Results With Syncardia Total Artificial Heart Beyond 1 Year

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Mechanical circulatory support devices have been increasingly used for long-term support. We reviewed outcomes in all patients supported with a SynCardia total artificial heart (TAH) for more than 1 year to assess its safety in long-term support. As of December 2011, all 47 patients who received the TAH from 10 centers worldwide were included in this retrospective study. Clinical data were collected on survival, infections, thromboembolic and hemorrhagic events, device failures, and antithrombotic therapy. The mean age of patients was 50 ± 1.57 years, the median support time was 554 days (range 365–1373 days). The primary diagnosis was dilated cardiomiopathy in 23 patients, ischemic in 15, and "other" in 9. After a minimum of 1 year of support, 34 patients (72%) were successfully transplanted, 12 patients (24%) died while on device support, and 1 patient (2%) is still supported. Five patients (10%) had a device failure reported. Major complications were as follows: systemic infections in 25 patients (53%), driveline infections in 13 patients (27%), thromboembolic events in 9 patients (19%), and hemorrhagic events in 7 patients (14%). SynCardia TAH has proven to be a reliable and effective device in replacing the entire heart. In patients who reached a minimum of 1 year of support, device failure rate is acceptable and only in two cases was the leading cause of death. Infections and hemorrhagic events were the major causes of death. Patients who remain supported beyond 1 year are still likely to survive to transplantation. *ASAIO Journal* 2014; 60:626–634.

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Implanted in patients with biventricular failure, the Syncardia TAH has over time asserted itself as a reliable bridge to transplantation,[1–6] and in 2004, it was approved by the United States Food and Drug Administration (FDA) and by the Centers for Medicare & Medicaid Service in 2008.[7] In recent years, the number of centers worldwide accredited for TAH implantation has increased dramatically with 93 implanting centers between Europe, Australia, and the United States in 2013.[8] An additional 35 centers are in the process of being credentialed.[8]

The approval of a portable external device (Freedom Driver) in March 2010 for the SynCardia TAH now allows patients to be discharged from the hospital.[9] This portability has improved the quality of life for patients with a TAH and opened the possibility for its use as a long-term or permanent implantation device.[9] Although not published, the longest survivor known with a TAH lived 1,374 days (almost 4 years) and subsequently went on to successful heart transplantation. These developments led to the FDA approval of the Syncardia TAH in April 2012 to be used as a destination therapy (DT) for humanitarian use device.[8]

Recently, the short-term quality of life of patients discharged home and supported with a SynCardia have been reported.[9] However, a paucity of published experience on the long-term use of the TAH leaves questions regarding its safety and utility as a DT. In an effort to investigate the use of SynCardia TAH as a long-term support device, we collected the outcomes of all patients supported for more than 1 year worldwide.

Methods

Patient Selection and Inclusion Criteria

All patients who received a SynCardia TAH between 1989 and December 2011 and had the device implanted for more than 1 year were included in the study. After the study period and at time of publication, an additional 29 patients had the SynCardia TAH implanted for more than 1 year (**Figure 1A**). SynCardia Systems Inc. provided the date of birth, date of implant, time of support, and center of implant of patients fitting this criteria. The individual institutions were then contacted to acquire the data. During this time period, a total of 13 centers had at least one patient with a SynCardia TAH implanted for more than 1 year. An online database was prepared to acquire each institutions data. The single centers were responsible to upload the database and verify the accuracy of the data inserted. SynCardia Systems Inc. did not receive access to the database. Patients were excluded if data were not complete or partially available.

Data Collection and Data Analysis

A review of the medical records and computerized hospital data was approved by the Clinical Investigation Committee

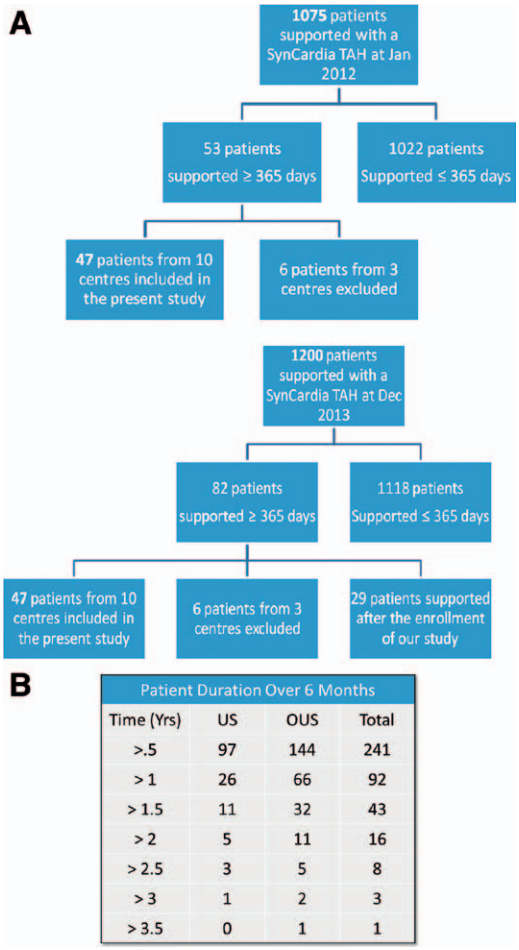

Figure 1. A: At January 2012, when we start the current study, 1,075 patients were supported with a SynCardia TAH and 53 of them were supported for more than 1 year. Six patients from three centers were excluded because lack of information provided. At December 2013, 1,200 patients have been supported with a SynCardia TAH and 82 of them were supported for more than 1 year. Of these 82 patients, 47 underwent transplantation, 15 died, and 20 are supported on the device. **B**: Patient supported with TAH over 6 Months. Data updated April 2014. (Data provided by Syncardia Inc.) US, United States; OUS, Outside United States; Yrs, years. full color online

of the University Hospital of Padua, and the procedures followed were in accordance to the institutional guidelines for retrospective record review and protection of patient confidentiality. Individual consent was not required for this study. Patients were not identified, and the chairperson of the Ethics Committee of each institution consented to send data for publication. The data reviewed were relative to the hospital course and to the follow-up clinical controls of patients supported with a Syncardia TAH for more than 1 year. Variables analyzed included demographics, preoperative clinical data, and postoperative data. Data were collected on survival, thromboembolic (TE) events, hemorrhagic events, device failure, and the antithrombotic therapy regimen. Definitions of these variables were in agreement with the INTERMACS registry.[10]

Because quantitative variables are not normally distributed, comparisons among groups were carried out by the Wilcoxon signed-rank test. The difference between proportions was assessed by Fisher exact test. Data were analyzed with SAS software, release 9.1.3 (SAS Stat 9.1, SAS Institute Inc, Cary, NC), and values of $p < 0.05$ were considered significant.

Results

A total of 1,075 patients received a SynCardia TAH during the study period (**Figure** 1A, B). The majority of these patients had the device implanted for less than 1 year. Fifty-three patients from 13 centers met the study criteria for enrolment. Six patients from three centers were then excluded from the study because of incomplete data. The remaining 47 patients from 10 centers worldwide who received a TAH for more than 1 year between 1989 and 2011 were included in the analysis. This composed of three centers from the United States and seven centers from Europe with each center entering between 1 and 23 patients into the database (median of four patients per center).

Patient Demographics

Patient demographics and preoperative data are stratified by preoperative diagnosis and presented in **Table 1**. There were 41 males (87%). Median age was 49 years (range 19–69 years); median weight was 85 kg (range 62.5–128 kg), median height 180 cm (range 155–202 cm). The median body surface area (BSA) was 2.02 square meters (range 1.64–2.4 square meters) with 11 patients (23%) having a BSA value below 1.8 m^2. Twenty-three (49%) patients had an initial diagnosis of dilated cardiomyopathy, 18 patients (32%) ischemic cardiomyopathy, and 9 patients (19%) were classified as having other causes for heart failure.

Thirty-three of 47 patients (70.2%) were ascribable to an INTERMACS class: 23 patients were in INTERMACS class I (crash and burn), 7 were in class II (sliding on inotropes), and 3 were on class III.

The median support time was 554 days (1.5 years) (range 365–1,374 days) and cumulative support time was 79.8 years.

Differences in the surgical implantation technique adopted in the centers enrolled were not recorded and we assumed

Table 1. Baseline Major Comorbidities by Cause of Heart Failure

	Dilatative N = 23 (49%)	Ischemic N = 15 (32%)	Others N = 9 (19%)	Total N = 47 (100%)
Previous LVAD/IABP, n (%)	8 (34.7%)	8 (53.3%)	6 (66.6%)	22 (46.8%)
Previous IPPV, n (%)	8 (34.7%)	10 (66.6%)	5 (55.5%)	23 (49%)
Previous Cardiac Surgery, n (%)	3 (13%)	12 (80%)	4 (44.4%)	19 (40%)
Previous RRT, n (%)	9 (39%)	4 (26.6%)	5 (55.5%)	18 (38%)

IABP, intraaortic balloon pump; IPPV, intermittent positive pressure ventilation; RRT, renal replacement therapy.

Table 2. Demographics and Events in Died Patients

Died	Cause of Death	Support (days)	BSA	Male	Hemodialysis	TE Events	HE Events	Driveline Infections	MOF	Device Failure
Patient 1	MOF—sepsis	381	1.65	0	1	0	0	0	1	0
Patient 2	ICB—CH	382	1.8	1	1	0	1	0	0	0
Patient 3	MOF—sepsis	422	2.4	1	0	0	0	1	1	0
Patient 4	ICB—CH	428	2	1	0	0	1	1	0	0
Patient 5	MOF—sepsis	466	1.8	0	1	0	1	0	1	0
Patient 6	Mediastinitis	521	2	1	0	1	0	1	0	0
Patient 7	MOF—sepsis	529	2	1	0	0	0	0	1	0
Patient 8	MOF—sepsis	540	1.8	1	0	0	1	1	1	0
Patient 9	AA rupture	543	1.8	1	0	1	0	0	0	0
Patient 10	ICB—CH	603	1.8	0	0	0	1	0	0	0
Patient 11	Device problem	971	1.99	1	1	0	0	0	0	1
Patient 12	Device problem	801	1.79	1	0	0	0	0	0	1
		M: 525	M: 1.79	9/12	4/12	2/12	5/12	4/12	5/12	2/12

AA, aortic aneurysm; BSA, body surface area; CH, cerebral hemorrhage; HE, hemorrhagic; ICB, intracranial bleeding; M, median; MOF, multiorgan failure; SAH, subarachnoid hemorrhage; TE, thromboembolic.

all patients received the TAH according to a standard surgical technique.[11]

Of the 47 patients included in the series, 12 patients (25%) died supported with SynCardia TAH (within a median time of 525 days—range 381–971 days) (**Table 2**), 34 patients (72%) underwent cardiac transplantation, and one patient remain supported with the device.

Of the 34 patients who underwent cardiac transplantation, three patients died at a median time of 145 days (range 50–328 days); graft rejection was the cause of death in all of them.

Mean intensive care unit (ICU) length of stay was 28 days (range 5–467). Delayed sternal closure occurred in 11 patients (23%) with a median time to delayed closure of 4 days (range 1–6 days). A wound infection occurred in two patients. New renal replacement therapy (RRT) was necessary in 12 patients (26%), while an additional 18 (60%) patients who required RRT preoperatively continued to require it postoperatively. Of all 30 patients requiring postoperative RRT, recovery of renal function occurred in 22 (73%), whereas persistent RRT was required in 8 (17%) at 1 year.

Forty patients (85%) were discharged home: 39 received an Excor drive support (available only in Europe), and 11 of them were then switched to a Freedom device. One patient was discharged with Freedom driver as the primary portable driver unit.

Of the seven patients who remained in-hospital, five were from the United States where, at the time of their TAH support, a portable driver was not available yet.

Anticoagulation/Thrombotic Complications and Infections

All patients received warfarin with a target INR range between 2.5 and 3.5. Thromboelastogram (TEG) was available and routinely used to set the antithrombotic therapy in 7 of 10 centers enrolled in the study.

Anticoagulation strategies are shown in **Figure 2**. Forty-two patients (89%) received antiplatelet therapy in addition to warfarin. Thromboembolic events complicated the postoperative course of nine patients (19%) and they occurred after a median time of 500 days from TAH implantation (range 159–815 days). Six patients (12.7 %) experienced a transitory ischemic attack, whereas three patients (6.3 %) suffered a major cerebrovascular accident with hemiparesis or aphasia (**Table 3**).

Hemorrhagic events occurred in seven patients (14%) after a median time of 249 days (range 174–598 days). A cerebral hemorrhage occurred in three patients, a subarachnoid hemorrhage in another two, and other two patients experienced a gastrointestinal tract bleeding (**Table** 3). Thus, eight strokes (three embolic and five hemorrhagic) or 0.083 strokes per patient year were observed.

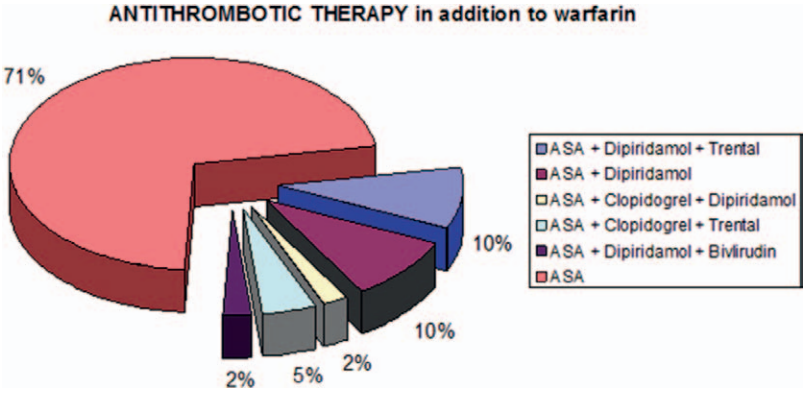

Figure 2. Antithrombotic therapy in addition to warfarin. ASA, aspirin. full color online

Table 3. Hemorrhagic and Thromboembolic Events

	Anticoagulation Therapy	BSA	Day of Support	Neurological Event	Outcome
Patients with thromboembolic events					
Patient 1	W + A + D + P	2.1	629	TIA	Transplanted alive
Patient 2	W + A	1.9	815	TIA	Transplanted alive
Patient 3	W + A	2.1	374	TIA	Transplanted alive
Patient 4	W + A	2	371	CVA hemiparesis	Died
Patient 5	W + A	2.2	629	TIA	Transplanted alive
Patient 6	W + A	1.9	500	TIA	Transplanted alive
Patient 7	W + A	1.8	159	TIA	Died
Patient 8	W + A	2.2	318	CVA hemiparesis	Transplanted alive
Patient 9	W + A	2.08	626	CVA aphasia	Transplanted alive
Patients with hemorrhagic events					
Patient 1	W + A + D + P	1.8	320	ICB - SAH	Transplanted alive
Patient 2	W + A + D	1.8	468	GI bleeding	Died
Patient 3	W + A	1.75	223	GI bleeding	Died
Patient 4	W + A	2	249	ICB—CH	Died
Patient 5	W	1.8	174	ICB—CH	Died
Patient 6	W + A + C + P	1.7	598	ICB—CH	Died
Patient 7	W + A	1.9	208	ICB—SAH	Transplanted alive

Anticoagulation therapy: A, aspirin; BSA, body surface area; C, clopidogrel; CH, cerebral hemorrhage; CVA, cerebrovascular accident; D, dipyridamole; GI, gastrointestinal; ICB, intracranial bleeding; P, pentoxifylline; SAH, subarachnoid hemorrhage; T, trental; TIA, transitory ischemic attack; W, warfarin.

Twenty-six patients (55%) used an antihypertensive treatment during their support, with one (15 patients) or more drugs (11 patients) per day.

Systemic infection requiring intravenous antibiotics occurred in 25 patients (53%). Driveline infections occurred in 13 patients (27%); in 11 patients, the infection was superficial and did not ascend to the mediastinum, in 2 patients, the infection was deep (4%) (mediastinitis) and it was the cause of death for one of them. Five patients died of sepsis with multiorgan failure. This is the most common cause of death in between our cohort of patients.

Device Failures

Five patients (10%) experienced a major device-related technical problem. Two patients died because of a device failure: in both cases, a membrane rupture occurred; one at 801 and the other at 971 days,. The three nonfatal events were 1) an Excor unit patient was observed to have a lower than usual left pump output 400 days after implantation with a right pump output higher than the left and increasing signs of pulmonary congestion. He was urgently admitted to the hospital and switched to a new Excor Unit with complete recovery. He was successfully transplanted 197 days after this event; 2) another patient reported a membrane rupture at 694 days postimplantation. The rupture was identified on a computed tomography scan of the chest and the patient was successfully transplanted; and 3) the last patient reported an air-hole in the driveline: no major changes in the pump output had been recorded, but he was admitted urgently and successfully transplanted 69 days after this event (**Table 4**).

Table 4. Device-Related Problem and Outcome Recorded in our Series

Device Technical Problems	Time of Device Failure (Days After TAH Implant)	Type of Technical	Outcome	Delay Htx—Technical Problem (Days)
Patient 1	971	Membrane rupture	Died	0
Patient 2	801	Membrane rupture	Died	0
Patient 3	694	Membrane rupture	Htx	2
Patient 4	400	Excor unit failure	Htx	197
Patient 5	390	Air-hole in driveline	Htx	69

Htx, heart transplantation.

When we stratified patients by BSA, we found important differences. Patients with a BSA < 1.8m^2 were found to have a increased incidence of death ($p = 0.0045$), hemorrhagic events ($p = 0.009$), and systemic infections ($p = 0.008$) (**Table 5**) (**Figure 3**).

The 47 patients were entered in a Kaplan–Meier survival curve. Kaplan–Meier estimate of the overall survival according to BSA resulted statistically significant ($p = 0.002$). No differences in freedom from device failure, freedom from transplant survival, and freedom from TE events were recorded when patients were tested for BSA < 1.8 m^2 and BSA >1.8 m^2 (**Figures 4–6**).

Table 5. Outcomes

	BSA ≤ 1.8 m^2 (N = 11)	BSA > 1.8 m^2 (N = 36)	*p*
Death on device	7 (63%)	5 (14%)	**0.005**
Hemorrhagic events	5 (45%)	2 (5.5%)	**0.009**
Systemic infections	10 (90%)	15 (41%)	**0.008**
Postoperative complications	10 (90%)	21 (58%)	0.09
Heart transplantation	4 (36%)	28 (77%)	0.03

BSA: body surface area

BSA, body surface area.

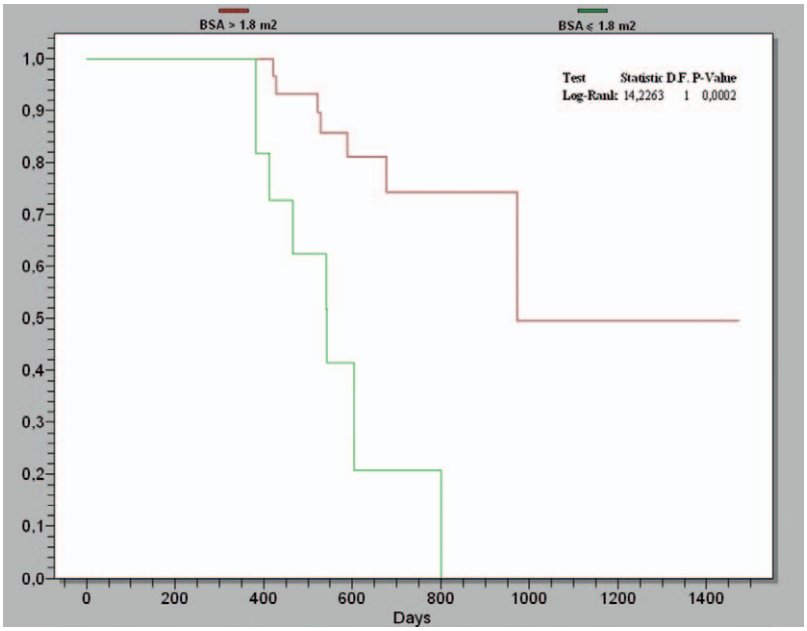

Figure 3. Kaplan–Meier estimate of the overall survival according to BSA (≤1.8 and >1.8 m²). $p = 0.0002$. Green curve: BSA < 1.8 m²; Red curve: BSA > 1.8 m². BSA, body surface area. full color online

Comment

According to the fifth INTERMACS annual report, DT represents an increasing application of continuous flow-left ventricular assist device and currently accounts for nearly one-third of overall mechanical circulatory support (MCS) activity in the United States.[12]

Despite these success in the treatment of left ventricle failure, refractory biventricular failure remains a major clinical and surgical challenge especially in long-term support.[13]

In the fourth INTERMACS report, survival at 3 and 6 months of patients with biventricular dysfunction supported with a TAH appeared to be higher than for patients supported with a BiVAD.[14] Despite this statistics, there is a paucity of data available on the outcomes of long-term support with a TAH.

We collected the entire international experience of patients assisted with a Syncardia TAH for more than 1 year to investigate the long-term application of this device.

In long-term support, the use of TAH was safe with only two deaths (4%) occurring secondary to device failure and over

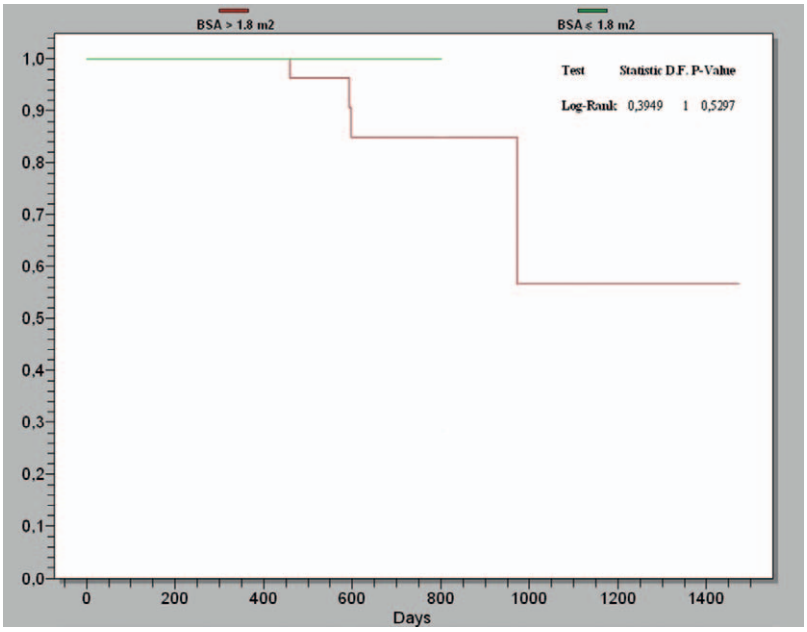

Figure 4. Kaplan–Meier estimate of the freedom from device failure according to BSA (≤1.8 and >1.8 m²). $p = 0.5297$. Green curve: BSA < 1.8 m²; Red curve: BSA > 1.8 m². BSA, body surface area. full color online

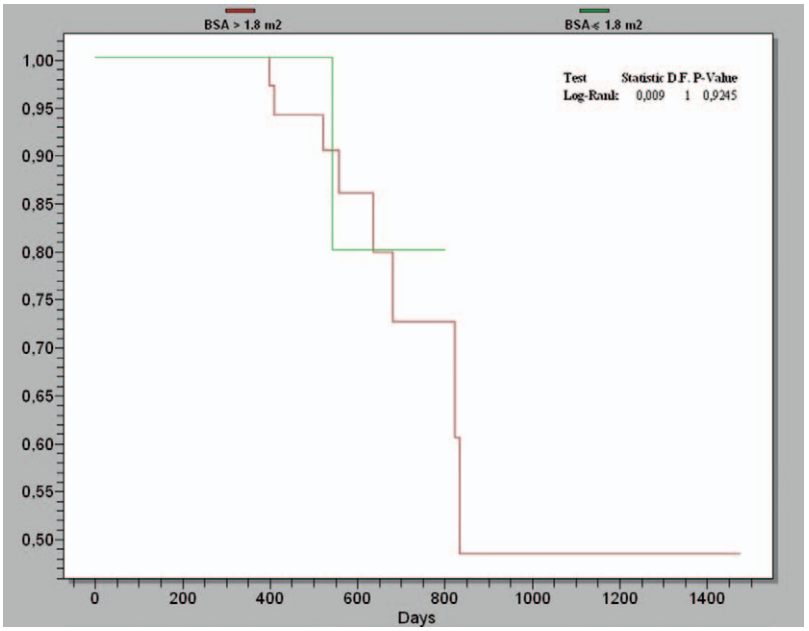

Figure 5. Kaplan–Meier estimate of the freedom thrombembolic events according to BSA (≤1.8 and > 1.8 m²). p = 0.9245. Green curve: BSA < 1.8 m²; Red curve: BSA > 1.8 m². BSA, body surface area. full color online

70% of patients being successfully transplanted with a median time of TAH support of 554 days (1.5 years).

Infections and hemorrhagic events were the leading cause of death in this series.

Role of Body Surface Area

One striking observation of this series is the role of BSA as a risk factor for death, infections, and hemorrhagic events. BSA is undoubtedly a marker for "fit complications" that have been noted since the introduction of the Jarvik-7 (100 ml) in the 1980s.[13] In fact, the United States FDA clinical protocol stipulates patients with a BSA of less than 1.7 m² should be excluded from receiving the Syncardia.[15]

The preliminary experience at LaPitiè-Salpetriere Hospital during the 1980s reported that a BSA < 1.7 was an independent risk factor for death with a TAH.[16] Clinically, the BSA is rarely used as a selection criterion in the algorithm for device selection. Instead, the SynCardia TAH is implanted as long as the patient is in INTERMACS class I or II and the anterior–posterior diameter of the mediastinum (by chest computed tomography) is least 10 cm to accommodate the device. The same French group reported

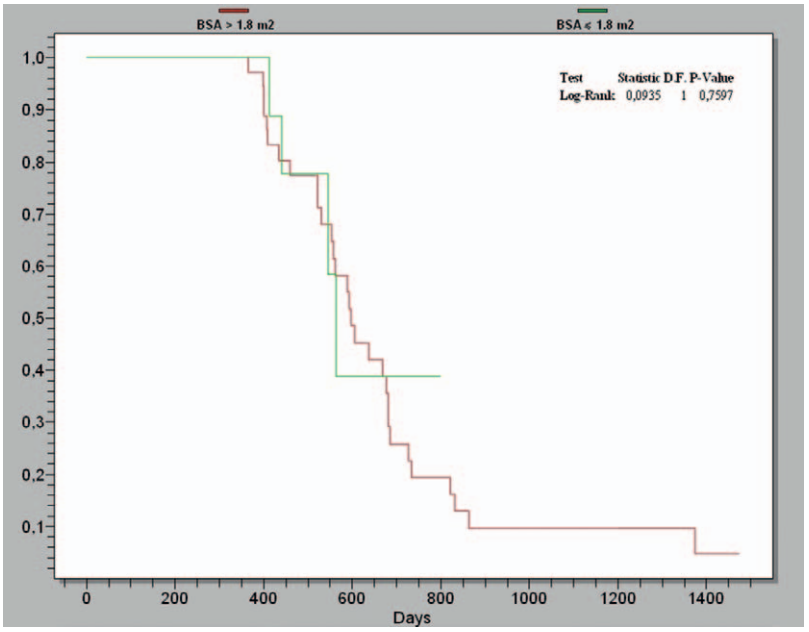

Figure 6. Kaplan–Meier estimate of the freedom transplantation according to BSA (≤1.8 and > 1.8 m²). p = 0.7597. Green curve: BSA < 1.8 m²; Red curve: BSA > 1.8 m². BSA, body surface area. full color online

Table 6. Membrane Rupture Published in the International Available Literature

Membrane Rupture International Literature Watch	Time of Membrane Rupture (Days After TAH Implant)	Year Published	Outcome
Arizona Group (USA)	123	Ann Thorac Surg 1999	Died
La Pitie Group (F)	2	J Heart Lung Transplant 2003	Re TAH Implantation
Bad Oeynhausen (G)	180	Ann Thorac Surg 2005	Transplanted
Current Study	971	2014	Died
Current Study	801	2014	Died
Current Study	694	2014	Transplanted

Htx, heart transplantation.

in their most recent series a survival rate that reached 75% in patients with a BSA < 1.7m^2. This result was achieved with short-term support with a median implantation time of 40 ± 50 days[17] and is because of more accurate surgical techniques used to implant the CardioWest TAH inside small chests.[10,17]

Our data show patients with a BSA < 1.8m^2 have an increased risk of death with long-term support (p = 0.0045). Indeed a benchmark of 1.8 m^2 or less is a risk factor for hemorrhagic (p = 0.009) and infection complications (p = 0.008), both representing 75% of the causes of death in our cohort. The increased incidence of intracranial hemorrhagic complications in these patients may be caused by the stroke volume mismatch and high blood pressure secondary to high cardiac output generated by the TAH.

The association of infection with the smaller BSA patients in our series is unclear. The majority of infections had a pulmonary source. Placing the TAH in a small chest could lead surgeons to laterally displace one of the artificial left ventricle into the left chest cavity[17] compromising normal lung physiology leading to a higher risk of pulmonary atelectasis and pneumonia. However, infections still represent a major cause of morbidity in all MCS patients. All of these devices have external drivelines, increasing the risk of ascending infection in the chest cavity.

A totally internally implantable MCS is in the process of being developed and would likely significantly decrease device-related infections.

Device Malfunction

To evaluate the use of TAH as a long-term strategy, an analysis of its safety is crucial. We recorded a total of five episodes (10%) of device malfunction and for two patients, it was the leading cause of death (**Table** 4). Including these three patients, six overall episodes of membrane rupture have been reported[5,18] (**Table 6**). It is difficult to assess the true incidence of this complication considering the only current data available about the safety of the internal membrane of TAH is provided by the Syncardia itself. Nevertheless, device malfunctions are generally referred to as a rare complication with the TAH, especially when used for short- to mid-term length support.[19–21] Interestingly, a recent study that included home discharged SynCardia TAH recipients recorded a 21% rate of device malfunction with no device dysfunction-related deaths.[9] In this subset of patients discharged home, an air leak in the pneumatic driveline was described. In our series, we also recorded an air leak from the driveline in a patient discharged home. After sealing the leak, this patient survived uneventfully for 69 days until he was transplanted. As patients regain mobility, thanks to the portable driver, the possibility for air leaks on the pneumatic pipeline has to be more closely monitored. This complication seems to be safely manageable by sealing the air leak while awaiting for a high priority organ allocation.[9]

Outcome and Heart Transplantation

Even after 1 year of support, the vast majority (72%) of patients with a TAH included in our series underwent successful cardiac transplantation within a median support time of 563 days. Despite the long-term presence of the TAH, no intraoperative mortality is reported at the time of the cardiac transplantation when the device is removed from the chest.

The outcome of heart transplantation in patients supported for long term with a TAH should be discussed cautiously using our data: a selection bias is present in our cohort because of the exclusion of all the patients supported for less than 1 year. Despite this, according to our results, patients who survive with a TAH for greater than a year still have a high rate of successful heart transplantation. Nevertheless in the experience of Copeland et al,[7] with 100 TAH implants (mean support time 87 ± 94.8 days), 70% of deaths occurred in the first 14 days and 90% occurred within the first 40 days after implantation, underlining a substantial stabilization of patient death events over time. These data are confirmed also in the most recent experience in France where the actuarial estimates of survival under TAH support is constant between 120 and 360 days.[22]

If the patient survives the initial surgery and complications of multiorgan failure experienced at the time of TAH placement, focusing on avoiding subsequent infections seems to play a major role in the survival of these patients. Six of 12 deaths in our cohort are ascribable to multiorgan failure secondary to an infectious origin. A bulky device with external connections tunnelized under the skin is more prone to develop in long-term potential lethal infections. Nevertheless, in patients supported with TAH death generally arrive after a long-term period of ICU where the hemodynamic conditions are guaranteed by the mechanical device and infections superimposed a clinical scenario of multiorgan failure. These data highlight the need for maintaining an extremely high index of suspicion for infection in patients supported long term with a SynCardia TAH.

Hemorrhagic and Thromboembolic Events

In our study, we recorded an incidence of 0.083 TE events per patient month comparable with the previous international experience achieved within 1 year of support (**Table 7**). Interestingly, this data show that long-term TAH support does not increase the risk of TE events. Moreover, a variety of anticoagulation protocols and monitoring were used in the centers enrolled in our study; however, these differences did not impact the rate of TE events. Even the recent experience at La

Table 7. Outcomes and Thromboembolic Events/Patients/Month Comparison Between Different Studies on Syncardia TAH

	Year	Patients	Mean Support Time (Days)	Percentage of Patients Transplanted	Thromboembolic Events/Patients/Month
Arizona group	1999	24	32	79%	0.03
La Pitie group	2003	127	60	74%	0.016
PMA NEJM	2004	81	80	79%	0.03
Bad Oynhausen group	2005	42	51	48%	0.04
Nantes group	2009	42	101	71,5%	0,03
La Pitie group	2013	90	84	61%	0,03
Arizona group	2013	99	87	69%	0,06
Current study	2013	47	554	72%	0.08

Pitie-Salpetriere Hospital in Paris illustrates that a simplification of the anticoagulation protocol of Szefner did not result in an increase in neurologic complications or thrombotic events.[22,23] Furthermore, the recent report from GRAM (Groupe de Relexion sur l'Assistance Mecanique) registry showed that Syncardia recipients experienced significantly fewer neurologic events compared with BiVAD recipients. There are likely elements to the design of this device, which may be responsible for reduced TE events.[24] Moreover, TE events had a more favorable clinical course (only 1/9 deaths) compared with hemorrhagic episodes (5/7 deaths). This data should be considered when addressing the anticoagulation strategy for patients supported with a TAH.

Study Limitations

Our cohort of patients represent only the 4% of the entire populations of patients supported with a Syncardia TAH. Up to now, this device is more extensively used as BTT in short-term support (<6 months) (**Figure 1B**). One of the major limitations of our study is the exclusion of the patients supported for less than 1 year by selection criteria. This choice was made to focus the attention on the outcomes of the few patients with long-term survival using a SynCardia TAH. Patient included in this study received a TAH within a broad time period (1988–2012) with different expertise and technologies available in the respective eras. Furthermore, the reason why these patients were supported for more than 1 year was not always specified by the included centers. It is likely that complications experienced while under the use of TAH caused prolonged support times and represent a selection bias of our population.

The current iteration of the TAH is far from ideal given the large size, external drivelines tunneled under the skin, the weight of the back pack, the high incidence of infections, and the noise associated with the device (75 dB)—all which impact the quality of life of patients. However, the SynCardia TAH has emerged as a robust form of mechanical circulatory support for patients with biventricular failure. This study illustrates that support using the Syncardia TAH beyond 1 year has acceptable outcomes, but further improvements in the device, patient selection, and long-term patient management need to be achieved to further reduce the major complications of infection, TE, and hemorrhagic events.

The future promises of new technologies will potentially overcome the current drawbacks and limitations and hence improve the quality of life and survival in patients.

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References

1. Slepian MJ, Smith RG, Copeland JG: The Syncardia CardioWest total artificial heart in Baughman K, Baumgartner WA (eds), Treatment of Advanced Heart Disease, Chapter 26. New York, Taylor and Francis, 2006, pp. 473–490.
2. Copeland JG, Smith RG, Cleavinger MR: Development and current status of the CardioWest C-70 (Jarvik-7) total artificial heart in Lewis T, Graham TR (eds), Mechanical Circulatory Support. Great Britain, Edward Arnold, 1995, pp. 186–198.
3. DeVries WC, Anderson JL, Joyce LD, *et al*: Clinical use of the total artificial heart. *N Engl J Med* 310: 273–278, 1984.
4. Leprince P, Bonnet N, Rama A, *et al*: Bridge to transplantation with the Jarvik-7 (CardioWest) total artificial heart: A single-center 15-year experience. *J Heart Lung Transplant* 22: 1296–1303, 2003.
5. El-Banayosy A, Arusoglu L, Morshuis M, *et al*: CardioWest total artificial heart: Bad Oeynhausen experience. *Ann Thorac Surg* 80: 548–552, 2005.
6. Copeland JG, Smith RG, Arabia FA, *et al*: Cardiac replacement with a total artificial heart as a bridge to transplantation. *N Engl J Med* 2004;351: 859–867, 2004.
7. Copeland JG, Copeland H, Gustafson M, *et al*: Experience with more than 100 total artificial heart implants. *J Thorac Cardiovasc Surg* 143: 727–734, 2012.
8. Data obtained from SynCardia Inc. Available at: www.syncardia.com. Accessed June 15, 2014.
9. Demondion P, Fournel L, Niculescu M, Pavie A, Leprince P: The challenge of home discharge with a total artificial heart: the La Pitie' Salpetriere experience. *Eur J Cardiothorac Surg* 44: 843–848, 2013.
10. Dowling RD, Gray LA Jr, Etoch SW, *et al*: Initial experience with the AbioCor implantable replacement heart system. *J Thorac Cardiovasc Surg* 127: 131–141, 2004.
11. Arabia FA, Copeland JG, Pavie A, Smith RG: Implantation technique for the CardioWest total artificial heart. *Ann Thorac Surg* 68: 698–704, 1999.
12. Kirklin JK, Naftel DC, Kormos RL, *et al*. Fifth INTERMACS annual report: Risk factor analysis from more than 6,000 mechanical circulatory support patients. *J Heart Lung Transplant* 32: 141–156, 2013.
13. Kirklin JK, Naftel DC, Pagani FD, *et al*: Long-term mechanical circulatory support (destination therapy): on track to compete with heart transplantation? *J Thorac Cardiovasc Surg* 144: 584–603, 2012.
14. Kirklin JK, Naftel DC, Kormos RL, *et al*: The Fourth INTERMACS Annual Report: 4,000 implants and counting. *J Heart Lung Transplant* ;31: 117–126, 2012.
15. Slepian MJ: The SynCardia temporary total artificial heart—evolving clinical role and future status. *US Cardiol* 8: 39–46, 2011.
16. Kawaguchi AT, Gandjbakhch I, Pavie A, *et al*: Factors affecting servival in total artificial heart recipients before transplantation. *Circulation* 82: IV322–327, 1990.
17. Leprince P, Bonnet N, Varnous S, *et al*: Patients with a body surface area less than 1.7m^2 have a good outcome with the CardioWest total artificial heart. *J Heart Lung Transplant* 24: 1501–1505, 2005.
18. Copeland JG, Francisco AA, Smith RG, Sethi GK, Nolan PE, Branchy ME: Arizona experience with CardioWest total artificial heart bridge to transplantation. *Ann Thorac Surg* 68: 756–760, 1999.

19. Leprince P, Rahmati M, Bonnet N, *et al*: Expanded polytetrafluoroethylene membranes to wrap surfaces of circulatory support devices in patients undergoing bridge to heart transplantation. *Eur J Cardiothorac Surg* 19: 302–306, 2001.
20. Copeland JG, Copeland H, Gustafson M, *et al*: Experience with more than 100 total artificial heart implants. *J Thorac Cardiovasc Surg* 143: 727–734, 2012.
21. Roussel JC, Sènage T, Baron O, *et al*: CardioWest (Jarvik) Total artificial heart: A single-center experience with 42 patient. *Ann Thorac Surg* 87: 124–130, 2009.
22. Kirsh M, Nguyen A, Mastroianni C, *et al*: SynCardia temporary total artificial heart as bridge to transplantation: Current results at L Pitiè Hospital. *Ann Thorac Surg* 95: 1640–1646, 2013XXX.
23. Copeland JG, Copeland H, Nolan P, Gustafson M, Slepian M, Smith R: Result with an anticoagulation protocol in 99 SynCardia total artificial heart recipients. *ASAIO J* 59: 216–220, 2013.
24. Kirsch M, Mazzucotelli JP, Roussel JC, *et al*: Survival after biventricular mechanical circulatory support: Does the type of devices matter? *J Heart Lung Transplant* 31: 501–508, 2012.