First serial in vivo results of mechanical circulatory support in children with a new diagonal pump

Thilo Fleck\textsuperscript{a,}\textsuperscript{*}, Christoph Benk\textsuperscript{b}, Rolf Klemm\textsuperscript{b}, Johannes Kroll\textsuperscript{b}, Matthias Siepe\textsuperscript{a}, Jochen Grohmann\textsuperscript{a}, René Höhn\textsuperscript{a}, Frank Humburger\textsuperscript{a}, Friedhelm Beyersdorf\textsuperscript{a} and Brigitte Stiller\textsuperscript{a}

\textsuperscript{a} Department of Congenital Heart Disease and Paediatric Cardiology, University Heart Centre Freiburg, Freiburg, Germany
\textsuperscript{b} Department of Cardiovascular Surgery, University Heart Centre Freiburg, Freiburg, Germany
\textsuperscript{c} Department of Anesthesiology, University Medical Center Freiburg, Freiburg, Germany

\* Corresponding author. Department of Congenital Heart Disease and Paediatric Cardiology, University Heart Centre Freiburg, Mathildenstrasse 1, 79106 Freiburg, Germany. Tel: +49-761-27046380; fax: +49-761-2704680; e-mail: thilo.fleck@universitaets-herzzentrum.de (T. Fleck).

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Abstract

OBJECTIVES: Mechanical circulatory support (MCS) is a rescue therapy for infants and children suffering from severe cardiorespiratory failure with specific system-related complications like bleeding, thromboembolism and device failure. Novel circuit components for temporary MCS with improved haemodynamic properties may improve patients' outcome and reduce system-related morbidities. The Deltastream\textsuperscript{®} DP3 (Medos Medizintechnik AG, Stolberg, Germany) is a newly designed rotational pump with a diagonally streamed impeller that can be used in children of all ages (priming volume 16 ml, flow 0–8 l/min). The aim of this study was to analyse the feasibility and safety of the DP3 pump system in children.

METHODS: We retrospectively investigated a consecutive series of 16 children [median age 0.9 months (0.1–55 months), median weight 3.2 kg (2.5–14 kg)]. The DP3 circuit was used 22 times in these children for different indications: (I) extracorporeal life support (ECLS) in post-cardiotomy heart failure \( n = 11 \), (II) ECLS in cardiopulmonary resuscitation (CPR) \( n = 7 \) and (III) extracorporeal membrane oxygenation (ECMO) in acute respiratory distress syndrome (ARDS) \( n = 4 \).

RESULTS: Median duration of MCS was 4 days (0–18 days), 12 patients (75\%) were weaned successfully from MCS, 4 of these children (25\%) died after weaning, with a median survival time of 15 days (6–28 days). Overall survival rate was 50\% and all 8 survivors were discharged home without neurological injury. There was no case of severe bleeding, thromboembolic complications or device failure. Mean lactate dehydrogenase (LDH) before MCS was 700 (±384) U/l, and increased to a maximum of 2279 (±2635) U/l during MCS \( P = 0.04 \). Baseline D-dimer values were 3.4 (±3.0) mg/l and rose significantly to 19.5 (±11.5) mg/l during MCS \( P < 0.001 \). The mean of the highest plasma-free haemoglobin during MCS was 21.0 (±42.9) mg/dl. The increase in plasma-free haemoglobin correlated moderately with the duration of MCS (Pearson’s \( r = 0.78 \)).

CONCLUSION: The use of the Deltastream\textsuperscript{®} DP3 seems to be safe and effective for MCS in children and may show a low degree of haemolysis. We observed no system-related complications and an overall good outcome in this demanding patient cohort.

Keywords: Congenital heart disease • Mechanical circulatory support • Extracorporeal life support • Extracorporeal membrane oxygenation • Rotational pump • Children

INTRODUCTION

Mechanical circulatory support (MCS) is an emergency treatment for children and neonates. It can be conducted as extracorporeal life support (ECLS) with venous-arterial cannulation in case of severe cardiac or cardiorespiratory failure after cardiopulmonary resuscitation (CPR) or in post-cardiotomy heart failure [1]. Extracorporeal membrane oxygenation (ECMO) with venovenous cannulation is used in cases of severe respiratory distress to ensure blood oxygenation [2].

ECLS and ECMO systems can be used as a bridging therapy to transplantation [3] or to recovery, but are associated with specific complications such as bleeding, thromboembolism and infections. There are few devices designed for the paediatric population. A recent US survey showed that roller-pumps are still in use in 70\% of neonatal and paediatric ECLS [4]. However, the use of centrifugal pump systems in ECLS has improved patient safety and outcome [5]. The implementation of the newest circuit components and designs might improve patients’ outcomes by lowering system-related morbidities.

The Deltastream\textsuperscript{®} DP3 (Medos Medizintechnik AG, Stolberg, Germany) is a rotational pump with a diagonally streamed impeller (Fig. 1). This diagonal pump system unifies the advantages of radial and axial pump systems: high hydraulic performance as in radial pumps combined with the low inertia and small size of an axial pump. The result is a small pump system with a priming
volume of ~16 ml generating a high flow of up to 8 l/min and producing pressures up to 600 mmHg [6]. The system is capable of operating at speeds up to 10,000 rpm. The flow control allows flow adjustments even at flow ranges below 0.5 l/min, and enables application in patients ranging from neonates to adults. The pump can be administered with optional operating methods producing pulsatility at 40–90 bpm, already tested successfully in vitro [7].

The pump circuit is composed of a single-use diagonal blood pump, motor, console and flow probe; it has obtained its CE Mark for 7 days of use. Several control systems offer safety functions: the preload control prevents cannula aspiration; the zero-flow mode allows even a brief interruption of the flow without backflow. This pump is multifunctional and can be used for all kinds of MCS such as ECMO [8], ECLS or as a ventricular assist device (VAD) for the right ventricular assist device or left ventricular assist device and as uni- or biventricular support. Wang et al. undertook a technical in vitro validation of this device, examining the relationship between blood flow, pump speed and circuit pressures [7]. The first preclinical studies in adult sheep demonstrated the DP3 pump’s ability to run for 7 days without incident in 5 of 6 animals while demonstrating a low degree of haemolysis in this animal model [9].

The aim of this study was to analyse the safety and feasibility of this novel pump in paediatric MCS and report about the first serial in vivo experience.

**MATERIALS AND METHODS**

We retrospectively investigated a consecutive series of children undergoing MCS with the Medos Deltastream® DP3 diagonal pump at the University Heart Centre Freiburg. The period of review was from December 2009 to February 2013. Approval from our local ethics committee to investigate and publish the data was obtained.

The extracorporeal circuit

The Deltastream® DP3 (MEDOS Medizintechnik AG diagonal pump is an updated version of the Deltastream® DP2 (MEDOS Medizintechnik AG). The torque transmission between the drive and pump head works by means of magnetic coupling between the driver and pump head. The old DP2 is pivot-mounted on a shaft for the impeller and driven by four magnets. In the new DP3, the impeller is pivot-mounted with a ring magnet and a ceramic ball-bearing for the impeller (Fig. 1). The DP3 pump is attached and controlled via a driving console: the Medos Delta Stream Console. The console consists of a detachable TFT-touchscreen monitor to visualize the course of all the perfusion parameters like flow, rotational speed, pressure and temperature (Fig. 2).

*Figure 1: A photo of the Deltastream® DP3 (MEDOS Medizintechnik AG) diagonal blood pump, which combines an axial and a radial pump. The impeller is pivot-mounted with a ring magnet and a ceramic ball-bearing associated with a low friction loss. Because of this new impeller design, the DP3 pump does not require a seal to prevent leakage into the driver.*

*Figure 2: This original photo shows the Medos Delta Stream Console being used in an infant. The detachable TFT-touchscreen monitor in the middle visualizes a flow of 0.78 l/min at a rotational speed of 6650 rpm. The combined heater-cooler device Deltastream® HC (MEDOS Medizintechnik AG) underneath is set at 35°C to regulate the patient’s temperature.*
Furthermore, the paediatric temporary MCS circuit at our institution (Fig. 3) consisted of either a plasma tight polyethylene hollow fiber oxygenator HILITE 800LT (MEDOS Medizintechnik AG) for flow rates up to 0.8 l/min with a static priming volume of 55 ml or a HILITE 2400LT oxygenator for flow rates between 0.8 and 2.4 l/min. The extracorporeal circuit is coated with reoparin to reduce thrombogenicity.

We used thin-walled polyurethane arterial cannulae with inner diameters from 8 to 16 Fr depending on the patient’s weight and venous cannulae with bevelled metal multiport tips in paediatric sizes from 12 to 20 Fr. A special cone tube measuring from 3/8 to 1/4 connected the 1/4 oxygenator connector to the pump’s 3/8 connector. We used the combined heater–cooler device Deltastream® HC (MEDOS Medizintechnik AG) to regulate patient temperature (Figs 2 and 3).

The ECLS circuit was primed with a crystalloid solution (Jonosteril, B. Braun Melsungen, Germany), and packed human red blood cells were added into the circuit to maintain the blood haematocrit at a level above 30%.

Patients

MCS with the DP3 was performed in 16 children (8 females, 8 males). Median age was 0.9 months with a range from 0.1 to 55.7 months. Median weight of the children was 3.2 kg, ranging from 2.5 to 14.4 kg. The patients’ height was a median of 52 cm (47–90 cm). Lowest body surface area was 0.18 m², with a median of 0.22 m² and a maximum of 0.61 m².

Patients’ management

All children were intubated and ventilated mechanically. Sedation was maintained with continuous intravenous fentanyl (4–20 µg/kg/h) and midazolam (4–20 µg/kg/min). Heart rate, systemic arterial blood pressure in the radial or femoral artery, transcutaneous oxygen saturation (SaO₂) and central venous pressure were monitored continuously, as is routine in the paediatric cardiac intensive care unit (PICICU).

Depending on the indication for MCS, the patients were divided into three different indication groups.

Figure 3: Original photo of the paediatric mechanical circulatory support circuit with the Deltastream® DP3 pump head connected to the hollow fibre oxygenator HILITE 800LT (MEDOS Medizintechnik AG). The blue tubes connect the heater–cooler device to the oxygenator to directly cool or heat the blood stream.

Cardiac: ECLS in early post-cardiotomy heart failure. MCS was performed in patients suffering from early post-cardiotomy heart failure, who could not be weaned from cardiopulmonary bypass (CPB), after surgical repair of complex cardiac malformations. Decisions to initiate ECLS were based on a consensus between the operating cardiac surgeon, anaesthesiologist, perfusionist and paediatric cardiologist in the operating theatre.

The adequacy of cardiac output was evaluated according to the blood pressure, heart rate, transcutaneous oxygen saturation, blood-gas analysis, serum lactate and central venous oxygen saturation together with cerebral oxygen saturation measured by near-infrared spectroscopy and urine output. Myocardial contractility, furthermore, was evaluated during weaning from CPB by transoesophageal echocardiography. Excessive need for catecholamines like adrenaline or noradrenaline (>0.3–0.5 µg/kg/min) to transfer the patient from the operating theatre to the PICICU was not acceptable and ECLS was implanted to facilitate myocardial recovery.

CPR: ECLS in prolonged CPR. During circulatory arrest, we performed CPR following the European Resuscitation Council guidelines, while a resuscitation team of cardiac surgeons and perfusionists was called. If adequate circulation did not resume within 20 min, the DP3 circuit was implanted via either a standard median sternotomy with direct cannulation of the atrium and aorta or via peripheral cannulation of the jugular vein and carotid artery via the Seldinger technique. The left atrium was not cannulated for left ventricular (LV) venting. A flow of ~3.5–4.5 l/min/m² was established and the blood temperature lowered immediately to 32–34°C using the heat exchanger in the ECLS circuit for at least 24 h as a neuroprotective strategy. Transcutaneous oxygen saturation, if achievable in non-pulsatile flow, was kept between 90 and 95% and arterial oxygen partial pressure maintained ~100 mmHg by regulating gas flow and fractionally inspired oxygen using the oxygenator of the ECLS circuit, to avoid oxidative stress after circulatory arrest.

Respiratory: ECMO in acute respiratory distress syndrome. Patients with acute respiratory distress syndrome (ARDS), despite optimized mechanical ventilation and optimal adjuvant treatment, received ECMO if the oxygenation index (OI) (OI = (100 × fractionally inspired oxygen × mean airway pressure)/PaO₂) was >40 or in case of severe respiratory acidosis [10].

The ECMO circuit was established by cannulating the jugular vein with an Avalon™ Bi-caval Dual Lumen Catheter. ECMO flow was adjusted to ~3.5–4.5 l/min/m², and fractionally inspired oxygen and gas flow of the oxygenator were regulated to achieve normal blood gases. Mean airway pressure on mechanical ventilation was usually lowered by reducing positive inspiratory pressure to diminish shear stress to the lung, and fractionally inspired oxygen on mechanical ventilation was lowered to 21% to allow lung recovery without exacerbating oxidative stress.

Anticoagulation

After implementing reoparin-coated extracorporeal circulation, anticoagulation was started within the first 24 h as long as there was no relevant bleeding. We anticoagulated our patients starting with heparin doses of 100 IU/kg/day increased stepwise, if necessary, to up to 700 IU/kg/day to keep the activated clotting time (ACT) at 150–180 s. Whether we moved towards the upper or
lower range of the ACT depended on the presence or absence of bleeding and the level of D-dimers.

To create a stable heparin effect, antithrombin III was monitored and substituted if it fell below 80%. Fibrinogen was kept at over 200 mg/dl and platelets were substituted when lower than 100,000/µl.

**Laboratory values**

Lactate dehydrogenase (LDH) levels were measured before and during MCS to estimate the degree of red blood cell destruction due to increased shear stress. Furthermore, we measured plasma-free haemoglobin to evaluate the degree of haemolysis. Plasma-free haemoglobin is present in the serum during significant haemolysis—when the serum’s haemoglobin concentration exceeds 100 mg/dl and haemoglobin can no longer bind to haptoglobin.

We measured D-dimers, which are only present in blood plasma when the coagulation system has been activated (i.e. because of thrombosis) pre-MCS in 12 of our patients. We compared the baseline values of D-dimers to the highest level during MCS in order to estimate the degree of coagulatory system activation.

**Statistics**

Depending on the normality of their Gaussian distribution, continuous measurements are presented as either the mean ± standard deviation or median (interquartile range). Descriptive measures were used to summarize patient characteristics and outcomes where appropriate.

Referring to the normally distributed laboratory values for haemolysis and thrombosis; we applied the Student’s t-test to determine whether the difference in the values before and during MCS was significant. P-values under 0.05 were considered statistically significant.

Pearson correlation coefficient (Pearson’s r) was used to measure the linearity of the correlation between two variables.

**RESULTS**

**Mechanical circulatory support indications**

In the 16 children we observed, the Deltastream® DP3 system was implanted 22 times for different indications (Table 1). An overview of the patients’ course is illustrated in Fig. 4. The indication for ECLS was early post-cardiotomy heart failure in 50% of the cases (Table 2). During this study’s observation period, we performed 450 operations in children with congenital heart disease. An ECLS system had to be employed in 1.7% of the operations. The 8 patients requiring post-cardiotomy MCS were mainly neonates with complex cardiac malformations. During the observation period, the Deltastream® DP3 system was used in all but one of the MCS cases. There were 7 cases (32%) in which we implanted the MCS with the Deltastream® DP3 pump during CPR. We had to perform ECMO in ARDS in 4 cases (18%). Two of our children had the DP3 implanted three times (Tables 1 and 2) for different indications. Two patients were on the rotational pump twice.

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**Table 1: Data overview of all patients**

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Sex (F/M)</th>
<th>Age (months)</th>
<th>Weight (kg)</th>
<th>Length (cm)</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>5.0</td>
<td>5.1</td>
<td>57</td>
<td>HLHS after extended Norwood II operation</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>5.7</td>
<td>14.4</td>
<td>90</td>
<td>Adenovirus infection</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>4.7</td>
<td>5.6</td>
<td>65</td>
<td>Klebsiella pneumonia</td>
</tr>
<tr>
<td>4.1</td>
<td>F</td>
<td>1.4</td>
<td>3.2</td>
<td>52</td>
<td>Myocarditis</td>
</tr>
<tr>
<td>4.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lung bleeding</td>
</tr>
<tr>
<td>4.3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Heart failure</td>
</tr>
<tr>
<td>5.1</td>
<td>M</td>
<td>0.3</td>
<td>3.5</td>
<td>52</td>
<td>d-TGA with intramural left coronary artery</td>
</tr>
<tr>
<td>5.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>After 1. Weaning from CPB</td>
</tr>
<tr>
<td>5.3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>After 2. Weaning from CPB</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>0.4</td>
<td>3.4</td>
<td>53</td>
<td>d-TGA after ASO, pericardial tamponade</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>0.1</td>
<td>3.2</td>
<td>52</td>
<td>Tricuspid atresia with ALCAPA</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>0.3</td>
<td>2.8</td>
<td>52</td>
<td>HLHS after Norwood I operation</td>
</tr>
<tr>
<td>9.1</td>
<td>F</td>
<td>0.4</td>
<td>3.2</td>
<td>49</td>
<td>Ebstein anomaly with PA after corrective surgery</td>
</tr>
<tr>
<td>9.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Ebstein anomaly after Starnes operation</td>
</tr>
<tr>
<td>10</td>
<td>F</td>
<td>1.5</td>
<td>2.5</td>
<td>48</td>
<td>Double outlet right ventricle, J-TGA</td>
</tr>
<tr>
<td>11</td>
<td>F</td>
<td>0.5</td>
<td>2.8</td>
<td>51</td>
<td>Double outlet right ventricle, PA, embolism into the RCA</td>
</tr>
<tr>
<td>12</td>
<td>F</td>
<td>4.1</td>
<td>4.2</td>
<td>55</td>
<td>HLHS after Norwood I, preclinical CPR</td>
</tr>
<tr>
<td>13</td>
<td>M</td>
<td>40.0</td>
<td>11.8</td>
<td>88</td>
<td>Adenovirus and Aspergillus pneumonia</td>
</tr>
<tr>
<td>14</td>
<td>M</td>
<td>1.5</td>
<td>2.9</td>
<td>47</td>
<td>Shone complex after Norwood type operation</td>
</tr>
<tr>
<td>15.1</td>
<td>M</td>
<td>0.5</td>
<td>2.9</td>
<td>51</td>
<td>Norwood I operation, shunt closure</td>
</tr>
<tr>
<td>15.2</td>
<td>F</td>
<td>0.1</td>
<td>3.0</td>
<td>49</td>
<td>Shunt revision</td>
</tr>
<tr>
<td>16</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>ccTGA, cAVSD and PA</td>
</tr>
</tbody>
</table>

All children are listed according to their patient number. Those with asterisks received mechanical circulatory support more than once. Sex: M = male, F = female.

Diagnosis: HLHS: hypoplastic left heart syndrome; TGA: d-transposition of the great arteries; ASO: arterial switch operation; ALCAPA: anomalous left coronary artery arising from the pulmonary artery; PA: pulmonary atresia; RCA: right coronary artery; CPR: cardiopulmonary resuscitation; cAVSD: complete atrioventricular septal defect; CPB: cardiopulmonary bypass.
In only 1 patient, presenting severe bleeding and pericardial tamponade leading to circulatory arrest and CPR, were we unable to establish sufficient flow after ECLS implantation because of the lack of preload that was not reversible with volume resuscitation. One child had low cardiac output after CPB and displayed no signs of myocardial recovery after 13 days; ECLS was, therefore, discontinued in accordance with the parents' wishes. One boy suffered severe ARDS after an adenovirus infection during chemotherapy for acute lymphoblastic leukaemia. The DP3 ECMO system was implanted in the paediatric intensive care unit on an emergency basis for severe hypoxaemia, and he was transferred to the PCICU. He was sufficiently oxygenated with the ECMO system for 18 days, but suffered pneumonia in addition to Aspergillus, thus the lung failed to recover and treatment was stopped in accordance with the parents' wishes.

None of our patients sustained severe bleeding or relevant thromboembolic events during MCS. In case of relevant post-operative bleeding, anticoagulation was safely paused for up to 48 h. We did not have to discontinue MCS with the Deltastream® DP3 because of technical problems or system-related complications in any of the patients. Elective pump changes were made after at least 7 days of continuous use.

### Patients' outcomes

Eight of our patients (50%) were discharged home in stable respiratory and haemodynamic condition. Neurological examination revealed no pathologies in all 8 patients at discharge.

One specific case required three different pump phases. A 1.4-month old baby with fulminant myocarditis was on ECLS and was successfully weaned after 8 days. Two days after weaning from the ECLS, she suffered lung bleeding with consecutive ARDS, probably because of a generally activated coagulation system; we, thus, put her on ECMO in the PCICU by cannulating the jugular vein. After 1 day on ECMO, she developed heart failure again, and the ECMO was switched to ECLS by cannulating the jugular vein and carotid artery. She was weaned successfully once again after 7 days on ECLS. At the last follow-up, 14 months after having undergone a total of 16 days of MCS, this girl is in excellent health and displays normal neurocognitive development.

### Haemolysis

Mean LDH (as an indirect marker for haemolysis) was 700 (±384) U/l in all patients before MCS. The normal paediatric laboratory values for children aged between 1 month and 5 years is 150–360 IU/l. The mean value of the maximum LDH on MCS was 2279 (±2635) U/l. Compared with the baseline LDH, the LDH level's increase was slightly significant with a P-value of 0.04. Maximum LDH values, however, showed no correlation with the duration of MCS (Pearson's r: 0.41).

The mean value of the highest plasma-free haemoglobin during MCS was elevated 21.0 (±42.9) mg/dl compared with the paediatric standard values of <10 mg/dl. The correlation between plasma-free haemoglobin and the duration of MCS revealed moderate linearity (Pearson's r: 0.78).

### Thrombosis

Baseline D-dimer values were 3.4 (±3.0) mg/l and rose significantly to 19.5 (±11.5) mg/l during MCS (P < 0.001). However, there was
no correlation between maximal D-dimer levels and the duration of MCS (Pearson’s r: 0.38).

**DISCUSSION**

In our study, we present the first serial in vivo results of MCS with the new Deltastream® DP3 rotational pump. The DP3 was used 22 times in these 16 children for different indications such as ECLS in heart failure after cardiac surgery, or in prolonged CPR, as well as ECMO for lung failure.

**Patients’ outcomes and mortality**

The median duration of MCS in our children was 4 days, and 71% of them were weaned successfully. In the Extracorporeal Life Support Organization (ELSO) registry, the overall weaning rate was 75%, but in the registry’s cardiac group, weaning was feasible in only 59% of the children [1]. Our children’s overall survival rate was 50%, and all of them were discharged home after MCS following normal neurological examination results. The results from a systematic neurological follow-up with neurodevelopmental testing and magnetic resonance imaging of the brain are pending. Our overall survival rate is slightly lower than 63% in the ELSO registry; however, 81% of our cases presented a cardiac indication for MCS. Only 41% of the cardiac children in the ELSO registry survived to discharge. As we had so few patients, it would have been statistically unfeasible to break them down into age and indication groups. A clinical trial with a comparable paediatric population reported results following MCS using the Endumo® 200 system with the ROTAFLOW® centrifugal pump (Maquet, Rastatt, Germany) [11]. The Endumo group in that study had a weaning rate of 56.3%, and 50% of their children were discharged. However, their median duration of MCS was considerably longer (7 days) than ours, and their outcomes might be significantly influenced by different weaning concepts.

**Mechanical circulatory support complications**

None of our children died from complications (like thromboembolism or haemorrhage) related to the MCS system or the DP3.

**Table 2: Data overview of all patients**

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Duration of MCS (days)</th>
<th>Indication of MCS (groups)</th>
<th>Type of cannulation (v-a/v-v)</th>
<th>Site of cannulation (cardiac/peripheral)</th>
<th>Weaning from MCS (yes/no)</th>
<th>Discharged home (yes/death)</th>
<th>Death after weaning (days)</th>
<th>Cause of death</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12</td>
<td>I. Cardiac</td>
<td>v-a</td>
<td>Cardiac</td>
<td>Switch to Berlin-heart</td>
<td>Death</td>
<td></td>
<td>Lack of myocardial recovery</td>
</tr>
<tr>
<td>2</td>
<td>7</td>
<td>III. ARDS</td>
<td>v-v</td>
<td>Peripheral v.jug</td>
<td>Yes</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>III. ARDS</td>
<td>v-v</td>
<td>Peripheral v.jug</td>
<td>Yes</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.1</td>
<td>8</td>
<td>II. CPR</td>
<td>v-a</td>
<td>Cardiac</td>
<td>Peripheral v.jug/a.carotis</td>
<td>Yes</td>
<td></td>
<td>Death 28</td>
</tr>
<tr>
<td>4.2</td>
<td>1</td>
<td>III. ARDS</td>
<td>v-v</td>
<td>Peripheral v.jug</td>
<td>Yes</td>
<td>Yes</td>
<td></td>
<td>Death on list to transplant</td>
</tr>
<tr>
<td>4.3</td>
<td>7</td>
<td>II. CPR</td>
<td>v-a</td>
<td>Peripheral v.jug</td>
<td>Yes</td>
<td>Yes</td>
<td></td>
<td>Cardiac tamponade Lack of myocardial recovery</td>
</tr>
<tr>
<td>4.4</td>
<td>3</td>
<td>I. Cardiac</td>
<td>v-a</td>
<td>Cardiac</td>
<td>Yes</td>
<td>No</td>
<td>Death 6</td>
<td>Brain death after preclinical CPR</td>
</tr>
<tr>
<td>4.5</td>
<td>6</td>
<td>II. CPR</td>
<td>v-a</td>
<td>Cardiac</td>
<td>Yes</td>
<td>No</td>
<td>Death 8</td>
<td>Sepsis</td>
</tr>
</tbody>
</table>

All patients are listed with their patients’ number. Patients were divided into three mechanical circulatory support indication groups: (I) Cardiac: ELS in early post-cardiotomy heart failure, (II) CPR: ELS in prolonged CPR and (III) ARDS: ECMO in ARDS. The two possible types of cannulation where: venous-arterial (v-a) or venovenous (v-v). Cardiac cannulation was performed after median sternotomy with cannulation of the right atrium and the ascending aorta. Peripheral cannulation was performed in the Seldinger technique by cannulation of the jugular vein (v.jug.) with a Bi-caval Dual Lumen Catheter (v-v) or venous-arterial (v-a) by cannulation of the jugular vein and the carotid artery (a.carotis).
pump itself. Furthermore, we experienced no technical complications such as sudden cessation of the pump or rupture of any components in the ECLS or ECMO system. This stands in contrast to a retrospective analysis of the ELSO database which revealed that 15% of those ECLS patients experienced a mechanical component failure associated with the duration of ECLS [12].

**Thrombogenicity and haemolysis**

One of the theoretical benefits of the DP3 is the diagonal blood flow through the pump, which aims to produce less haemolysis than other pump systems [13]. Because of the new impeller design, the DP3 pump does not require a seal to prevent leakage into the driver, and this may prevent clotting in the pump. Prototype animal testing revealed low thrombogenicity and haemolysis associated with the DP3 blood pump, and only minuscule thrombus formations on the rotor or bearing pin (not altering the pump’s function) were observed in all survivors [9]. An animal study group who employed the Levitronix UltraMag reported similar findings (Levitronix LLC, Waltham, MA, USA), namely small thrombi within the impeller blade during the in vivo testing in a lamb model [14]. In our study, we observed no large thrombi (which cause the MCS system to stop working). D-dimers as a marker for thrombogenicity showed a significant increase during MCS in our study population, which can be explained not just by the flow through the pump itself, but by the thrombogenicity of the oxygenator, tubings and any other component in the MCS circuit as well. We noted a slightly significant increase in LDH levels during MCS. However, LDH levels also increase after cardiac surgery and may not only be associated with haemolysis. Plasma-free haemoglobin, a more specific parameter for haemolysis, was only slightly increased, and this increase correlated with the duration of MCS. A similar increase in plasma-free haemoglobin was reported during in vivo use of the Levitronix UltraMag in lambs [14].

An in vitro study compared the degree of haemolysis produced by the ROTAFLOW® and CentriMag (Thoratec Corporation, Pleasanton, CA, USA) centrifugal flow devices [15]. The blood trauma performance of the ROTAFLOW device was similar or better compared with the CentriMag pump, which had to operate at higher average pump speeds in order to maintain a constant flow of 4.2 l/min [15].

**Technical considerations**

The DP3 pump is non-occlusive; limiting the risk of creating extreme negative pressures and cavitation bubbles—an advantage over the roller pump. In an in vitro setting, Wang et al. [7] showed that the Medos Deltastream® DP3 generates effective pulsatile flow without backflow and that it provides higher flow rates and pressures in the pulsatile mode than in the continuous-operation mode. The pump, therefore, might meet the requirements of a new perfusion concept. However, we did not carry out an in vivo test of the pulsatile operation mode in this study, and thus cannot judge whether its use is beneficial in children.

Unlike the older DP2 pump originally designed for cardiac surgery only, the DP3 has received approval for usage in Europe for up to 7 days of continuous use. We experienced no system-related complications during MCS lasting as long as 18 days. However, for safety reasons, we changed the entire DP3 system after at least 7 days, which is easy and quick to do with the help of a talented team of intensivists, perfusionists and cardiac surgeons. The whole procedure can be done in the intensive care unit with minimal blood loss and no flow phase lasting <30 s. It may be feasible to use this pump for longer than 7 days, but that was not possible during our study, as it would have exceeded the pump’s clinically approved duration of use. Long-term testing of this system should be done in an in vitro or animal model in order to judge whether its continuous use for >7 days is conceivable.

The pump system’s flexible-position option permits shortened tube lengths to minimize priming volumes and reduce blood contact with foreign surfaces. The minimized blood contact with foreign surfaces may result in lower activation of the coagulation system and a diminished inflammatory response. The ROTAFLOW® centrifugal pump in comparison has a higher priming volume (32 ml) and demonstrated thrombus formation in the LV cavity in 2 children with myocarditis [11].

Another centrifugal pump applicable in paediatric MCS is the PediV AS (Levitronix LLC) [16, 17]. It has a priming volume of 14 ml and its advantage over the DP3 pump system is CE approval for 30 days of use. Preclinical studies of its pump system in bovine models showed good results with low haemolysis and thrombogenicity and low degrees of platelet activation [18]. Like the DP3, the PediVAS can be used in a pulsatile mode; it revealed good haemodynamic performance during in vivo testing [19]. However, the PediVAS has a maximum pump flow of 1.7 l/min with attached cannulae and is therefore applicable in a smaller range of patients. Clinical in vivo results of the PediVAS in a paediatric population have not yet been published. Further investigations of the clinical use of new MCS components in this challenging population of patients are necessary in order to identify the device demonstrating the best performance and lowest complication rate.

**Limitations**

Unfortunately, our results are limited by the fact that we were unable to evaluate exactly the inflammatory response, as our data are retrospective. Furthermore, our data can only be considered preliminary because of the small number of patients.

**CONCLUSION**

We have demonstrated in this study that the new Deltastream® DP3 pump system is safe and effective for MCS in children and seems to produce only a low degree of haemolysis. It has since been adopted as the standard blood pump for MCS in neonates and children in our institution.

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