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CORRESPONDENCE

COVID-19 pneumonia and ROX index: Time to set a new threshold for patients admitted outside the ICU. Author's reply



We appreciate the interest of Gallardo et al. in our paper “COVID-19 Pneumonia and ROX index: Time to set a new threshold for patients admitted outside the ICU”.¹ We are grateful to the authors for their positive comments, and brilliant insights on the advantages and disadvantages of using the ROX index as a predictor of failure of high-flow nasal cannula in patients with pneumonia due to SARS-CoV-2. We believe these remarks will foster an important debate regarding the interpretation of the ROX index.

The first issue regards the specific strategy to treat acute hypoxemic respiratory failure (AHRF). In their letter,² they state that high flow nasal cannula (HFNC) has been shown to be more effective than standard oxygen therapy and it is recommended as first-line treatment for AHRF. This, however, is not true in patients with COVID-19–related acute hypoxemic respiratory failure in which there was no significant difference between an initial strategy of HFNC compared with conventional oxygen therapy. Instead, an initial strategy of continuous positive airway pressure (CPAP) significantly reduced the risk of tracheal intubation or mortality compared with conventional oxygen therapy.³

Secondly, it is very true what the authors suggested regarding that the parameters that are evaluated can easily vary throughout the day or in different clinical situations (fever, mobilization, fatigue, pain, acidosis, hypotension). Nevertheless, our study assessed the ROX index 4 times in the first 24 hours, so that in this time frame it is very possible to detect any major clinical variation. Indeed, there are already on the market instruments able to monitor continuously this index,⁴ and therefore in the right context it should not be considered a static index.

Furthermore, we totally agree with the authors that a small effect may be observed in the ROX index using different flow in terms of the pressure effect in the airway and favour the lavage of the dead space or increased end-expiratory volume and decreased respiratory rate and work of

breathing. Owing to the fact that the large majority of the studies have mainly used the setting at 50–60 L.min⁻¹ in patients with acute respiratory failure,^{5–7} we used the same flow rate in all patients so as not to bias the sample. Indeed, the index has been so far proposed only in hypoxic patients and some of these physiological mechanisms you are referring to are typical of hypercapnic patients (i.e. lavage of dead space). Also, the generation of airways pressure is never constant, despite the flow used. In other words, HFNC is not equivalent to CPAP in terms of pressure, as you stated. While HFNC controls the flow with a variable pressure, CPAP controls the pressure with a variable flow rate.⁸ Moreover, during HFNC, pressure is also strongly dependent on the closure of the mouth and on average quite small, not overpassing the limit of 4–5 cmH₂O.

In conclusion, above all, we would like to congratulate Gallardo et al who were able to clearly summarize in a few words which parameters to take into account when using the ROX index to monitor a patient with AHRF.

Conflicts of interest

The authors have no conflicts of interest to declare.

References

1. Vega ML, Dongilli R, Olaizola G, et al. COVID-19 pneumonia and ROX index: time to set a new threshold for patients admitted outside the ICU. *Pulmonology*. 2022;28(1):13–7. <https://doi.org/10.1016/j.pulmoe.2021.04.003>.
2. Gallardo A, Zamarrón- López E, Deloya-Tomas E, et al. Advantages and limitations of the ROX Index in Critically ill Patients With High Flow Nasal Cannula. *Pulmonology* 2022. Article in Press.
3. Perkins GD, Ji C, Connolly BA, et al. Effect of noninvasive respiratory strategies on intubation or mortality among patients with acute hypoxemic respiratory failure and COVID-19: the RECOVERY-RS randomized clinical trial. *JAMA*. 2022;327(6):546–58. <https://doi.org/10.1001/jama.2022.0028>.
4. Vega ML, Pisani L. Nasal high flow oxygen in acute respiratory failure. *Pulmonology*. 2021;27(3):240–7. <https://doi.org/10.1016/j.pulmoe.2021.01.005>.

5. Frat JP, Thille AW, Mercat A, et al. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. *N Engl J Med*. 2015;372(23):2185–96. <https://doi.org/10.1056/NEJMoa1503326>.
 6. Mauri T, Turrini C, Eronia N, et al. Physiologic effects of high-flow nasal cannula in acute hypoxemic respiratory failure. *Am J Respir Crit Care Med*. 2017;195(9):1207–15. <https://doi.org/10.1164/rccm.201605-0916OC>.
 7. Grieco DL, Menga LS, Raggi V, et al. Physiological comparison of high-flow nasal cannula and helmet noninvasive ventilation in acute hypoxemic respiratory failure. *Am J Respir Crit Care Med*. 2020;201(3):303–12. <https://doi.org/10.1164/rccm.201904-0841OC>.
 8. Mündel T, Feng S, Tatkov S, et al. Mechanisms of nasal high flow on ventilation during wakefulness and sleep. *J Appl Physiol* (1985). 2013;114(8):1058–65. <https://doi.org/10.1152/jappphysiol.01308.2012>.
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