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CORRESPONDENCE

$ECCO_2R$ in COPD exacerbation only for the right patients and with the right strategy

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Dear Editor,

We read with interest the article by Braune et al. recently published in *Intensive Care Medicine*, whose study demonstrated that treatment of COPD exacerbation unresponsive to noninvasive ventilation (NIV) with $ECCO_2R$ prevented endotracheal intubation in 56 % of patients [1]. The results of this study, which are substantially different to those of a previous investigation with similar concept and design [2], trigger a few important considerations.

1. It is of crucial importance to select the right patient population that may benefit from $ECCO_2R$, as $ECCO_2R$ may have a number of putative physiological benefits [3], but it does not cure sepsis or pneumonia, resulting in worsening secretions and hypoxaemia. It was surprising to observe that five patients required intubation for severe secretions and six patients for progressive hypoxaemia due to evolving infiltrates. The presence of abundant respiratory secretions is one of the criteria to shift from NIV to invasive mechanical ventilation (IMV) [4], and should therefore be used as an exclusion criterion in a study that aims to use $ECCO_2R$ to avoid endotracheal intubation. Moreover, it is unusual to observe such a high number of COPD patients developing severe hypoxaemia requiring IMV [5], those should thus probably be excluded. Finally, haemodynamic instability should also be an exclusion criterion, as this is per se a potential indication for endotracheal intubation. In the present study, haemodynamic instability was not listed as an exclusion criterion, and it would be important to know how many patients required vasoactive drugs.
2. The timing of $ECCO_2R$ initiation is also a crucial issue. If it is started too early, patients are exposed to unnecessary $ECCO_2R$-related complications. However, if it is started too late, the potential effect in preventing intubation may be lost. In this regard, the investigators included patients with SAPSII >40 and criteria of established NIV failure rather than patients "at risk" for NIV failure, and therefore they may have been too severely compromised to benefit from $ECCO_2R$.
3. The features of the $ECCO_2R$ circuit are also of crucial importance in determining treatment success. The investigators applied an average $ECCO_2R$ blood flow of 1.3 L/min, which is higher than what is typically applied in COPD exacerbations [6], and may have induced greater damage to platelets, contributing to the higher rate of bleeding events. It is possible that the potential gain provided by the $ECCO_2R$ in preventing intubation has been blunted by the occurrence of bleeding complications. The relatively higher extracorporeal blood flow used in this trial may have also caused oxygenation issues, as the consequent higher amount of CO_2 removal may have potentially led to excessive reduction of tidal volume, increasing the risk of atelectasis and hence hypoxaemia. In addition, higher CO_2 removal results in greater modification of the respiratory quotient, contributing to the development of hypoxaemia.
4. The $ECCO_2R$-treated group was matched to historical controls and their outcomes compared. However, the methods to identify the controls and to perform the matching were not clearly explained, reducing the strength of the results. In matched case–control studies, the risk of selection bias is high and can be

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reduced by performing matching with advanced strategies and using available databases that have undergone quality control [2, 7, 8] rather than newly identified historical cases.

Overall, for the design of a randomized controlled trial investigating the efficacy of $ECCO_2R$ to treat patients with hypercapnia due to COPD exacerbation in order to prevent IMV, it will be important to define the right patient population and the right strategy.

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Compliance with ethical standards

Conflicts of interest
The authors do not have conflicts of interest to declare.

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