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Brief Report
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Early Percutaneous Heparin-Free Veno-Venous Extra Corporeal Life Support (ECLS) is a Safe and Effective Means of Salvaging Hypoxemic Patients with Complicated Chest Trauma

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Background: The objective of this study was to assess the feasibility and safety of heparin-free veno-venous extracorporeal life support (VV ECLS) as a means of salvaging polytrauma patients with life-threatening hypoxemia.

Methods: This is a retrospective observational study on 7 consecutive trauma patients who underwent VV ECLS for severe chest trauma unresponsive to conventional measures.

Results: The median time to ECLS was within 10 hrs (IQR 2-53) of mechanical ventilation. Surgical interventions were performed before and during ECLS based on management priorities consistent with advanced trauma life support guidelines. No heparin was used for at least 4 days in this group with activated coagulation time (ACT) approximating 170 seconds by the 3rd and 4th day. There were no thromboembolic complications. Four patients were successfully discharged and three of these survivors had concomitant traumatic brain injury (TBI) without neurologic sequel.

Conclusions: Early VV ECLS can be used for salvage of patients with traumatic lung injury. Acute trauma care can be continued as needed under heparin-free ECLS without the fear of thromboembolic complications.

Key Words: Adult respiratory distress syndrome • Extracorporeal life support • Multiple trauma • Thoracic injury • Traumatic brain injury

INTRODUCTION

Injury accounts for about 9% of overall deaths worldwide and over 40% of deaths among young people (persons between 10 and 24 years of age).[1] Polytrauma patients usually die from lethal head or thoracic injuries. Most of these deaths occur onsite or within 48 hours of admission, corresponding to the first two peaks of the tri-model distribution.[2] Compared to head injury patients, deaths from severe chest injury are more time-dependent and potentially reversible. In our previous study on trauma fatalities, lethal chest injury was identified as a significant culprit in over 50% of onsite deaths, 57% of early deaths (< 48 hours of admission), and 8% of late deaths (> 48 hours of admission). In contrast, deaths from severe head injuries occurred more sporadically and usually as late deaths.[3] Therefore, managing lethal chest injuries is emerging as a primary focus of acute trauma care. During the acute stage of injury, heparin-free veno-venous extracorporeal life-support (VV ECLS) may be an effective means of salvaging pa-

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tients with hypoxemia that are non-responsive to conventional treatment.

MATERIALS AND METHODS

This is a retrospective observational study on trauma patients who underwent ECLS at a regional trauma center in northern Taiwan. We serve approximately 1000 trauma patients annually, and treat around 70 major trauma cases per year. At our hospital, advanced trauma life support (ATLS)-qualified, in-house staff arrive at the emergency room (ER) within 10 minutes of trauma-team activation. All other surgical subspecialties arrive within 30 minutes of emergency consultation. From September 2009 till September 2012, seven major trauma patients admitted to our hospital received ECLS. Indications for ECLS initiation include tracheal injury irresponsive to conventional means of airway management, Murray score[4] of ≥ 2.5, or a partial pressure of arterial oxygen (PaO_2) in mmHg to fraction of inspired oxygen (FiO_2) ratio (P/F ratio) < 100 mmHg despite optimized mechanical ventilatory support. The decision for ECLS initiation was made by one of two cardiovascular surgeons specializing in trauma care and mechanical organ support. Contraindications for ECLS include fatal cerebral lesion, and out-of-hospital cardiac arrest (OHCA) with return of spontaneous circulation (ROSC) but fully dilated pupils. ECLS is not used for cardiopulmonary resuscitation (ECPR) at our hospital. Hemodynamic compromise after trauma is managed by conventional measures including damage control surgery (DCS), fluid resuscitation, blood transfusion, vasopressors, and inotropes. Thus, venoarterial (VA) ECLS plays a limited role in our acute trauma care, reserved only for patients with severe myocardial stunning or malignant arrhythmias.

VV ECLS is established via the right common femoral vein (RCFV) and the right internal jugular vein (RIJV) using the Seldinger technique. An 18F femoral venous cannula (Medos, Germany) is inserted into the RCFV for venous outflow into the ECLS. A 16F femoral artery cannula (Medos, Germany) is inserted into the RIJV for venous inflow back to the body. We routinely use a centrifugal pump (Rotaflow™), rheoparin® coated ECLS circuit (Medos, Germany), and the HILITE 7000 hollow fiber oxygenator (Medos, Germany). ECLS flow rate is initiated at 500 ml/min to allow for hemodynamic adaptation. Pump flow and gas flow rates are then progressively adjusted to the patient's requirement. All trauma patients are maintained heparin-free until clinical signs of bleeding can be controlled. Afterwards, minimal (or none) systemic heparinization is used to meet the target activated coagulation time (ACT) at 170 seconds.

Acute trauma care under VV ECLS is generally not different from other major trauma patients. However, three basic principles deserve emphasis. First, mechanical ventilation settings followed a lung protection protocol targeting peak inspiratory pressure (PIP) < 30 cm H_2O, mean airway pressure (MAP) < 15 cm H_2O, and fraction of inspired oxygen (FiO_2) < 60%. The second principle is mild hypothermia (34-36 °C) for TBI or post-resuscitated patients. Hypothermia is usually maintained around 34 °C for at least 24 hours or until increased intra-cranial pressure (IICP) can be controlled. The third principle is adequate control of bleeding. In addition to DCS, massive transfusion (component therapy) and anti-fibrinolytic therapy are applied no differently from non-ECLS trauma patients. Following hemorrhage control, we generally keep the hematocrit (Hct) ≥ 30%, and platelet ≥ 50,000/uL unless otherwise indicated.

Statistical analysis

Continuous variables are reported as mean with standard deviation or median with interquartile range (IQR). Categorical and discrete variables are presented as frequencies and percentages. All analyses were performed using SPSS version 15.0.

RESULTS

Indications and timing for ECLS

From September 2009 till September 2012, seven polytrauma patients admitted to our hospital required ECLS. Table 1 lists the baseline characteristics and peri-ECLS interventions of all patients. The median age in this group was 31 years (IQR 21-49) with the majority being male (n = 6, 85.7%). The mechanism of injury was primarily traffic accident (n = 5, 71.4%) followed by fall (n = 2, 28.6%). Injury severity score (ISS) median is 36 (IQR 27-57). Severe injury, defined as abbreviated injury

Table 1. Characteristics of polytrauma patients undergoing VV ECLS

Case	Age	Sex	Mechanism and Injuries	ISS	Intervention before ECLS	Murray score and P/F ratio	Pre-ECLS MV (h)	Intervention on ECLS
1	67	M	Fall down staircase 1.Right hemopneumothorax 2.Re-expansion lung injury with ARDS	16	1.Tube thoracostomy	2.75 P/F 35.9	2	Nil
2	49	M	Crush between 2 trucks 1.OHCA with ROSC 2.Left hemopneumothorax 3.Right lung contusion with 5-9th rib fracture 4.Heart contusion with myocardial stunning (LVEF 25%) 5.Hypoxic encephalopathy	75	1.Tube thoracostomy	2.75 P/F 61.4	10	1.Hemodialysis catheter insertion + CRRT
3	31	M	Vertical fall (4^{th} floor) 1.Bilateral lung contusion with multiple rib fx 2.Rt hemopneumothorax, intrapulmonary hemorrhage 3.Open fx of mandibular bone	27	1.Tube thoracostomy	3.0 P/F 55.8	63	1.Hemodialysis catheter insertion + CRRT
4	21	F	Motorcycle crash into construction vehicle 1.Traumatic tracheal rupture 2.Bilateral hemopneumothrax s/p tube thoracostomy 3.Multiple rib fx (right 5-7, left 1,10) 4.Left temporal ICH (TBI) 5.Deep tongue laceration wounds 6.Left knee PCL rupture	36	1.Tube thoracostomy, bilateral	2.75 P/F 105.0	2	1.Partial sternotomy with tracheal repair
5	21	M	Motorcyclist-to-car collision 1.Head injury with severe brain swelling, RSE (TBI) 2.Bilateral lung contusion, intrapulmonary hemorrhage 3.Rt femoral fx 4.Lt humeral head fx 5.Liver hematoma 6.Spleen hematoma	45	Nil	3.0 P/F 56.8	53	Nil
6	31	M	Car crash into ramp on expressway 1.Bilateral hemopneumothorax 2.Right flail chest 3.Left pericardial rupture 4.Traumatic SAH with brain swelling (TBI) 5.Liver laceration 6.Spleen laceration 7.Left olecranon and mid-shaft fx 8.Bilateral calcaneal fx 9.Nasal bone fx	34	1.Left thoracotomy + evacuation of blood clot 2.Pericadial repair + hemostasis 3.Right tube thoracostomy 4.Craniotomy + ICP monitor + EVD insertion	2.75 P/F 65	6	1.ORIF with locking plate of left olecranon and mid-shaft fx 2.Close reduction and slpint fixation of bilateral calcaneal fx
7	19	M	Motorcyclist-to-car collision 1.Left hemopneumothorax 2.Bilateral lung contusion 3.Traumatic SAH with severe brain swelling (TBI) 4.Skull base fracture 5.Jejunal peforation with intra-abdominal bleeding 6.Pelvic fracture 7.Bilateral femoral shaft fracture	57	1.Tube thoracostomy 2.Craniotomy + ICP monitor 3.DPL	3.0 P/F 48.3	23	1.Laparotomy + jejunal repair + abdominal drainage + Bogota bag closure 2.Hemodialysis catheter insertion + CRRT

ARDS, acute respiratory distress syndrome; CRRT, continuous renal replacement therapy; DPL, diagnostic peritoneal lavage; EVD, external ventricular drain; F, female; fx, fracture; ICH, intracranial hemorrhage; ICP, intracranial pressure; M, male; MV, mechanical ventilation; OHCA, out-of-hospital cardiac arrest; P/F, PaO_2/FiO_2 ratio; ROSC, return of spontaneous circulation; RSE, refractory status epilepticus; SAH, subarachnoid hemorrhage; TBI, traumatic brain injury; VV ECLS, veno-venous extracorporeal life support.

score (AIS) ≥ 3, was predominantly in the chest (100%) followed by the head and neck region (5/7, 71.4%), the abdomen (2/7, 28.6%), and the extremities (1/7, 14.3%). Lung injury was generally severe as assessed by a Murray score of 2.75-3.0. The primary indication for ECLS was to correct hypoxemia (defined by a P/F ratio < 100 mmHg under FiO_2 100% and peak end expiratory pressure (PEEP > 10 cmH_2O) for at least 2 hours of conservative management). The median time to ECLS was within 10 hours (IQR 2-53) of mechanical ventilation.

Surgery before and under ECLS

Surgical interventions were performed as needed based on priorities suggested by the ATLS guidelines. ECLS was initiated after hemorrhage control and confirmation of hypoxemia intractable to optimal conventional measures for at least 2 hours. Invasive procedures performed before and under ECLS are as listed in Table 1.

Heparinization

VV ECLS was routinely initiated without systemic heparinization. The mean ACT level during the first 96 hours without heparinization is depicted in Figure 1. No intervention was made to elevate the ACT level. Correction of the lethal triad in trauma (hypothermia, coagulopathy, and acidosis) was attempted as routine upon trauma admission. The patient's body temperature was maintained at 34-36 °C, platelet was kept above 50,000/uL, and hematocrit was kept above 30%. There was no evidence of thromboembolic complication in any of the patients.

Outcome

Five of 7 patients were successfully weaned off ECLS. However, one patient died from irreversible brain damage 3 days later. The remaining four survivors were followed at our out-patient department for at least 18 months. Only 2 patients were unsuccessfully weaned off ECLS (Table 2).

Traumatic brain injury (TBI)

Four of 7 patients had concomitant TBI. Two had

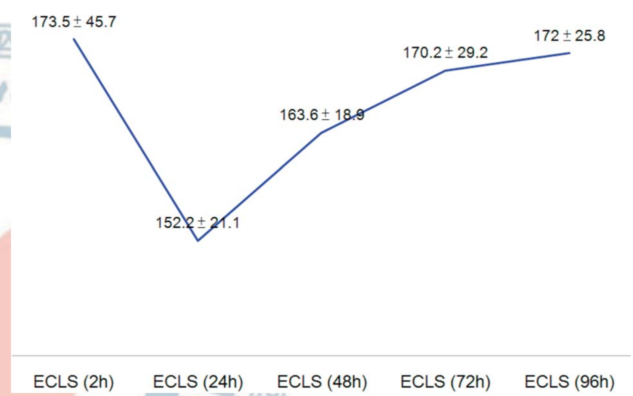

Figure 1. *Activated coagulation time (ACT) levels during heparin-free veno-venous extra corporeal life support (VV ECLS).*

Table 2. Outcome

Case	On ECLS (d)	Weaned off ECLS	ICU (d)	LOS (d)	Cause of death	Complications (In-Hospital)	Follow-up duration
1	9	Yes	26	37	N/A	ARF Acute pancreatitis	2010/1/9-2011/7/6
2	5	No	5	5	Irreversible brain damage with vasodilatory shock	ARF Brain swelling	N/A
3	9	No	11	11	Septic shock with MOF	ARF Sepsis	N/A
4	5	Yes	15	27	N/A	Transient memory deficit	2010/8/30-present
5	17	Yes	24	48	N/A	Nil	2010/10/13-present
6	17	Yes	23	37	N/A	Nil	2012/6/29-present
7	4	Yes	7	7	Irreversible brain damage with vasodilatory shock	Acute lung edema ACS ARF Brain swelling	N/A

ACS, abdominal compartment syndrome; ARF, acute renal failure; ECLS, extracorporeal life support; ICU, intensive care unit; LOS, length of stay; MOF, multiple organ failure; N/A, not applicable.

SAH and required surgical intervention. Two patients were treated conservatively. Only one patient died in this group due to irreversible brain damage. Heparin-free ECLS lasted from 4-17 days depending on individual needs. All three survivors attained full neurologic recovery during follow-up (Table 2).

DISCUSSION

Indications for ECLS in trauma

Acute lung injury (ALI) and hypoxemia irresponsive to conventional therapy

Similar to most reported series, all patients in our study received VV ECLS due to clinical evidence of severe chest injury and hypoxemia irresponsive to conventional therapy (lung protective ventilation[5] and fluid conservative therapy[6]). It has been known for decades that the lung is the most likely organ to fail following trauma and is associated with the highest mortality. In our previous study analyzing trauma fatalities, severe chest trauma (AIS ≥ 3) was the most significant predictor of death within the first 48 hours.[3] During this period, VV ECLS can be a powerful tool to stabilize hypoxemia, avoid immediate death, and facilitate subsequent treatment of circulatory or hemodynamic compromise. Beyond the first 48 hours, correction of hypoxemia is also crucial because respiratory dysfunction is the major contributor to early multi-organ failure (MOF).[7] Thus, hypoxemia irresponsive to conventional therapy is the most important indication for ECLS intervention in patients with severe polytrauma.

How is hypoxemia from post-traumatic ALI defined?

Post-traumatic ALI is typically secondary to either direct lung injury (ie. pulmonary contusion, inhalation injury) or indirect lung injury (ie. overwhelming sepsis, transfusion, pancreatitis).[8] Similar to medical acute respiratory distress syndrome (ARDS), the severity of post-traumatic ALI is defined by the P/F ratio. In this series, we initially adopted the criteria for fast entry enrollment of ECLS as reported by Huang et al (P/F ratio < 60 mmHg at PEEP > 10 cmH2O, after at least 2 hours of conservative management)[9] However, a more liberal threshold of P/F ratio < 100 mmHg as adopted by more recent studies[10] was later utilized.

Contraindications to VV ECLS in trauma?

The only absolute contraindication to VV ECLS during acute polytrauma is fatal cerebral lesions and states of observed prolonged hypoxia.[10] Relative contraindication to ECLS is uncontrolled bleeding.

Timing

When to initiate VV ECLS?

Timing is crucial for VV ECLS. In our series, 5 patients were treated within 48 hours, and 2 patients were treated within 72 hours of admission. Early experiences from the University of Michigan showed a clear advantage in both recovery and survival among trauma patients treated with ECLS within 5 days of mechanical ventilation support.[11] In 2006, Cordell-Smith also reported a clear distinction in pre-ECLS intubation time between survivors (61 hours) and non-survivors (87 hours). However, ECLS in these earlier studies were aimed at the management of respiratory failure as a part of late MOF (> 48 hours). In today's setting, ECLS is intended for the rescue of trauma patients with acute intractable hypoxemia. In our previous study on trauma fatalities, over 90% of trauma deaths presenting with severe chest injury died within 48 hours.[3] Rapid correction of hypoxemia during this period may have improved survival in this population. We currently adopt a modified fast-entry approach with initiation of VV ECLS within 2 hours of aggressive therapy if oxygenation cannot be maintained (if P/F < 100 mmHg under 100% FiO_2, PEEP 10 cmH_2O, and peak inspiratory pressure 30 cmH_2O).[9] As with most trauma centers, ECLS is initiated at the emergency room (ER), intensive care unit (ICU), or operating room (OR) depending on the patient's priority in trauma care and the patient's actual cardiopulmonary deterioration.[10] In the event of uncontrolled bleeding, DCS should be performed to control bleeding before, or at least in conjunction to ECLS initiation in the operation room.

Heparinization

Traditionally, systemic heparinization was required during all ECLS runs. The use of ECLS was often deterred in trauma patients who had active bleeding and required surgical intervention. Early experiences from the University of Michigan group proposed to taper the ACT level from 180-200 seconds down to 140-170 seconds in trauma patients with active bleeding.[11] Nonetheless, most trauma centers refrained from ECLS use in patients requiring aggressive surgical intervention and allowed only simple bedside procedures during ECLS treatment due to the risk of bleeding.[12] In today's setting, a heparin-free ECLS protocol can be integrated into the ATLS management protocol without fear of thromboembolic or bleeding complications.

Initial Heparin-free protocol (< 48 hours) is generally safe

In patients suffering from severe chest trauma and active bleeding, heparin-free VV ECLS can be safely performed for the first 48 hours or till bleeding tendency is controlled.[10] Coexisting hemorrhagic shock can be treated before and on ECLS with fluid resuscitation and massive blood transfusion using units of packed red blood cells, fresh frozen plasma, platelets and coagulation factor (e.g., prothrombin complex and fibrinogen).[10] In general, treatment of severe bleeding in trauma patients requiring ECLS can be regarded the same as treatment of hemorrhagic shock and coagulopathy in trauma patients without ECLS.[10] Once the bleeding and signs of shock has been controlled, heparin can be initiated keeping aPTT at 50-60 seconds[13] or an ACT value around 150 seconds[10] depending on institutional protocols.

TBI

TBI with Intracranial bleeding is not a contraindication for ECLS

To date, TBI and/or intracranial bleeding are still considered to be a contraindication for ECLS therapy at many hospitals. Therefore, experiences of ECLS for patients with TBI remain limited. The first report on successful craniotomy under ECLS in a multiply traumatized patient with severe thoracic and brain injuries was reported by Friesenecker in 2005. This successful treatment with beneficial neurological outcome suggested that ECLS should not be withheld from severely injured patients with combined brain and thoracic trauma presenting with life-threatening hypoxemia. However, heparin-free protocol was not used and the ACT was closely controlled at 150 seconds.[14] In a more recent report by Muellenbach et al., three trauma patients suffering from ARDS combined with TBI were successfully treated with heparin-free VV ECLS.[15] In 2013, Biderman reported a series of 10 patients including 7 with TBI and six patients survived. The median Glasgow Coma Scale (GCS) score on arrival was 7 (range, 5-9) and improved in all survivors to 14 (range, 12-15). All but two patients regained normal neurologic status during follow-up. Follow-up computed tomography were performed in all patients during hospitalization, and no patient demonstrated worsening of cerebral bleeding.[16] In our series, VV ECLS was not withheld from patients with TBI despite evidence of intracranial bleeding. Prolonged heparin-free ECLS was used. All survivors recovered full neurologic status during our follow-up (up to 4 years).

Management of TBI can be performed as routine (IICP control, anti-fibrinolytics, transfusion)

The management of TBI can be performed as routine before and during VV ECLS. This includes the control of IICP, the use of anti-fibrinolytics, and blood transfusion.[10] Mild hypothermia (34 °C) can also be induced in patients with severe TBI without significant bleeding complications.[16] Furthermore, ECLS can provide excellent temperature control and optimal oxygen delivery to injured brain tissue.

CONCLUSIONS

Clinical trials to assess the role of ECLS in acute trauma care are difficult to conduct simply because major trauma patients with hypoxia die quickly. Thus, evidence can only be built from cumulative case experiences. To date, there is growing support for its use and some suggestions can be proposed. First, VV ECLS is primarily indicated for trauma patients with ALI and hypoxemia irresponsive to conventional measures. Once indicated, it should be initiated early to avoid build-up of oxygen debt which leads to early death or MOF. However, bleeding with shock must be effectively controlled with DCS either before or in conjunction with initiation of ECLS. Bleeding with coagulopathy can be treated with routine anti-fibrinolytics and component therapy under heparin-free ECLS without the fear of circuit failure or thromboembolic events. Finally, TBI is not contraindicated for ECLS and routine management including mild hypothermia (34 °C) can be tolerated under heparin-free VV ECLS.

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