Extracorporeal membrane oxygenation for the treatment of children with severe hemodynamic alteration in perioperative cardiovascular surgery

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Background: **This article summarizes the use of extracorporeal membrane oxygenation (ECMO) for the treatment of children with severe hemodynamic alteration in perioperative cardiovascular surgery.**

Methods: **Four children with congenital heart disease (CHD) (3 boys and 1 girl, aged 6 days to 4 years and weighing 2.8-15 kg) associated with severe heart failure and/or hypoxemia were treated with ECMO cardiopulmonary support in perioperative cardiovascular surgery between July 2007 and July 2008. We retrospectively analyzed the medical records of the 4 children.**

Results: **Of the 4 children, 2 survived and 2 died. The survivors were treated with venoarterial (VA) ECMO due to severe low output syndrome after arterial switch operation. They were weaned successfully from 22-hour and 87-hour ECMO support, and discharged 20 days and 58 days after ECMO explantation, respectively. The other boy treated with venovenous ECMO died of severe hypoxemia and metabolic acidosis. The other girl with VSD, treated with VA ECMO because of failure to wean from cardiopulmonary bypass, died from irreversible heart failure 11 hours after ECMO explantation. The main complications in this series included pulmonary hemorrhage, blood tamponade, surgical site bleeding, hemolysis and hyperbilirubinemia.**

Conclusions: **ECMO is an effective therapy for patients with severe heart failure in the perioperative cardiovascular surgery. The keys to successful ECMO are selection of indications, time to set up ECMO, and good management of complications during ECMO.**

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Introduction

Extracorporeal membrane oxygenation (ECMO), a modified form of cardiopulmonary bypass, is used to prolong tissue oxygen delivery in patients with respiratory and/or cardiac failure. ECMO is performed by draining venous blood, removing carbon dioxide and adding oxygen through an artificial lung, and returning the blood to the circulation via a vein or artery (Fig. 1). ECMO is an accepted therapeutic modality for neonates, children and adults, who have failed in conventional therapy and in whom cardiac and/or respiratory insufficiency is potentially reversible.[1] Extracorporeal life support (ECLS) for neonatal and pediatric cardiac surgery showed the rates of weaning and hospital discharge were 60%-61% and 39%-44%, respectively.[2,3] ECMO has been used with satisfactory results around the world for years. In China, its development and clinical application are still very low, especially in neonates and children. Four children with severe heart failure and/or hypoxemia were supported with ECMO in the perioperative period from July 2007 to July 2008 at our hospital. Of these children, 3 had ECMO removed and 2 survived.

Case report

Case 1

A 2-day-old boy weighting 2.8 kg was admitted to our

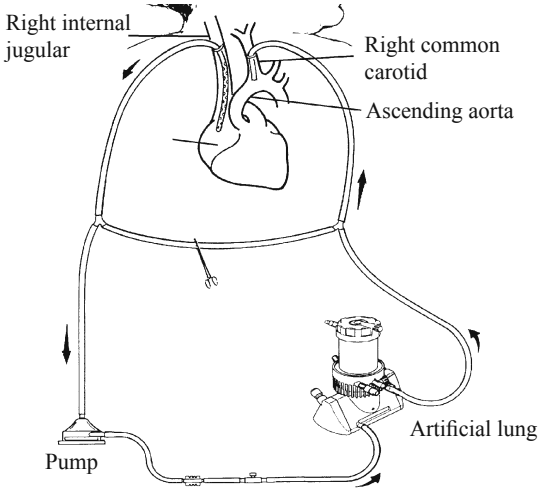

Fig. 1. A diagrammatic representation of venoarterial extracorporeal membrane oxygenation.

hospital because of cyanosis and tachypnea after birth on July 14, 2007. He was diagnosed with D-transposition of the great arteries (TGA), atrial septal defect (ASD), and patent ductus arteriosus (PDA). Arterial switch, ASD repair and PDA ligation were performed together with a conventional cardiopulmonary bypass (CPB) on July 18, 2007. The aorta was clamped for 72 minutes. During the clamping, 30 ml/kg 4:1 cold cardioplegic solution was infused twice intermittently. The heart re-beated automatically after removal of the clamp. Pacemaker was applied to increase the native heart rate (105 bmp) and keep a pace rate of 150 bmp. Ultrafiltration was used. Hematocrits, blood gas and electrocytes were normal near the end-time of CPB. Due to failure to wean from CPB (CPB lasting for 263 minutes) with acidosis (blood lactate: 8.8 mmol/L), low blood pressure (39/30 mmHg), increased left atrial pressure (>20 mmHg), and decreased urine output (<1 ml/kg per hour), a venoarterial (VA) ECMO was used for cardiopulmonary support. Direct cannulation of the ascending aorta (Edward FEM008A) and right atrium (Edward TF18090), Medtronic pediatric ECMO package (CB2503R1) and a centrifugal pump system (bio-console 560) were applied. The patient was transported to the intensive care unit with the chest open.

The patient was weaned from ECMO successfully after 87 hours. Pulmonary hemorrhage, surgical bleeding and blood tamponade occurred on the day of ECMO implantation. Hemolysis and hyperbilirubinemia (270.5 μmol/L total) occurred on the third day after ECMO implantation, but were improved by surgical hemostasis, clearance of blood clot, lowering of pump speed, and diuretic and blue light treatment. Left ventricular function improved rapidly. Left ventricular ejection fraction (LVEF) rate on day 1, 2, and 3 after ECMO was 20%, 34% and 43% respectively. The circulation system was stable after weaning from ECMO with inotropic medicine (epinephrine 0.2 μg/kg per minute, dopamine and dobutamine 8 μg/kg per minute, and milrinone 0.56 μg/kg per minute). On off-ECMO day 4, the chest of the patient was closed. On off-ECMO day 22, the patient was extubated. On day 58 after ECMO removal, the patient was discharged from the hospital. Ultrasound imaging revealed no intracranial hemorrhage or infarction during and after ECMO. The function of the brain, heart, lung, liver and kidney was normal during a 1.5-year follow-up.

Case 2

A 37-day-old boy weighing 4 kg was admitted to our hospital because of cyanosis and tachypnea on January 28, 2008. He was diagnosed with TGA and ASD and ventricular septal defect (VSD). Arterial switch, VSD occlusion and ASD repair were performed under CPB. The aorta was clamped for 100 minutes. 30 ml/kg 4:1 cold cardioplegic solution was infused intermittently four times during the clamping of the aorta. The heart re-beated automatically after removal of the clamp. The heart rate was 169 bpm; blood gas and electrocytes were normal; blood lactate was 2.1 mmol/L. But systemic blood pressure maintained at 36/25 mmHg at the first attempt to wean from CPB. Echocardiography showed that VSD amplatzer occluded mitral chordae tendience. After re-clamping of the aorta, the amplatzer was taken out and VSD was repaired with pericardial patch under CPB. The patient was transferred directly from CPB to VA ECMO after operation because of long-term CPB and unstable circulation. The establishment of ECMO was the same as in case 1. The patient was transported to the intensive care unit with the chest open.

The patient was successfully weaned from 22-hour ECMO support. Surgical bleeding and tamponade occurred on the day of ECMO implantation. The bleeding was stopped by surgical homeostasis and clearance of blood clot. The blood circulation was stably supported by dobutamine 5 μg/kg per minute after ECMO removal. On off-ECMO day 4, the chest was closed. On off-ECMO day 20, the patient was discharged home. Ultrasound imaging revealed no intracranial hemorrhage or infarction during and after ECMO. The function of the brain, heart, lung, liver and kidney remained normal during the half year of follow-up.

Case 3

A 19-day-old boy weighing 3.5 kg was admitted to our neonatal intensive care unit because of cynosis and tachypnea on January 31, 2008. The boy was diagnosed with TGA, ASD and PDA. He was intubated urgently after admission because of severe hypoxemia induced by PDA closing. After salvage for several hours, blood gas still showed severe metabolic acidosis (pH 7.14, BE -7.3). A venovenous (VV) ECMO was intervened

for correcting the intra-environmental derangement by cannulating the right internal jugular vein with a Joustra double-lumen (12F) cannula. A Medtronic hollow fiber heparin-coated Carmeda oxygenator and a centrifugal pump system (CB2503R1) were applied. The patient died on ECMO from severe hypoxemia and metabolic acidosis after ECMO running for 15 hours.

Case 4

A 4-year-old girl weighing 15 kg was admitted to another hospital on July 18, 2008 because of heart murmur for 3 years. She was diagnosed with VSD. Repair of VSD was performed through a right chest lateral incision on conventional CPB 3 days after admission. The VSD (0.4 cm) was stitched directly. The aorta was clamped for only 14 minutes. The heart re-beated 8 minutes after removal of the clamp, with poor cardiac constriction even arrest during closing of the chest. Unfortunately, the patient was hardly weaned from CPB though conventional treatment was given. Echocardiography showed marked ST segment elevation and the level of serum lactate was 8.9-9.8 mmol/L after CPB support for 3 hours. The circulation was unstable. Echocardiography showed poor cardiac function, LVEF 26%, non-reflux of the tricuspid and aortic valves, and residual shunt. The patient had myocardial stunning and severe low output syndrome induced possibly by ischemia-reperfusion injury. VA ECMO was inserted via a CPB cannula (the right atrium and ascending aorta).

The condition of the patient was stable on ECMO except bleeding at the cannula, and blood tamponade occurred on the day of ECMO implantation. After 18-hour ECMO support, heart rate was 100-120 bpm and blood pressure 70/50 mmHg. The level of hemoglobin rose rapidly from 47 g/L to 100 g/L and the level of serum lactate decreased from 10.5 mmol/L to 2.0 mmol/L. Inotropics reduced rapidly to a lower level since adequate perfusion was achieved. Ventilator settings were reduced to the "rest condition" for minimizing lung injury (positive end-expiratory pressure, 6 cmH_2O; FiO_2 0.25; volume tide, 5 ml/kg per minute; respiratory rate, 12/min). "ECMO lung" appeared on the second day of ECMO and recovered 2 days after intravenous administration of laxis and methylprednisolone. Up to day 6 on ECMO, the patient recovered with normal function of the lung, liver and kidney. The values of creatine kinase-MB (<0.06 nmol/L), platelet (70×10^9/L), hematocrit (35%), and lactate (2.0 mmol/L) recovered except QRS waves which were very low (Fig. 2). Echocardiography indicated poor systolic and diastolic function, especially a LVEF rate of 22%-28%. Three attempts failed to wean from ECMO. Because of irreversible cardiac failure and no heart donor was available, ECMO was withdrawn after 16-day (380 hours) support and the patient died 11 hours after ECMO.

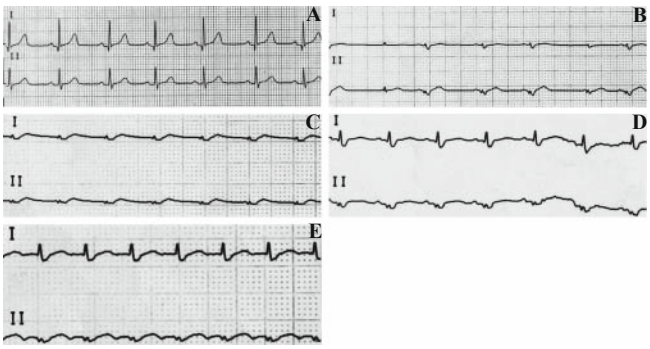

Fig. 2. Series of electrocardiogram pictures of case 4. **A:** preoperation; **B:** on the day of extracorporeal membrane oxygenation (ECMO) implantation; **C:** on the 2nd day of ECMO implantation; **D:** on the 7th day of ECMO implantation; **E:** on the 16th day of ECMO implantation.

Discussion

ECMO is effective in controlling severe hemodynamic[4] or respiratory[5] alteration in the perioperative period of cardiovascular surgery. This allows the recovery of target organs[6] or serves as a bridge for transplantation in irreversible cases.[7-9] ECMO support can be offered perioperatively to any patient with potentially reversible pulmonary, cardiac or cardiopulmonary failure, excluding those with irreversible outcome.[10]

The recovery of reversible cardiac and pulmonary failure after repair of congenital heart malformation, especially stunning due to the recovery from ischemic-reperfusion injury, takes about 4-6 days of ECMO support.[11] A good repair of anatomic malformation is essential to successful ECMO in postoperative patients. In this series, cases 1 and 2 had an ideal anatomic correction after arterial switch, with a smooth blood flow in coronal arteries except the left ventricular function that can not bear systemic circulation pressure load in a short time. ECMO assistance for a couple of days dramatically improved cardiac function with a good response to vasoactive drugs. In case 4, the patient had received effective assistance of ECMO for 16 days. She survived the low cardiac output period and had time for functional recovery of the brain, lung, liver and kidney. Unfortunately, the heart could not recover well enough to work independently. Vectorcardiographically, a large number of cardiac myocytes were found to be necrotic, and residual myocardial cells could not effectively bear the function of the heart. Air emboli were suspected to enter coronal arteries during the operation, leading to myocardial infarction. But we could not make a final diagnosis because of a lack of endomycardial biopsies and coronarography. Hence it is difficult to identify

whether there was reversible ventricular dysfunction by the current clinical criteria. New insights are required for the pathophysiology of intraoperative myocardial injuries and the determinants of myocardial recovery.[11]

Timing of intervention remains a challenge. It is clear that if anatomic correction is adequate, early and appropriate support before end-organ injury, severe metabolic derangement or cardiac arrest can lead to excellent results. Theoretically, ECMO support can improve preoperative hypoxia, ensuring a chance of operation. But in case 3 of this series, severe hypoxia and extreme acidosis caused poor results of ECMO.

ECMO complications include hemorrhage, thrombosis, hemolysis, renal failure, sepsis, neurological insult, distal limb ischemic and ECMO circuit system disorder. Hemorrhage remains the most common complication of ECMO for cardiac surgery.[12] In this series all children after operation had surgical bleeding around the left atrial pressure monitoring cannula and aortic cannula. ECMO was stable after surgical hemostasis and blood transfusion.

In 3 of our 4 cases there was no secondary injury to vital organs. The tenets of successful ECMO included timely implantation of ECMO to assure neurons oxygen provision; maintenance of moderate ventilator setting to reduce the lung's work and prevent alveolar lapse; regulation of vasoactive drugs to maintain appropriate cardiac workload and prevent thrombosis; maintenance of activated coagulation time between 180 and 230 seconds, prothrombin time <14 seconds or activated partial thromboplastin time <80 seconds so as to prevent disseminated intravascular coagulation; transfusion of fresh frozen plasma and platelets to 50-80 $\times$ 10^9/L; maintenance of a level of 35%-40% for hematocrits to warrant adequate oxygen transport to tissues; and maintenance of normal plasma colloid osmotic pressure for sputum drainage and diuresis. A good ECMO system should include monitoring continuous negative pressure, pre-oxygenator and post-oxygenator pressure, checking circuit and pump head thromboses, monitoring free hemoglobin concentration every day (less than 50 mg/L), and observing urine color. If the color deepens, it is necessary to replace the system in time to prevent renal failure.

ECMO implanting, transporting, running and weaning are very complex, even a tiny mistake can lead to disastrous results. Theoretical and technical training must be done before the use of ECMO. ECMO team members must pay attention to every detail to prevent failure of the nervous system, kidney and liver.[13] ECMO technology and management involve multi-disciplinary knowledge and the cooperation of surgeons, ECMO technicians and intensive care unit doctors.

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