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Case Report

Recurrent Use of VV ECMO in Refractory Hypoxemia After Penetrating Lung Injury and Multifocal Pneumonia in a Single Individual's ICU Stay

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PENETRATING CHEST trauma, although much less common than blunt chest trauma, is associated with the highest mortality rate compared with all other types of trauma.[1,2] In the small percentage of patients who survive the initial penetrating injury, the risk of mortality is due to the ensuing operative interventions, open chest, and mechanical ventilation. This scenario creates a complex and high-risk setting for several pulmonary complications. These complications include inter-related pathologies such as pulmonary contusions, pulmonary hemorrhage, acute respiratory distress syndrome (ARDS), pulmonary embolism, pneumonia, empyema, and pulmonary edema.[3]

To overcome the sequalae from the injury, complex ventilation strategies including inverse ratio ventilation, airway pressure release ventilation, and low stretch ventilation may be used to limit secondary alveolar damage.[4] Advanced airway maneuvers, such as single- lung ventilation with bronchial blockers and double- lumen endotracheal tubes, may be used to protect potential staple lines and avoid ventilation of large bronchopleural fistulae. Additional management with inhalation medications, including epoprostenol and nitric oxide, can be used as pulmonary vasodilators if needed. Despite all these techniques, extracorporeal membrane oxygenation (ECMO) can be used for refractory situations. Several large studies have described the use of ECMO in ARDS secondary to pneumonia, and several studies have described the use of ECMO in blunt trauma-induced ARDS; however, to the authors' knowledge no case reports have described the use of ECMO twice in the same patient for 2 different indications in a single intensive care admission. This case presents a patient who was placed on venovenous (VV) ECMO first in the setting of a penetrating gunshot wound to the lung hilum that required clamshell resuscitative thoracotomy with successful ECMO decannulation and second, several days later, for ARDS secondary to a complicated ventilator-associated pneumonia.

Case

A 23-year-old man presented to the authors' emergency room with 2 gunshot wounds via police drop-off so no prehospital resuscitation was performed. Primary assessment revealed diminished breath sounds on the left, palpable radial and

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femoral pulses, and a GCS of 14. Exposure revealed 1 posterior bullet wound entering left of the thoracic spinal cord with no exit wound, and a second bullet wound over his left posterior thigh causing crepitus and bone instability. Focused Assessment with Sonography for Trauma examination was negative. Given concern for hemodynamic compromise and likely hemothorax, an emergently placed left tube thoracostomy was performed, which drained 200 mL of frank blood. After thoracostomy tube placement, the patient developed hematemesis and was intubated for airway protection. Given the combination of positive-pressure ventilation, administration of- rapid sequence medication, and massive hemothorax, the patient's compensatory mechanisms were overcome and he became pulseless. Due to the loss of vital signs, a left resuscitative thoracotomy was performed. More than 2 liters of blood were evacuated from the left chest cavity. Aortic cross-clamp was applied, and blood was noted to be emanating from the left pulmonary hilum and parenchyma. Direct cardiac massage was performed followed by several doses of intravenous epinephrine, calcium, and bicarbonate. The incision was extended into a clamshell thoracotomy after the determination of right-sided hemothorax and expanding superior mediastinal hematoma. In addition to the pulmonary injuries, there were also significant vascular injuries, including lacerations to the superior vena cava and pulmonary artery, which were repaired first. After 15 of minutes of direct intermittent cardiac massage, vascular access, and hilar clamping, 2 doses of direct intra-cardiac epinephrine were administered, which in combination with other resuscitative efforts, led to ventricular fibrillation. Direct paddle cardiac defibrillation with 20 joules of energy was administered 3 times, and the heart regained organized rhythm followed by a sustained blood pressure confirmed by end-tidal capnography and palpable carotid pulse. At this point, the patient was emergently taken to the operating room.

In the operating room, the patient underwent exploration of the chest through the clamshell incision, and the lacerations in his superior vena cava and left superior pulmonary artery were definitively repaired. The displaced superior bronchus was also repaired. A complete left lung tractotomy was performed attempting to ligate all surgical bleeding sites through the gunshot wound tract. Once surgical stabilization was reached, the chest was temporarily closed with an Abthera VAC (3M-KCI), and the patient was taken to the intensive care unit for further management. With ongoing resuscitation, intraluminal blood clots and extraluminal pulmonary bleeding, pulmonary contusions, $\dot{V}/\dot{Q}$ mismatch, and trauma-related ARDS, the patient progressively deteriorated to treatment-refractory hypoxemia. Initial maneuvers, including airway pressure release ventilation and addition of epoprostenol, were unsuccessful at maintaining saturations greater than 80%. Fiberoptic bronchoscopy revealed severe left luminal bleeding and clot; therefore, a bronchial blocker placement was attempted but unsuccessful. The chest was re-opened at the bedside and hemothorax evacuated. The previous repairs were inspected and found to be intact, with bleeding from the lateral musculature and raw surfaces. This maneuver transiently improved hemodynamic parameters but oxygenation remained low. At this point, a total of 8 hours since admission, the patient had received 1 unit of whole blood, 18 units of packed red blood cells, 14 units of fresh frozen plasma, 5 pooled packs of platelets, and 10 units of cryoprecipitate. Attempted ratio for administration of blood product was 1:1:1, with replacement driven by thromboelastography.

The lung rescue team was consulted at this point due to refractory hypoxemia, and the patient was then placed on venovenous ECMO (VV ECMO) through a 25- French multistage right femoral inflow cannula and 18- French end- hole right internal jugular outflow cannula, with TEE guidance at the bedside. No heparin bolus was administered. At the time of cannulation, the ventilator settings were assist control volume control with a respiratory rate of 34 breaths per minute (bpm), tidal volumes of 300 (4 mL/kg), a positive end-expiratory pressure (PEEP) of 15 mmHg, and an Fio_2 of 100%. His lung mechanics were a peak airway pressure of 50 mmHg, a plateau pressure of 40 mmHg, an I:E ratio of 1:1.6, and a compliance of 20 (100 mL/cm H_2O). His vital signs included an invasive blood pressure of 70/51 and pulse oximeter of 71% oxygen saturation. His arterial blood gas prior to ECMO cannulation was pH 7.07, $PaCO_2$ of 92 mmHg, and Pao_2 of 59 mmHg. Heparin was not used for bolus or maintenance of ECMO circuitry. His initial ECMO settings were 4.43 LPM, 3583 RPM, on 100% O_2 with a sweep of 4 LPM. The patient had an excellent response to VV ECMO, and noted saturations were 100% on pulse oximeter with a Pao_2 of 430 mmHg, and he was able to maintain his blood pressure. Over the next several days, the patient required fewer vasoactive infusions, and successful weaning from VV ECMO was accomplished. His sweep gas was rapidly reduced from 4 LPM to 1 LPM over 2 days, and his Fio_2 was reduced to 40% over 7 days. The decision was made to hold off on anticoagulation due to the repeat nature of going to the operating room daily until chest closure. Five days after his initial presentation, he underwent chest re-exploration and closure. Two days postclosure he was decannulated from ECMO after a total of 7 days of extracorporeal support. His ventilator settings at the time of decannulation were assist control volume control, respiratory rate of 16 bpm, tidal volume of 400 cc, PEEP of 10, Fio_2 of 60%. His compliance at the time of decannulation was 45 (100 mL/cm H_2O), and his plateau pressure was 26 mmHg. After decannulation he was placed on a heparin infusion for lower extremity deep venous thrombosis (DVT). Following decannulation, the patient remained intubated but progressing on the ventilator; however, 3 days later he developed a leukocytosis and fever. Bronchoalveolar lavage specimens revealed pseudomonas species. Repeat chest computed tomography (CT) revealed a loculated pneumothorax, right lower lobe atelectasis, and an infiltrate consistent with pneumonia in the right lung. He progressively deteriorated during the course of 3 days after the CT scan. In response, multiple ventilator strategies were attempted for lung- protective measures in addition to paralysis and deep sedation. Broad-spectrum antibiotics were initiated. Given his deteriorating condition, 1 week after decannulation from VV ECMO, he was re-evaluated for VV ECMO secondary to refractory hypoxemia from infectious ARDS. His ventilator

settings at this time were assist control volume control with a respiratory rate of 32 bpm, tidal volumes set at 300 mL, PEEP of 20, and Fio_2 of 100%. His peak airway pressure was 76 and compliance was 10. His arterial blood gas was pH 7.1, $PaCO_2$ 61, and Pao_2 76, and demonstrated a combined hypercarbic and hypoxemic respiratory failure.

His second cannulation strategy was a 25- French multistage left femoral venous inflow cannula and 18- French end -hole right internal jugular outflow cannula. This was performed by the lung rescue team at the bedside with TEE guidance. A bolus of 5000 units of heparin was administered at the time of cannulation. His initial ECMO settings were 4.4 LPM, 3650 PRM, 100% Fio_2. and a sweep of 4 LPM. Heparin infusion with a goal activated partial thromboplastin time (aPTT) of 40- to- 50 seconds was used throughout the second ECMO cycle per the authors' institutional protocol. The second run time for VV ECMO was 3 weeks. After meeting criteria for decannulation he was removed from the ECMO circuit. The day after he had a tracheostomy placed and he had a successful 10-day mechanical ventilator wean with progressive pressure support trials. Three months postinjury, he was discharged to a rehabilitation facility cognitively and neurologically intact, ventilator liberated, tracheostomy decannulated, ambulating, and fully verbal. He had no limitations and was followed up in the trauma clinic 1 month after being discharged after successfully completing his physical therapy rehabilitation.

Discussion

Twenty-five percent of all trauma-related deaths are the result of chest injury. Much of the literature is focused on the more common blunt chest injury. Penetrating chest injury remains a smaller subset of all chest injury, and survival after the initial insult is less common. A small study from 2 trauma centers described 25 patients who had penetrating chest injury and survived the damage control thoracotomies. Six of 25 (24%) patients eventually died of coagulopathy or persistent bleeding. Mattox et al. described their experience with operative thoracic trauma during a 15-year period, and the mortality in 397 patients was 27%.[1,5] Here the authors present a case of a patient who presented after penetrating gunshot wound lung injury requiring an emergency thoracotomy complicated by persistent hypoxemia. Eight hours into his hospital stay, due to the combination of blast injury, massive resuscitation, and arteriovenous shunting, the patient developed multifactorial ARDS requiring initiation of VV ECMO. It is difficult to pinpoint the exact mechanism of injury that led to refractory hypoxemia, but it was likely multifactorial in nature. Ballistic lung injuries can cause pulmonary contusions and parenchymal edema, both pathologic processes that prevent gas exchange. In this case, the patient had an open chest after a resuscitative thoracotomy. This resulted in the inability to maintain PEEP. When mechanical ventilation is done without PEEP, the alveoli repetitively fall below the lower inflection point, and this is theorized to cause further alveolar resultant damage.[6] Additionally, tractotomy and acute ligation of arterial blood supply to the lung can cause shunting of blood from potential gas exchanging units, causing $\dot{V}/\dot{Q}$ mismatch. Furthermore, intraluminal bleeding and intracellular inflammatory agents can lead to difficulty with gas exchange across the alveolar membrane.[7] In 1 retrospective study, 51.7% of polytrauma patients with thoracic injury developed ARDS and 21.5% developed pneumonia.[2,8] The median time to ARDS in the thoracic injury population was 2 days. In major thoracic trauma vessel injury, bilateral lung contusion, bilateral flail chest, and structural heart injury were found to be independent risk factors for worsened mortality.[3]

Extracorporeal membrane oxygenation (ECMO) is a platform that can provide cardiac or pulmonary support.[9] The CESAR trial for refractory ARDS demonstrated that VV ECMO had a survival of 75% versus 47% with conventional ventilator management.[10] The subsequent Extracorporeal membrane oxygenation for severe Acute respiratory distress syndrome trial also demonstrated a 35% mortality rate for VV ECMO compared with 46% with conventional treatment; this trial, however, did not reach statistical significance.[11] Of note, 28% of the patients in the conventional arm crossed over to the ECMO treatment arm, leading the authors to conclude that earlier application of ECMO may have resulted in a statistically significant improvement and survival benefit. Therefore, these data are suggestive that salvage rescue VV ECMO might be too late to expect lung recovery. For patients who fail standard management, early ECMO is emerging as a primary option. There are drawbacks to early ECMO, which include the potential need for anticoagulation. Decision to initiate anticoagulation in a trauma patient is challenging. The risk and benefit of anticoagulation need to be weighed against the presence of trauma-induced coagulopathy. Furthermore, exposure to the ECMO circuit also can cause consumption of clotting factors and lead to platelet dysfunction and reduction in platelet count. Thus far, many case reports and observational studies have demonstrated a survival benefit of ECMO in trauma patients refractory to the standard management.[12] However, the survival benefit of ECMO remains undefined, especially because active hemorrhage remains a contraindication to ECMO.[13] VV ECMO provides a platform in which "lung rest" with low tidal volumes limits barotrauma and halts the inflammatory cascade related to mechanical ventilation. Cordell-Smith et al.[14] reported a retrospective review over 8 years in which 28 trauma patients were placed on ECMO for severe respiratory failure. Twelve of these patients had blunt chest trauma requiring ECMO. In this group the average Murray score was 3.1, and 10 of 12 thoracic trauma patients survived.[14] A second, more recent study, from Ahmad et al.[12] described 46 patients placed on VV or VA ECMO after chest trauma; 39 of these patients were on VV ECMO and 7 patients on VA ECMO. They had no survivors in the VA cohort. Of the 39 patients placed on VV ECMO, 5 patients had penetrating chest trauma; 49% of patients on VV ECMO survived to hospital discharge. The researchers found that anticoagulation was not an independent risk factor for mortality or ECMO-related complications. They did note that this could be based on selection bias, as patients who were actively coagulopathic and in hemorrhagic shock were not deemed good candidates for VV ECMO to begin with.[12]

A literature review by Bedeir et al. published a survival range of 50% to 79% for ECMO in trauma.[15] The most recent study, using the largest dataset available from ELSO, queried 87,366 ECLS runs and found a total of 279 patients in whom ECMO was used in trauma settings. Thoracic trauma accounted for the largest number of trauma diagnoses, and the most common indication was ARDS. Ninety percent of the patients were placed on VV ECMO.[16] A separate study of the Extracorporeal Life Support Organization database looked at blunt thoracic trauma and demonstrated that the mean duration of VV ECMO was 207.4 hours +/- 23.8 hours, and survival to discharge was 74.1%.[17] This study was limited to blunt thoracic trauma, and no cases described the use of repeat prolonged ECMO use. Duration of ECMO was associated with worsened outcome. These data did suffer from selection and publication bias; nonetheless, it highlighted that with appropriate and judicious selection criteria, ECMO outcomes in trauma can be comparable to the EIOLA mortality for nontrauma ARDS of 35%.

The advent of newer generation technologies including cannula design, oxygenators, and centrifugal pumps with lower risk of thrombosis, can help reduce or eliminate the maintenance anticoagulation requirements.[13] In the authors' particular case, in the setting of massive blood transfusions and ongoing bleeding, they elected not to heparinize the circuit at the initiation or in the maintenance phase of the first ECMO run. Forgoing anticoagulation increases the risk of thrombosis and clot formation when the blood contacts the foreign surfaces; however, there have been several studies reporting the successful use of VV ECMO without anticoagulation or with low aPTT/ACT targets.[18] Furthermore, in this case the authors did not appreciate a decline in the oxygenator capacity or experience any arterial or venous limb clots. On the other hand, thrombosis needs to be balanced with the increased bleeding risks associated with the ECMO circuit exposure. It is well documented that exposure to the extracorporeal circuit promotes bleeding owing to platelet activation, loss of Von Willebrand Factor, activation of inflammatory cascade molecules, and consumption of clotting factors.[18] Additionally, the tubing, oxygenator, and centrifugal pump cause shear stress and decrease platelet counts. These risks need to be assessed prior to using VV ECMO in the penetrating trauma setting. In this patient, it was possible that although circuit clot did not occur, the patient still developed DVTs and pulmonary embolisms, which accelerated his respiratory failure.

Pseudomonas pneumonia and sepsis were the indications for the second ECMO run. This was evidenced by the week-long progressive increase in white blood cell count, CT scan with infiltrates, and bronchoalveolar lavage consistent with pseudomonas. Furthermore, the ventilator settings were consistent with decreased compliance and increased airway secretions. According to 1 study, patients with thoracic trauma who are mechanically ventilated are at risk of pneumonia, once intubated for longer than 108 hours.[19] The authors believed that the improvement of mechanical ventilator parameters including improvement in lung compliance demonstrated that these 2 indications for ECMO were distinct. For the second course of VV ECMO, the authors heparinized with a bolus dose of 5000 units during cannulation and maintenance dose targeting aPTT of 40 to 50 for the duration of 3 weeks. The authors thought that the patient was well out of the window for coagulopathy secondary to acute trauma and now was in the second phase, which included a prothrombotic state. This was evidenced by the presence of several DVTs in the lower extremities.

The challenging decision-making in this case was the repeat use of VV ECMO. ECMO is a high-cost, resource-intense service using multiple physicians, perfusionists, nursing staff, and ICU space. It could be argued, in retrospect, that the initial decannulation from ECMO may have been too early; however, the patient had met criteria for decannulation. He had increased compliance, lower PEEP levels, and decreased ventilator Fio_2 settings and progressed to chest closure. Once Fio_2 and sweep gas levels have stabilized, patients who meet criteria should be decannulated to avoid prolonged exposure to ECMO. General complications for prolonged ECMO include DIC, membrane oxygenation failure, bleeding, stroke, and thrombosis. Therefore, early and expeditious removal of ECMO is warranted when possible. The discussion revolving around the second ECMO cannulation also hinged on the idea of palliation versus treatment. At the time of the second ECMO cannulation the patient was critically ill, paralyzed, had completed 1 ECMO run, survived direct cardiac massage, and had a clamshell thoracotomy. Palliative care groups have introduced the term "bridge-to-nowhere" for patients who are on a mechanical support device with no exit strategy. The authors used a multidisciplinary approach in their decision prior to recannulating for VV ECMO. After several discussions, they thought that this second cause of ARDS was infectious in nature and a treatable problem. They therefore proceeded with VV ECMO. The patient slowly progressed and eventually was weaned after completing 2 series of antibiotic treatments.

In conclusion, this patient showed the advanced application of ECMO in trauma ARDS and pneumonia ARDS. This case is unique, highlighting the application of anticoagulation-free ECMO and the repeat application of ECMO in the same patient, which to the authors' knowledge, has not been described. ECMO is an advanced treatment modality; however, this should not deter cardiac or intensivist anesthesiologists from the application of this lifesaving tool. The authors advise readers to set a realistic expectation to both caregivers and families with prolonged or heroic ECMO use. This decision needs to involve the ECMO team as well as intensivists, anesthesiologists, and surgeons.

Conflict of Interest

None.

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