CASE REPORTS OF THE UNIVERSITY OF PUERTO RICO
SCHOOL OF MEDICINE HOSPITALS

Extracorporeal Membrane Oxygenation: Successful Bridge to Pediatric Heart Transplantation

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Since the year 2000, extracorporeal membrane oxygenation (ECMO) support for cardiac failure has been employed in the post operative care of children at the Centro Cardiovascular de Puerto Rico y el Caribe. Our experience with the application of ECMO had been limited to circulatory support after repair of congenital cardiac lesions. We report the first case in Puerto Rico where ECMO was used successfully as bridge to pediatric heart transplantation.

Key words: Extracorporeal membrane oxygenation; Pediatric heart transplant; Circulatory support; Cardiogenic shock

An 11 year-old male patient without history of systemic illness was doing well until 3 days prior to admission when he developed muscle cramps, nausea and vomiting. He also complained of dyspnea upon effort and chest pain associated with physical activity. Symptoms persisted in spite of anti- inflammatory medications. CPK and CPK-MB levels were elevated and he was referred to the University Pediatric Hospital for further evaluation. His past medical history was negative for cardiac disease, Kawasaki disease or recent viral or respiratory infections.

Hospital course. Physical examination on admission revealed: a regular heart rate of 80/bpm, blood pressure 92/59 mmHg, temperature 37.9°C and a respiratory rate of 23/min. His nutritional status was good, the lungs were clear to auscultation and the heart sounds were normal. No cardiac murmur or dysrhythmia were present. The liver and the spleen were not enlarged and pre-tibial edema was absent. The chest roentgenogram demonstrated a normal cardiac silhouette and clear lungs. Admission laboratory data revealed elevated serum CK and CPK-MB (>18000U/L and 715U/L, respectively) and troponin (>500ng/ml) levels. Other significant laboratory findings included hypocalcemia, hypomagnesemia and hyperphosphatemia. Electrocardiography showed sinus rhythm with ST segment inversion in leads V_1 to V_6. The QTc interval was 0.51 seconds. M-mode echocardiography revealed dilatation of all chambers with mitral and tricuspid valve regurgitation and generalized hypokinesis of the left ventricle with an ejection fraction of 24%.

During the next few hours the patient became increasingly dyspneic and was transferred to the pediatric intensive care unit with supplemental oxygen by non-rebreathing mask and dobutamine infusion at 5 mcg/kg min. Digitalization was initiated but the patient failed to show a significant improvement and continued to deteriorate. There was evidence of poor peripheral perfusion, desaturation and air hunger, he became dusky in appearance and developed gallop rhythm, hepatomegaly, (liver 4 cm below costal margin), prolonged capillary refill and non-palpable peripheral pulses. Chest radiography revealed bilateral pleural effusion, a 12-lead ECG showed sinus tachycardia (160/ beats/min), low voltage and persistence of abnormal ST depression in the ECG. Dobutamine was discontinued and patient was started on milrinone at 0.5 mcg/kg/min. The patient failed to improve and required endotracheal intubation and ventilatory assistance.

In spite of maximal medical therapy including inotropic and afterload reducer support, digitalis, diuretics, calcium and magnesium supplementation. The patient continued with low cardiac output state. High ventilator parameters were required to achieve adequate oxygenation. Broad spectrum antiobiotic therapy as well as intravenous immunoglobulins were given.

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The patient was transferred to Centro Cardiovascular de Puerto Rico y el Caribe for extracorporeal membrane oxygenation (ECMO) support. He was taken to the operating room and through a median sternotomy incision transthoracic cannulation of the ascending aorta and right atrium was done. Because of severe left ventricular dysfunction, an additional cannula was placed to decompress the left ventricle. Anticoagulation was maintained by continuous heparin infusion, mechanical ventilation was continued with reduced inspired oxygen concentration and lower ventilatory settings.

Cardiac function was assessed by serial echocardiographic examination and hemodynamic testing at reduced ECMO flow. There were no signs of myocardial recovery. The echocardiogram revealed poor biventricular contraction and a LVEDF of 10%, so the patient was enrolled on the United Network for Organ Sharing (UNOS) waiting list for cardiac transplantation.

On the 6th hospital day a suitable donor was identified so the patient was taken to the operating room for orthotopic heart transplantation. One surgeon procured the donor heart while the other transplant surgeon began the operation. Transplantation was performed using the modified Shumway's technique using bicaval anastomosis. Total donor ischemia time was 19 minutes; the transplanted heart returned to sinus rhythm and patient was weaned from cardiopulmonary bypass assisted by low dose epinephrine infusion (0.02mcg/kg/min). Inmunosupression was started with steroids, tacrolimus, mycofenolate mofetil and monoclonal antibodies.

Table 1.

Patient	Age	Diagnosis	Procedure	Indication for ECMO	Duration of CPR	ECMO duration	Complications
#1	3 months	Tetralogy of Fallot	Total repair CBP 89 min AXC 33 min	ARDS RV and LV dysfunction	----------	106 hours	Bleeding Discharged home
#2	2 months	Single ventricle Dextrocardia Hypoplastic RV	4 mm Rt. Modified BTS	ARDS Low cardiac output	----------	139 hours 27 minutes	Bleeding HFOV for 14 days Death
#3	1 months	Tetralogy of Fallot	Total repair CPB 81 min AXC 32 min	CR arrest	35 min	40 hours 56 minutes	Discharged home
#4	5 months	Tetralogy of Fallot	Total repair CPB 125 min AXC 105 min	Low cardiac output	---------	75 hours 30 minutes	DIC MOF Death

One day after the transplantation the patient became hemodynamically stable at low dose epinephrine and dobutamine drips. Echocardiogram revealed an ejection fraction 64%; he was on minimal ventilatory assistance with adequate oxygenation and inmunoprophylaxis was continued. The following day the patient was successfully extubated and remained hemodynamically stable without inotropic support. On the 14th hospital day the patient was discharged home asymptomatic, on inmunosupression therapy and calcium supplements.

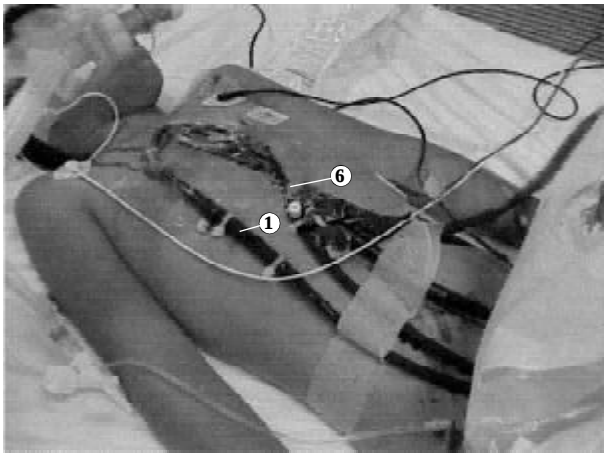
Discussion

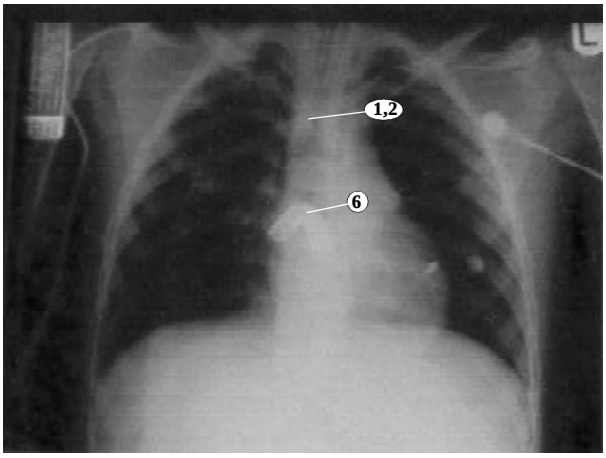
The first heart transplant in Puerto Rico was performed on June 27, 1999 at the Centro Cardiovascular de Puerto Rico y el Caribe. Since then, 44 adult patients and 3 pediatric patients have been successfully transplanted. Two patients have died; the first died 3 month after transplant due to uncontroled sepsis and multiorgan failure and the second patient died 2 years after transplant due to fulminant pancreatitis. The patient reported here was the first who received extracorporeal membrane oxygenation support as a bridge to cardiac transplant.

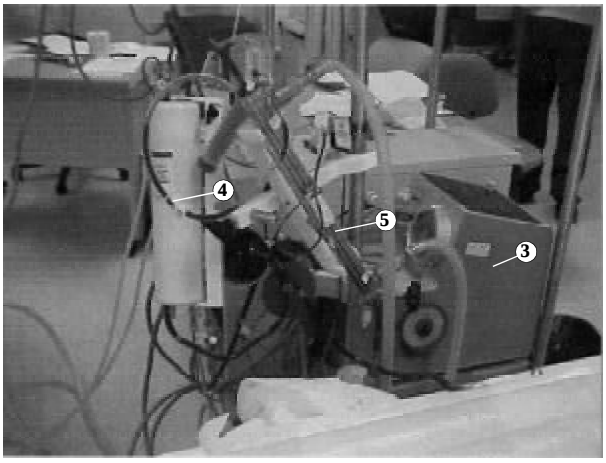
In the Extracorporeal Life Support Organization Registry, there have been an increasing number of children receiving circulatory support with ECMO after cardiotomy or for cardiac support (1). Since the year 2000 we have been using ECMO for circulatory support in children after repair of congenital cardiac lesions (Table 1). The goal of ECMO support in patients after cardiac surgery is to maintain adequate tissue perfusion while providing complete or nearly complete cardiac bypass. In the case presented, we used ECMO as a rescue therapy for a severe myocardial failure and cardiogenic shock. The aim was twofold: to allow time for the heart to recover function and to allow time for a donor heart to become available.

The pioneering use of ECMO in patients with severe cardiac failure was first reported in the 1950's but ECMO was not commonly used until the 1980's. Several types of ECMO have been developed according to cannulation site and method of mechanical ventilation. However, the basic circuit is similar for all modes. The two basic types are venoarterial (VA) and veno-venous (VV). This terminology describes the direction of blood flow: outflow is always from the venous system, whereas inflow can be either into the arterial (VA) circulation or the venous (VV) circulation. VV ECMO can only be used when the patient does not require circulatory support.

In the case presented, venoarterial ECMO circuit was used (Figure 1-3). It consists of a venous cannula draining desaturated systemic venous blood from the right atrium







Venoarterial ECMO circuit: It consists of a venous cannula (1) draining desaturated systemic venous blood from the right atrium (2) to a closed reservoir. Blood is drawn from the patient by gravity drainage and a centrifugal pump (3) is used to advance the blood through a membrane oxygenator (4), where gas exchange occurs. Oxygenated blood then flows through a heat exchanger (5), where it is warmed before returning to the patient aorta (6).

to a closed reservoir. Blood is drawn from the patient by gravity drainage and a centrifugal pump is used to advance the blood through a membrane oxygenator, where gas exchange occurs. Oxygenated blood then flows through a heat exchanger, where it is warmed before returning to the recipient aorta. Access ports for medication and fluid administration, pressure monitoring, and blood sampling are located at various sites along the circuit. Oxygen saturation of venous blood is monitored by a photoelectric device providing an essential way of estimating the adequacy of tissue oxygenation. The patient is heparinized as early as possible to attain an activated clotting time (ACT) between 180 and 220 seconds. ACT determined bedside, provides a gauge for adjusting the heparin dose to avoid either a catastrophic circuit clotting or bleeding complications. Platelet sequestration in the ECMO circuit is a constant problem and patients are usually transfused to keep a platelet count of 80,000mm^3 to 100,000mm^3. There are reports in which platelets were transfused only when the count was less than 50,000 mm^3, unless a bleeding complication was present (2). Fresh frozen plasma and cryoprecipitate are given to keep coagulation factors to normal levels.

The output of the ECMO circuit is determined by the amount of venous blood that is withdrawn from the patient and enters the circuit. Venous flow to the ECMO circuit is gravity dependent, generated by the pressure difference between the column of blood in the venous cannula and the reservoir. Because the venous cannula can drain only as much blood as the right atrium receives, adequate systemic venous return must be maintained. Fluid and electrolytes are managed according to patient's need.

ECMO flow is initiated at 50ml/kg/min and increased in 50 to 100 ml increments. Pediatric patients usually require about 90ml/kg/min of ECMO flow to maintain adequate oxygen delivery. This patient (weight: 22kg) was receiving approximately 1.5 L/min flow. The hematocrit is maintained at 30% to 35%. Although low hematocrit/hemoglobin reduces blood oxygen-carrying capacity and blood oxygen content [(Cao_2 = CO (SaO2 x Hb x 1.34) + (0.003 x PaO2)], high hematocrits increase the risk of stagment flow in the ECMO circuit.

In the patient undergoing ECMO, total systemic cardiac output (CO) is determined by both the ECMO pump flow and the patient's left ventricular output. By limiting the pump flow VA-ECMO can be complete or partial. We used partial VA-ECMO because studies have shown that complete bypass of the pulmonary circulation may lead to pulmonary alkalosis and ischemia. It can also cause direct damage to the pulmonary bed and can contribute to cardiac ischemia since coronary arteries are primarily supplied by blood ejected from the left ventricle (4)

Nevertheless, the blood entering the pulmonary circuit is minimal, and manipulating the ventilator settings has little effect on blood gas tensions. Ventilation and oxygenation depend primarily on the function of the ECMO circuit. During ECMO mechanical ventilation in pediatric patients include the use of positive end inspiratory pressure (PEEP) to maintain functional residual capacity and low positive inspiratory pressure (PIP) and oxygen concentration to reduce lung injury and toxicity.

ECMO provides an optimal environment for myocardial recovery. In 1995, Black et al. (3) reported that the maximum time required for recovery for cardiotomy patients and those with myocardytis should be 6 days and that initial recovery can be seen in the first 48 hours of ECMO. Dalton et al. (4) reported 79 % recovery of myocardial function during ECMO. Our patient received 48 hours of initial ECMO support. During that period his cardiac function was assessed by serial echocardiographic examinations and hemodynamic testing at reduced ECMO flows. In view of no improvement in cardiac function ECMO was used as a bridge for cardiac transplantation.

In a revision of ECMO support as a bridge to transplantation del Nido (1) reported 14 patients accepted as candidates for transplantation. Duration of ECMO was 109+/- 20 hours. In our case, a suitable donor was identified in less than 24 hrs. Donor heart procurement and the start of the recipient operation were coordinated to minimize donor heart ischemia time. The ischemic time (the time from aortic cross-clamp of the donor to release of aortic cross-clamp in recipient) and the autonomic nervous system denervation of the transplanted heart will both impact the recovery of heart rate of the transplanted heart. A longer ischemic time may correlate to a longer time to recovery of the sinoatrial (SA) node (5).

The transplantation was performed using the technique first described by Lower and Shumway in 1960. Recipient cardiectomy was done leaving the posterior walls of both atria in place to be later anastomosed to the donor heart. In this case aortoplasty and pulmonary artery arterioplasty were necessary due to larger size of donor's heart vessels. End-to-end anastomoses were made between the donor and recipient aortas and pulmonary arteries.

Post cardiac transplant care at the pediatric intensive care unit includes mechanical ventilation assistance for at least the first 24 hours, stabilization of hemodynamics, nutrition, strict reverse isolation, and immunosuppressive medications. Recovery time after transplant will vary but, typically, patients can expect to be discharged within 8 days after surgery. Survival after pediatric heart transplantation was reported by the International Registry to be 60% at 7 years and 50 % at 10 years (6) Success is dependent not only in preoperative condition, post-operative management and immediate outcome but on the long term follow-up and patient's compliance with therapy. Psychological maladaptation is worrisome but little has been studied in this area. It should be part of our goals as health providers to identify strengths and weaknesses in this child new life to create an environment where strengths are magnified and weaknesses are minimized.

Based on our experience and the current literature reports we can conclude that pediatric patients with severe myocardial dysfunction who fail conventional medical therapy can be successfully supported with ECMO as a rescue therapy and bridge to heart transplantation.

Resumen

El Centro Cardiovascular de Puerto Rico y el Caribe es el único hospital en Puerto Rico donde se realizan cirugías correctivas para enfermedades congénitas cardiacas en niños. En dicha institución se ha utilizado en ocasiones la oxigenación por membrana extracorpórea (ECMO) desde el año 2000 como parte del manejo para fallo circulatorio refractario a la terapia médica convencional luego de la reparación quirúrgica de estos defectos. En este artículo informamos nuestra experiencia con el uso de ECMO como puente para transplante de corazón en un niño de once años con disfunción severa del miocardio y fallo cardiaco congestivo persistente.

Acknowledgement

The authors would like to thank to the pediatric residents, medical staff and nursing staff of the University Pediatric Hospital-University of Puerto Rico and to all the medical and nursing staff of the Centro Cardiovascular de Puerto Rico y el Caribe for their commitment with the pediatric health and the humanistic and high quality of care they always provide to our patients. We particularly thank Dr. Ivan Gonzalez Cancel and Dr. Hector Banch for their contributions, participation and support on the care and follow up of our heart-transplanted pediatric patients.

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