

Minimizing Reperfusion Injuries: Successful Resuscitation Using eCPR After Cardiac Arrest on a Post-Operative Norwood Patient

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Abstract: In patients with hypoplastic left heart syndrome (HLHS), the left ventricle is too small to circulate adequate oxygenated blood. If left untreated, HLHS is fatal. A 3-staged palliative procedure ultimately leading to a single ventricle physiology is the preferred management strategy for HLHS in most pediatric cardiac centers in the United States. In this report, a 1-month-old infant developed cardiac arrest 3 weeks after undergoing a Norwood procedure as an initial palliation for HLHS. After 151 minutes of cardio-pulmonary resuscitation (CPR) with intermittent, but non-sustainable return of spontaneous circulation, extracorporeal cardio-pulmonary resuscitation (eCPR) was used. Utilizing the carotid artery and internal jugular vein for cannulation, we

connected our extracorporeal membrane oxygenation (ECMO) circuit to the patient. To minimize reperfusion injury, immediate cooling, arterial/venous shunting, minimal calcium, and hemodilution strategies were used. Once $\text{paCO}_2/\text{pvCO}_2$ gradients were minimized, we instituted sweep gas and gradually increased FiO_2 as pH normalized. The patient was successfully weaned from ECMO and discharged. eCPR was used successfully in the resuscitation of this patient and reperfusion injuries were minimized despite prolonged CPR. **Keywords:** extracorporeal cardiopulmonary resuscitation, reperfusion injury, hypoplastic left heart syndrome, Norwood procedure, Pediatric, ischemia/reperfusion. *JECT. 2010;42:238–241*

Hypoplastic left heart syndrome (HLHS) is a congenital cardiac defect that requires multiple staged procedures for palliation (1). This defect is characterized by a hypoplastic ascending aorta and aortic arch, hypoplastic left ventricle, mitral and/or aortic atresia, large patent ductus arteriosus (PDA) supplying the only source of blood flow to the body, and an atrial septal defect allowing pulmonary venous blood to mix with systemic venous return. Because the left heart is underdeveloped and incapable of pumping oxygen-rich blood to the body, the right ventricle has to provide circulation to both the systemic and pulmonary beds (2). Thus, having a PDA is crucial to allow the blood from the right ventricle to reach the systemic circulation. In the absence of a PDA, patients with HLHS will die without surgical intervention

Surgical management of patients with HLHS includes orthotopic heart transplantation or a 3-stage palliative procedure eventually leading to a single ventricle physiology (3).

The Norwood procedure usually consists of an atrial septectomy to ensure unobstructed mixing of pulmonary venous blood with systemic venous blood, aortic arch augmentation, and conversion of the right ventricle into the systemic ventricle by funneling the outflow of the right ventricle into the newly augmented distal ascending aorta (2). The pulmonary blood flow is provided by one of two sources: a systemic-to-pulmonary shunt (Blalock-Taussig (BT) shunt) connecting the innominate artery to the pulmonary artery or a ventricular to pulmonary shunt (Sano shunt) connecting the right ventricle to the pulmonary artery (2). Of the mortalities associated with the management of HLHS, most occur after the Norwood procedure. Even with many recent improvements in the perioperative and operative management of these patients, most pediatric cardiac programs still have a 10–20% post-operative (post-op) mortality rate (4). Here we report the details of a successful eCPR case with emphasis on reinstatement oxygen therapy for a profoundly ischemic patient.

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DESCRIPTION OF TECHNIQUE

Exemption from Institutional Review Board 09.174 was granted to meet the requirements of this case report under 45-CFR-46. A classic Norwood procedure with a right-sided

modified BT shunt was performed on a 6-day-old, 51 cm, 3.2 kg (body surface area .22 m²) male infant with HLHS at Inova Fairfax Hospital. Cardiopulmonary bypass was 227 minutes, aortic cross clamp was 71 minutes, and hypothermic circulatory arrest time was 9 minutes. The patient's lactate level stabilized and gradually dropped to normal levels, and his pulmonary-to-systemic ratios and systemic blood pressure were stable immediately after surgery with minimal amount of inotropic support. Three days after surgery, the sternum was successfully closed. At 17 days post-op, the patient was transferred to the step-down telemetry unit. He remained there until the day before anticipated discharge (28 days post-op), where he developed bradycardia and hypotension (probable vasovagal episode) shortly after the passage of a nasogastric feeding tube. Cardiopulmonary resuscitation (CPR) was initiated. Multiple doses of intravenous epinephrine, calcium chloride, sodium bicarbonate, atropine, milrinone, packed red blood cells (pRBCs), and tromethamine were used during the CPR effort.

The patient's blood gas and chemistry were measured using an I-Stat analyzer (Abbott, Princeton, NJ). Due to ischemia, arterial/venous (A/V) pCO₂ was >130 mmHg, pH was <6.771–7.111, and lactic acid was >20 mmol/L. Aggressive amounts of sodium bicarbonate were administered in attempt to correct the acidosis. By treating acidosis medically, the systemic sodium levels rose to >160 mmol/L due to the disassociation of sodium and bicarbonate, which may have contributed to the elevated pCO₂ levels. During the next 151 minutes of CPR, the patient intermittently

developed perfusing rhythms punctuated with cardiac arrest. Due to the inability to sustain an adequate perfusing cardiac rhythm, eCPR was initiated.

Because this patient had a right-sided modified BT shunt, he was cannulated for eCPR using an 8-french arterial cannula (Medtronic, Minneapolis, MN) in the left carotid artery and a 10-french venous cannula (Medtronic, Minneapolis, MN) in the left internal jugular vein. The extracorporeal membrane oxygenation (ECMO) circuit consisted of a roller head heart lung machine (Stockert S3, Sorin, Arvada, CO), a 1/4" x 1/4" arterial-venous loop (Medtronic, Minneapolis, MN), biocompatible coating (Carmeda, Upplands Väsby, Sweden) with an inline reservoir (Better Bladder, Oyster Bay, NY), and oxygenator (Terumo Baby RX, Ann Arbor, MI), and primed with PlasmaLyte A (Baxter, Deerfield, IL). We added 100 units of porcine heparin (APP Pharmaceuticals, Schaumburg, IL) to the prime. This was followed by 250 mL of 5% albumin (Baxter, Deerfield, IL) to coat the circuit. One unit (350 cc) of <7 days old leukocyte reduced, irradiated, cytomegalovirus negative, homologous pRBCs, was slowly added to the prime while removing most of the clear prime from the circuit. The perfusate was cooled to 32°C with a heater/cooler (Cincinnati Sub-Zero, Cincinnati, OH). The patient's hematocrit was 33%.

eCPR prime was cooled to 32°C to reduce the patient's metabolic demand, while attenuating the pCO₂ by increasing carbon dioxide solubility. Patient's temperature had drifted to 36°C. eCPR was started initially at a flow rate of .29 L/min. Sweep gas was not turned on to reduce the likelihood of reperfusion injury (Table 1). Note that the BT

Table 1. CPR to initiation of eCPR.

Time	Hgb g/dL	Hct %	pH (A/V)	pvCO ₂ mmHg	pvO ₂ mmHg	paCO ₂ mmHg	paO ₂ mmHg	Ca ⁺⁺ mEq/L	Sweep Gas L/min	fiO ₂	Pump Flow L/min
1059	11.6	34	6.771	>130	27			4.8			
1111	9.9	29	6.889	>130	29			2.9			
1118	11.2	33	7.018	>130	19			4.4			
1140	6.1	18	7.111	>130	11			1.8			
1148	7.1	21	6.974	>130	22			3			
1205	9.2	28	6.972	>130	12			2.2			
1218	11.2	33	6.891	>130	13			2.8			
1226	10.9	32	6.958	>130	20			2.5			
1240	11.2	33	6.974	>130	14			2.8			
1302									0	.21	.29
1306			7.224			61.5	59		0	.21	.29
1308	12.2	36	7.153	66.7	56				0	.21	.29
1309									.15	.21	.29
1314	12.2	36				62	57	2.6	.15	.21	.29
1331									.3	.4	.46
1415	19.5	56.7							.3	.4	.46
1419			7.449	27	73				.3	.4	.46
1423	17	50		27	64			2.2	.35	.5	.41
1449						31.2	185	2.3	.35	.5	.41

Ca⁺⁺, ionized calcium; fiO₂, fraction of inspired oxygen; g/dL, grams per deciliter; Hct, Hematocrit; Hgb, Hemoglobin; L/min, Liters per minute; mEq/L, milliequivalents per Liter; mmHg, millimeters of mercury; paCO₂, partial pressure of carbon dioxide in arterial blood; paO₂, partial pressure of oxygen in arterial blood; pH, potential Hydrogen; pvCO₂, partial pressure of carbon dioxide in venous blood; pvO₂, partial pressure of oxygen in venous blood.

shunt was providing some blood flow to the lungs while the patient was being positive-pressure ventilated. The premise for turning off the sweep and oxygen was to circulate the cool deoxygenated hemodilute blood through the patient's tissue beds to mobilize areas of metabolic waste (lactic acid, CO₂, and acidosis) and to minimize the impact of reactive oxygen species to reperfusion injury prone organs, particularly the brain. This technique was used to slowly reinstitute oxygen therapy when the paCO₂/pvCO₂ gradient was minimal. Room air (fiO₂ .21) sweep gas was started at .15 L/min after A/V blood gases were drawn confirming a small A/V pCO₂ gradient (7 minutes without sweep gas). Over the next 30 minutes, the perfusion flow rate was increased to .46 L/min. and the sweep gas and fiO₂ were increased to .3 L/min and 40% respectively. The patient was cooled to 34°C. Once stabilized on ECMO settings he was transferred to the Pediatric Intensive Care Unit (PICU).

Shortly after arriving in the PICU, patient developed hypertension, which subsided with sedative and analgesic agents. A few seizure-like episodes occurred during the first 12 hours after eCPR, which were controlled with phenytoin.

The patient was successfully weaned off ECMO support after 67 hours and 52 minutes and then decannulated. No further seizure activity was recorded. Magnetic resonance imaging (MRI) showed a global hypoxic hypoperfusion injury, post ischemic demyelization/infarction of corpus callosum and cerebral hemisphere deep white matter, cortical infarction with laminar necrosis through perirolandic cortex and diffusely throughout the supratentorial hemispheres, relative sparing of the brain stem, basal ganglia, thalami, cerebral hemisphere, and temporal lobes. The patient was successfully extubated 3 days after decannulation and was discharged home 21 days after weaning from ECMO without further incident. At 6 months of age he had a bidirectional Glenn procedure, which connected his superior vena cava to the pulmonary artery, and his BT shunt was taken down. The operation was successful, and the patient was discharged home without complication.

DISCUSSION

During the post-operative, Stage 1 period, 10–20% will die (4). That percentage can be reduced by an effectively instituted eCPR protocol. The minimization of reperfusion injury seems to be just as important as a rapid deployment strategy (less than 15 minutes of CPR conversion to eCPR) (5). Thus, providers should strive for both rapid deployment and elimination of reperfusion injury. However, in our patient, the deleterious effects of prolonged CPR were minimized via effective eCPR.

Some reperfusion injury will likely occur after prolonged CPR, but it can be minimized with several strategies: 1) cooling systemically (6–8) as recommended by

the International Liaison Committee on Resuscitation and the American Heart Association CPR Guidelines; 2) full eCPR (9); 3) normalizing A/V pCO₂ gradient (10); 4) reducing calcium chloride, which may induce the mitochondrial transition pore that could lead to organ damage (9) and is associated with increased mortality (11,12); and 5) addressing acidosis (13) prior to institution of sweep gas/fiO₂. This last technique seemed to be critical during the initiation of eCPR on our patient when a majority of reperfusion injuries occur (14). We suggest that little oxygenated blood makes it to the hypoxic brain in patients with a BT shunt during a prolonged CPR effort. Thus, such patients have improved cerebral protection from a lack of reperfusion injury associated with intermittent oxygenated blood flow to ischemic tissue. In other words, ischemic tissues are most viable when prolonged acidosis is reduced using the aforementioned strategy.

Seizure activity can be a side effect of neurologic ischemia (6). Due to the aggressive treatment of acidosis with sodium bicarbonate during the resuscitation, the patient's sodium levels were high (>160 mEq/L) which likely exacerbated temporary neurologic damage shown in the MRI study. However, initial cerebral ultrasounds and electroencephalograms both produced results within normal limits.

With current CPR protocols, there is only a 27% survival to hospital discharge with a high incidence of major neurologic sequela (15) in witnessed pediatric cardiac arrest patients. As experience is gained in the field of eCPR, some practitioners are attempting it after longer CPR intervals and/or with older patients yielding minimal reperfusion injury (16,17). Because the greatest risk of mortality during the three stages of a Norwood procedure is post-operative Stage 1 (2), an eCPR protocol should be a universal precaution for these patients. An excellent institutional mortality average of post-surgical Stage 1 Norwood procedures is 10–20% (4). We suggest that some of these deaths could be prevented with an eCPR program in place.

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