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Initial experience with intracorporeal continuous flow LVAD in pediatric patients in Poland

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Abstract: The aim: The aim of the study is to present the initial experience with continuous flow left ventricle assist device (CF-LVAD) in pediatric patients with BSA below 1.5 m^2.
Material and Methods: Between 2016 and 2017, CF-LVAD (the Heartware System) have been implanted in three pediatric patients in the Department of Pediatric Cardiac Surgery, Jagiellonian University, Krakow, Poland. The indications for initiating CF-LVAD were end-stage congestive heart failure due to dilated cardiomyopathy in all children.
Results: Implanted patients have had BSA of 1.09, 1.42, 1.2 m^2, and 37, 34, 34 kg of body weight and the age 12, 11, 12 years, respectively. The time of support was 550 days in two patients and 127 in another one, and is ongoing. The main complication has been driveline infection.
Conclusion: The outcomes from our single-center experience using the HeartWare CF-LVAD have been excellent with a low incidence of complication and no necessity to reoperation in our patients. Children could be successfully and safely discharged home.

Key words: mechanical circulatory support, continuous flow left ventricle assist device, congestive heart failure in children.

Introduction

In the last decade, the mechanical circulatory support (MCS) has become a valuable therapeutic option in patients with end-stage congestive heart failure (CHF). Several generations of devices have been developed, but they are mainly designed for adult population. The only available solution dedicated particularly to infants and small children is the pulsatile system Berlin Heart. Its superiority in long-term MCS as compared to extracorporeal membrane oxygenation (ECMO) has been established [1], demonstrating at the same time many disadvantages, such as neurological complications, incidences of pump thrombosis, necessity of readmissions and important limitations of quality of life. At present, the intracorporeal continuous flow left ventricle assist device (CF-LVAD) offers excellent patient mobility and low complication rates in the adult population.

The use of these devices in the pediatric population is constrained mainly by small patient size, but few centers have reported early experiences with CF-LVAD devices in the pediatric population [2–5]. The aim of the study is to present the initial experience with CF-LVAD in pediatric patients with BSA below 1.5 m^2.

Method

Between 2016 and 2017, three pediatric patients were implanted CF-LVAD in the Department of Pediatric Cardiac Surgery, Jagiellonian University, Krakow, Poland. The indications for initiating MCS were end-stage CHF due to dilated cardiomyopathy in all the patients. Taking into consideration the size of the devices, the Heartware System (HeartWare Inc, Miami Lakes, FL) was chosen for implantation. The system has been previously described in details. Briefly, it consists of a centrifugal pump, an integrated inflow cannula, an outflow graft, and a percutaneous driveline connected to an electronic controller. The pump has the displacement volume of 50 cc and weighs 140 g. The diameter of the pump is 49 mm, the total height of the pump is 58 mm. The inflow part has a diameter of 20.5 mm and is 25 mm long. The outflow tube has a diameter of 10 mm, and the percutaneous driveline a diameter of 4.2 mm. All the implants were performed with cardiopulmonary bypass. A standard median sternotomy was performed during the surgical procedure. The patient was put on cardiopulmonary bypass after sewing of the ring to the myocardium and coring of the ventricular wall, the inflow cannula was inserted slightly anteriorly to the left ventricular apex. The outflow graft was anastomosed to the ascending aorta, using partial clamping. The driveline was then tunneled under the sternum to the right upper abdominal quadrant and connected to the controller. The position of CF-LVAD with respect to the heart could be observed on postoperative chest X-rays of all the patients. All the patients were supported with CF-LVAD alone, despite the fact that all

had a high degree right heart dysfunction. Postoperative management is characterized in Table II, but in general, the management strategy was similar to that applied in patients with Fontan physiology, including nitric oxide application, a special technique of ventilation and even leaving the chest open in the early post-implantation period.

A transesophageal and subsequently transthoracic echocardiography were used as a primary tool in monitoring ventricular function and optimization of pump speed while weaning the patient from cardiopulmonary bypass following implantation, and for further adjustments.

Results

Patient demographics and preoperative characteristics are listed in Table 1. All the patients met the criteria for INTERMACS score 1 before CF-LVAD implantation. Of the three patients forming the study cohort, all were on intravenous inotropes prior to CF-LVAD initiation, two were on prolonged mechanical ventilation, while one patient was supported with veno-arterial ECMO. Two patients needed resuscitation procedures to be performed several times.

Table 1. Pre-implantation characteristics of CF-LVAD patients.

Characteristics	Patient I	Patient II	Patient III
Age [years]	12	11	12
Gender	M	F	M
Weight [kg]	37	34	34
Diagnosis	Dilated CMP	Dilated CMP	Dilated CMP
BSA [m^2]	1.09	1.42	1.20
Drainage of pleural cavity	YES	YES	YES
LVEDD [mm]	60	44	55
Pre-op inotropes	milrinone, dopamine, levosimendan, amiodarone, adrenaline	milrinone, dopamine, levosimendan, adrenaline	milrinone, dopamine, levosimendan, adrenaline
Mechanical ventilation	Yes	Yes	Yes
ECMO	Yes	No	No
LVEF [%]	20	23	18

BSA — body surface area, LVED — left ventricular end-diastolic diameter, LVEF — left ventricular ejection fraction, CMP — cardiomyopathy, ECMO — extracorporeal membrane oxygenation.

The operative results on the day of implantation of CF-LVAD are summarized in Table 2. All the patients remained on VAD support as the bridge to transplant. Patient 1 and 2 have been over 550 days on VAD support and continue to be supported. The post-operative chest X-ray images of the patients are shown in Fig. 1. None of the patients have developed significant end-organ dysfunction, either in early or long-term follow up. In none of our patients have we observed symptoms of device malfunction. In patient I and III, signs of depression and feeding intolerance were observed.

Table 2. Post implantation clinical outcomes in CF-LVAD patients.

Characteristics	Patient 1	Patient 2	Patient 3
Operation time [min]	225	195	340
CPB time [min]	96	106	120
Outcome data [days]	570	550	127
Pump speed range [rpm]	2850–2900	2800–3200	2400–2600
Pump flow during first 30 days [L]	2–4	4–5.1	3–4.2
Post-op NO	Yes	Yes	Yes
Delayed chest closure	No	No	Yes

CPB — Cardiopulmonary bypass, NO — nitric oxide.

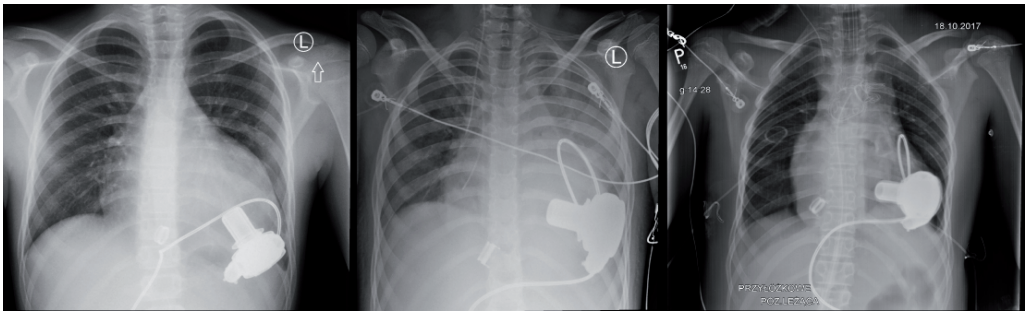

Fig. 1. Position of CF-LVAD after implantation in 3 children on chest X-ray.

In all the patients, only the LVAD system was implanted in spite of biventricular dysfunction. The prolonged cardiopulmonary bypass time (Table 2) was related to right ventricular dysfunction and attempts to eliminate the implantation of the right ventricular assist device.

Postoperative anticoagulation was started with unfractionated heparin (the target activated partial thromboplastin time of 50 to 60 s). As the patients tolerated

oral nutrition, heparin was switched to warfarin. The targeted INR for this cohort was well within the recommended range of 2–3. The platelet inhibitors used in the patients were acetylsalicylic acid 1 to 2 mg/kg/day. All the patients and their families were trained prior to discharge home. All the patients received treatment after discharge including metildigoxin, aspirin and acenocoumarol with the dose adjusted according to INR. Patient II and III additionally received sildenafil, ACE inhibitors and occasionally furosemide. The patients were advised to check INR, initially every 2 days, then on a weekly basis. Readmission occurred two times in patient 1 and one time in patient 2. The reason for readmissions and adverse events are presented in Table 3. In patient I, drive line infection (defined as appearance of erythema or purulent discharge around the exit site of the drive line) was the reason of several readmissions. CF-LVA-related thrombosis or signs of stroke were not present in any patient. Supra-ventricular arrhythmia was observed only during the post op period in patient II and III, but only in the course of the early post-implantation period. An emergency reference card displaying contact telephone numbers and an algorithm for emergency care was provided to all the patients. Before reintegration to school, school staff members were educated by the family caregiver.

Table 3. Readmission and adverse events in CF-LVAD patients.

Adverse event	Patient 1	Patient 2	Patient 3
Exit site infection	1	0	0
Sepsis	0	0	0
LVAD-related infection	0	0	0
Local non-LVAD infection	Tooth	0	0
Device replacement	NR	NR	NR
Right heart failure requiring RVAD	NR	NR	NR
Renal dysfunction	0	0	0
Hepatic dysfunction	0	0	0
Cerebrovascular dysfunction	0	0	0
LVAD thrombosis	0	0	0
Cardiac arrhythmia	0	SVT	SVT
Respiratory failure	0	0	0
Unscheduled readmissions	Driveline infection	Subtherapeutic INR	0
Readmission (No. of times)	2	1	0

Present — 1, Absent — 0, Not required — NR, SVT — supraventricular tachycardia.

Discussion

In this study, we have demonstrated that children with low weight and BSA <1.5 m^2 can be successfully implanted with CF-LVAD and supported for long periods. Moreover, all our pediatric patients have been discharged home and attend their schools [6].

There is a growing body of evidence that CF-LVAD is currently the optimal method of long-time MCS, even in pediatric patients. The borderline body weight oscillates about 20 kg, when the patients can be supported, whereas the pulsatile systems, such as the Berlin Heart, remains the option for patients with lower body weight, when the volume of the employed paracorporeal pumps is adjusted to the body mass.

One of the major advantages of the CF-LVAD systems is the possibility of discharging patients home; they can even attend schools and be active in everyday life. All the patients in our group are physically very active, what may even pose a risk of damaging the driveline.

All our patients demonstrated end-stage CHF, with enhanced pharmacotherapy, being on mechanical ventilation, and in one case on ECMO as the bridge to CF-LVAD. It seems to be one of the reasons that the time from admission to discharge home was about one month. With the center gaining experience, the threshold for starting the MCS may be optimized, so that the patients might be implanted CF-LVAD before reaching the critical status, what may influence the post-implantation course. Some data suggest that ECMO should be generally viewed as increasing the risk of LVAD support in the majority of children. On the other hand, it is possible that ECMO, when used strictly for short-term resuscitative support to normalize end-organ function immediately prior to VAD implant, may improve LVAD candidacy in selected patients.

Patients with significant problems with left ventricle function have very frequently concomitant right ventricular dysfunction, so the decision must be reached whether the patient needs LVAD only or the biventricular MCS system implantation. The biventricular system is highly demanding and is associated with poorer final results. This is why the majority of centers prefer to start only LVAD and manage patients with RV failure on pharmacological support. Appreciating this strategy, we dedicated much effort to preventing biventricular MCS, what was the reason of prolonged time of cardiopulmonary bypass, which was not related to technical issues of CF-LVAD implantation.

In our experience, the management strategy in the post-op period was very similar to that employed in patients after the Fontan operation, including special ventilation settings, nitric oxide administration, or even leaving the chest open shortly after initiation of CMS. Despite aggressive medical support of RV, a certain proportion of

patients will still develop RV failure requiring temporary mechanical RV support to restore blood flow to the pulmonary circulation and increase LV preload [7]. Studies suggest that an early planned biventricular assist device (BiVAD) is associated with better survival as compared to delayed implantation [8, 9]. Therefore, performing a thorough preoperative risk assessment for RV failure is necessary to implant BiVAD or total artificial heart.

Currently, different options on temporary RV support are expressed [10]. Temporary ECMO support for RV failure after LVAD implantation was successfully performed in 29 (91%) patients. The results achieved in this cohort showed the one-year survival rate of 74% [11], what is comparable to data from previous reports on temporary and permanent mechanical RV support with 6-month survival rates of 50–60%. However, the number of thromboembolic events was higher in ECMO as compared to the true RVAD group with cannulation of pulmonary artery [12, 13].

The choosing of optimal MCS systems depends mainly on the size of the device, especially in patients with borderline body weight. There is hope that miniaturization of the devices will eliminate the size limitations for CF-LVAD systems. The HeartWare MVAD (HeartWare International Inc.) small axial pump, about one-third the size of the HeartWare HVAD, has been tested in animal studies [14, 15]. The MVAD pump is capable of delivering flows ranging from 1 to 7 L/min. This provides the advantage of the pump being possibly used in patients of less than 20 kg (BSA <1 m^2), in whom the use of the HeartWare HVAD has been limited by dimensions and restriction of flow to a minimum of 2 L/min. It is known that the usage of the Berlin Heart Excor for children with body weight below 5 kg is related to worse outcomes.

In patients with a limited space in the pericardium, the technique of infradiaphragm implantation has been developed. In our patients, we were able to locate the device in the pericardial sac and the position could be observed in chest X-ray pictures. In adult patients, the MCS is thought to be "the bridge to transplant" or even destination therapy, especially when the heart transplantation is not possible. The longest reported time of MCS is about 6 years, what suggests that MCS cannot be recommended as the destination therapy in the pediatric population in terms of life time expectancy. On the other hand, the shortage of donors may cause the patients to be on waiting list for months or even years. The strategy when the CMS is applied as the bridge to recovery is possible mainly when the substrate of the underlying diagnosis has a reversible nature, as in the case of myocarditis.

The present study includes a total of three patients who underwent CF-LVAD implantation, with all of them (100%) successfully discharged home. It has a significant implication for psychosocial wellbeing of patients and their families. As the device technology continues to improve, the approach to pediatric MCS aims not only at supporting life, but also at improving quality of life of patients. D'Alessandro *et al.* [16] reflected on the "potential benefits that facilitate hospital

discharge, and a rapid return to activities of daily living" when they published the first reported use of HVAD in an adolescent as the bridge to transplant in the United States. Padalino *et al.* also reported two children discharged home on HVAD support. They suggested that the patients and their families had a more positive psychosocial experience with the HVAD, and were more accepting of their condition as they had few constraints and limitations [17]. When a patient can be discharged home safely, it has an impact on the financial status of the said patient and his family, as the child can return to school and the parents can resume work.

We report a low rate of adverse events and complications in the outpatient setting. Driveline infection was the most common complication present in patient 1, as is similarly reported in adult VAD series [18–20]. There were no neurologic events or life-threatening incidents reported. Technical malfunction, controller failure, drive line disconnection, loss of power support and pump thrombosis can lead to life-threatening events in LVAD patients [21]; none of these adverse events were observed in our subjects. Product training for paramedics is essential, as they have the potential to significantly affect patient outcome in crisis situations [21–23].

We recommend hotline services for outpatients on VAD so that they could be easily accessible to all families, care providers and necessary community personnel, as it is done in many adult centers [24–26].

Strategies aiming at prevention and treating perioperative right heart failure include optimization of LVAD speed guided by echocardiography, support with inotropes and/or use of selective pulmonary vasodilators, such as inhaled nitric oxide or sildenafil, to reduce PVR [27–29].

Sparks and colleagues recently reported their experience with the HeartWare HVAD as the bridge to transplant in adolescents with end-stage heart failure. The outcomes were compared with a matched cohort of adult patients. The incidence of adverse events and survival after HVAD implant were very satisfactory and similar between the two groups [30]. Niebler *et al.* published a case of successful support with the HeartWare HVAD in a patient with failed Fontan circulation as the bridge to cardiac transplantation, opening the path for a potential application of the device in this setting [31]. The published multi-institutional report showed only 42% success rate in bridging failing single ventricles to either recovery or transplant, using the Berlin Heart EXCOR VAD [32]. The present single center institutional study is the initial experience of implantation of CF-LVAD in pediatric patients with small body size in Poland, and it demonstrates that discharge home, outpatient management and school integration is feasible and safe.

The limitations of this study include its retrospective nature, a small number of patients and single-center experience.

Conclusions

The outcomes from our single-center experience using the CF-LVAD have been excellent with a low incidence of complications and improved survival, free of stroke and no necessity to reoperation for device repair or replacement in our patients. Children could be successfully and safely discharged home.

Conflict of interest

None declared.

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