Abstract

The ventricular assist device (VAD) is a life-saving option for patients in heart failure refractory for conventional therapy. The aim of study was to assess the influence of VAD on heart transplantation (HT) outcome in children <16 years. Between October 1988 and August 2008, 73 children underwent HT: Group 1 (n=9) who received VAD as bridge to HT (left ventricular – 4, biventricular – 5), and Group 2 (n=64), without previous VAD. Diagnoses included cardiomyopathy (n=50 (68.5%)) and congenital heart defects (n=23 (31.5%)). Retrospective analysis of perioperative and long-term follow-up data was performed. The mean follow-up was 7.22±4.7 years. The diagnosis of cardiomyopathy appeared more often in Group 1 (P=0.074), but the difference was not significant. The two groups did not differ with respect to age (P=0.123) and weight (P=0.183). Mortality in long follow-up was: 11.1% (n=1) in Group 1 and 14.1% (n=9) in Group 2 (P=0.782). Analysis of preoperative end-organs function did not reveal significant differences between groups. There was also no significant differences with respect to waiting time for transplant (P=0.948), postoperative ventilatory support time (P=0.677), duration of hospital stay (P=0.711) and incidence of acute rejection episodes (P=0.156). VAD used as a bridge for HT in children does not negatively influence the outcome.

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Keywords: Ventricular assist device; Pediatric heart transplantation; End-organ function

1. Introduction

For more than thirty years now, heart transplantation (HT) has been used as a last treatment option for children with end-stage heart failure refractory to medical therapy [1]. The organ availability in this age group is poor, especially among the smallest children. The waiting time for transplantation is usually longer than in adults and continues to increase [2]. The mortality rate on the waiting list is also higher, ranges in infants from 25% to 31% [3, 4]. Pulsatile paracorporeal ventricular assist devices (VAD) have been proved to be an effective long-term strategy to keep children alive while awaiting HT [3, 5–7]. VAD systems give the chance to recover from secondary to resuscitation end-organs dysfunction [8], and have a higher rate of successful bridge to transplantation than short-term devices [9]. Mechanical circulatory support with VAD is unfortunately not free from potential complications, e.g. immunization (substitution of blood products) or adhesions (VAD implantation), which may have a crucial impact on transplantation results.

The aim of the study was to assess the influence of mechanical support with pulsatile VAD systems in children <16 years old before HT on the HT outcomes.

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2. Materials and methods

We retrospectively analyzed patients younger than 16 years, who underwent orthotopic HT in our center between October 1988 and August 2008. Review identified 73 children, 43 (58.9%) boys and 30 (41.1%) girls, with a mean age of 6.3 years (range, 5 days–15.9 years) and a mean weight of 19.9 kg (range, 3.3–69.6 kg). The indications for mechanical support were: dilated cardiomyopathy in 50 (68.5%) children (all without previous thoracic surgery), and congenital heart defect in 23 (31.5%) patients (16 children had 1–3 previous sternotomies). All children were divided into two groups. Group 1 (n=9) consisted of patients supported with VADs before HT, Group 2 (n=64) was constituted by children without VADs before HT (Table 1).

For mechanical support, two long-term systems were used: Berlin Heart Excor in five and Medos system in four children. The Berlin Heart VAD system (Excor, Berlin Heart AG, Berlin, Germany) consists of a paracorporeal polyurethane blood pump (with 10, 25, 30, 50, 60 ml stroke volume) with polyurethane valves, silicone cannulas and the stationary driving unit (IKUS 2000). The pump is driven by a pulsatile electromechanical system. All blood-contacting surfaces are coated with heparin (Carmeda process, Carmeda, Upplands Väsby, Sweden). Medos HIA VAD (Medos
Clinical cardiac rejection was defined as biopsy grade III or greater rejection associated with clinical heart failure or death. Severe acute renal failure was defined as renal failure requiring dialysis.

The quantitative data are represented as a median value and range. Mean value and standard deviation (S.D.) were reported when statistically relevant. For qualitative data, frequencies were given. Patient survival was estimated using the Kaplan–Meier method. The statistical analysis was carried out by means of $\chi^2$-test with Yates correction and Mann–Whitney U-test. Differences were considered statistically significant at a $P<0.05$.

### 3. Results

Follow-up was complete up to September 2008 (mean, 7.22 ± 4.7 years; range, 1.1–16.53 years). There were no significant differences between the groups regarding the operative body weight and age (Table 1). Diagnosis of congenital heart disease was more frequent in Group 2 (all the children in Group 1 had dilated cardiomyopathy), but the difference was not significant ($P=0.074$) (Table 1). Immediately before transplantation the overall mean bilirubin was $0.9\pm0.6$ mg/dl (0.1–4.0 mg/dl), aspartate aminotransferase was $34.9\pm34.2$ U/ml (5–222 U/ml), alanine aminotransferase was $41.1\pm69.1$ U/ml (7–411 U/ml), urea was $41.3\pm26.6$ mg/dl (8–162 mg/dl) and creatinine was $0.6\pm0.3$ mg/dl (0.3–2.0 mg/dl). Data regarding both groups are presented in Table 2, showing no differences in end-organ function between the groups shortly before HT. The mean waiting time for heart was 59.2±88.1 days (median, 30 days; range, 1–443 days), and did not differ between the groups ($P=0.948$) (Table 2).

Major adverse events during VAD support included re-exploration for bleeding in 5 (55.6%) children, failure of primary device because of thrombus in the pump chamber requiring change(s) of the chambers in 3 (33.3%) patients, ischemic stroke (with spastic hemiparesis) and peripheral embolism (femoral artery) in 1 (11.1%) patient and infection (local) in 1 (11.1%) child.

Immediately before transplantation, 2 (3.1%) patients in Group 2 and nobody in Group 1 showed evidence of HLA sensitization ($P=0.581$).

There was no difference between the groups regarding postoperative ventilatory support time ($P=0.677$), duration of hospital stay ($P=0.711$) and incidence of acute rejection episodes ($P=0.179$) (Table 2).

The mortality in long-time follow-up was 11.1% ($n=1$) in Group 1 and 14.1% ($n=9$) in Group 2. We did not find any statistically significant differences in post-transplantation mortality between groups ($P=0.782$). Fig. 1 shows the actuarial survival using Kaplan–Meier method. The causes of death were: in Group 1: graft failure – 1 (11.1%); in Group 2: acute rejection – 5 (7.8%), graft failure – 3 (4.7%) and sudden death in 1 (1.6%) case.

In Group 1 in early post-transplantation period, only 1 (11.1%) child required rethoracotomy because of bleeding. The most common late complications in Group 1 were: arterial hypertension – 3 (33.3%), renal insufficiency – 2 (22.2%) and rhythm disturbances – 2 (22.2%). The most common early complication in Group 2 was heart tampon-
ade in 4 (6.3%) children. In the late post-transplantation period the most frequent complications in Group 2 were: renal insufficiency – 16 (25%) (one patient underwent renal transplantation), arterial hypertension – 10 (15.6%), rhythm disturbances – 10 (15.6%) [4 (6.3%) children required pacemaker implantation], cytomegalia virus reactivation – 9 (14.1%), transplant vasculopathy – 3 (4.7%) (one child underwent heart re-transplantation, and another stent implantation in right coronary artery), and associated with Epstein–Barr virus infection lymphoma in 2 (3.1%) – one was fatal.

4. Discussion

Since 1992, when the first miniaturized pulsatile devices (Berlin Heart) became available, long-term mechanical circulatory support systems have been successfully implanted even in small infants and newborns suffering from cardiogenic shock, as a bridge to HT or recovery [5, 11, 12]. Outcome in VAD support in infants is no longer inferior to that of adult patients [5]. However, ECMO is still the most often applied mechanical support for young children [6]. ECMO provides total cardiopulmonary support, can be rapidly implanted – centrally or peripherally (neck or femoral vessels), is inexpensive, readily available and was proved to be the safest form of support in children when the anticipated waiting time for transplantation is likely to be short (i.e. weeks) [3, 7]. In comparison with ECMO, current available for pediatric application paracorporeal or complete implantable VAD systems have many advantages: can offer medium- or long-term support, do not require high level of anticoagulation, have lower incidence of blood trauma (hemolysis), require only a little technical attention after implantation, children can be extubated, fully mobilized and ambulatory controlled [3, 6, 7, 9, 14]. In the current era, the waiting time for HT often exceeds the time which patients can be successfully supported by ECMO [9].

Implantation of VAD systems allows improvement or complete recovery of end-organs function and optimizes the patient condition before HT [2, 10, 12]. All our patients were in critical condition during the VAD implantation and recovered completely until HT. Comparison of the most important parameters of end-organ function, shortly before HT reveals no significant differences between children on VAD and children electively referred to transplantation. We conclude that long-term support with VAD offers enough time to restore end-organ function.

In our observations, after implantation of left VAD (LVAD), right ventricle very often improves markedly within minutes, which was also noticed by others [5, 8]. LVAD combined with pharmacological right heart support can provide satisfactory circulatory support, allowing for recovery of end-organ function, especially in small children. We usually first implant LVAD and then decide, depending on the right ventricular function about the right heart support. Sometimes, we use right heart reperfusion using standard cardiopulmonary bypass (cannulation of the right atrium and pulmonary artery) for a few minutes, which is usually sufficient for right ventricular recovery [15]. In small children only LVAD implantation facilitates also primary chest closure [14].

Our analysis demonstrates that post-transplantation survival for pediatric patients who were bridged with VAD is similar to that of other children, who did not require support. These results are confirmed by other authors [8, 9]. One of the most important factors which seems to have enormous impact on early and long-term survival after
transplantation is the history of previous sternotomy itself [8]. VAD implantation requires sternotomy and almost always substitution of blood products. On the other hand, among pediatric candidates for HT a large group constitutes the children with congenital heart defects after previous surgery. There seems to be no difference between VAD implantation and corrective or palliative surgery regarding the development of sensitization and, as a consequence, an increased risk of acute rejection after transplantation. Use of VAD in our series did not appear to significantly increase the risk of antibody sensitization before HT, which is also observed by others [7].

The use of VAD support before transplantation did not significantly influence the post-transplantation complications. The incidence of the most frequent complications after HT, for example: acute rejection, infection, graft failure, is usually constant in the biggest so far published series [2, 8].

The most important limitation of the study was the small number of patients which influences the value of carried on statistics, retrospective nature of the data collection, and the inclusion criterion to the study, i.e. performed HT. In studies which analyze the overall results after implantation of VADs in children, the survival to transplantation/recovery ranges between 76% and 86% [3, 6, 7, 9]. Many authors emphasize the fact that diagnosis of congenital heart defect is associated with worse outcome in children on VAD [7–9]. All our patients on VAD had diagnosis of cardiomyopathy and because of this we could not confirm these observations.

Pneumatically driven pulsatile systems used in children, who would otherwise die, are effective in keeping them alive and allow complete recovery of the end-organ function. The post-transplantation course, complication and survival are comparable to non-VAD patients.

References


