model. A *p*-value of  $< 0.05$  was considered statistically significant. Analyses were performed using SAS 9.4 software (SAS Institute Inc., Cary, NC).

## Results

### Patient characteristics

Complete follow-up data were available from all 450 patients (87% men) who underwent TAH-t implantation during this period, yielding 197.0 patient-years. Mean follow-up was 5.3 months (median, 3.3 months). Patients were an average age of 50 years (range, 19–72 years), 75% were on inotropes, 80% were IPP 1 or 2, and 20% were supported with extracorporeal membrane oxygenation (ECMO). Dilated cardiomyopathy was the etiology leading to biventricular failure in 50% of the patients. More than 95% of patients were on the active list for a heart transplant or underwent TAH-t as a bridge to candidacy.

### Baseline characteristics as predictors of RV failure

Baseline characteristics that describe RV failure at the time of implant were present in 82% of patients, including

include dialysis, ECMO, ventilator support-dependent, severely reduced RV ejection fraction, temporary MCS, or moderate or severe tricuspid valve insufficiency (Supplementary Table S1, online).

## Patient's size

Weight, body surface area (BSA), and body mass index were examined as potential risk factors in the multivariable analysis but did not reach statistical significance for entry into the model. The cumulative distribution functions for ranges of weight and BSA are included in Supplementary Figures S2 and S3, online.

## Hemolysis

The mean lactose dehydrogenase (LDH) value was  $574.2 \pm 579.7$  U/liter (Supplementary Figure S4, online). However, LDH values were available in INTERMACS for only 33% of patients both before and after implantation. The values from the currently available data show LDH remained stable from before implantation throughout the follow-up period.

## Survival

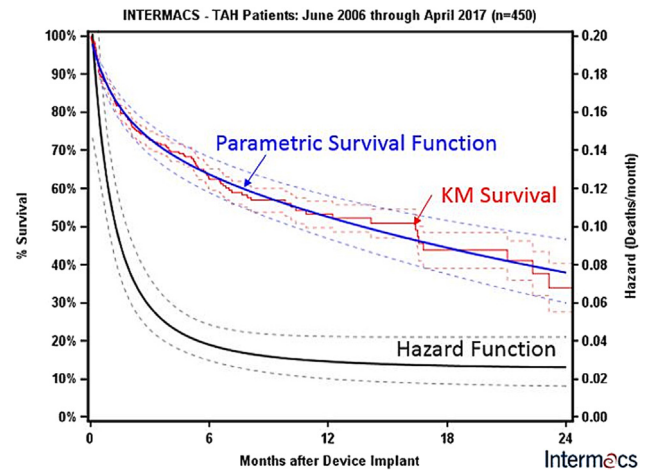
Transplantation was performed in 266 patients, and 162 patients died on support. Survival according to Kaplan-Meier estimates was 53.2% at 1 year and 33.9% at 2 years (Figure 1). Hazard function analysis showed an early rapidly decreasing risk that merged with a constant phase at about 4 months. By competing outcome analysis, the overall rate of transplantation was 53%, mortality was 34%, and 13% were alive on a device by 12 months (Figure 2). Survival outcome was highest for patients with an IPP of 3 (Supplementary Figure S5, online) Table 1.

## Causes of death

The most common cause of death was multisystem organ failure (36% of deaths), followed by neurologic injury (18%) and elective withdrawal of support (12%; Table 2). Differences in the distribution of causes of death by era or center volume were not significant.

## Risk factors for death

A 2-phase multivariable model was developed to determine pre-implant risks factor for death (Table 3). Older age at implantation and the need for dialysis before implantation were significant risk factors for early mortality. The greatest age effect was among patients younger than 40 years, who had more a favorable survival likelihood compared with other age groups (Figure 3). Patients with a history of pre-implant dialysis had a particularly high (> 50%) 6-month mortality (Supplementary Figure S6, online). High creatinine and low serum albumin were risk factors for late mortality.

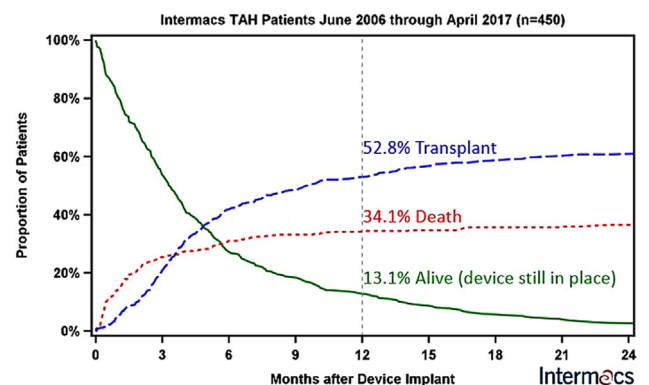


**Figure 1** Parametric survival curve and associated hazard function for total artificial heart (TAH) patients. The event modeled is death on a device censored at transplant. The Kaplan-Meier (KM) survival estimates are plotted to show the agreement with the fitted parametric model. The dashed lines indicate the 70% confidence limits. INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support.

The cumulative center TAH-t volume of  $\leq 10$  implants was a significant risk factor in the constant phase (Figure 4). The cutoff at a center volume of 10 implants was identified as the best descriptor of center volume as a risk factor. The 12-month survival was 64.8% for centers with more than 10 implants vs 36.7% for those with 10 or fewer ( $p = 0.001$ ). The relationship between age and center volume (Figure 5) shows the particularly favorable outcomes in younger patients in centers with more experience.

## Adverse events

The most common AEs early (<3 months) were bleeding and infection. After 3 months, minor device malfunction and infection were most prevalent (Table 4). The AE rates for bleeding, infection, and neurologic dysfunction for TAH-t



**Figure 2** Competing outcomes depiction for patients who received a total artificial heart (TAH) from June 2006 through April 2017 ( $n = 450$ ). At any point in time, the sum of the proportions of each outcome equals 1. INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support.

**Table 1** Interagency Registry for Mechanically Assisted Circulatory Support Total Artificial Heart Patients—Characteristics (June 2006 through April 2017)

Characteristics	TAH patients (n = 450)
Age at implant, years	50.1 ± 12.7
Male	393 (87.3)
Weight, kg.	90.5 ± 20.2
Body surface area, m <sup>2</sup>	2.1 ± 0.3
Diagnosis	
Congenital heart disease	15 ( 3.3)
Dilated myopathy	225 (50.0)
Hypertrophic cardiomyopathy	13 ( 2.9)
Ischemic cardiomyopathy	92 (20.4)
Restrictive cardiomyopathy/other	105 (23.3)
INTERMACS Patient Profile	
1 (critical cardiogenic shock)	189 (43.1)
2 (progressive decline)	163 (37.1)
3 (stable but inotrope dependent)	43 ( 9.8)
4 (resting symptoms)	32 ( 7.3)
5-7 (less sick)	12 ( 2.7)
Device strategy	
Bridge to transplant, listed	267 (59.3)
Bridge to candidacy	169 (37.6)
Destination therapy	7 (1.6)
Rescue therapy, other	7 (1.6)
Hemoglobin, g/dl	10.5 ± 2.1
Creatinine, mg/dl	1.6 ± 1.0
INR, international U	1.4 ± 0.6
Platelets, ×10 <sup>3</sup> /μl	176.5 ± 86.4
Albumin, g/dl	3.3 ± 0.8
Total bilirubin, mg/dl	2.1 ± 3.1
Brain natriuretic peptide, ng/liter	1,338.9 ± 1,164.4
Blood urea nitrogen, mg/dl	32.4 ± 21.7
Alanine aminotransferase, U/liter	126.0 ± 330.4
Aspartate aminotransferase, U/liter	131.7 ± 370.4
Sodium, mEq/liter	134.5 ± 5.9
Cardiac index, liter/min/m <sup>2</sup>	2.3 ± 1.4
Pulmonary artery	
Diastolic pressure, mm Hg	25.4 ± 8.7
Systolic pressure, mm Hg	45.3 ± 14.5
Wedge pressure, mm Hg	25.4 ± 8.3
Right atrial pressure, mm Hg	16.6 ± 7.9
Ascites	53 (16.4)
LVEDD, cm	6.3 ± 1.4
LVEF	
< 20 (severe)	243 (55.7)
20-29 (moderate/severe)	87 (20.0)
30-39 (moderate)	24 ( 5.5)
40-49 (mild)	16 ( 3.7)
> 50 (normal)	34 ( 7.8)
Not recorded or documented/unknown	32 (7.4)
Regurgitation (moderate/severe)	
Mitral	192 (44.0)
Tricuspid	218 (50.0)
Aortic	20 ( 4.6)
RVEF (severe)	146 (33.5)
ECMO	94 (20.9)

ECMO, extracorporeal membrane oxygenation; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; LVEDD, left ventricular end-diastolic dimension; LVEF, left ventricular ejection fraction; RVEF, right ventricular ejection fraction.

Continuous data are presented as mean ± standard deviation and categorical data as number (%).

**Table 2** Interagency Registry for Mechanically Assisted Circulatory Support Total Artificial Heart Patients—Primary Cause of Death (June 2006 through April 2017, n = 450)

Primary cause of death	Patients No. (%)
Multisystem organ failure	59 (36.4)
Neurologic dysfunction	29 (17.9)
Withdrawal of support	19 (11.7)
Major infection	17 (10.5)
Respiratory failure	8 (4.9)
Heart Failure	7 (4.3)
Device malfunction	5 (3.1)
Bleeding	4 (2.3)
Gastrointestinal disorder	3 (1.9)
Hepatic dysfunction	3 (1.9)
Fluid/electrolyte disorder	1 (0.6)
Pulmonary embolism	1 (0.6)
Other	6 (3.7)
Total	162 (100)

were higher in the early phase compared with data from the INTERMACS registry of patients receiving LVADs.

The likelihood of major infection approached 70% within 6 months ([Supplementary Figure S7](#), online). There were 556 infections documented in 450 patients. Pulmonary infections after implantation were the most common type, with bacteria being the most common pathogen ([Supplementary Tables S2 and S3](#), online).

A total 188 neurologic dysfunction events occurred. The incidence of stroke was 22.7% within the first 6 months: 13.5% ischemic and 10.2% hemorrhagic strokes ([Supplementary Figure S8](#), online). A modified Rankin scale was applied to only 51 events; the scores indicated that 12% of these events resulted in moderate-severe disability and 39% in severe disability.

Approximately 20% of patients experienced a major gastrointestinal hemorrhage within 6 months of implantation ([Supplementary Figure S9](#), online). The incidences of major and minor device malfunction were 7.1% and 28.2% at 6 months, and the incidence of thrombosis was 1.6% during this same interval ([Supplementary Figure S10](#), online).

**Table 3** Interagency Registry for Mechanically Assisted Circulatory Support Total Artificial Heart Patients—Multivariable Model (June 2006 through April 2017, n = 450)

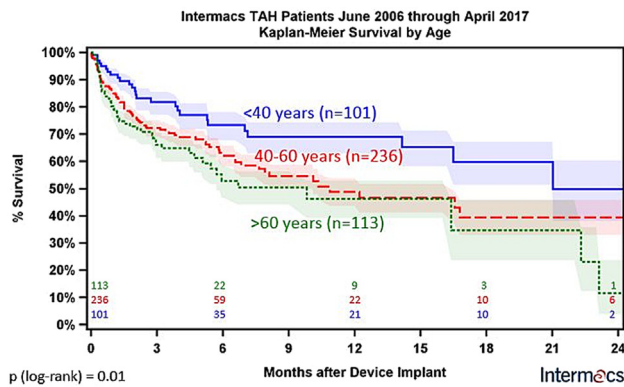
Pre-Implant Risk Factor for Death	Early hazard		Constant hazard	
	HR	p-value	HR	p-value
Age, year (older) <sup>a</sup>	1.6	0.001		
Pre-implant dialysis	2.5	0.006		
Creatinine (higher)			1.3	0.008
Albumin, g/dl (lower) <sup>b</sup>			1.9	<0.001
Total center TAH volume ≤10			3.0	<0.001

HR, hazard ratio; TAH, total artificial heart.

<sup>a</sup>The hazard ratio depicts the increase in hazard when age increases from 50 to 60 years

<sup>b</sup>The hazard ratio depicts the increase in hazard when albumin decreases 1 unit.



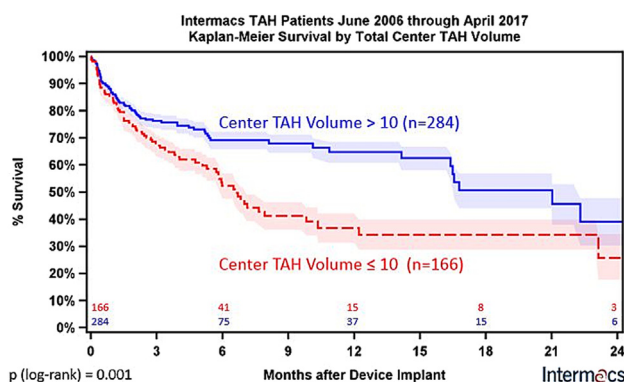


**Figure 3** Kaplan-Meier survival curves for total artificial heart (TAH) patients stratified by age. INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support.

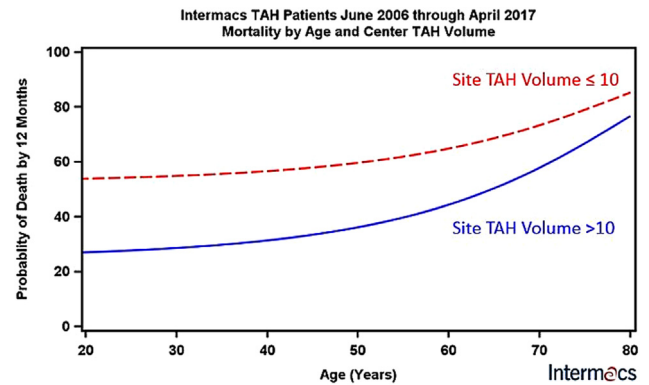
Pre-implant dialysis was performed in 51 patients (11%). For the 399 patients who did not require dialysis before implantation, 114 (29%) began dialysis after TAH-t implantation. We were unable to identify the number of patients who were weaned from dialysis. The mean creatinine and serum urea nitrogen values remained stable from baseline to 6 months after implantation (Supplementary Figures S11 and S12, online). To determine a relationship between hemolysis and renal failure dysfunction, LDH levels were analyzed to determine whether hemolysis was a risk factor for dialysis. Pre-implant and post-implant (follow-up) LDH levels were compared in 2 groups: (1) no dialysis before and after implantation and (2) no dialysis before implantation but with the need for dialysis after implantation. The difference in LDH levels for both groups was not statistically significant (Supplementary Figure S13, online). All AE rates for the TAH-t cohort were highest during the first 3 months.

### Discharged home and hospitalization

Overall, 109 patients (24%) were discharged with device support: 91% were discharged to a home setting, and 4% were discharged to a rehabilitation unit. Of the 370 patients who received an LVAD after 2010, 99 (27%) were



**Figure 4** Kaplan-Meier survival curve for total artificial heart (TAH) patients stratified by total center volume. INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support.



**Figure 5** Predicted probability of mortality by 12 months by total center total artificial heart (TAH) volume. Predicted 12-month survival is based on a multivariate parametric hazard model using the average patient characteristics. INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support.

discharged home on the device. The median time from implantation to discharge home for discharged patients was 1.6 months (interquartile range, 1.1–2.3 months). The number of patients discharged increased in the most recent area (Supplementary Tables S4–6, online).

### Likelihood of transplantation

The possibility of undergoing heart transplantation differed widely by era and center volume. Among centers implanting more than 10 TAH-t during the study period, 58.4% of patients received a heart transplant within 12 months vs 43% in lower-volume centers (Figure 6). The year of

**Table 4** Interagency Registry for Mechanically Assisted Circulatory Support Total Artificial Heart Patients—Adverse Events (June 2006 through April 2017,  $n = 450$ )

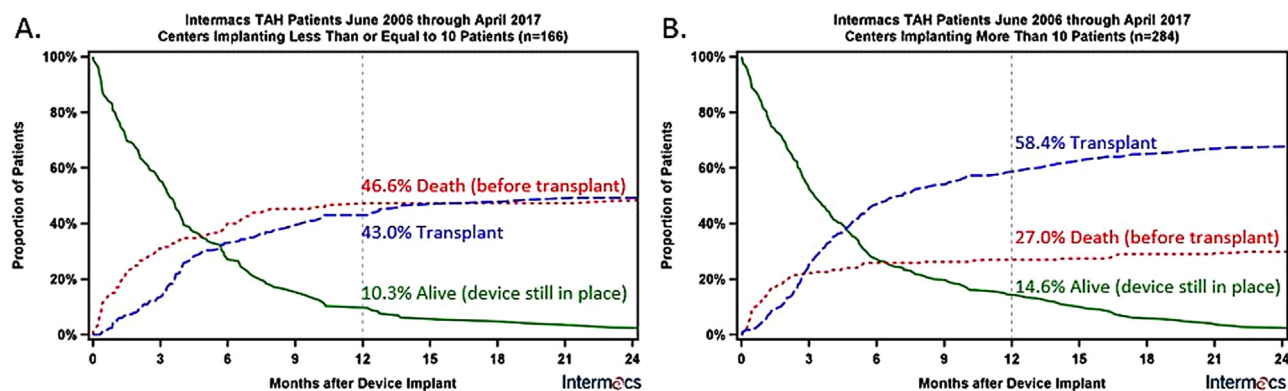
Event	Early <sup>a</sup>		Late <sup>a</sup>		$p$ -value <sup>c</sup>
	Events	Rate <sup>b</sup>	Events	Rate <sup>b</sup>	
Thromboembolism					
Venous	17	1.7	3	0.2	0.0001
Arterial non-CNS	20	2.0	2	0.1	<0.0001
Bleeding	414	41.3	96	7.1	<0.0001
Device malfunction					
Major	13	1.3	34	2.5	0.04
Minor	50	5.0	203	14.9	<0.0001
Pump thrombus	4	0.4	3	0.2	0.4
Hepatic dysfunction	52	5.2	11	0.8	<0.0001
Infection	389	38.8	167	12.3	<0.0001
Neurologic dysfunction	148	14.7	40	2.9	<0.0001
Pericardial drainage	63	6.3	1	0.1	<0.0001
Renal dysfunction	162	16.1	21	1.5	<0.0001
Respiratory failure	219	21.8	38	2.8	<0.0001

CNS, central nervous system.

<sup>a</sup>Early indicates  $\leq 3$  months of device implant. Late indicates  $> 3$  months after device implant

<sup>b</sup>Rates are reported per 100 patient-months.

<sup>c</sup>The  $p$ -values compare early and late rates.



**Figure 6** Competing outcomes for centers implanting (A)  $\leq 10$  patients ( $n = 166$ ) and (B)  $> 10$  patients ( $n = 284$ ). At any point in time, the sum of the proportions of each outcome equals 1. INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; TAH, total artificial heart.

implantation also had an effect on the chances of transplantation (Figure 7), with a higher likelihood of transplant within 1 year for implants taking place before 2012.

## Discussion

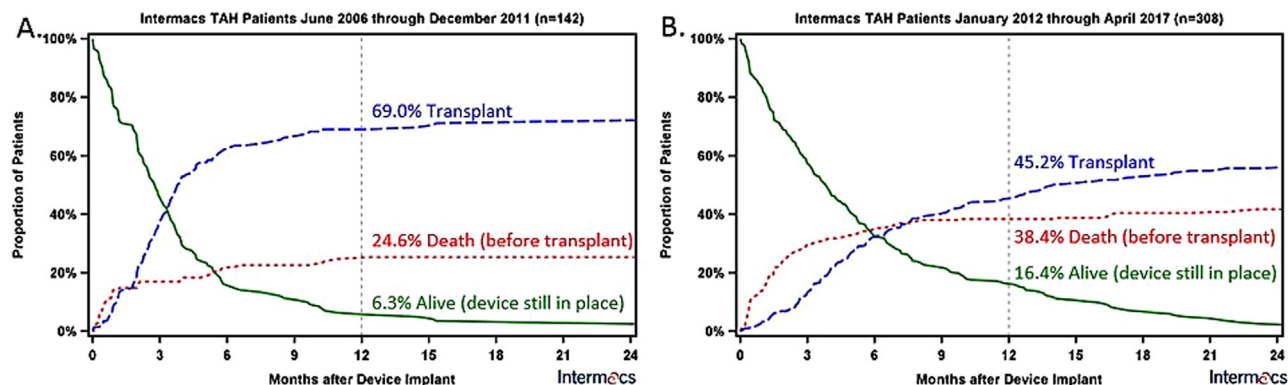
Several publications during the last few decades have shown a wide range of outcomes in patients undergoing TAH implantation.<sup>22–32</sup> This analysis of initial data from the INTERMACS database represents a comprehensive multi-institutional investigation of the TAH-t experience, providing outcomes, risk factors for death, and AE rates to establish benchmarks. Future analyses of the INTERMACS database will provide in-depth understanding of patients' renal function before and after implantation, rates of hemolysis and neurologic events, quality of life, hospitalization and functional capacity, and their care after hospitalization.

Outcomes data for TAH-t obtained from INTERMACS are typically reported annually, with the most recent being in 2015 and 2017<sup>33,34</sup>; the results of the first analysis of data from the Pediatric Interagency Registry for Mechanical Circulatory Support database (the pediatric-specific portion of INTERMACS) were published in 2016.<sup>35</sup> The current analysis of the INTERMACS database shows

that the patient cohort that received TAHs-t was sicker (IPP 1 and 2) than patients who received LVADs (more frequently IPP 2 and 3). One or more characteristics of RV failure were present in 82% of patients implanted with a TAH-t.

These characteristics are not surprising, because severe biventricular failure is the indication for the TAH-t. However, each center that implants the TAH-t has developed different criteria to select the appropriate patient with biventricular failure, ranging from determining RV functional parameters calculated preoperatively, etiology of biventricular failure (potential for RV function reversibility) to perioperative hemodynamic assessment with intraoperative visual inspection of RV contractility.

Although the overall 6-month survival for the TAH-t cohort is lower than that of patients who received an isolated LVAD, these patient sub-sets are not comparable in that the TAH-t was selected because LVAD support was deemed inappropriate secondary to biventricular failure.<sup>36,37</sup> Initial consideration was given to comparing the TAH-t cohort to patients in INTERMACS who had received BiVAD support, but this proved to be a challenge. Patients who have received BiVAD in the INTERMACS database were implanted with permutations of different LVADs and RVADs. Furthermore, the outcomes of some of the



**Figure 7** Competing outcomes by implant era: (A) June 2006 through December 2011 ( $n = 142$ ) and (B) January 2012 through April 2017 ( $n = 308$ ). At any point in time, the sum of the proportions of each outcome equals 1. INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; TAH, total artificial heart.

BiVAD configurations have been studied (retrospectively, prospectively, or randomized). Some configurations use different energy sources or are implanted off-label.

The major period of risk for mortality with the TAH-t was the first 3 months. Further analysis showed that center experience with the TAH-t (particularly with >10 implants) is an essential determinant of success, with no discernible difference in the level of patient sickness at the time of implantation. The observed decrease in survival between eras can be attributed to an increase in newer programs performing a small number of implants. The Kaplan-Meier survival estimate by center volume shows a survival advantage when the center volume exceeds 10 devices implanted, a value that differentiates the high-volume from the low-volume centers at 3 months and beyond (i.e., the constant phase).

The mortality in the early phase, which is similar at both high-volume and low-volume centers, is the result of the severity of the patient's condition. The mortality in the constant phase is primarily the result of medical issues (i.e., elevated creatinine and low albumin concentrations) and management (experience). This finding suggests that not only the severity of the patient's illness but also the level of experience of the team managing the patient is important. The improvement in TAH survival could be the result of surgical experience with device implantation, a better understanding of patient selection, the timing of intervention, and patient management. The survival from the high-volume centers at 1 year is approximately 66%, and destination therapy LVAD survival at 1 year is 78%. Although these survival outcomes are dissimilar, they are within range of one another. The improvement in medical management because of more experience argues in favor of performing destination therapy in patients with TAHs in high-volume centers. The outcome gap that exists between low-volume and high-volume centers must improve to provide overall better outcomes.

The device malfunction rate was high in the period of 3 to 24 months because of frequent changes that the Freedom Driver required, not because of pump-component failure or thrombosis. The higher AE rates in the early phase after the implantation of TAH-t vs LVAD were multifactorial and might represent the patient severity of illness, coagulation state, and center experience. AEs decrease over time as the patient moves away from the pre-implant physiologic state and the surgical intervention. Pericardial drainage decreased as the risk of mediastinal bleeding decreased over time.

This retrospective analysis indicated that the primary application of the TAH-t has been in the very ill patient with biventricular failure. According to the data from INTERMACS, principal pre-implant diagnoses have been dilated and ischemic cardiomyopathies. During the past few years, those diagnoses have changed to include failing heart transplant (acute or chronic), restrictive and infiltrative cardiomyopathy, congenital abnormalities, malignant arrhythmias that do not respond to other interventions, large post-infarction ventricular septal defects, partial ventricular thrombosis, cardiac malignancies, and Chagas disease.

Rebridging with a TAH-t has been successful in some patients who experience LVAD/BiVAD failure.<sup>38</sup>

The challenges for early MCS referral continue to be multifactorial. The timing of referral and intervention might make the difference for some etiologies between successful implant of an LVAD and irreversible RV dysfunction requiring a TAH-t. Nonetheless, as LVADs continue to improve and become ubiquitous, there remains a group of patients whose diagnoses appear best treated with heart replacement. The TAH-t allows for home discharge and outpatient follow-up while the patient awaits transplantation.<sup>39</sup>

The benefits of LVADs in providing significant survival and quality of life benefit for those patients with progressive hemodynamic deterioration are well summarized.<sup>40</sup> The increase in mortality with patients in cardiogenic shock (IPP 1) has led to a decrease in the proportion of such patients receiving LVAD devices. The recent increase in the use of short-term MCS has proven to be encouraging for the severely ill patient in cardiogenic shock as a bridge to decision and durable LVAD. However, this use is associated with an increase in early mortality, partly because of unrecognized RV failure.<sup>41</sup> The encouraging survival in this patient sub-set with the TAH-t, particularly with sufficient center experience, provides support for consideration of the TAH as an alternative to the use of right-sided or left-sided VADs in patients with severe biventricular failure.<sup>42</sup> Pre-implant dialysis is a risk factor for death but is not a contraindication for the use of TAH-t. Successful bridging to heart-kidney transplantation has been performed.<sup>43</sup> A small number of patients are still alive 5 years after implantation of their original TAH-t, leading to the development of an ongoing destination therapy trial of TAH in the United States and Europe.

The concept of TAH continues to evolve as more efficient drivers are developed for the SynCardia TAH-t. The CARMAT TAH has started a trial in Europe.<sup>44</sup> The BiVACOR TAH is a design using magnetic levitation technology that can generate continuous or pulsatile flow.<sup>45</sup> The quest for a long-term heart replacement continues with designs in the form of the ReinHeart TAH,<sup>46</sup> CCFTAH,<sup>47</sup> OregonHeart TAH,<sup>48</sup> Helical Flow TAH,<sup>49</sup> and a hybrid CF-TAH.<sup>50</sup> The concept of a bioartificial TAH has also been proposed.<sup>51</sup>

The patients who benefit from the TAH are among the sickest patients we encounter. Regardless of whether we accept the current technology, the present-day TAH has taught us how to select and manage patients with complex cardiac conditions. This knowledge will serve as the foundation for the future management of patients with the TAH and technologies to come. The concept of heart replacement continues to have value in patients with otherwise fatal biventricular failure.

This study has some limitations. Including the significant amount of data available in the INTERMACS database is not possible in a single report. Some areas that need further analysis include transplant survival after TAH bridge, need for heart-kidney transplant, quality of life, and more data regarding modified Rankin Scale scores for those patients



with neurologic events. Further analysis of the INTERMACS database will be performed to address these relevant issues.

## Disclosure statement

F.A.A. and V.K. are consultants and trainers for SynCardia Systems. I.G. and F.E. are principal investigators in SynCardia Systems clinical trials. R.G.S. is a consultant for SynCardia Systems. None of the other authors has a financial relationship with a commercial entity that has an interest in the subject of the presented manuscript or other conflicts of interest to disclose.

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## Appendix A. Supporting information

Supplementary data are available in the online version of this article at [www.jhltonline.org](http://www.jhltonline.org).

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