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CLINICAL STUDY

Successful support of biventricular heart failure in an adult patient by the Berlin Heart EXCOR system as a bridge to transplant: literature review

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ABSTRACT
Right heart failure is a huge challenge in left ventricular assist device therapy and its occurrence is associated with increased mortality and morbidity. Other options include the use od temporary right ventricular assist device, use of two continous flow biventricular assist devices, use of total artificial heart and the use of paracorporeal biventricular assist devices.
In this report we described the successful use of the paracorporeal pulsatile Berlin Heart EXCOR system as a bridge to transplant in a 62 years old patient with end-stage biventricular heart failure *(Tab. 1, Fig. 3, Ref. 22)*.
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KEY WORDS: biventricular heart failure, mechanical circulatory support, biventricular assist device, Berlin Heart EXCOR system, heart transplantation.

Introduction

Mechanical circulatory support (MCS) is an established therapy for advanced heart failure. Patients can be bridged to heart transplantation with an acceptable quality of life by the use of continuous-flow pumps as durable left ventricular assist devices (LVAD) (1). However, in a subgroup of patients with advanced biventricular heart failure, LVAD implantation alone or LVAD implantation in combination with temporary right ventricular assist device (RVAD) does not lead to favorable outcomes (2).

Immediate mechanical support of both ventricles becomes necessary to overcome cardiogenic shock and multiorgan failure. Such options are the total artificial heart (TAH) (3) and the pulsatile paracorporeal biventricular support devices (BiVAD) (4, 5).

The purpose of this report is to describe our initial experience and evaluate the outcome of an adult patient with end-stage biventricular heart failure who received a paracorporeal pulsatile BiVAD, the Berlin Heart EXCOR system (Berlin Heart, GmbH, Berlin, Germany) as a bridge to heart transplantation. Moreover, we provide a review of the latest main literature concerning its use in end-stage biventricular heart failure in adult patients.

Patient

A 62 years old patient with diabetes mellitus, permanent atrial fibrillation, and end-stage biventricular heart failure due to dilated cardiomyopathy, unsuitable for left-sided support only, was indicated for biventricular assist device with the Berlin Heart EXCOR system (Berlin Heart, GmbH, Berlin, Germany) as bridge to transplant. In the past he underwent implantation of a cardiac resynchronization pacemaker-defibrillator (CRT-D).

The standard surgical approach was median sternotomy. The implantation procedure was performed on cardiopulmonary bypass (CPB). Heparin (300 IU/Kg) was given and standard cannulation to the distal ascending aorta and bicaval venous cannulation were established. Once, on CPB the implantation started with the implantation of the left apical cannula, followed by the cannula to the distal pulmonary artery trunk, the right atrium and the ascending aorta. Interrupted pledged sutures were used for the apical and right atrial cannulae, running sutures for the pulmonary artery and aorta. After channelling all four cannulas throughtout the chest, the chambers were connected accordingly after proper de-airing. An 80 ml pump for the left side and a 60 ml pump on the right side, both with bileaflet valves, were applied. After complete connection of both pumps, initial test ejections were accomplished to assure correct function, followed by a stepwise reduction of the CPB flow

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Fig. 1. Blood pump of the EXCOR system (Courtesy of the Berlin Heart, GmbH).

with a simultaneous increase of BiVAD pump rate. After successful weaning and de-cannulation from CPB, protamine was used to completely reverse heparin. Coseal (Baxter Healtcare, Zurich, Switzeland) was applied to all anastomoses. GoreTex pericardial membrane (GORE-TEX WL Gore and Associates, Flagstaff, AZ.USA) was used to cover all cannulae and the heart to avoid adhesions as much as possible, for future chest reentry for heart transplantation. Both pleural spaces were opened and drained to prevent pericardial tramponade and to drain pleural effusions.

Anicoagulation was started 24h after surgery, after cessation of perioperative bleeding with continuous heparin controlled by partial thromboplastin time (active partial thromboplastin time 50s–80s, ratio 1.5–2.0). Warfarin treatment was started after the removal of the chest tubes and the risk of postoperative bleeding was low with a target International Normalization Ratio (INR) of 2.5 to3.5. The patient also received aspirin 100 mg daily.

During the postoperative course, the patient underwent repeated re-explorations due to mediastinal and pleural bleeding, and he was treated for sacral decubitus. Moreover the patient had a Pseudomonas Aeruginosa urinary tract infection which was treated with intravenous antibiotics and transient renal failure with no need of dialysis. Thrombotic deposits were observed in both the left and right sides, but didn´t led to any fatal complications or device malfunction.

The pulsatile BVAD was able to improve the impaired renal and liver function of the patient: there was a significant decrease in creatinine values from 123 umol/l before BVAD implantation to 87 umol/l at discharge as well as a decrease in bilirubin values from 30.1 umol/l before BVAD implantation to 10.7 umol/l at discharge.

Wound care and dressing changes were performed according to EXCOR instructions for use.

On postoperative day 123 the patient was discharged in stable condition with the mobile driving system, and after 74 days he underwent heart transplantation.

Berlin Heart EXCOR ventricular assist device

The Berlin Heart EXCOR system (Berlin Heart, GmbH, Berlin, Germany) is a paracorporeal, pneumatically driven blood pump

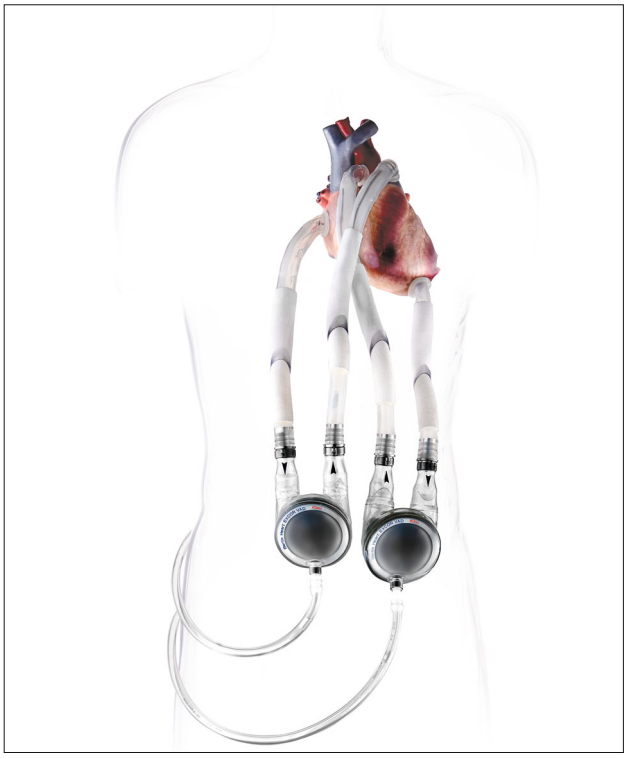

Fig. 2. EXCOR system configuration (Courtesy of the Berlin Heart, GmbH).

Fig. 3. A: Paracorporeal stationary driving unit. B: Mobile driving system (Courtesy of the Berlin Heart, GmbH).

that delivers a pulsatile flow and can provide a durable support of the left, right or both ventricles. The device is available in different pump sizes that are developed to support both children and adults and with different valves (tri-leaflet polyurethane or bileaflet mechanical valves). In adults a 80ml pump is used to support the left ventricle and a 60ml pump to support the right ventricle. The ventricles are checked 3 times a day and exchanged when significant thrombi are visible. In Europe, the system is approved for both children and adults, but in the United States, its use is only granded for children (Figs 1, 2, 3).

Tab. 1. Literature review of recent case series in adults.

Year	Author	Number of adult patients	Indication	Outcome
2018	Schmack et al (5)	12	INTERMACS level 1,2 Bridge to transplant	Median support time 248 (57–381) days 1 year survival 92% 1 year post implantation 6 patients heart transplant Complications 3 patients: thoracic bleeding, exit site infection, ischemic cerebrovascular accident
2021	Bartfay S-E et al (6)	29	INTERMACS level 1 Bridge to transplant	Median support time 136 (81–185) days 24 patients heart transplant 1 patient recovery 4 patients' death on device
2022	Michael S et al (7)	90	INTERMACS level 1 Bridge to transplant	Median support time 37 (0–487) days 37 patients heart transplant 43 patients died on support 30-day survival 70.1% 1 year survival 41.2% Complications: stroke 16, bleeding 13, driveline infection 13, re-thoracotomy 41, pump thrombosis 40 patients
2022	Kremer J et al (8)	58	Median INTERMACS level I (I–III) Bridge to transplant	30 patients heart transplant after support time 316±240 days 28 patients BiVAD thrombosis 140 chamber exchanges Causes of death: multiorgan failure 25%, septic shoch 17.9%, cerebral hemorrhage 14.3%, bleeding 14.3%,embolic events 14,3%

BiVAD = biventricular support device

Literature review

Recent dedicated studies (case series) on the use of the paracorporeal the Berlin Heart EXCOR system (Berlin Heart, GmbH, Berlin, Germany) in adults are presented in Table 1.

Moreover, in the published literature, there are few case reports presenting successful biventricular support with the EXCOR system or describing different complications. Herrmann FEM et al (9) and Bireta C et al (10) presented successful implantations as a bridge to transplant in a young patient with Marfan syndrome or as a long-term support in a 76 years old patient with giant-cell myocarditis, respectively. On the contrary, Volt S et al (11) presented a case of acute tamponade caused by mechanical defect in the membrane of the arterial chamber, Attisani M et al (12) presented a case with device -related infection and multiple splenic infarctions, and Oto O et al (13) presented a case of serious infection in cannulation and driveline sites treated with vacuum-assisted therapy.

Discussion

The number of continous flow (cf)-LVAD implantation has significantly increased worldwide (14). However, right heart failure is a huge challenge in LVAD therapy and its occurrence is associated with increased mortality and morbidity (15). The use of temporary RVAD after LVAD implantation shows inferior results compared to planned BiVAD implantation (2). If a right ventricular recovery is expected, the trremporary RVAD should go along with the LVAD. As to long-term BiVADs, there can be continuous flow and pulsatile BiVADs. The use of 2 continous flow pumps as BiVAD has been described as a modern option compared to the use of the bigger paracorporeal pulsatile BiVAD (16). However, as to cf-BiVADs there are several issues that need to be adressed. The use of 2 cf-devices is complex and off-label. Moreover, the pumps are controlled independently from each other, which makes predictions of systemic and pulmonary flow almost impossible. Also, the use of 2 cf-devices HeartMate 3 (Abbot Cardiovascular, Plymouth, MN), as a total artificial heart was described (17).

In contrast pulsatile systems such as the Berlin Heart EXCOR system (Berlin Heart, GmbH, Berlin, Germany) coordinate flows for the left and right side using one contoller. Also, they perform real cardiac output measurements as a product of stroke volume and pump rate.

The second annual ISHLT Mechanically Assisted Circulatory Support Registry shows superior 1-year survival rates in pulsatile BiVAD (57.8 %) versus continous flow BiVAD (53.1 %) versus pulsatile total artificial heart (TAH) (47.8 %) (18).

Another option in such patients with severe end-stage biventricular failure and INTERMACS level 1 or 2 is the use of the pulsatile total artificial heart TAH SynCardia (3). Since 2017 until the end of 2021, the time when the CE registration in Europe was suspended due to logistical reasons, 11 SynCardia TAH devices were successfully implanted in our institute (19).

Based on the above reasons, we have decided to implant the pulsatile paracorporeal Berlin Heart EXCOR system (Berlin Heart, GmbH, Berlin, Germany) as bridge to transplant in an adult patient on INTERMACS level 1.

The implantation of the device in our report was made in the standard way. Some authors published different modifications of the recommended implation technique. Bigdeli AK et al (20) presented a modification of the implantation technique to reduce perioperative complications and to facilitate cardiac transplanta-

tion after mechanical circulatory support. Another modification is the combination of Berlin Heart cannulas with the Levitronix CentriMag device (Abbot Cardiovascular, Plymouth, MN), in order to enable successful bridge to long-term EXCOR support in case of no myocardial recovery (21).

In our institute we use the standard intravenous UFH protocol for prevention of pump thrombosis and its sequele. Taking into account the difficulties in establishing therapeutic heparin levels, the potential use of bivalirudin was described in the literatute (22).

Intrathoracic bleeding postoperative complications and thrombotic deposits were also reported by other authors (5). Thrombotic depostits may lead to pump replacement and fatal complications, such as pulmonary embolism.

The Excor paracorporeal BVAD provides full pulsatile haemodynamic support of the circulation. Compared to continues flow devices, which show only a calculated flow, the Excor device provides the real cardiac output as a product of stroke volume and heart rate. A pulsatile BVAD can even generate a higher than normal cardiac output (e.g. 10 l/min) that is necessary to overcome vasodilatatory shock. Postoperative management of these very sick patients is facilitated, and their organisms recover quite well, as the patient who is presented in this report, within a short time period, preconditioning them for the following heart transplantation.

In conclusion, the paracorporeal pulsatile Berlin Heart EXCOR system is a reasonable and reliable therapeutic option as a bridge to transplant in patients with end-stage biventricular heart failure.

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