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ORIGINAL ARTICLE

Mechanical cardiac support in children with congenital heart disease with intention to bridge to heart transplantation†

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Abstract

OBJECTIVES: A significant number of children affected by congenital heart disease (CHD) develop heart failure early or late after surgery, and heart transplantation (OHTx) remains the last treatment option. Due to shortage of donor organs in paediatric group, mechanical circulatory support (MCS) is now routinely applied as bridging strategy to increase survival on the waiting list for OTHx. We sought to assess the impact of MCS as intention to bridge to OHTx in patients with CHD less than 16 years of age.

METHODS: From 1998 to 2013, 106 patients received 113 episodes of MCS with paracorporeal devices as intention to bridge to OHTx. Twenty-nine had CHD, 15 (52%) with two-ventricle (Group A) and 14 (48%) with single-ventricle physiology (Group B). In Group A, 5 children had venoarterial extracorporeal membrane oxygenation (VA ECMO), 6 left ventricular assist device (LVAD), 2 biventricular assist device (BIVAD), 1 VA ECMO followed by BIVAD and 1 BIVAD followed by VA ECMO. In Group B, VA ECMO was used in 7 children, univentricular assist device (UVAD) changed to VA ECMO in 4, UVAD in 2 and surgical conversion to two-ventricles physiology with BIVAD support changed to VA ECMO in 1.

RESULTS: Twenty-one of 29 (72%) children survived to recovery/OHTx. Seven of 29 (59%) survived to discharge. In Group A, 11/15 (73%) survived to recovery/OHTx and 9/15 (60%) survived to discharge. Four of 15 (27%) died awaiting OHTx. One child had graft failure requiring VA ECMO and was bridged successfully to retransplantation. One child dying after OHTx had acute rejection, was supported with VA ECMO and then BIVAD but did not recover. One patient had an unsuccessful second run on BIVAD 1 year after recovery from VA ECMO. In Group B, 10/14 (71%) survived to recovery/OHTx and 8/14 (57%) survived to discharge. Four of 14 (29%) died awaiting OHTx. Of deaths after OHTx, 1 occurred intraoperatively and 1 was consequent to graft failure and had an unsuccessful second run with VA ECMO.

CONCLUSIONS: Children with CHD can be successfully bridged with MCS to heart transplantation. Single-ventricle circulation compared with biventricular physiology does not increase the risk of death before transplant or before hospital discharge.

Keywords: Mechanical circulatory support • Extracorporeal membrane oxygenator • Heart transplantation • Congenital heart disease

INTRODUCTION

Patients affected by congenital heart disease (CHD) can increasingly survive to adulthood due to improvements in surgical, cardiological and intensive care treatments [1]. A significant proportion develop heart failure either acutely or chronically after cardiac surgery [2]. Heart transplantation offers an improvement in survival to these patients. However, donor organ shortage remains a persistent and hitherto an insurmountable barrier [3]. Mechanical circulatory support (MCS) as bridge to transplantation offers a strategy to allow prolongation of window of opportunity to transplantation in this group. This has allowed more cardiac transplantations to be undertaken albeit with increased early morbidity and mortality [4–6]. However, this group still remains poorly studied with amalgamation of disparate categories such as dilated cardiomyopathies to confound the analysis. In addition, MCS for single ventricle also provides an increasingly challenging category [7–9].

In order to define the feasibility of MCS in patients with CHD, we assessed our 15 years' institutional experience of congenital patients less than 16 years old receiving mechanical assist device for heart failure as bridge to transplantation, comparing the outcomes of biventricular and single-ventricle physiology.

METHODS

Institutional Review Board approval was obtained for the study and the board waived individual patient consent. The database of

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all patients less than 16 years of age who underwent MCS was retrospectively analysed and stratified by diagnosis. The bridge for transplantation programme at Freeman Hospital commenced in 1998. This has undergone transformation from an initial use of just venoarterial extracorporeal membrane oxygenator (VA ECMO) to the present use of Berlin Heart EXCOR device since 2005. Several combinations of various MCS strategies have been used including bridge-to-bridge strategy for the acutely ill child with initial resuscitation with VA ECMO and thereafter conversion to Berlin Heart for prolongation of support. Levitronix Centrimag® device has also been employed in some instances.

The National Health System in the UK has regionalized the care for children with end-stage heart failure to two centres, Freeman hospital being one of them. The use of mechanical support as bridge to transplantation and transplantation is exclusively undertaken in these centres. Accordingly, the majority of patients being treated at the Freeman hospital are tertiary referrals from other congenital cardiothoracic units: some of them electively for assessment and further management and some others in emergency, already on MCS after previous cardiac arrest requiring ECMO cardiopulmonary resuscitation.

Patients

Between January 1998 and September 2013, 106 patients received 113 episodes of MCS with paracorporeal devices as intention to bridge to transplantation. Of these, 29 patients had CHD as their primary diagnosis. Fifteen (52%) had biventricular circulation (Group A), while 14 (48%) had single-ventricular physiology (Group B). In the biventricular group, 5 children received VA ECMO, 6 left ventricular assist device (LVAD), 2 biventricular assist device (BIVAD), 1 VA ECMO followed by a BIVAD and 1 BIVAD followed by a VA ECMO (Table 1). In the single-ventricle group, 7 children were supported with VA ECMO, 2 with univentricular assist device (UVAD) and 4 with UVAD changed to VA ECMO; a child was surgically converted to a biventricular circulation and assisted with a BIVAD followed then by a VA ECMO (Table 2).

Surgical strategies

ECMO was instituted via central cannulation (in case of failed weaning from cardiopulmonary bypass) or via neck vessel cannulation, initially using a roller pump and since 2010 the Levitronix Centrimag LVAS®. When used as second step after BIVAD or UVAD, ECMO was established using the Berlin Heart cannulas left *in situ*. In particular instances, such as recurrent clot formation in the pulsatile devices or need to add an oxygenator in the circuit in case of lung dysfunction, the Berlin Heart pump was replaced with a continuous flow Levitronix Centrimag®, using the same cannulas.

In biventricular circulation, Berlin Heart EXCOR devices were implanted in routine position, with right atrial and pulmonary artery cannulas for the pulmonary (right) ventricle and with apical left ventricle and aortic cannulas for the systemic (left) ventricle.

In the setting of single-ventricle palliation, the surgical strategy to implant a Berlin Heart EXCOR device was adapted to the anatomical (situs, stage of palliation, multiple previous operation) and haemodynamic (pulmonary vascular resistance, passive blood flow drainage in the lungs, presence of venovenous collaterals) variables. Five patients with failing bidirectional Glenn circulation were assisted with UVAD (apical and aortic cannulation) using larger size Berlin Heart ventricles to achieve successful haemodynamic support (Fig. 1). In case of inadequate empting of the single ventricle, the option of switching the inflow cannula from the apex to the single atrium was considered. Coil embolization was applied in the presence of large venovenous collateral to achieve a better oxygen saturation. Finally, in case of recurrent hypoxia, persistent end-organ failure and inotropes dependency despite the UVAD support, elective conversion to venoarterial ECMO through the Berlin Heart cannulas was established. Of 2 children with failing first stage palliation (in the presence of modified Blalock–Taussig (BT) shunt), 1 was assisted with UVAD (apical

Table 1: Group A (biventricular)

n	Age (m)	Weight (kg)	Anatomy	Cardiac arrest pre-MCS	MCS (type)	Length of support (days)	Outcome
1	34	12.5	DORV, TGA, CoA	Yes	VA ECMO	8	Transplant
2	21	10	CAV disease	No	VA ECMO	21	Death
3	157	69	pAVSD	No	BIVAD (Berlin Heart) → VA ECMO	76	Death
4	14	7	CAV disease	Yes	VA ECMO → BIVAD (Berlin Heart)	127	Transplant
5	167	37	CAV disease	Yes	LVAD (Levitronix)	8	Transplant
6	26	10	Shone's complex	Yes	VA ECMO	17	Explant
7	118	23	cAVSD	Yes	BIVAD (Berlin Heart → Levitronix)	24	Death
8	34	12	TGA, VSD, PS	Yes	LVAD (Berlin Heart)	39	Transplant
9	62	19	ccTGA	No	LVAD (Berlin Heart)	146	Transplant
10	14	7.5	CAV disease	Yes	LVAD (Berlin Heart)	219	Transplant
11	74	25	cAVSD	No	VA ECMO	7	Transplant
12	192	44	DORV, TGA, PS	No	VA ECMO	4	Transplant
13	1.6	4	TGA	No	LVAD (Berlin Heart)	79	Explant
14	7	7	IAA	No	LVAD (Berlin Heart)	42	Explant
15	8	5.5	ALCAPA	No	BIVAD (Berlin Heart)	30	Death

MCS: mechanical circulatory support; DORV: double-outlet right ventricle; TGA: transposition of great arteries; CoA: aortic coarctation; VA ECMO: venoarterial extracorporeal membrane oxygenator; CAV: congenital aortic valve; LVAD: left ventricular assist device; pAVSD: partial atrioventricular septal defect; BIVAD: biventricular assist device; cAVSD: complete atrioventricular septal defect; VSD: ventricular septal defect; PS: pulmonary stenosis; ccTGA: congenital corrected transposition of great arteries; IAA: interrupted aortic arch; ALCAPA: anomalous origin of left coronary artery from pulmonary.

Table 2: Group B (single ventricle)

n	Age (m)	Weight (kg)	Stage of palliation	Cardiac arrest pre-MCS	MCS (type and cannulation site)	Length of support (days)	Outcome
1	89	18	Fontan	Yes	VA ECMO	13	Transplant
2	172	53	Fontan	Yes	VA ECMO	2	Transplant
3	35	8	BCPC	Yes	UVAD (Berlin Heart, RV-AO)	7	Transplant
4	18	15	BCPC	No	UVAD (Berlin Heart, RV-AO)	4	Transplant
5	6	4.5	BCPC	Yes	UVAD (Berlin Heart, RV-AO) → VA ECMO	8	Transplant
6	22	12	BCPC	No	UVAD (Berlin Heart, RV-AO) → VA ECMO	61	Death
7	14	9	DKS+BTS	No	UVAD (Berlin Heart, RV-AO) → VA ECMO	21	Death
8	6	6.5	Norwood	No	BIVAD (Berlin Heart, SVC/IVC-PA–RV-AO → Levitronix, SVC/IVC-PA–RV-AO) → VA ECMO	42	Death
9	17	8.5	BCPC	No	UVAD (Berlin Heart, RV-AO) → VA ECMO	31	Death
10	0.2	3	Norwood	No	VA ECMO	5	Transplant
11	53	17	Fontan	Yes	VA ECMO	15	Transplant
12	11	7	BCPC	Yes	VA ECMO	10	Explant
13	60	18	Fontan	Yes	VA ECMO	3	Explant
14	96	17	BCPC	No	VA ECMO	15	Transplant

MCS: mechanical circulatory support; VA ECMO: venoarterial extracorporeal membrane oxygenator; BCPC: bidirectional cavopulmonary connection; UVAD: univentricular assist device; RV: right ventricle; AO: aorta; DKS: Damus–Kaye–Stansel anastomosis; BTS: Blalock–Taussig shunt; BIVAD: biventricular assist device; SVC: superior vena cava; IVC: inferior vena cava.

and aortic cannulation) and the systemic-to-pulmonary artery shunt was reduced by narrowing the shunt to limit pulmonary blood flow (Fig. 2). The other child was converted to a biventricular physiology, disconnecting the shunt, dividing the systemic venous return from the pulmonary venous return and creating a new chamber between the superior and the inferior venae cava. A BIVAD was then established with a right ventricle assist device through the new chamber and pulmonary artery, and an LVAD through the apex of the single ventricle and the aorta (Fig. 3). The BIVAD was subsequently changed to a venoarterial ECMO.

Institutional protocol of care in ventricle assist device patients

Patients assisted with ventricular assist devices (VADs) (in form of Berlin Heart EXCOR and Levitronix Centrimag®) are not anticoagulated for 24–48 h to reduce excessive bleeding. Intravenous Heparin infusion is then started at 25 units/kg/h and continued during the time of MCS, keeping the anti-Xa levels between 0.35 and 0.7 units/ml. Once postoperative bleeding ceases, antiplatelet therapy is commenced, starting 1 mg/kg of Dypiridamole 6-hourly and thereafter adding Aspirin 1 mg/kg twice a day. A value of 7 g/l of haemoglobin is considered the threshold for institution of blood transfusion.

Infection prophylaxis is continued for 48 h after the implantation using broad-spectrum antibiotics and antifungal drugs. Wound care consists of daily dressings using sterile saline 0.9% and avoiding alcoholic solutions. Once the drains are removed, the wound and cannula dressings are changed twice a week and swabs of the wound and of the cannula sites are sent once a week.

After implantation of MCS, all patients are listed for heart transplantation. However, an institutional protocol was established in order to allow recovery from VAD. During the implantation procedure, a left ventricle apical biopsy is performed to assess the degree of fibrosis and to achieve the correct diagnosis. In Berlin Heart EXCOR patients, the plan for potential recovery is based on weekly echocardiographic examination and, once a month, formal testing. This is undertaken with and without inotropic support. Echocardiographic, haemodynamic and biochemical examinations are undertaken at 10 min.

Clinical assessment

A retrospective cross-sectional clinical analysis was performed. Demographic and surgical variables were collected. All children were followed from the time of MCS implantation and censored at the time of recovery/explantation (removal from waiting list), death during support (death awaiting transplantation), transplantation leading to death before discharge and transplantation with survival to hospital discharge. Outcomes of biventricular and univentricular patients receiving MCS were compared in terms of major complications (renal support, chest exploration for bleeding and sepsis), survival to explantation/transplantation and survival to discharge. Major bleeding was considered an episode of haemorrhage requiring reoperation and blood transfusion; and sepsis was considered as evidence of systemic involvement by infection manifested by positive blood culture and/or hypotension [10].

Statistical analysis

A descriptive statistical analysis was performed. Continuous data are presented as mean ±standard deviation, reporting confidence interval (CI) at 95%, and compared through the Student *t*-test. Categorical data are expressed as proportions and compared through the χ^2 test. All hypothesis tests used a 0.05 significance level. Analyses were performed using the STATA v 11.0 software.

RESULTS

Demographic characteristic of the population are reported in Table 3. Children with univentricular physiology were younger at the time of MCS implantation, but not in a significant way. Age between 1 and 10 years was mostly represented in both groups,

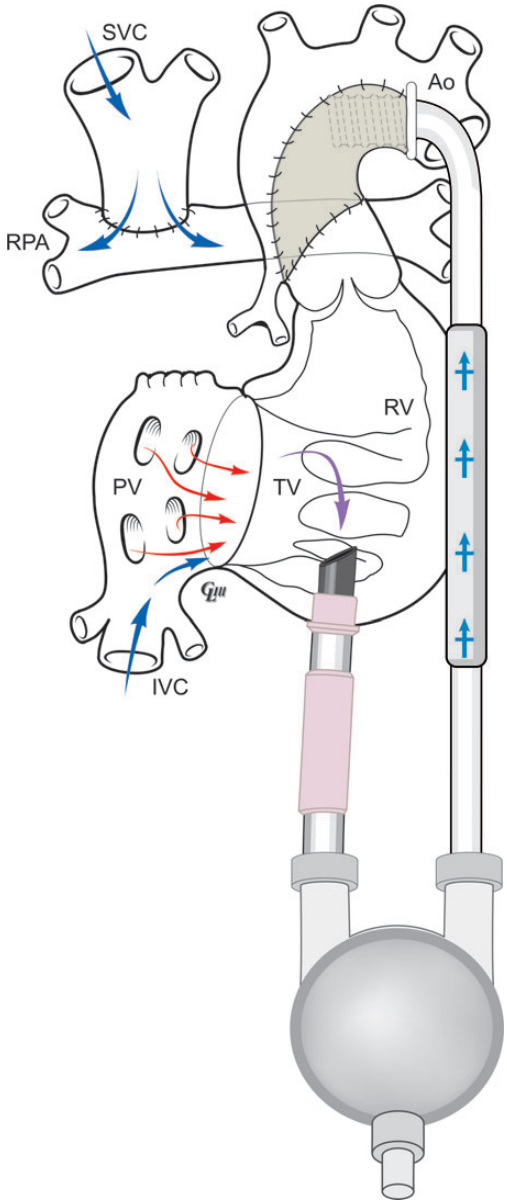

Figure 1: Schematic view of UVAD placement in single-ventricle anatomy after second stage palliation (Glenn circulation) of hypoplastic left heart syndrome. The inflow cannula is inserted in the apex of the single right ventricle and the outflow cannula at the level of the Damus–Kaye–Stansel anastomosis.

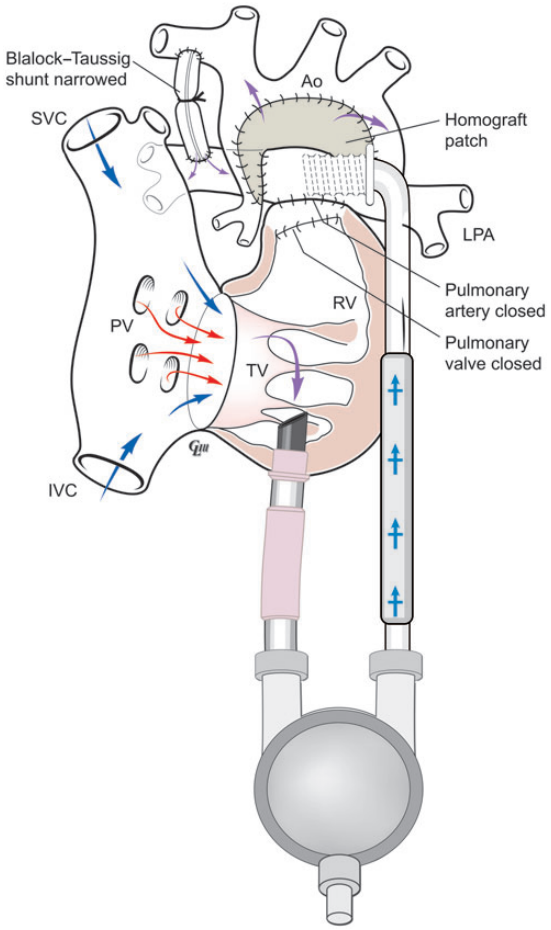

Figure 2: Schematic view of UVAD placement in single-ventricle anatomy after first stage palliation (Norwood with modified BT shunt) of hypoplastic left heart syndrome. The inflow cannula is inserted in the apex of the single right ventricle and the outflow cannula at the level of the Damus–Kaye–Stansel anastomosis, leaving the shunt open to allow the pulmonary circulation.

without significant differences comparing infants, bigger children and adolescents. The mean weight at time of circulatory support was similar in both groups. Tables 1 and 2 describe the demographic characteristics, the diagnosis, the MCS types and the outcome of each individual patient with biventricular and single-ventricle physiology, respectively. In nearly 50% of the cases, with similar frequency in both groups, MCS was established after an episode of cardiac arrest requiring cardiopulmonary resuscitation. The mean overall length of support on the extracorporeal circulation was significantly longer in the biventricular group ($P = 0.03$), with a peak of 219 days in an infant on LVAD with Shone's complex and 61 days in a child after failing Glenn circulation. The duration of mechanical ventilation during MCS was similar in both groups.

Clinical outcomes are reported in Table 4. Morbidity and mortality of MCS for patients with single and biventricular circulation were compared. A greater proportion of patients with univentricular physiology required renal support during MCS ($P = 0.03$), with filter placement during venoarterial ECMO, peritoneal dialysis in the smallest children and continuous venovenous haemofiltration in the biggest. A significant number of new neurological events occurred in patients (6/15, 40%) with biventricular physiology on mechanical assist device ($P = 0.04$), this group had a significantly longer length of the paracorporeal support. Three of these children were in Berlin Heart LVAD: 1 had an embolic event during the 219 days (the longest in this series) of support before successful transplantation; 1 had a stroke at the time of VAD testing and was successfully explanted; 1 developed a neurological event because of recurrent clotting formation that required several Berlin Heart ventricles replacement and switching of the pulsatile circulation to a Levitronix Centrimag® machine with continuous flow. The incidence of tracheostomy for long-term ventilation, chest exploration for bleeding and sepsis did not differ significantly between the groups during MCS.

Five children successfully recovered after MCS, with explantation of the device (3 in the biventricular group and 2 in the single-ventricle group, P = NS). One child with two-ventricle physiology required a second run of MCS 1 year after explantation and died on the waiting list during support with Berlin Heart BIVAD. Eight patients, 4 per group, died during mechanical

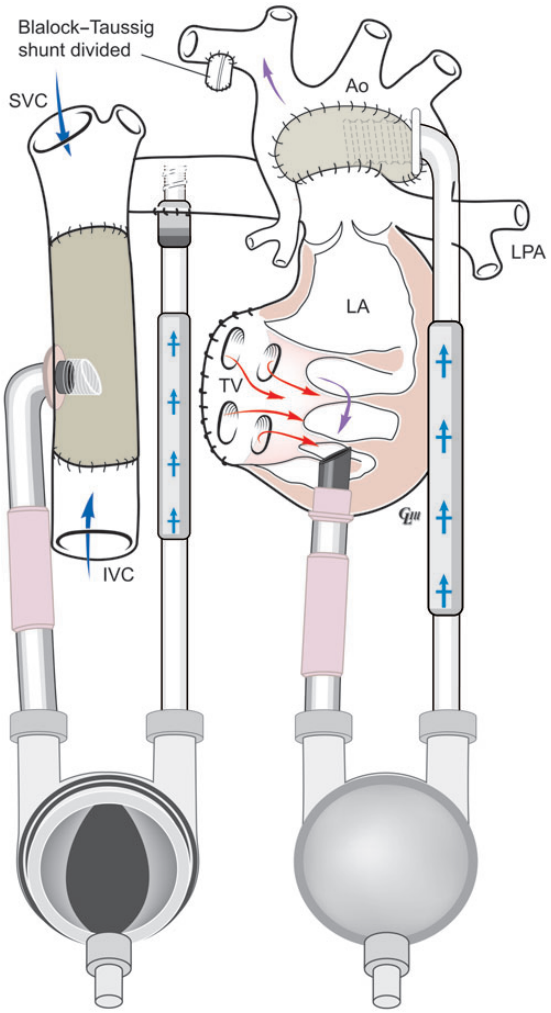

Figure 3: Schematic view of BIVAD placement in single-ventricle anatomy after first stage palliation (Norwood with modified BT shunt) of hypoplastic left heart syndrome. The physiology is converted to a biventricular circulation dividing the systemic venous return from the pulmonary venous return and creating a new chamber joining the superior and the inferior venae cava with a Dacron graft. The pulmonary circulation is established placing the inflow cannula through the Dacron graft and the outflow cannula in the confluence of the pulmonary arteries. The systemic circulation is provided inserting the inflow cannula in the apex of the single right ventricle and the outflow cannula at the level of the Damus–Kaye–Stansel anastomosis. The shunt is disconnected or ligated.

support (P = NS) and 16 patients, 8 per group, were successfully bridge to transplantation (P = NS). Two infants in the biventricular group required a second run of MCS after transplantation for acute graft failure: 1 died after 29 days of Berlin Heart BIVAD for multiorgan failure and 1 was supported for 5 days on ECMO and then successfully retransplanted. In the single-ventricle group, 1 patient had an unsuccessful second run of MCS (ECMO) after transplantation.

The overall survival to recovery/transplantation of MCS in paediatric congenital heart patients was 72% and the overall survival to discharge was 59%. Both, survival to recovery/transplantation (73 vs 71%, P = NS) and survival to discharge (60 vs 57%, P = NS) did not differ significantly when comparing the biventricular and the single-ventricle physiology, respectively.

All children surviving to hospital discharge are alive at an average follow-up of 4.5 ± 3.4 years.

DISCUSSION

The improvement in survival following cardiac surgery for the treatment of congenital heart surgery is a modern day success story [1]. This has, however, generated an increasing number of patients who develop heart failure either acutely or chronically. These patients would ultimately require transplantation for either improvement in quality-of-life or survival [11]. Since the successful use of ECMO for respiratory support, it was just a matter of time before this modality would be used to support this group of patient to transplantation. We first used ECMO to successfully bridge to transplantation in 1998. However, it soon became clear that most of the patients would require cardiac support longer than could be achieved with ECMO. This came in the form of Berlin Heart EXCOR, which was first implanted in 1990 [12]. Since then, with improvement in Berlin Heart technology, implantation techniques and anticoagulation management, there have been several reports of good medium-term support with this device [4–6]. In addition, Berlin Heart has been shown to be superior to ECMO in length and quality of support [10]. However, this prolonged support is not without an increase in morbidity [5, 6].

Berlin Heart has been predominantly used in patients with myocardial disease and there are only a few reports of its use in patients with CHD [4–6]. This is not surprising due to a higher mortality and morbidity associated with its use in this group [13, 14]. However, in a recent paper reviewing the US use of Berlin Heart EXCOR by Almond *et al*. [6], there was no increased risk with the usage of Berlin Heart. Similarly, the use of ECMO prior to insertion of the Berlin Heart was also not a risk factor in the entire cohort. We also found similar results in our overall experience with paediatric MCS [5].

The use of MCS in single-ventricle support still remains a challenge. This is due to complex anatomy coupled with competing physiological demands. Not surprisingly, there are only a few reports in the literature of use of MCS in this group [8, 9]. In patients with Fontan completion our approach has been to undertake ECMO support. This has been a successful strategy for us due to the urgent allocation system for heart transplantation in the UK, which preferentially allocates hearts to the paediatric patients from adult donors. These patients are older and have larger body weight making them suitable for this strategy. However, there have been recent reports of successful LVAD support using a HeartMate device [15] and Berlin Heart [16] in patients who previously had a failing Fontan circulation.

Our strategy in supporting patients with failing bidirectional cavopulmonary connection has evolved over time [9]. These were due to a complex set of interaction between ventricular dysfunction and altered pulmonary resistance. Our initial problems were related to placement of a ventricular chamber commensurate with the body weight recommendation by the Berlin Heart group. But we felt that a larger chamber was required to provide a larger cardiac output than the prescribed size could provide. However, in some patients we found worsening of lung function after an apparent satisfactory initial result from the Berlin Heart insertion, resulting in hypoxia, ventilator dependency and ongoing inotropic support. This necessitated changing these patients to VA ECMO support but still continuing to use the Berlin Heart cannulas, thus essentially converting them to centrally cannulated ECMO. Using this modality, we were able to successfully transplant a patient in semielective condition after extubation on ECMO (Patient 5 in Table 2).

Table 3: Demography

	Two-ventricles, *n* = 15	Single ventricle, *n* = 14	*P*-value
Age at MCS (months)	66 ± 62 (CI 95% 31.4)	46 ± 46 (CI 95% 24.1)	NS
<1 year	3 (20%)	4 (27%)	
1–10 years	9 (60%)	9 (64%)	
>10 years	3 (20%)	1 (9%)	
Weight at MCS (kg)	21 ± 15 (CI 95% 7.6)	14 ± 11 (CI 95% 5.8)	NS
Pre-MCS cardiac arrest	7 (47%)	7 (50%)	NS
Overall length on MCS (days)	56 ± 60 (CI 95% 30.4)	16 ± 16 (CI 95% 8.4)	0.03
Days of ventilation during MCS (days)	21 ± 20 (CI 95% 10.1)	13 ± 12 (CI 95% 6.3)	NS

MCS: mechanical circulatory support.

Table 4: Outcomes of MCS

	Two-ventricles, *n* = 15	Single ventricle, *n* = 14	*P*-value
Renal support during MCS	2 (13%)	7 (50%)	0.03
Neurological events during MCS	6 (40%)	1 (7%)	0.04
Tracheostomy during MCS	6 (40%)	6 (43%)	NS
Chest exploration for bleeding during MCS	3 (20%)	3 (22%)	NS
Sepsis during MCS	4 (27%)	3 (22%)	NS
Explanted	3 (20%)	2 (14%)	NS
Died on MCS	4 (27%)	4 (29%)	NS
Transplanted	8 (53%)	8 (57%)	NS
Survival to recovery/transplantation	11 (73%)	10 (71%)	NS
Post-transplant MCS	2 (13%)	1 (7%)	NS
Retransplanted	1 (7%)	None	NS
Survival to discharge	9 (60%)	8 (57%)	NS
Mortality stratified by age			
<1 years	1/3	2/4	NS
1–10 years	4/9	6/9	NS
>10 years	1/3	0/1	NS

MCS: mechanical circulatory support.

In 1 child with progressive heart failure after Norwood palliation, and severe tricuspid regurgitation and high pulmonary vascular resistance, we tried an experimental approach separating the circulation and using a BIVAD: the pulmonary venous return was separated from the systemic venous return and the superior vena cava (SVC) and inferior vena cava (IVC) were joined together with a 14 mm Dacron tube, the shunt was ligated, a 10 ml Berlin Heart pulsatile pump was implanted with the inflow cannula placed in the artificial connection between the SVC and IVC and the outflow cannula in the pulmonary arteries and another 10 ml Berlin Heart ventricle was implanted inserting the apical cannula in right ventricle and the outflow cannula in the Damus–Kaye–Stansel anastomosis (Fig. 3). The child remained in BIVAD Berlin Heart for 13 days, requiring numerous ventricle changes: for that reason, the MCS was switched to a BIVAD using Levitronix Centrimag for 5 days and subsequently switched to a venoarterial ECMO due to inadequate systemic oxygenation and impaired lung function. In spite of our unsuccessful attempt, we feel that this approach could work in patients with elevated pulmonary vascular resistance.

Single-ventricle support with VAD remains a challenging group; we only had limited success in this group. The patients undergoing successful transplantation in this cohort were lucky to have received a donor organ in a relatively short period. We feel the complex anatomical and physiological nature of failing single ventricle was not conducive to longer support. This is evident in our experience where we had to switch the modality of support to cope with increasingly difficult haemodynamic conditions. Morbidity represents a significant problem in patients requiring MCS for CHD. Patients with single ventricle were particularly prone to renal replacement support ($P = 0.03$). This is not surprising as this is the sickest of the sick group. The management of anticoagulation therapy again remains problematic, since the right equilibrium between clotting and bleeding is difficult to achieve. Despite a meticulous approach to the latter, the number of cerebrovascular events still bedevils the outcomes of children undergoing MCS, representing the leading cause of death in most of the series [4–6]. We found a significant incidence of new neurological events in the biventricular group ($P = 0.04$). This is perhaps due to longer length of support required in this group compared with the patients with single ventricles ($P = 0.03$).

The present clinical experience suggests that children with CHD supported with mechanical assist devices for acute or end-stage heart failure can be satisfactorily bridged to heart transplantation despite the significant cumulative morbidity. Nearly two-third of them survive to discharge after transplantation. Most importantly, single-ventricle when compared with the biventricular circulation does not increase the risk for death before transplantation and hospital discharge.

Conflict of interest: none declared.

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APPENDIX. CONFERENCE DISCUSSION

Dr M. Kostolny *(London, United Kingdom)*: You presented 29 patients basically divided into two groups based on whether they were single or biventricular physiology. Coming from a unit that also has a mechanical and transplantation programme, I know that there is a lot of work behind it.

I would like to ask you to focus on the group of patients with univentricular physiology. You had 14 patients there, and approximately half of those patients were started on VA-ECMO. Only two patients of the whole group of 14 were successfully supported with a VAD in the form of a Berlin Heart. So my question would be: Do you think that VAD support for univentricular physiology really works?

Dr De Rita: I think this is the most important point of this paper, because we know for sure from our experience that if we can have short-term support in the univentricular patients we can achieve a successful transplantation.

And if you have a look at the different settings starting with the Fontan, for example, our policy is to use VA-ECMO in the Fontan patients because we can transplant these bigger children with bigger hearts and chest walls with an adult size heart and they can receive an organ from the adult donor pool. In the Fontan patient, the length of support on ECMO is quite short. And I can reasonably say that we can transplant this kind of patient within a month after putting the patient on the transplant list.

Regarding the Glenn circulation, we know that we can't assist these patients on VA-ECMO with the classic approach through the neck, so we have to give something different. And we change our management with the univentricular VAD in these patients because of the complex anatomy and the complex physiology. One of the problems was to use a bigger ventricle compared to the size of the ventricle referred by the Berlin Heart, because with the bigger ventricle we could achieve more cardiac output. But in 4 of 6 patients we had to change the support to VA-ECMO because of worsening of the lung function. And with this strategy we were able to transplant one patient.

Dr Kostolny: Okay, thank you, I think that answers my question. But I also noticed that those two patients who were supported with VAD had a relatively short time on support in the univentricular group. So it just supports my question: Does it really work? Because you can't really say that if you have only a short time on support.

Anyway I would like to ask you another question. Can you perhaps elaborate more on the subgroup of Fontan patients? I mean, were they all patients with impaired function or failing Fontan physiology? In other words, what was the time interval between the surgery and support? And I'm asking that because you had some patients who recovered, for example, who were explanted, and even one patient in the Fontan group.

Dr De Rita: Yes. But this patient was successfully transplanted a few weeks after the explantation. Anyway, I think the reason for using the VA-ECMO is because it's difficult also to distinguish whether it's a pump problem or a failing circulation. So we can easily use the VA-ECMO to support Fontan patients also because I think we can easily find an organ for these patients. You know, we are one of the two transplant centres in the UK.

Dr Kostolny: Thank you. I have one more question. There is a relatively high incidence of neurological events, especially in the biventricular group. Could you just briefly perhaps mention your anticoagulation protocol.

Dr De Rita: The anticoagulation protocol starts with heparin infusion usually after 36 or 48 h. And we manage the coagulation with the anti-Xa level. So after reaching one week's satisfactory level of anti-Xa, we start the antiplatelet drugs. And in some children we use warfarin, but basically in paediatric patients that have to stay in the hospital, at least in HDU with a VAD, we prefer to place a line for long-term infusion of heparin.

Dr H. Lindberg *(Oslo, Norway)*: I saw that there was a high incidence of renal failure in your patients, especially in the two-ventricle group. So did any of your patients need a renal transplant or have persistent renal failure afterwards?

Dr De Rita: No. Renal support was used in a patient with ECMO in the form of filtration during ECMO, or in the form of CVVH in the bigger children, but none of the patients required renal transplantation.

Dr Lindberg: And as you said, this is the sickest of the sickest. So especially in the single-ventricle group, do you have any information on the long-term survival?

Dr De Rita: Oh, the survival of all the patients that we transplanted is good. But I don't have any data about recent follow-up.

Dr Lindberg: I mean survival after 5–10 years, or something?

Dr De Rita: I don't know about 5–10 year survival, but they are alive at the moment.

Dr I. Afridi *(Rawalpindi, Pakistan)*: My question is: When these kids are stable, can they be taken home for social welfare reasons during the bridging procedures or not?

Dr De Rita: Out of the hospital, you mean?

Dr Afridi: Yes.

Dr De Rita: No. The best we can do for these children is to put them in the high dependency unit, but not out of the hospital, because at the moment we don't have any transportable device as in the adult patients, so they have to stay in the hospital.