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REVIEW

# Extracorporeal $CO_2$ removal: Technical and physiological fundaments and principal indications☆

E. Romay[a], R. Ferrer[a,b,*]

[a] Servicio de Medicina Intensiva, Hospital Universitario Mútua de Terrassa, Universidad de Barcelona, Terrassa, Barcelona, Spain
[b] Centro de Investigación Biomédica en Red de Enfermedades Respiratorias, Spain

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**Abstract** In recent years, technological improvements have reduced the complexity of extracorporeal membrane oxygenation devices. This has enabled the development of specific devices for the extracorporeal removal of $CO_2$. These devices have a simpler configuration than extracorporeal membrane oxygenation devices and uses lower blood flows which could reduce the potential complications. Experimental studies have demonstrated the feasibility, efficacy and safety of extracorporeal removal of $CO_2$ and some of its effects in humans.

This technique was initially conceived as an adjunct therapy in patients with severe acute respiratory distress syndrome, as a tool to optimize protective ventilation. More recently, the use of this technique has allowed the emergence of a relatively new concept called ''TRA-protective ventilation'' whose effects are still to be determined. In addition, the extracorporeal removal of $CO_2$ has been used in patients with exacerbated hypercapnic respiratory failure with promising results.

In this review we will describe the physiological and technical fundamentals of this therapy and its variants as well as an overview of the available clinical evidence, focused on its current potential.


**PALABRAS CLAVE**
Respiración artificial;
Dióxido de carbono;
Circulación extracorpórea;

**Eliminación extracorpórea de $CO_2$: fundamentos fisiológicos y técnicos y principales indicaciones**

**Resumen** Recientemente las mejoras tecnológicas han permitido reducir la complejidad de los dispositivos de oxigenación por membrana extracorpórea, dando paso al desarrollo de dispositivos específicos para la eliminación extracorpórea de $CO_2$. Estos dispositivos tienen un

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* Corresponding author.
*E-mail address:* rferrer@mutuaterrassa.es (R. Ferrer).

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montaje más simple y utilizan flujos sanguíneos más bajos, lo que potencialmente disminuye las complicaciones vasculares y hemodinámicas. Estudios experimentales han demostrado la factibilidad, eficacia y seguridad de la eliminación extracorpórea de $CO_2$ y algunos de sus efectos en humanos.

Esta técnica, que fue concebida como un tratamiento complementario en los pacientes con SDRA grave, permite la optimización de la ventilación protectora e incluso ha abierto el camino a nuevos conceptos, como lo que se ha denominado ventilación «ultraprotectora»'', cuyos beneficios aún están por determinarse. Además, la eliminación extracorpórea de $CO_2$ se está implementando en pacientes con insuficiencia respiratoria hipercápnica agudizada con resultados prometedores.

En esta revisión describiremos los fundamentos fisiológicos y técnicos de esta terapia y sus distintas variantes, así como la evidencia clínica disponible hasta la fecha, enfocados en su potencial en el paciente con insuficiencia respiratoria.


## Introduction

In recent years, different strategies and technological improvements have made it possible to reduce the size and complexity of extracorporeal membrane oxygenation (ECMO) devices–thereby allowing a gradual increase in the use and safety of these systems.[1,2]

In concordance with these advances, and with the aim of contributing to this simplification process, Gattinoni and Kolobow were the pioneers in describing the need to dissociate oxygenation support from exclusive ventilation extracorporeal support, with the purpose of optimizing lung protection during mechanical ventilation. This gave rise to the extracorporeal $CO_2$ removal (ECCO2R) devices,[3] which extract $CO_2$ from venous blood by passing it through a membrane similar to that used in ECMO. The main difference is that the blood flow rates used in this case are much lower, and the arterial and venous cannulas are therefore smaller.[4] These systems were initially conceived mainly for patients with severe acute respiratory distress syndrome (ARDS), where the protective ventilation strategies produce important hypercapnia.[5] More recently, however, the technique has also been used in patients with exacerbated chronic obstructive pulmonary disease (COPD).[6]

In ARDS, the strategy of the ARDSNet of using a low tidal volume (Vt) (6–8 ml/kg ideal body weight) to reduce lung distension, and a high PEEP to improve oxygenation, resulted in a very important decrease in mortality.[7] In addition, hyperinsufflation and alveolar opening and closure intrinsically lead to a condition known as ventilator-induced lung injury, which is minimized by using this strategy.[8] In a *post hoc* analysis of the study of the ARDSNet, both the patients receiving low Vt and those receiving high Vt were seen to benefit from a plateau pressure (Pplat) of <30 $cmH_2O$, thus evidencing that additional reductions in Vt may be needed in order to maintain Pplat <30 $cmH_2O$.[9] In this same line, it has been shown that the use of low Vt can prevent the development of ARDS in patients at risk.[10] However, despite the described benefits, adherence to the protective ventilation strategy is still not adequate or uniform, and in some cases it may prove insufficient.[11]

## Effects of hypercapnia

The effects of hypercapnia have been extensively studied in animals and have been corroborated in a number of observational clinical studies.[12,13] While hypercapnic acidosis may cause vasodilatation in tissues such as the brain, at pulmonary level it causes vasoconstriction, with an increase in mean pulmonary artery pressure. This, added to the effects of positive pressure ventilation, leads to an important increase in right ventricle afterload.[14] The pulmonary hypertension induced by hypercapnia can contribute to the appearance of *cor pulmonale* in patients with ARDS, with an associated increase in mortality.[15] Likewise, hypercapnia and acidosis are established risk factors for the appearance of arrhythmias, which further complicate the management of these patients. In other tissues, hypercapnic acidosis can increase gastric secretion and induce a degree of systemic vasodilatation.

In contrast, some studies have found that high $CO_2$ concentrations reduce lung injury through attenuation of the effects of the free radicals and a decrease in the activity of neutrophils[16] and other immunological factors, and may even exert protective effects against endotoxin-induced lung damage.[17] However, many of these changes might be explained not only by hypercapnia but also by acidosis, and may even be independent–as occurs in the alveolar epithelial monolayers, where hypercapnia with a compensated pH affords no benefit and may even cause damage.[18]

Different authors have proposed the use of ultraprotective mechanical ventilation (3–4 ml/kg ideal body weight) combined with ECCO2R, with the ultimate aim of preventing acute ventilator-induced lung injury. In potential, this strategy would avoid the risks of hypercapnia and would reduce the needs for sedation.[19,20]

## Technical and physiological fundaments of extracorporeal $CO_2$ removal

Technical simplification has caused the development and potential applications of extracorporeal $CO_2$ extraction