

Extra Corporeal co2 Removal in Critical Care : A Review

Seyed Mohammad Reza Hashemian^{*}, Negin Kasiri

Chronic Respiratory Diseases Research Center (CRDRC), National Research Institute of Tuberculosis and Lung Diseases (NRITLD),
Shahid Beheshti University of Medical Sciences, Tehran, Iran

Abstract

Hypoxia and hypercapnia are the consequences of respiratory failure. Correcting hypercapnia with a low risk of ventilator induced lung injury has drawn the attention of the researchers to extracorporeal technologies that facilitate extracorporeal CO₂ removal (ECCO₂ R). In this review article, we briefly discussed the definition, the physiology of ECCO₂R and its role as an adjunct to mechanical ventilation in acute respiratory distress syndrome. In patients with chronic obstructive pulmonary disease, when noninvasive ventilation fails, ECCO₂R could be an alternative to mechanical ventilation. Patients awaiting lung transplantation, who are more prone to life threatening hypercapnia, benefit from ECCO₂R.

Keywords :

Introduction

Respiratory failure refers to a condition in which the respiratory system is unable to maintain adequate gas exchange to satisfy metabolic demands. An important syndrome leading to respiratory failure in critically ill patients is the acute respiratory distress syndrome (ARDS), which leads to poor lung function with hypoxemia, hypercapnia, and low respiratory system compliance. In these conditions, mechanical ventilation provides adequate oxygenation and facilitate CO₂ removal. Nonetheless, ventilation occurs at the expense of a secondary injury to the lung (ventilator-induced lung injury or VILI) due to inhomogeneous lung over distension. In this situation, inflammatory mediators are released and cause multiple organ failure. Ultra protective ventilation strategy employs lower tidal volumes, a lower respiratory rate, lower driving pressures, and lower plateau pressures while maintaining an adequate mean airway pressure to avoid a reduction in functional residual capacity. However, the strategy puts its user at the risk of hypercapnia and its consequences include systemic and cerebral vasodilatation, cardiovascular depression, arrhythmia, and pulmonary vasoconstriction with an increase in pulmonary arterial pressure. Acute pulmonary hypertension increases right ventricular (RV) afterload and causes acute cor pulmonale which is associated with high mortality rates [12]. The need to correct hypercapnia without exposing the lung to mechanical trauma has drawn the attention of the researchers to extracorporeal CO₂ removal (ECCO₂ R).

Definition and physiology of ECCO₂R:

ECCO₂ R is a technique of partial respiratory support that

removes CO₂ from the blood through a low blood flow (0.4–1 L/min) extracorporeal circuit, without any significant effect on blood oxygenation. Consider that extracorporeal membrane oxygenation (ECMO) uses blood flows of 3–7 L/min to provide total respiratory support with significant oxygenation and CO₂ removal. In many expert centers the devices used to provide ECMO and ECCO₂R support are the same. Although the original purpose for ECCO₂R was to provide additional CO₂ clearance in patients with severe ARDS to reduce tidal volumes and inspiratory pressures, it can also be employed for the patients suffering from Chronic Obstructive Pulmonary Disease (COPD) and work as a bridge to transplant or facilitate thoracic surgery.

Blood oxygenation is dependent on blood flow, whereas CO₂ exchange is dependent on ventilation, gas flow, blood CO₂ content, hemoglobin [13] and the efficacy of the gas exchange membrane.

An ECCO₂R circuit consists of a drainage cannula placed in a large central vein (or artery), a membrane lung, and a return cannula into the venous system. In the case of arterio venous (AV) systems, the patient's blood pressure provides the driving pressure across the membrane, while veno venous systems require a pump to be placed within the circuit. (Figure 1, 2) [26]

Access to the circulation is obtained either through separate arterial and venous cannula (AV systems or pump less systems) or by using double-lumen cannula (VV systems).



Figure : 1



Figure : 2

The AV system needs two single-lumen wire reinforced cannula, one in the femoral artery to access blood and one in the femoral vein to return the blood to the venous side. Disadvantages of this cannula are arterial injury and limb ischemia which is thought to relate to operator experience, patient factors such as peripheral vascular disease, and the size of arterial cannula. The venous cannula is usually larger than the arterial cannula to reduce resistance to blood flow. They can be placed in any large central vein although the jugular and femoral approaches are most commonly used [14]. Some cannulae have heparin coatings to decrease the risk of thrombosis.

Evidence shows that by using ECCO2R, PaCO₂ can be reduced and arterial pH due to respiratory acidosis improved [15]. AV ECCO2R has also been shown to reduce minute ventilation in an uncontrolled cohort of 159 patients over 10 years [16]. Similarly VV ECCO 2 R can effectively decrease PaCO₂, tidal volume and airway pressures in patients with ARDS [17,18].

The role of extracorporeal CO₂ removal as an adjunct to mechanical ventilation in ARDS:

Dominant features of ARDS include injury to the alveolar-capillary membrane, which results in severe hypoxemia,

decrease in pulmonary compliance, and increase in pulmonary vascular resistance [1,2]. Despite new hopeful therapeutic interventions such as protective ventilation, prone positioning, use of neuromuscular blockers and conservative fluid balance, ARDS remains a devastating disease [3,4]. Mortality rates are still remains near 40%, because of hemodynamic complications of this syndrome [5]. Positive-pressure mechanical ventilation is the important part of symptomatic treatment for ARDS [3], but may further increase pulmonary hypertension and right ventricular (RV) afterload, leading to acute cor pulmonale and RV failure [6]. Mechanical ventilation induces additional lung injuries due to overdistention, repeated stretch to the alveoli, atelectotrauma, and increased inflammatory mediator levels [7]. Ventilation strategy involving limitation of mean tidal volume to 6 ml/kg, as compared with a more traditional tidal volume of 12 ml/kg [3], shows a reduction in mortality. However, utilization of lower tidal volumes leads to permissive hypercapnia. Indeed, the need to substantially reduce tidal volume and improve the outcome in ARDS patients remains questionable [8]. As the discussion about optimization of mechanical ventilation in ARDS patients continues, extracorporeal CO₂ removal (ECCO2R) come up. Modern technology used for optimization, could effectively remove metabolically produced CO₂ while permitting significant reductions in minute ventilation in preclinical [9,10] and clinical settings [11]. Specifically, combination therapy using reduction in tidal volumes to around 4 ml/kg along with ECCO2R has been shown to effectively manage permissive hypercapnia in ARDS [11]. In moderate to severe ARDS, ECCO2R should be considered as a therapeutic adjunct which is combined with further decrease in tidal volume. Recent major technological improvements in devices make them simpler, safer, less invasive and more efficient, requiring lower blood flow rates and smaller access cannulas with reduced anticoagulation requirements.

ECCO₂R as an alternative to mechanical ventilation when noninvasive ventilation fails in COPD:

In severe COPD exacerbations, hypercapnia is the result of high airway resistance, ventilation/perfusion mismatch, dynamic hyperinflation, and increased work of breathing with increased CO₂ production.

ECCO2R is being considered as an adjunctive therapy to noninvasive respiratory support (NIV) to promote the withdrawal of NIV, avoid intubation, or facilitate early extubation. The feasibility of using VV ECCO2R for acute hypercapnic respiratory failure due to COPD exacerbations has been demonstrated in several recent cases and cohort studies [19-22].

In a retrospectively propensity matched cohort study it was found that AV ECCO2R could consistently decrease PaCO₂

, improve respiratory acidosis, and reduce respiratory rate in 21 patients suffering from acute hypercapnic respiratory failure (mainly COPD) who were failing NIV [23]. In this study 90% of the patients treated with AV ECCO2R did not require intubation and invasive mechanical ventilator support, and showed a tendency towards a reduced length of hospital stay, but not mortality.

There has been a recent retrospective cohort study using historical controls reported from Italy where 25 patients at high risk of NIV failure who received ECCO2R via a dual-lumen cannula in the femoral vein. They experienced lower intubation rates (HR 0.27) and a lower mortality [24]. But 36% of patients experienced device malfunctions and 12% of patients had bleeding complications, including one vessel perforation.

ECCO2R can be a bridge to transplant

The Patients awaiting lung transplantation, who are prone to life-threatening hypercapnia, may benefit from ECCO2R as bridge to transplantation. The mortality of patients with an acute deterioration requiring mechanical ventilation is substantially increased when compared with those patients who do not require mechanical ventilation. The possible advantages of ECCO2R are the avoidance of intubation and mechanical ventilation.

In a study of 20 patients, the most common underlying diagnoses were reported to be bronchiolitis obliterans syndrome, cystic fibrosis, and idiopathic pulmonary fibrosis. Hypercapnia and acidosis were corrected in all patients within the first 12 h of ECCO2R therapy: nineteen patients (95%) were successfully transplanted. Hospital and 1-year survival were 75 and 72%, respectively [25].

ECCO2R and complementary continuous renal replacement therapy (CRRT)

In patients with acute kidney injury (AKI), volume overload and activation of inflammatory factors with excretion of cytokines, induce apoptosis of pulmonary cells endothelium, leads to respiratory distress. On the other hand, in acute lung injury, hypoxia, hypercapnia and respiratory acidosis could lead to AKI. Increasing the level of positive end-expiratory pressure (PEEP) cause decreasing cardiac output and renal blood flow which follows by renal cell apoptosis. Considering, atrial natriuretic peptide production suppress, so oliguria and volume overload occurs. In respiratory distress, pro inflammatory cytokines could cause renal injury too. As a result continuous renal replacement therapy (CRRT) is needed. Addition of gas exchanger to this renal circuit could combine ECCO2R and CRRT, leads to protection against respiratory distress effect and acidosis. Patients usually require several central venous catheters; there for using a single pathway for ECCO2R and CRRT might be beneficial. (28, 29)

Conclusion:

Technological advances in ECCO2R, can create an opportunity for an extended role of partial extracorporeal CO₂ removal. For patients with moderate-severe ARDS and patients with hypercapnic respiratory failure, it can serve as a supportive modality. The potential complications of ECCO2R need to be assessed when considering patients for extracorporeal support.

References:

1. Cancio LC, Batchinsky AI, Dubick MA, et al. Inhalation injury: pathophysiology and clinical care proceedings of a symposium conducted at the Trauma Institute of San Antonio, San Antonio, TX, USA on 28 March 2006. *Burns*. 2007;33:681–92.
2. Lheritier G, Legras A, Caille A, et al. Prevalence and prognostic value of acute cor pulmonale and patent foramen ovale in ventilated patients with early acute respiratory distress syndrome: a multicenter study. *Intensive Care Med*. 2013;39:1734–42.
3. The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. The Acute Respiratory Distress Syndrome Network. *N Engl J Med*. 2000;342:1301–8.
4. Zambon M, Vincent JL. Mortality rates for patients with acute lung injury/ ARDS have decreased over time. *Chest*. 2008;133:1120–7. Morimont et al. *Critical Care* (2015) 19:117 Page 6 of 7
5. Squara P, Dhainaut JF, Artigas A, Carlet J. Hemodynamic profile in severe ARDS: results of the European Collaborative ARDS Study. *Intensive Care Med*. 1998;24:1018–28.
6. Lheritier G, Legras A, Caille A, et al. Prevalence and prognostic value of acute cor pulmonale and patent foramen ovale in ventilated patients with early acute respiratory distress syndrome: a multicenter study. *Intensive Care Med*. 2013;39:1734–42.
7. Slutsky AS, Ranieri VM. Ventilator-induced lung injury. *N Engl J Med*. 2013;369:2126–36.
8. Ijland MM, Heunks LM, van der Hoeven JG. Bench-to bedside review: hypercapnic acidosis in lung injury – from ‘permissive’ to ‘therapeutic’. *Crit Care*. 2010;14:237.
9. Batchinsky AI, Jordan BS, Regn D, et al. Respiratory dialysis: reduction in dependence on mechanical ventilation by venovenous extracorporeal CO₂ removal. *Crit Care Med*. 2011;39:1382–7.
10. Batchinsky AI, Chung K, Cannon J, Cancio LC. Respiratory dialysis is not extracorporeal membrane oxygenation. The authors answer. Extracorporeal membrane oxygenation and respiratory dialysis: our expending tool box. *Crit Care Med*. 2011;39:2788–9.
11. Terragni PP, Del Sorbo L, Mascia L, et al. Tidal volume lower than 6 ml/kg enhances lung protection: role of extracorporeal carbon dioxide removal. *Anesthesiology*. 2009;111:826–3.
12. Morimont P, Batchinsky A, Lambermont B. Update on

the role of extracorporeal CO₂ removal as an adjunct to mechanical ventilation in ARDS. *Critical Care* (2015) 19:117.

13. M. Park, E. L. V. Costa, A. T. Maciel et al., "Determinants of Oxygen and Carbon Dioxide Transfer during Extracorporeal Membrane Oxygenation in an Experimental Model of Multiple Organ Dysfunction Syndrome," *PLoS ONE*, vol. 8, no. 1, Article ID e54954, 2013.

14. C. E. Ventetuolo and C. S. Muratore, "Extracorporeal life support in critically ill adults," *American Journal of Respiratory and Critical Care Medicine*, vol. 190, no. 5, pp. 497–508, 2014.

15. Health Quality Ontario, "Extracorporeal lung support technologies—bridge to recovery and bridge to lung transplantation in adult patients: an evidence-based analysis," *Ontario Health Technology Assessment Series*, vol. 10, no. 5, pp. 1–47, 2010.

16. B. Flöorchinger, A. Philipp, A. Klose et al., "Pumpless extracorporeal lung assist: a 10-year institutional experience," *Annals of thoracic Surgery*, vol. 86, no. 2, pp. 410–417, 2008.

17. M. E. Cove, G. MacLaren, W. J. Federspiel, and J. A. Kellum, "Bench to bedside review: extracorporeal carbon dioxide removal, past present and future," *Critical Care*, vol. 16, no. 5, article 232, 2012.

18. A. Pesenti, N. Patroniti, and R. Fumagalli, "Carbon dioxide dialysis will save the lung," *Critical Care Medicine*, vol. 38, no. 10, supplement, pp. S549–S554, 2010.

19. D. C. Abrams, K. Brenner, K. M. Burkart et al., "Pilot study of extracorporeal carbon dioxide removal to facilitate extubation and ambulation in exacerbations of chronic obstructive pulmonary disease," *Annals of the American Thoracic Society*, vol. 10, no. 4, pp. 307–314, 2013.

20. R. Roncon-Albuquerque, G. Carona, A. Neves et al., "Venovenous extracorporeal CO₂ removal for early extubation in COPD exacerbations requiring invasive mechanical ventilation," *Intensive Care Medicine*, vol. 40, no. 12, pp. 1969–1970, 2014.

21. N. K. Burki, R. K. Mani, F. J. F. Herth et al., "A novel extracorporeal CO₂ removal system: results of a pilot study of hypercapnic respiratory failure in patients with COPD," *Chest*, vol. 143, no. 3, pp. 678–686, 2013.

22. S. Cole, N. A. Barrett, G. Glover et al., "Extracorporeal carbon dioxide removal as an alternative to endotracheal intubation for non-invasive ventilation failure in acute exacerbation of COPD," *Journal of the Intensive Care Society*, vol. 15, no. 4, pp. 344–346, 2014.

23. S. Kluge, S. A. Braune, M. Engel et al., "Avoiding invasive mechanical ventilation by extracorporeal carbon dioxide removal in patients failing noninvasive ventilation," *Intensive Care Medicine*, vol. 38, no. 10, pp. 1632–1639, 2012.

24. L. Del Sorbo, L. Pisani, C. Filippini et al., "Extracorporeal CO₂ removal in hypercapnic patients at risk of noninvasive ventilation failure: a matched cohort study with historical control," *Critical Care Medicine*, vol. 43, no. 1, pp. 120–127, 2015.

25. P. Schellongowski, K. Riss, T. Staudinger et al., "Extracorporeal CO₂ removal as bridge to lung transplantation in lifethreatening hypercapnia," *Transplant International*, vol. 28, no. 3, pp. 297–304, 2015.

26. P. P. Terragni, G. Maiolo, T. Tenaglia, J. Pernechele, V. M. Ranieri. "Extracorporeal CO₂ removal and O₂ transfer: A review of the concept, improvements and future development." *Anesthesia and critical care*, Volume 1, Issue 3, Pages 123–127, 2011.

27. A Lung Technologies, Inc. Low-Flow ECCO₂R for Acute Exacerbation of COPD, p1-6, 2014.

28. Quintard el. Partial Extracorporeal Carbon Dioxide Removal Using a Standard Continuous Renal Replacement Therapy Device: A Preliminary Study. *ASAIO Journal* 2014. 564-569

29. Forster et al.: Low-flow CO₂ removal integrated into a renal-replacement circuit can reduce acidosis and decrease vasopressor requirements. *Critical Care* 2013 17:R154