Extracorporeal Carbon Dioxide Removal in the Management of Complex Bilateral Flail Chest Injury

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Flail chest is an uncommon consequence of traumatic injury. Medical management includes mechanical ventilation for internal pneumatic stabilization. Control of respiratory drive is necessary to avoid paradoxical movement and impairment of recovery. Traditional approaches include sedation and neuromuscular blockade, but these measures are at odds with current trends of keeping patients awake and implementing active rehabilitation. We hypothesized that extracorporeal carbon dioxide removal (ECCO2R) would suppress the respiratory drive sufficiently to permit synchronous mechanical ventilation, allowing rib fracture healing in an awake patient with extensive bilateral flail chest. A patient with 21 fractures underwent ECCO2R for 6 weeks to permit internal pneumatic stabilization with mechanical ventilation, targeting a PaCO2 of 25–30 mm Hg. The first 2 weeks were performed with extracorporeal membrane oxygenation (ECMO) for bilateral pulmonary contusions and acute respiratory distress syndrome. The last 4 weeks was with low-flow ECCO2R. Respiratory drive was suppressed during both ECMO and ECCO2R phases when the targeted hypocapnia range of 25–30 mm Hg was achieved, permitting synchronous positive pressure ventilation in an awake and cooperative patient undergoing active rehabilitation. Extracorporeal carbon dioxide removal targeting hypocapnia is a potential adjunct in extensive flail chest injury undergoing nonsurgical management. *ASAIO Journal* XXX; XX:00–00.

Key Words: blunt chest trauma, flail chest, pulmonary contusion, extracorporeal membrane oxygenation, extracorporeal carbon dioxide removal

Traumatic injury is the leading cause of death in young people. Thoracic injury resulting from trauma and complications related to such injuries are responsible for up to 25% of deaths from traumatic injuries.[1] Flail chest, defined as the fracture of four or more consecutive ribs in at least two sites in each rib, is rare but can be a life-threatening injury.[2,3] The injury results in paradoxical motion of the chest wall during spontaneous respiration which leads to increased work of breathing, hypoxemia, and hypercarbia. Flail segments can be unilateral or bilateral. Flail chest represents 10% of thoracic trauma cases and has a reported mortality rate between 10% and 20%, and bilateral flail chest has a higher mortality than unilateral.[4] Flail chest often presents as a complex injury with associated underlying pulmonary contusion that contributes further to hypoxemia and altered pulmonary compliance.

Management consists of aggressive pulmonary toilet, appropriate analgesia, and noninvasive or invasive ventilatory support to provide internal pneumatic stabilization.[5] Despite appropriate therapy, flail chest is associated with high morbidity, high treatment costs, and long intensive care unit (ICU) stays.[6] Supported spontaneous ventilation may have a better outcome than controlled mechanical ventilation.[7] One of the challenges in the use of spontaneous ventilation in the severe spectrum of flail chest is that altered chest wall compliance leads to ineffective tidal ventilation and hypercapnia, dyspnea, and increased respiratory effort, undermining the therapeutic goal of stabilizing the chest wall.

We hypothesized that extracorporeal removal of carbon dioxide (ECCO2R) could be a useful adjunct to manage hypercapnia and dyspnea in flail chest, allowing the application of internal pneumatic stabilization in the awake patient using supported ventilation by diminishing respiratory drive sufficiently to allow synchronous mechanical ventilation.

Extracorporeal removal of carbon dioxide can be achieved with extracorporeal membrane oxygenation (ECMO), which provides both oxygenation and carbon dioxide (CO2) removal, and with ECCO2R, which provides CO2 removal without significant oxygen transfer. ECMO has been used for the management of severe hypoxemic respiratory failure in the adult since 1971.[8] Initially used in a limited number of centers, the advent of improved pump systems and artificial membrane lungs, supported by findings from the CESAR trial,[9] and catalyzed by the needs of the 2009 H1N1 pandemic, the application of ECMO has dramatically increased.[10] A more recently introduced concept, ECCO2R, targets CO2 removal through the use of low blood flow rates,[11] permitting smaller cannulas and simplified circuits, and can be used in hypercapnic states or to support lung-protective ventilation in hypoxemic respiratory failure.[12,13] Thus, CO2 can be removed with both ECMO and ECCO2R, with and without oxygenation, respectively.

Case Report

A 35-year-old Caucasian male with extensive chest wall and pulmonary trauma following vehicular ejection was transferred to our trauma center. His injuries consisted of unilateral pelvic fracture, left clavicle injury, bilateral pulmonary contusions, and fractures of the right second to 12th and left first to 10th ribs. His flail chest and pulmonary injury were initially managed with sedation, neuromuscular blockade, and controlled

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mechanical ventilation. Over 96 hours he developed progressive severe hypoxemic respiratory failure (posttraumatic acute respiratory distress syndrome) requiring extracorporeal support. Extracorporeal membrane oxygenation was initiated in the venovenous configuration initially to provide both oxygenation and CO_2 removal. Vascular access was obtained by percutaneous cannulation with a 31 Fr dual lumen Avalon Elite bicaval cannula (Maquet Cardiopulmonary GmbH, Rastatt, Germany) *via* his right interior jugular vein. The extracorporeal system included a Rotaflow centrifugal blood pump and Quadrox-D oxygenator (Maquet Cardiovascular, LLC, Wayne, NJ). Blood flow rates were initiated at 50 ml/kg/min (3.5 L/min) and titrated as needed to optimize oxygen delivery. Anticoagulation with argatroban targeted an activated partial thromboplastin time of 50–70 seconds.

During ECMO, support ventilator settings were reduced to lung-protective levels (PPLAT < 26 cm H_2O), whereas oxygen saturation and arterial CO_2 partial pressure were initially normalized with ECMO. Tracheotomy was performed to facilitate rehabilitation. Reduction in sedation, however, was complicated by dyspnea with increased respiratory drive preventing chest wall stabilization. This was managed by increasing the sweep gas flow of the circuit to induce hypocapnia (target $PaCO_2$ 25–30 mm Hg) and suppress the respiratory drive. This approach was effective in suppressing the respiratory drive allowing synchronized controlled ventilation in an awake, cooperative patient.

Following 2 weeks of ECMO support, his hypoxemia improved and he was decannulated. Post decannulation, his sedation was further weaned to allow for more intensive physical therapy. Pain medications were adjusted to prevent oversedation while maintaining an acceptable level of pain control. Despite support with mechanical ventilation post ECMO, he continued to have ineffective ventilation from chest wall instability that progressed to hypercapnic respiratory failure. As an alternative to employing deep sedation, neuromuscular blockade and controlled mechanical ventilation at this stage, $ECCO_2R$ was implemented with the goal of reducing ventilatory requirements and eliminating his respiratory drive while avoiding sedation and paralysis. Extracorporeal carbon dioxide removal was initiated with the same circuit components as ECMO following cannulation of the left internal jugular and left femoral vein with 16 Fr single lumen cannulae. Blood flow was maintained at a lower flow of 1.0–1.5 L/min to minimize risk of hemolysis[14] and sweep gas maximized at 10 L/min. Similar anticoagulation targets were maintained as during the ECMO support phase. As before, his target $PaCO_2$ was maintained between 25 and 30 mm Hg, suppressing his respiratory drive.

This strategy was maintained without ventilator weaning attempts for an additional 4 weeks to allow for rib fracture healing. Surgical management was not considered because of the extensive involvement of the thoracic cage and the risks associated with anticoagulation. He was then decannulated and subsequently weaned from mechanical ventilation with eventual removal of his tracheostomy. In a follow-up visit 1 month after discharge, he had a normal 6-minute walk test.

Discussion

Blunt thoracic trauma complicated by flail chest can result in paradoxical movement of the flail segment during spontaneous ventilation, with reduced minute ventilation and development of hypercapnia. Concomitantly, atelectasis and altered ventilation-perfusion matching lead to mild to moderate hypoxemia. The primary management goal for flail chest is stabilization of the chest wall to prevent paradoxical chest wall movement, prevent or correct hypercapnia, and maintain functional residual capacity until sufficient fibrous callous formation develops in about 6 weeks. Secondary goals include correction of hypoxemia with supplemental oxygen, management of secretions, and analgesia to support effective ventilation. The traditional and most common stabilization approach is to use positive intrathoracic pressure (internal pneumatic stabilization). In patients breathing spontaneously with small flail segments, continuous positive airway pressure is usually sufficient. A prospective study by Gunduz *et al.*[7] in moderate severity flail chest compared noninvasive CPAP and mild sedation with invasive mechanical ventilation and sedation plus neuromuscular blockade, demonstrating a higher survival in the CPAP group. These findings are consistent with recent practices of minimizing sedation to allow for intensive physical rehabilitation. Surgical stabilization with the aim of reducing duration of positive pressure support can be considered in selected patients, but there is no widely accepted device, technique, or timing.[5] In the presence of severe pulmonary contusion, surgical stabilization is relatively contraindicated since mechanical ventilation is still required to support oxygenation.[15]

In more extensive flail injury, tachypnea and increased inspiratory work of breathing can thwart attempts at stabilization with mechanical ventilation. Greater respiratory effort can also lead to high transpulmonary pressures with the development of ventilator-induced lung injury.[16] The traditional way of managing these patients is to induce deep sedation with neuromuscular blockade to eliminate the respiratory drive. However, this approach requires prolonged immobilization that can lead to long-term neuromuscular complications and diaphragm dysfunction as well as hospital-acquired pulmonary infections.[17–19]

Control of respiratory drive can be achieved in patients with extracorporeal support. Early experimental studies by Kolobow *et al.*[20] demonstrated that spontaneous breathing in lambs with normal respiratory drive could be completely suppressed when CO_2 removal equaled CO_2 production. Langer *et al.*[21] repeated similar experiments in a sheep model with acute respiratory distress syndrome (ARDS). Their results indicated that although control of respiratory drive could be achieved in ARDS, it required higher levels of CO_2 removal compared with normal lungs. This was confirmed in a study of patients recovering from ARDS, in which $ECCO_2R$ resulted in a decrease in P0.1 (inspiratory airway occlusion pressure at 100 ms, a measure of inspiratory effort) as well as support level during neurally adjusted ventilatory assist or pressure support.[22]

Our patient had essentially a complete flail chest (21 rib fractures) with severe pulmonary contusions and ARDS requiring early ECMO to maintain adequate arterial oxygen saturation. ECMO removes CO_2 more efficiently than it provides oxygen transfer, and this was exploited to reduce the patient's ventilatory drive through the induction of hypocapnia. With a reduced drive, he was able to have his sedation reduced and removed and to participate in a program of physical rehabilitation, previously demonstrated to decrease length of ICU stay.[23] He was not considered for surgical fixation due to his anticoagulation and extent of injury requiring intervention. Extracorporeal membrane oxygenation was explanted after 2 weeks of support when ARDS resolved sufficiently, and it was no longer needed for oxygenation. However, his respiratory drive increased, and he showed signs of increased respiratory effort with inadequate stabilization of the flail chest. Increasing sedation and using neuromuscular blockade was not considered an attractive option because of his rehabilitation progress, so he was placed on ECCO2R to reinduce hypocapnia. This was effective in sufficiently reducing his respiratory drive for the duration of time felt adequate for fracture healing, allowing continued mobility and rehabilitation. At 6 weeks following his injury, he was given a trial without ECCO2R support and was able to maintain stable thoracic excursions with supported ventilation. He was transferred to an inpatient rehabilitation facility to complete his weaning from mechanical ventilation and continue an aggressive physical therapy program.

Based on this experience, ECCO2R may be considered as an adjunctive therapy in selected patients with flail chest when there is a need to reduce respiratory drive and effort when supporting patients with medical management. Further study of this hypothesis is warranted. Modern application of ECCO2R is associated with low risk of complications, the most common of which is bleeding, but rarely life-threatening and usually manageable. A new generation of extracorporeal systems designed for simplified application of ECCO2R is under development and may further simplify the application of this type of support.

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