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Mechanical support of the functionally single ventricle

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CHILDREN WITH A FUNCTIONALLY SINGLE ventricle constitute just over 1% of congenital cardiac defects.[1] A majority of children with the functionally univentricular circulation undergo a three-staged reconstruction to achieve completion of the Fontan circulation. The first stage is usually performed in the neonatal period, and is either banding of the pulmonary trunk, an aorto-pulmonary shunt alone, or the shunt included as part of the first stage of reconstruction. In recent years, a conduit placed from the right ventricle to the pulmonary arteries is being used as an alternate source of flow of blood to the lungs. The second stage is the bidirectional cavopulmonary anastomosis, the two surgical variations being the so-called "hemifontan", and "bidirectional Glenn" procedures, while the third stage is the completion of the Fontan circulation, the two surgical variations being either construction of a lateral tunnel, or placement of an extra-cardiac conduit, each being possible with or without a fenestration. In many centres, patients with the functionally univentricular circulation make up one-fifth of the total surgical volume. The syndrome of low cardiac output is quite common in this population through all three stages of reconstruction, and some of these patients will eventually require cardiac transplantation. While conventional therapy, with inotropic support and afterload reduction, remains the mainstay of therapy for the failing heart in children, mechanical support is being increasingly used.[3] Most of this experience is limited to extracorporeal membrane oxygenation.[2–5] In this review, we discuss the current experiences with extracorporeal membrane oxygenation in patients with a functionally univentricular circulation, and describes some of their unique features. We also focus on the pulsatile ventricular assist devices capable of providing support over the longer term, and other new devices that may have a role in the future in these patients.[6]

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Types of mechanical support

Mechanical support can be divided into the following categories:

- short-term (less than 30 days) mechanical support devices:
  - extracorporeal membrane oxygenation
  - centrifugal ventricular assist device
- long-term (more than 30 days) mechanical support devices:
  - pulsatile types
  - axial types.

Extracorporeal membrane oxygenation in patients with a functionally univentricular circulation

The role of extracorporeal membrane oxygenation is well established in children with refractory ventricular dysfunction after cardiac surgery.[7–9] The reported survival of children supported in this fashion for cardiac indications is between 40% and 50%. Due to the poor outcome, and overall limited experience, functionally univentricular physiology is a relative contraindication for mechanical support in many centres.

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Extracorporeal membrane oxygenation in neonates after the first stage of reconstruction for hypoplastic left heart syndrome and its variants

There is very little data regarding the role of extracorporeal life support in infants with the functionally univentricular circulation.[10–15]A majority of this experience is in neonates with hypoplastic left heart syndrome and its variants. Reported indications in this patient population include:

- inability to separate from cardiopulmonary bypass
- cardiopulmonary arrest
- acute shunt thrombosis
- progressive low cardiac output syndrome
- elective mechanical support.

Morris et al.[12] published the results of extracorporeal membrane oxygenation for cardiac indications at a hospital for children providing tertiary care over a period of 6.5 years. Of the 137 children supported in this fashion, 28% had a functionally univentricular circulation, and almost two-fifths of the overall group survived to be discharged from hospital. In this large series, there was no difference was found in survival between those with functionally biventricular and univentricular circulations.

The registry of the Extracorporeal Life Support Organization[13] recently reported the outcome of extracorporeal support for neonates with cardiac indications from 1996 to 2000. The registry recorded 740 neonates who were placed on extracorporeal life support for cardiac indications at less than 30 days. There were 118 neonates with hypoplastic left heart syndrome. It is worth noting that the number of neonates with hypoplastic left heart syndrome increased from over five-fold in 2000. There was no significant difference in survival between patients with hypoplastic left heart syndrome compared with other defects. For those with hypoplastic left heart syndrome, placement on extracorporeal life support at greater than 15 days of age was significantly associated with better survival. For the whole group, placement on extracorporeal life support at less than 3 days of age was significantly associated with better survival. Survivors also had a shorter duration of support.

We have also reviewed our own experience at the Children's Hospital of Philadelphia with "non-elective" extracorporeal membrane oxygenation after the first stage of reconstruction for hypoplastic left heart syndrome and its variants over a period of 7.5 years.[14] Of the 382 infants who underwent the first stage of reconstruction during the period, almost one-tenth required extracorporeal membrane oxygenation in the post-operative period. These included 22 infants with hypoplastic left heart syndrome. Indications for extracorporeal membrane oxygenation included inability to separate from cardiopulmonary bypass in 14 infants, and cardiopulmonary arrest due to circulatory failure or severe hypoxia in 22. Of this group, almost two-fifths (38.8%) survived to hospital discharge or transfer. Risk factors are shown in Table 1. Longer duration of cardiopulmonary bypass, the need for extracorporeal membrane oxygenation early in the post-operative period, and longer duration of support were associated with worse survival. Among the survivors, only one-fifth required extracorporeal membrane oxygenation less than 24 hours after the first stage of reconstruction, whereas three-quarters of those who died required it within 24 hours. All five infants who had a cardiac arrest due to thrombosis of a shunt survived, as opposed to one-third of those arresting due to other causes. The mean duration of support was significantly less for those who survived. As with the report from the registry,[13] there was a trend toward a longer time to extracorporeal membrane oxygenation after the first stage of reconstruction among survivors. In our study, cannulation via the neck vessels was associated with better survival. This is consistent with better survival of infants who required it later in their post-operative course. There was also a trend toward a higher incidence of low birth weight in infants who died, along with the presence of renal failure and liver dysfunction. Extracorporeal life support was discontinued in 22 patients, due to refractory ventricular dysfunction, intraventricular haemorrhage, and multiorgan including necrotizing enterocolitis in almost comparable numbers. Half of the infants are alive at a median follow-up of 20 months.

Table 1. Difference between survivors and non-survivors.

	Survivors (n = 14)	Non-survivors (n = 22)	p
CPB (minutes)	103.9 ± 30.0	150.1 ± 70.0	0.01
DHCA (minutes)	44.3 ± 10.0	53.7 ± 19.6	0.06
ECMO < 24 hours after Stage I	5/14 (22%)	17/22 (61%)	0.02
Time to ECMO after Stage I (days)	6.6 ± 7.5	2.5 ± 5.8	0.07
Neck cannulation	11/14 (78%)	9/22 (40%)	0.04
ECMO hours	50.1 ± 12.5	125.2 ± 25.0	0.01
LFT > 500	1 (7%)	8 (36%)	0.06
Creat > 2	0 (0%)	5 (23%)	0.1
Seizures	6 (43%)	11 (50%)	0.4

Risk factors for survival after use of extracorporeal membrane oxygenation after the Norwood procedure. Modified from: Ravishankar C, Dominguez TE, Kreutzer J, et al. Outcome of extracorporeal membrane oxygenation after the Norwood operation [Abstract]. Crit Care Med 2004; 32: A50

Abbreviations: CPB: cardiopulmonary bypass; DHCA: deep hypothermic circulatory arrest; LFT-ALT/AST greater than 500 units/litre; ECMO: extracorporeal membrane oxygenation; Creat–creatinine

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Ungerleider et al.[15] have suggested that mechanical assistance should be routine in the first stage of reconstruction, arguing that this approach simplifies post-operative management and improves hospital survival. They have used their protocol in 18 consecutive patients undergoing the Norwood operation, with a mean duration of mechanical support of 3 plus or minus 0.1 days. Survival to discharge was 87%, with improved early neurodevelopmental outcomes. Such routine mechanical support after the Norwood operation is a novel approach that addresses the increased cardiac output demands in the immediate post-operative period, and as argued, simplifies post-operative care. The approach, nonetheless, will likely increase cost and the need for additional support personnel.

Techniques for extracorporeal membrane oxygenation

It is possible to use a standardized circuit, including a servo-regulated system driven by a roller pump or a centrifugal pump, for mechanical support. The majority of patients requiring extracorporeal membrane oxygenation immediately after cardiopulmonary bypass remain cannulated via the median sternotomy, with an atrial cannula and an arterial cannula in the neo-aorta. Patients requiring it later in their post-operative course are more likely to be cannulated via the right internal jugular vein and right carotid artery. Bleeding is a major complication of extracorporeal membrane oxygenation after cardiac surgery. Re-exploration of the mediastinum is often necessary when transthoracic cannulation is used, increasing the risk of displacement of the cannulas and infection. The aorto-pulmonary shunt can be left open as long as the flows are adjusted to maintain adequate systemic blood pressure, tissue perfusion, and gas exchange. Due to significant runoff through the shunt towards the pulmonary circulation, some patients may require flows as high as 150–200 millilitres/kilogram/minute. In a majority of patients, the membrane can be isolated, and the circuit utilized as a ventricular assist device. Mechanical ventilatory support, and/or sweep gas, should be adjusted to maintain adequate gas exchange. A continuous infusion of heparin is used to achieve an activated clotting time of between 180 and 200 seconds, unless there is excessive post-operative bleeding, in which case a lower value can be tolerated.

Initiation of "non-elective" mechanical support in the early post-operative period after the first stage of reconstruction in the Norwood sequence, therefore, is associated with poor outcome. This is likely secondary to irreversible myocardial ischemia and/or residual haemodynamic issues such as obstruction in the aortic arch. On the other hand, extracorporeal membrane oxygenation can be lifesaving in infants with otherwise fatal conditions. It is particularly useful in potentially reversible conditions, such as acute thrombosis of the shunt, and transient depression of ventricular function. Due to this, in many centres, including our own, a circuit is always primed and ready for use, and the team responsible for extracorporeal membrane oxygenation is mobilized if haemodynamic stability is not returned promptly during a brief period of cardiopulmonary resuscitation for cardiopulmonary arrest in the post-operative period after the first stage of reconstruction. It is also imperative to perform a cardiac catheterization while on mechanical support if the aetiology of the cardiovascular collapse is not entirely clear, and particularly to rule out residual anatomic issues.

Extracorporeal membrane oxygenation after cavopulmonary connections

There is very limited experience with mechanical support in patients with cavopulmonary connections.[16,17] The registry of Extracorporeal Life Support reported survival in one-quarter of patients with this physiology. Indications for mechanical support in patients with cavopulmonary connections include:

- inability to separate from cardiopulmonary bypass
- progressive low cardiac output in the post-operative period
- recalcitrant arrhythmia in the post-operative period
- post-operative cardiac arrest
- respiratory failure
- "failing Fontan" late after the Fontan operation
- destination therapy.

The largest experience reported is the series of 20 patients with cavopulmonary connections supported with extracorporeal membrane oxygenation from 1984 to 2002.[18] Indications for support in this group included myocardial failure or respiratory failure immediately after a fenestrated Fontan operation, progressive low cardiac output syndrome in patients who had previously undergone a Fontan operation, and a cardiopulmonary arrest during an intervention in the cardiac catheterization laboratory. Of the patients, three suffered a cardiac arrest and underwent cannulation during cardiopulmonary resuscitation. Indications for support in the patients with a bidirectional Glenn shunt included low cardiac output syndrome in the immediate post-operative period, progressive myocardial failure late after the Glenn operation, and acute decompensation in the cardiac catheterization laboratory. Half of these patients suffered a cardiac arrest and were cannulated during cardiopulmonary resuscitation. The outcome for the

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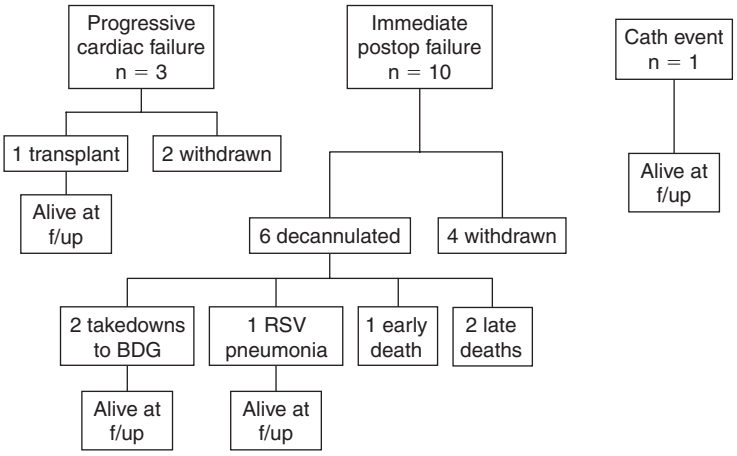

Figure 1.
The results of use of extracorporeal membrane oxygenation in the series of 14 patients reported by Booth et al.[18] with the Fontan circulation. Reproduced with permission from Society of Thoracic Surgery.

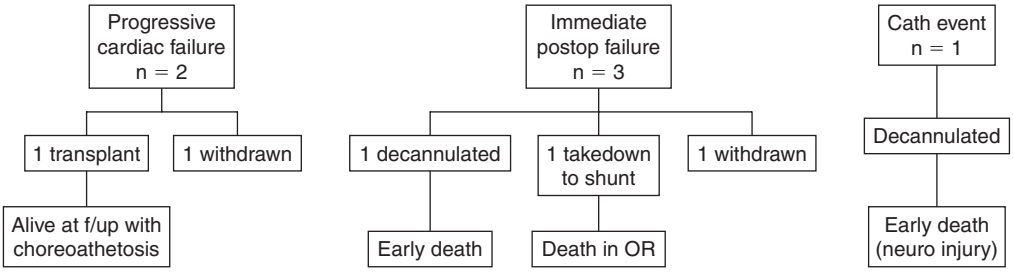

Figure 2.
The results of use of extracorporeal membrane oxygenation in the series of six patients reported by Booth et al.[18] with bidirectional cavopulmonary shunts. Reproduced with permission from Society of Thoracic Surgery.

patients is shown in Figures 1 and 2. In patients with a bidirectional Glenn, only one survived, and this patient sustained severe neurological damage. In those with the Fontan circulation, half survived to discharge, and one-third are alive at follow-up. This report highlights some of the technical difficulties in this challenging group of patients. Patients with cavopulmonary connections are difficult to resuscitate effectively with conventional cardiopulmonary resuscitation. During resuscitation, the increase in intrathoracic pressure may restrict effective flow of blood to the lungs and oxygenation, as well as increasing cerebral venous pressure that may further limit cerebral perfusion. This study also demonstrates the inability to maintain adequate venous drainage and systemic perfusion in these patients. The cannulation of the patient with a bidirectional Glenn shunt is particularly challenging because of the separation of the systemic venous drainage. A majority of patients in this series required placement of multiple venous cannulas.

Despite the limited experience, extracorporeal membrane oxygenation can be used successfully in patients after completion of the Fontan circulation as a manoeuvre to stabilize the situation pending takedown, or for respiratory indications. Venous drainage should be maximized using multiple venous cannulas, specifically with the initial cannula placed above, and the second cannula placed below the diaphragm. In patients with bidirectional Glenn physiology, it is particularly important to achieve adequate and early decompression of the superior caval vein to maximize cerebral perfusion pressure, and thus improve neurological outcome.

Long-term mechanical assist devices

The experience with long-term pulsatile devices in children has been growing.[19] Advantages of these devices include their chronic support capability, ease of use, mobility for cardiac rehabilitation, need for low-level anticoagulation, and the pulsatile nature of their flow.

The available long-term mechanical assist devices include:

- Pulsatile devices:
  - Berlin Heart or EXCOR, and Medos for neonates and infants
  - Thoratec and Heartmate
- Axial devices:
  - Heartmate II
  - DeBakey.

The Berlin heart is a paracorporeal pulsatile device that has been available for use in a miniaturized version

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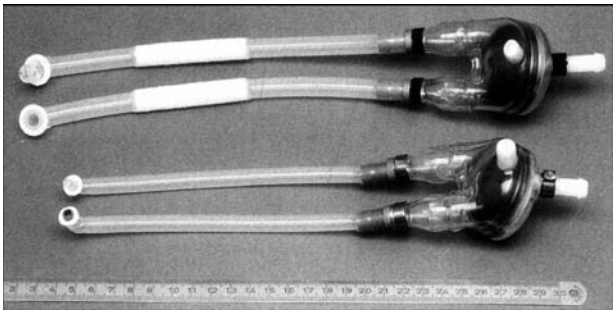

Figure 3.
Two examples of the Berlin heart.

since 1992. The inlet is cannulation via the ventricular apex, and the outlet is to the aorta or pulmonary trunk, with both cannulas exteriorized (Fig. 3). The polyurethane pumps have a wide range of stroke volumes of 10, 25, 50, and 60 millilitres. Three membranes provide stability, and the system is heparin coated. A rechargeable battery can provide up to 5 hours of independent power supply. This device can provide support in univentricular fashion for either the right or left ventricles, or biventricular support.[20,21] Survival of half of 28 patients with ages ranging from 6 days to 16 years has been reported for mean support of 17 days, with a range from 12 hours to 98 days. The early complication of thrombosis has been lessened with the use of a heparin-coated system. Post-operative care includes the use of heparin initially, followed by the addition of aspirin and dipyridamole. This device has been successfully used in infants as a bridge to transplantation. There is no reported use of this device in infants with a functionally univentricular circulation. There is also some limited experience in Europe with the MEDOS device.[22,23] Survival of one-third has been reported in children up to 16 years of age, including an infant with a body surface area less than 0.3 metre squared.

There is some experience in adolescents with the use of the Thoratec ventricular assist device. In a large series of 101 patients supported with this device, survival was two-thirds.[24] The smallest child in this series weighed 17 kilograms, with a body surface area of 0.7 metre squared. Although the experience in children with axial devices, such as the DeBakey device, is limited to a few adolescents, its smaller size holds promise for future use in children. This class of devices consists of relatively small axial pumps that involve an impeller with its housing that is entirely implantable (Fig. 4). The advantages of such an axial system are the relative ease of implantation, decreased infection, and its continuous flow provides unloading throughout the cardiac cycle. Disadvantages include the need for a large-sized ventricular apical cannulation, and current limitation to children with body surface area greater than 1.5 metre squared.

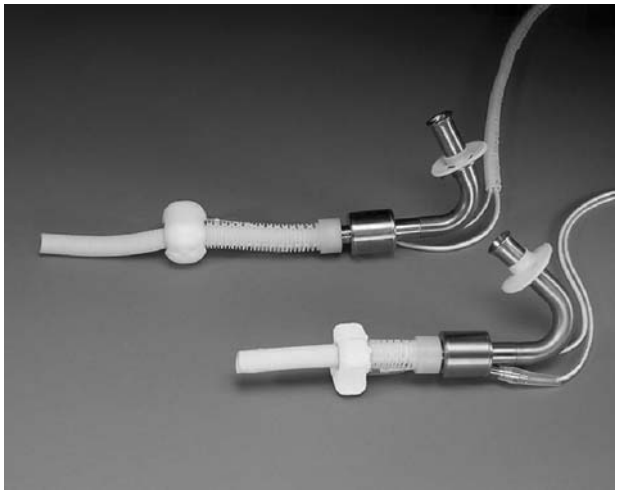

Figure 4.
Two examples of the DeBakey device.

As previously reported, a roller pump or centrifugal pump can be used as a short-term ventricular assist device after the first stage of reconstruction in the Norwood sequence. As far as we know, there are no reports of use of a long-term ventricular assist device in patients with a functionally univentricular circulation. One may speculate that in patients with a failing Fontan circulation due to ventricular dysfunction or protein-losing enteropathy, there may be a role for elective rather than emergency circulatory support with an implantable ventricular assist device, either as a bridge to transplantation or as definitive therapy in patients who are not suitable candidates for cardiac transplantation.

Conclusions

Extracorporeal membrane oxygenation can be effective for resuscitation of infants after a cardiopulmonary arrest in the post-operative period after the first stage of Norwood reconstruction, though mortality remains high. There may be a role for circulatory support with a long-term ventricular assist device such as the Berlin heart in a select group of patients, particularly as a bridge to transplantation. There is limited experience with extracorporeal life support after the cavopulmonary connection, and mortality remains high in this group of patients. In general, an anticipatory strategy for institution of mechanical support is preferable to a resuscitative situation. The role of a long-term ventricular assist device as a bridge to transplantation, or as definitive therapy, in these patients is unknown.

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