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SynCardia total artificial heart as a bridge to transplant: Current results at the National Institute of Cardiovascular Diseases in Slovakia

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Abstract. In this case series we present our initial experience with the implantation of the SynCardia total artificial heart (TAH) in three patients, the first of which was the first SynCardia TAH implantation in the Visegrad Four (V4) countries. The first and the third patients, after 195 and 126 days of TAH support respectively, experienced successful heart transplants, while the second patient on postoperative day 11 died due to a ruptured undiagnosed brain aneurysm. Our results show that the SynCardia TAH is an alternative therapy in patients with severe end-stage biventricular heart failure waiting for heart transplantation. It is an intermediate step until the development of genetically modified animal hearts, engineered bioartificial hearts or hearts from induced pluripotent stem cells could replace the failing heart in patients with end-stage heart disease. Tab. 2, Fig. 1, Ref. 27, on-line full text (Free, PDF) www.cardiologyletters.sks.sk

Key words: biventricular heart failure – total artificial heart – Syncardia TAH – biventricular assist device – heart transplantation

End-stage heart failure is a public health problem affecting an increasing number of patients each year. A variety of options exist for its treatment, but heart transplantation remains the gold standard (1). The lack of donors is now leading to increased use of ventricular assist devices (VAD) as a bridge to transplant (BTT) or as a destination therapy (2). Among patients with advanced heart failure, those with biventricular failure have the worst prognosis and very few available options while awaiting transplantation (1). Implantation of a total artificial heart (TAH) is an alternative to durable biventricular VAD support in the adult, as well as in the pediatric, population (3-5).

The number of heart transplants in Slovakia is 15-20 per year in a population of 5,5 million people and the median time on the waiting list is 13 months. Up to the end of 2017 there were 51 patients on the waiting list and 60% of them were on LVAD support, and during the last few years 5 patients with biventricular failure on paracorporeal BiVAD underwent successful heart transplants. The TAH enables these patients with biventricular failure to be discharged from the hospital while awaiting heart transplant. Alternative strategy for these patients is the use of durable biventricular VAD support.

In our institute the preferred strategy is the TAH support, and in this report we present our initial experience with the implantation of the SynCardia TAH in three patients awaiting heart transplantation with critical biventricular failure. The first patient underwent the first SynCardia (TAH) implantation in the Visegrad Four (V4) countries.

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Patients and methods

From January 2017 up to now 27 durable circulatory assist devices have been implanted in our institution. Biventricular assist devices were required in three patients, all of whom received the SynCardia TAH as a bridge to transplant. The decision to implant a TAH over LVAD was made owing to the presence of conditions most often associated with multiorgan failure, severe preoperative right ventricular dysfunction, and high pulmonary vascular resistance in one patient. Preoperative hemodynamic parameters including right heart catheterization have been recorded during evaluation for heart transplant eligibility. Before BiVAD implantation we emphasize right ventricular assessment. A BiVAD is indicated when the majority of the following echocardiographic parameters are present: functional area change (FAC)<20%, tricuspid annular plane systolic excursion (TAPSE)<8mm, S/L axis <0.6, R/L in 4D<0.72, right ventricular absolute peak longitudinal strain<9.6% and severe tricuspid regurgitation. Patients with a functional New York Heart Association (NYHA) class IV and body surface area (BSA) equal to or greater than 1.7 m^2 or with an antero-posterior diameter greater than 10 cm (measured at T10 from the sternum to the anterior border of the vertebral body on chest computed tomography (CT) were eligible for TAH implantation.

The patients' demographics and clinical characteristics and causes of heart failure are shown in **Table 1.**

Table 1 Preoperative patients' characteristics

Variable	Patient 1	Patient 2	Patient 3
Demographics			
Age	47	60	62
Sex	male	male	male
BSA, m^2	1.94	2.33	2.14
BMI, kg/m^2	25.18	29.09	27.32
Etiology	No-virus negative myocarditis	Dilated cardiomyopathy	Ischemic cardiomyopathy
Prior cardiac surgery	no	no	yes, CABG 22 years ago
Preoperative hemodynamics			
Systolic arterial pressure, mmHg	96	93	91
MBP, mmHg	87	77	75
central venous pressure,mmHg	24	19	15
Systolic PAP, mmHg	34	46	64
PCWP, mmHg	31	29	27
PVR,Wood units	1.5	3	5.3
TPG, mmHg	4	10	18
CI, $l/m^2/min$	1.13	1.5	1.6
LVEF, %	10	20	20
NYHA class	IV	IV	IV
INTERMACS status	1	2	2
RVFAC, %	25	18	25
TAPSE, mm	10	10	8
Preoperative laboratory data			
Sodium.mmol/l	130	139	144
Creatinine, µmol/l	112	116	108
Urea,mmol/l	8.9	13.3	12.9
total bilirubin, , µmol/l	37	43.1	27.4
AST, µKat/l	0.86	0.34	0.55
ALT, µKat/l	0.97	0.38	0.45
Hemoblobin, g/l	150	138	155
NTpro BNP, ng/l	13301	7639	2454
Preoperative circulatory support			
ECMO	yes	no	no
Duration of ECMO support, days	4	0	0

BSA – body surface area, BMI – body mass index, MBP – mean blood pressure, CABG – coronary artery bypass grafting, PAP – pulmonary artery pressure, PCWP – pulmonary artery capillary wedge pressure, PVR – pulmonary vascular resistance, TPG – transpulmonary gradient, LVEF – left ventricular ejection fraction, NYHA – New York Heart Association, INTERMACS – Interagency Registry for Mechanically Assisted Circulatory Support, RVFAC – right ventricle functional area change, TAPSE – tricuspid annular plane systolic excursion, AST – aspartate aminotransferase, ALT – alanine aminotransferase, NTproBNP – N-terminal pro brain natriuretic peptide, ECMO – extracorporeal membrane oxygenation

SynCardia TAH is a pneumatically driven TAH that replaces the failing native ventricles. The prosthetic ventricles are made of polyurethane and are attached to the left and right atria. Four monodisk mechanical prostheses (Medronic-Hall, Medronic Inc) provide unidirectional blood flow. Each ventricle has a volume of 70 ml and comprises a silicone diaphragm separating blood from the pneumatic chamber. The pulsed injection of compressed air allows the movement of the diaphragm, thus filling and evacuating both ventricles, which are connected to an external console via 2 drivelines (**Figure 1**). The advent of mobile (Companion II) and portable (Excor TAH-t and Freedom) drivers has allowed out-of-hospital care for SynCardia TAH recipients (6).

The surgical implantation technique has been described previously (7, 8). Briefly, the native ventricles were excised at the level of the atrioventricular valves, the atrial connectors were placed in the right and left atrial cuffs, the anastonosis of both the great arteries was performed and the ventricles of the total artificial heart were implanted. The Dacron aortic and pulmonary grafts are sealed with Coseal (Baxter Healthcare SA, Zurich, Switzerland) surgical sealant.

Postoperatively the patients were anticoagulated systematically with acetylsalicylic acid 100 mg daily and warfarin with target INR 2-3.5.

Clinical and laboratory data were collected from our transplantation and heart failure database. We obtained informed consent from each patient and approval from the institutional review board in order to present these patients.

Results

Patients status before implantation

One patient was presented with acute heart decompensation with critical end stage biventricular failure. For circulatory stabilization a peripheral veno-arterial extracorporeal membrane oxygenator (VA-ECMO) was implanted with left ventricular apical venting. Four days later the VA-ECMO was explanted and the SynCardia TAH was implanted as a BTT strategy. All three patients had chronic hepatic and renal failure with elevated levels of aspartate and alkaline aminotransferases, total bilirubin and creatinine. Patients were on INTERMACS status1 or 2 and NYHA class IV.

Operative characteristics

Duration of the aortic clamp and cardiopulmonary bypass for the three patients were 105 and 130, 106 min and 117 and 124, 155 min respectively. For further heart transplant the pericardium was fully reconstructed with a polytetrafluoroethylene membrane (PTFE) in order to simplify the re-entry for transplantation. Two of the patients left the operating room with open chest, which was closed the next day as

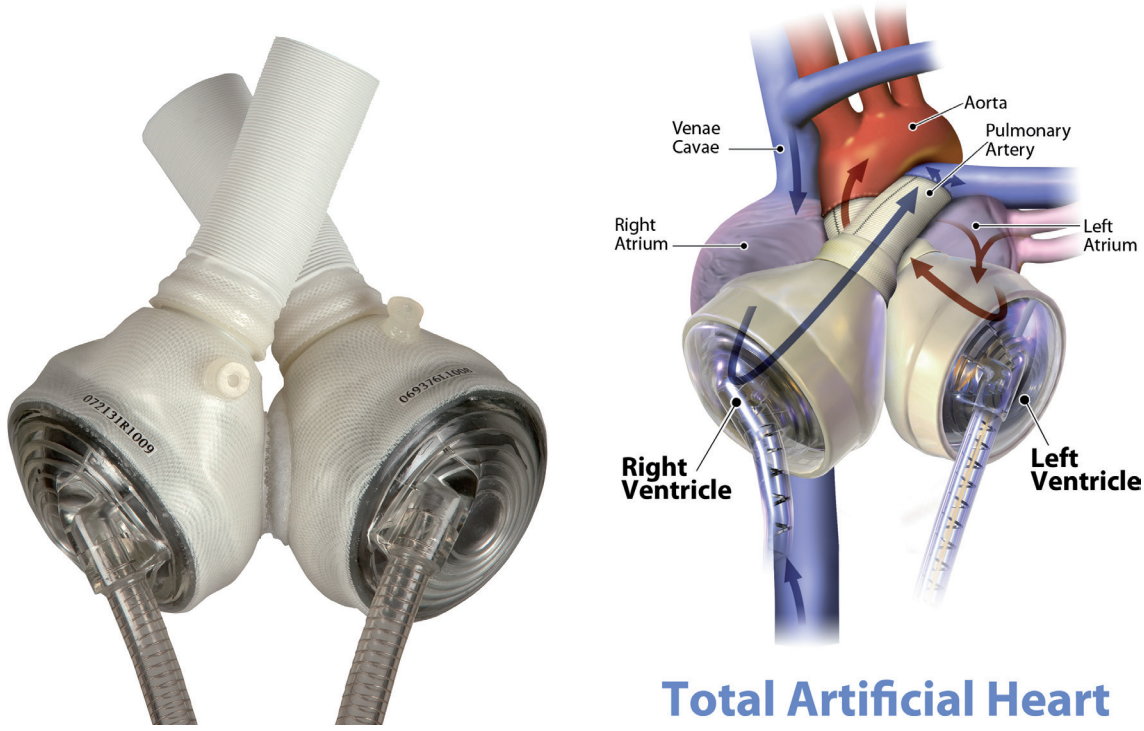

Figure 1 Image and illustration of the SynCardia total artificial heart (Courtesy of syncardia.com)

a preventative measure in the event of severe postoperative bleeding that would need surgical re-exploration.

Outcomes and complications while on support

The first and the third patient were successfully transplanted, the second patient died while on support after 7 day. On the postoperative day 67 and 31 (POD), with stable clinical condition and normal device function, the first and the third patient were discharged with the Freedom driver. The cause of death of the second patient was brain bleeding due to a ruptured undiagnosed brain aneurysm, found later in the postmortem examination.

Postoperative complications are listed in **Table 2**. Two patients suffered either ischemic stroke presented as expressive aphasia or hemorrhagic stroke. Also, one patient had acute renal failure that required dialysis and two patients had systemic infections. No patient experienced severe postoperative bleeding or gastrointestinal complications, neither was any device failure observed. One patient later in the follow-up had a sternal wound infection. The length of stay in the intensive care unit was 14, 7 and 11 days respectively. All three patients between POD 2 and 4 were weaned from mechanical ventilator support.

In one patient during the Freedom driver period, one malfunction of the driver appeared due to mechanical damage of the system controller. Cessation of the pump function was managed successfully by controller change.

Table 2 Outcomes of total artificial heart support

Variable	Patient 1	Patient 2	Patient 3
Duration of support, days	195	7	126
Outcome			
Ongoing	no	no	no
Died on support	no	yes	no
Transplanted	yes	no	yes
Neurologic events			
TIA, < 24h	no	no	no
Stroke	yes	yes	no
Cerebral bleeding	no	yes, rupture of undiagnosed brain aneurysm	no
Ischemic stroke	yes	no	no
Bleeding requiring reoperation	no	no	no
Infection	yes	no	yes
Gastrointestinal complications	no	no	no
Acute renal failure requiring dialysis	no	yes	no
Device failure	no	no	no
Sternal wound infection	no	no	yes

TIA – transitory ischemic attack

Outcomes after transplantation

Two patients were successfully bridged to transplant after 195 and 126 days of TAH support respectively. Before, they were discharged on POD 67 and 31 respectively with a portable console (Freedom driver). In the first patient the postoperative course was complicated by a primary graft dysfunction that was treated with a temporary right ventricular assist device (RVAD) and few surgical re-explorations due to severe postoperative bleeding. On POD 42 he was discharged home and nine months after the heart transplant he is in good condition. In the second patient, the postoperative course was complicated by right ventricular dysfunction that was managed conservatively and by postoperative bleeding that required surgical re-exploration. Also, on POD 41, he was discharged home in stable condition.

Discussion

In the present study we have reviewed our recent experience with patients undergoing mechanical bridge to transplant using the SynCardia TAH. Our results showed that this device provides acceptable survival rates to transplantation. Clinical investigations showed that the INTERMACS profile has an impact on survival, where INTERMACS profile 1 had reduced survival to transplantation compared with less sick profiles (9).

Patients with concurrent right ventricular failure in addition to left ventricular failure have poorer outcomes with left ventricular assist devices (LVAD) than patients with isolated left ventricular failure (10). In these patients biventricular support is indicated. While the TAH provides definite biventricular support, paracorporeal biventricular VAD (BiVAD) provides an alternative strategy and this includes temporary and durable RVAD. Initial biventricular mechanical support for critically ill patients usually provides higher cardiac output which can help resuscitate end organ malperfusion (10). Among the various devices available to support patients with biventricular failure, the SynCardia TAH is used less frequently than paracorporeal BiVADs according to the latest INTERMACS Registry (2). Our group uses preferentially the SynCardia TAH in this indication while other devices are employed only if myocardial recovery is expected or in case of a contraindication to the TAH. Other indications for which we consider the use of SynCardia TAH are in patients with malignant uncontrolled ventricular tachyarrhythmias, patients with complex congenital heart diseases and those with ventricular morphology unsuitable for LVAD implantation.

Moreover, our BTT preferred strategy with the use of the SynCardia TAH is based on the following reasons i) in the Slovakian health system, the use of the SynCardia TAH is a cheaper alternative than the use of durable LVAD and RVAD devices ii) the use of durable LVAD and RVAD devices requires its optimal synchronization, where to the contrary the use of the SynCardia TAH does not need such synchronization

iii) the SynCardia TAH provides a pulsatile flow which is more physiologic in contrast to the continuous flow that is provided by the current durable LVAD and RVAD devices iv) there is no need for extra anticoagulation management since it is the same as with the current LVAD and RVAD devices v) LVAD-related complications like right heart failure, aortic valve insufficiency, mitral and tricuspid valve regurgitation and arrhythmias (atrial fibrillation, ventricular tachycardia/fibrillation) are eliminated with TAH and finally vi) in the near future, the new SynCardia TAH devices would be less noisy which would mean an important improvement in the patients' quality of life.

While no head-to-head prospective randomized controlled trials have compared these two types of mechanical circulatory support, one small retrospective study showed no difference in mortality for patients implanted with a TAH compared with BiVAD (11). Conversely, analysis of the latest INTERMACS registry has suggested improved survival of patients implanted with a TAH compared to BiVADs by 9% (2).

Non-randomized studies showed that survival as BTT and after heart transplant is similar between TAH and BiVAD support (12). In our study two patients underwent successful heart transplant after 195 and 126 days of TAH support respectively, and at the latest follow-up both patients are in good condition.

Larger studies (3,13,14) showed that SynCardia TAH is an alternative therapy with low incidence of neurologic events in extremely complex patients awaiting transplantation. Nevertheless, our observed stroke incidence in this limited series was higher than that observed with current generation continuous flow LVADs (12,15). Furthermore, a report from the GRAM registry showed that SynCardia TAH recipients had significantly fewer neurologic events than BiVAD recipients (11). Further reduction of stroke can be expected with TAH devices using bioprosthetic heart valves for unidirectional blood flow (16) but with the expense of probable limited durability due to high levels of mechanical stress in assist devices that might accelerate structural changes of the bioprosthetic heart valves.

One patient had renal failure that needed postoperative replacement therapy, and two patients had systemic infection. These results are comparable to those reported around the world (12). Comparative studies showed that the renal failure rate was significantly higher in the TAH support group than the BiVAD support group after implantation (12). On the other hand, the infection rate after implantation was significantly lower in the TAH group than the BiVAD group (12). Most commonly infections in the TAH group were respiratory and genitourinary. Two of our patients experienced systemic infections.

In our study, no patients experienced severe bleeding events or device malfunction. Bleeding events were reported to be between 43% and 62% in the TAH group patients (12). Previous studies also showed that the surgical revision for bleeding or hematoma was significantly lower in the TAH group than the BiVAD group (23% Vs 42%). Of these events, 50% occurred during TAH implantation and were mainly tamponade or mediastinal bleeding within 21 days.

In our study in accordance with other published series (17), the two patients that underwent successful heart transplant after the TAH implantation had an improvement in pulmonary artery pressures, trans-pulmonary gradient and pulmonary vascular resistance during the TAH support. It seems reasonable that patients who receive a TAH implant amid elevated pulmonary artery pressures should benefit from direct monitoring, and a novel method with the CardioMEMS Heart Failure system (St. Jude Medical, Little Canada, MN) had been successfully used (18).

Finally, device malfunction is reported to be in non-randomized studies between 10% and 25% of the patients in the TAH group (11). In our cases, only one mechanical malfunction of the Freedom driver system controller due to mechanical damage appeared in one patient, which was managed successfully by controller change. Mechanical damage of the system controller of the Freedom driver has not yet been reported. In 2015 the Federal Drug Agency issued a Class I recall of a select number of the SynCardia systems total artificial heart Freedom driver. A specific part of the Freedom driver mechanism could fail causing driver failure without any advanced warning.

Common problems in the long-term management in both surviving patients were anemia of unknown origin and a need of high doses of diuretics for edemas and adequate diuresis. Mankad et al. (19), also reported that patients implanted with a TAH had laboratory evidence of hemolysis and persistent anemia that resolved only after heart transplant. Similar evidence of laboratory hemolysis our patients also had. The association of hemolysis, ineffective erythropoesis, and inflammation with the TAH warrants further studies. In TAH implantation, resection of the native ventricles results in a rapid decrease of endogenous brain natriuretic peptides (BNP) and this may induce a decline in renal function as in our cases, where in the long-term management high doses of diuretics were needed (20).

Conclusion

Based on our limited experience, the SynCardia TAH is an alternative therapy in patients with end-stage biventricular heart failue awaiting heart transplant. Whether TAH technology advances to the point where it becomes a viable alternative to transplantation remains to be seen. There are several challenges to overcome. Achieving adequate durability (>5 years), minimizing thromboemboli and hemolysis, better efficiency, maintaining pulmonary-systemic circulatory

balance and reduced size to accommodate women and small adolescents and children are examples (21). Greater autonomous balance between pulmonary and systemic flow intrinsic to rotary pumps might lead to rotary TAHs succeeding where previous attempts have failed (22-26). Finally, the next future step is the development of bioartificial engineered hearts, although a number of technological barriers remain before a bioartificial heart can move toward preclinical testing, and eventually to clinical application (27).

Learning points

The SynCardia total artificial heart as a bridge to transplant is a viable alternative method in patients with severe biventricular heart failure.

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