

## UNDERSTANDING THE DISEASE



# Understanding hypoxemia on ECCO<sub>2</sub>R: back to the alveolar gas equation

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Extracorporeal CO<sub>2</sub> removal (ECCO<sub>2</sub>R) is a promising technique for ARDS and for severe acute exacerbations of COPD [1]. However, ECCO<sub>2</sub>R carries its own risk of complications and side effects. Beyond hemorrhagic and thrombotic complications and hemolysis, the occurrence of progressive hypoxemia has been reported in COPD patients treated by ECCO<sub>2</sub>R, leading to a tracheal intubation rate of 28% in the prospective series from Braune et al. [2]. Obviously, progressive hypoxemia can be explained by pulmonary complications such as evolving infiltrates, even if other factors such as modification of the respiratory quotient have been proposed [2, 3]. Accordingly, we illustrate such a mechanism, intrinsically linked to the ECCO<sub>2</sub>R technique and not involving any worsening of lung function by itself.

A 76-year-old man was admitted because of a very severe hypercapnic acute exacerbation of a chronic respiratory failure due to non-cystic fibrosis bronchiectasis. Invasive mechanical ventilation (Carescape R860 GE Healthcare) was initiated because of non-invasive ventilation failure. ECCO<sub>2</sub>R was started 24 h later with the goals of limiting hypercapnia and dynamic hyperinflation and promoting a rapid weaning process [4]. The iLA-Active system (Xenios-Novalung, Heilbronn) was used with a 22-Fr right jugular veno-venous catheter. Since weaning was a very difficult process, the sweep gas flow was progressively increased during the next 7 days from 1 to 9 L/min, while the extracorporeal blood flow varied between 0.8 and 1.2 L/min. During the same period, the PaO<sub>2</sub>/FiO<sub>2</sub> ratio progressively decreased from 251 to 145, with no obvious pulmonary complication.

Table 1 indicates the corresponding ABG and PaO<sub>2</sub>/FiO<sub>2</sub> values as well as the DA-aO<sub>2</sub> values calculated either using the classical simplified alveolar air equation, i.e.,  $PAO_2 = PiO_2 - PACO_2/0.8$ , or the exact simplified alveolar air equation using the 0.3 value of the respiratory quotient displayed by the ventilator. Despite the apparent changes in PaO<sub>2</sub>/FiO<sub>2</sub> ratio, the correct DA-aO<sub>2</sub> and PaO<sub>2</sub> were compatible with clinically negligible changes in intrapulmonary shunt, oscillating around 15%, even if we cannot totally exclude confounding factors inferring with the shunt calculation such as a higher mixed venous PO<sub>2</sub> (even if it is generally believed that ECCO<sub>2</sub>R exerts only minimal oxygenation effects), a release of hypoxic pulmonary vasoconstriction due to a higher FiO<sub>2</sub>, or a shunt decrease in relation to higher FiO<sub>2</sub> as described in moderate ARDS. The observed changes in PaO<sub>2</sub>/FiO<sub>2</sub> were therefore mainly justified by changes in PAO<sub>2</sub> due to changes in the VCO<sub>2</sub>/VO<sub>2</sub> ratio of the patient's own lung, rather than to changes in its oxygenation function. Accordingly, no specific pulmonary complication was diagnosed during the following days.

ECCO<sub>2</sub>R exerts predominantly an effective extracorporeal CO<sub>2</sub> removal, without significant effect on oxygenation which accordingly occurs very predominantly in the native lungs, resulting in a decreased native lung respiratory quotient. It is therefore very important to use during ECCO<sub>2</sub>R the exact calculations of PAO<sub>2</sub> and DA-aO<sub>2</sub> when a suitable monitoring system is available, or at least to interpret with great caution any PaO<sub>2</sub>/FiO<sub>2</sub> worsening, which could, at least in part, reflect an ECCO<sub>2</sub>R-induced modification of the alveolar gas content [5].

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**Table 1 Oxygenation values, ABG values, and invasive mechanical ventilation parameters recorded immediately before initiation of ECCO<sub>2</sub>R and under ECCO<sub>2</sub>R after raising the sweep gas flow to 9 L/min**

	Immediately before ECCO <sub>2</sub> R	ECCO <sub>2</sub> R day 7
PaO <sub>2</sub> /FiO <sub>2</sub>	251	145
PaO <sub>2</sub> (mmHg) simplified	186	360
PaO <sub>2</sub> (mmHg) exact	–	248
DA-aO <sub>2</sub> (mmHg) simplified	98	273
DA-aO <sub>2</sub> (mmHg) exact	–	161
R (native lungs) measured by the ventilator	–	0.3
pH	7.31	7.38
PaO <sub>2</sub> (mmHg)	88	87
PaCO <sub>2</sub> (mmHg)	51	54
Ventilatory mode	ACV	ACV
VT (mL/kg IBW)	6	6
RR (/min)	12	10
PEEP (cmH <sub>2</sub> O)	0	5
FiO <sub>2</sub>	0.35	0.6

A alveolar, DA-aO<sub>2</sub> difference between alveolar and arterial O<sub>2</sub> partial pressures, R respiratory quotient displayed by the ventilator, *simplified* assuming that R is equal to 0.8, *exact* using the measured value of R, ACV assist-controlled ventilation, VT tidal volume, RR respiratory rate

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#### Compliance with ethical standards

#### Conflicts of interest

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#### Ethical statement

Treatment with ECCO<sub>2</sub>R was performed as part of a specific registry (Registry on the EXperience of Extracorporeal CO<sub>2</sub> Removal in Intensive Care Units, NCT02965079), benefiting from an approval (07 March 2016) from the Ethics Committee of the French Intensive Care Society.

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