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Darryl Abrams
Roberto Roncon-Albuquerque Jr.
Daniel Brodie

What's new in extracorporeal carbon dioxide removal for COPD?

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D. Abrams (✉) · D. Brodie
Division of Pulmonary, Allergy and Critical Care,
Columbia University College of Physicians and Surgeons,
New York-Presbyterian Hospital, 622 W. 168th St, PH 8E 101,
New York, NY 10032, USA
e-mail: da2256@cumc.columbia.edu

D. Brodie
e-mail: hdb5@cumc.columbia.edu
Tel.: +1 212 305 9817

R. Roncon-Albuquerque Jr.
Department of Emergency and Intensive Care Medicine,
Centro Hospitalar S. Joao, Porto, Portugal

R. Roncon-Albuquerque Jr.
Department of Physiology and Cardiothoracic Surgery,
Faculty of Medicine of Porto, Porto, Portugal

Interest in the use of extracorporeal carbon dioxide removal (ECCO$_2$R) is increasing, owing to advances in the technology of extracorporeal devices and the efficiency of these devices in removing carbon dioxide at blood flow rates significantly lower than what is required for extracorporeal oxygenation. Because lower blood flow targets allow for the use of smaller cannulae, ECCO$_2$R may have a more favorable risk profile than traditional ECMO cannulation strategies [1, 2].

An area of re-emerging interest in ECCO$_2$R is its use in respiratory failure due to exacerbations of chronic obstructive pulmonary disease (COPD). With the potential to modulate the hypercapnia and the respiratory acidosis associated with respiratory failure in this setting, ECCO$_2$R may facilitate the withdrawal or avoidance of invasive mechanical ventilation along with its associated complications. Recent studies have offered a modern proof-of-concept, although randomized studies are still needed to define the role of ECCO$_2$R in the management of COPD.

Evolving role of ECCO$_2$R in hypercapnic respiratory failure

The concept of using an extracorporeal membrane to manage carbon dioxide is hardly new. Extracorporeal membranes are more efficient at carbon dioxide removal than oxygenation [3], and Gattinoni et al. [4] had previously demonstrated the ability to control ventilation via an extracorporeal device at relatively low blood flow in the context of acute respiratory failure, with the intention of minimizing ventilator-associated lung injury. With newer technology and an improved risk–benefit profile, ECCO$_2$R is being pursued as a means of maximizing a lung-protective ventilation strategy by correcting the hypercapnia and acidemia associated with the application of very low tidal volumes and airway pressures [1, 5, 6]. The same technology may be applied to acute exacerbations of COPD, where hypercapnia and severe respiratory acidosis often require non-invasive ventilation (NIV) or endotracheal intubation and invasive mechanical ventilation (IMV). IMV is associated with multiple complications, including ventilator-associated lung injury, ventilator-associated pneumonia, dynamic hyperinflation and elevations in intrinsic end-expiratory pressure, impaired delivery of aerosolized medications, and decreased mobility. Those patients requiring IMV after a failed trial of NIV have mortality rates as high as 30 % [7]. ECCO$_2$R, by correcting the respiratory acidosis, may both minimize dyspnea and either facilitate rapid weaning from IMV or obviate the need for IMV, prior to resolution of the COPD exacerbation. This strategy helps to avoid the complications associated with endotracheal intubation and IMV and maximizes the potential for active physical therapy, including ambulation [7–9]. Early $ECCO_2R$ systems used pumpless arteriovenous configurations, which have been associated with complications of arterial cannulation [5, 10–12]. The use of a pump-assisted venovenous configuration avoids these risks and allows for better control of extracorporeal blood flow rates [5, 10].

Evidence for $ECCO_2R$ in COPD exacerbations

The feasibility of using venovenous $ECCO_2R$ for acute hypercapnic respiratory failure due to COPD exacerbations has been demonstrated in several recent studies [7, 8, 13]. Burki et al. [13] demonstrated variable success of $ECCO_2R$ in managing a heterogeneous group of patients ($n = 20$), including patients receiving NIV with a high likelihood of requiring IMV, those who could not be weaned from NIV, and those unable to be weaned from IMV. A 15.5-Fr dual-lumen cannula was used for institution of $ECCO_2R$, with a mean blood flow of 430 mL/min (Table 1). This strategy was successful in improving hypercapnia (reduction in $PaCO_2$ from 78.9 to 65.9 mmHg) and respiratory acidosis (increase in pH from 7.25 to 7.36), with variable success in avoiding IMV or liberating patients from positive pressure ventilation. Significant bleeding events occurred in three patients, and one patient died as a consequence of retroperitoneal hemorrhage associated with femoral venous cannulation. In a feasibility study by Abrams et al. [7], five patients with acute respiratory acidosis in the setting of COPD exacerbations who had failed NIV and required IMV were initiated on $ECCO_2R$ to facilitate endotracheal extubation and mobilization. Bicaval, dual-lumen cannulae (20–23 Fr) were introduced into the internal jugular vein under imaging guidance, with extracorporeal blood flow rates of 1–1.7 L/min. All five patients were successfully extubated within 24 h (median duration, 4 h) and ambulating within 48 h of $ECCO_2R$ support. Resolution of dyspnea correlated with correction of pH. Only two minor bleeding complications occurred and there were no device malfunctions. This approach of using $ECCO_2R$ post-NIV failure was reproduced by Roncon-Albuquerque Jr. et al. in a feasibility study of two patients [8]. Each patient underwent $ECCO_2R$ via a 19-Fr dual-lumen cannula introduced into the internal jugular vein with blood flow rates of 0.7–1.0 L/min. Both patients were successfully extubated within 24 h after $ECCO_2R$ initiation, and mobilized during $ECCO_2R$ support without any bleeding or device-related complications.

Table 1 Extracorporeal blood flow rates and cannula sizes used in studies of $ECCO_2R$ for acute hypercapnic respiratory failure

References	$ECCO_2R$ blood flow rate (L/min)	Cannula size (Fr)
Abrams et al. [7]	1.0–1.7	20–23
Burki et al. [13]	0.43	15.5
Del Sorbo et al. [14]	0.18–0.33	14
Kluge et al. [10]	1.1	13–15 (arterial), 13–17 (venous)
Roncon-Albuquerque Jr. et al. [8]	0.7–1.0	19

In a recent study by Del Sorbo et al. [14], patients deemed to be at high risk of NIV failure ($n = 25$) were managed with $ECCO_2R$ via a 14-Fr dual-lumen cannula in the femoral vein with blood flow rates of 177–333 mL/min. Compared to a matched group of historical controls ($n = 21$), the risk of being intubated was significantly lower in the $ECCO_2R$-assisted group (HR 0.27; 95 % CI 0.07–0.98; $p = 0.047$). Thirty-six percent of patients experienced device malfunctions and 12 % of patients had bleeding complications, including one vessel perforation. The relatively low rate of intubation in the control group highlights the difficulty in predicting patients most likely to fail NIV. Although avoidance of endotracheal intubation in this patient population would be preferred, such a strategy has to be weighed against the use of $ECCO_2R$, with its potential complications, in patients who might never have required intubation [15].

Areas of future research

With increasing interest in $ECCO_2R$, there have been a variety of devices developed, each with different blood flow capabilities, catheters, and risk profiles. The field would benefit from a better understanding of these devices' physiological capabilities and complication rates. Randomized controlled trials are ultimately needed to define the role of $ECCO_2R$ for COPD, including the potential economic impact, before such a strategy can be endorsed for widespread clinical use.

Whether $ECCO_2R$ should be instituted before or after endotracheal intubation is a matter of debate. However, given the complication rates of $ECCO_2R$ in some reports, and the inability to reliably predict NIV failure, it may be prudent to focus initially on the role of $ECCO_2R$ only after patients require IMV.

Conflicts of interest Dr. Roncon-Albuquerque Jr. has received honoraria from Maquet-CP-AG for lectures on $ECCO_2R$. Dr. Brodie reports receiving research support and providing research consulting for Maquet Cardiovascular (all compensation paid to Columbia University) and serving on the Medical Advisory Board of A Lung Technologies (all compensation paid to Columbia University). Dr. Abrams has no conflicts of interest to report.

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