Reply to: High-Flow versus Venturi Mask Oxygen Therapy to Prevent Re-intubation: A Matter of Time or Device?

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From the Authors:

We thank Dr. Mandal et al. for their letter regarding our study (1).

They asked if we used the ROX index (the ratio of percutaneous oxygen saturation, SpO_2, over the inspired oxygen fraction, FiO2, divided by the respiratory rate) to monitor patients randomized to receive high-flow nasal oxygen in our trial. Although we collected data on SpO_2, FiO_2 and respiratory rate, we did not formally compute the ROX index, we did not use it to assess the risk of failure of high-flow nasal oxygen, nor ROX index was included among the predetermined criteria used to establish the need for endotracheal intubation. We have calculated *a posteriori* the ROX index in patients who received high-flow nasal oxygen and the results are shown in Figure 1. Mean ROX index during the initial 12 hours of treatment was 9.98 in patients who needed endotracheal intubation within 72 hours vs. 12.30 in patients who did not (mean difference 2.31 [CI95%: 0.44 to 4.19], repeated measures ANOVA p=0.016). Values of ROX index in patients who were subsequently intubated are significantly higher than those reported for patients with acute hypoxemic respiratory failure. The pathophysiology of *de novo* hypoxemic respiratory failure may be different from that of post-extubation respiratory failure (2,3) and this may explain the higher ROX values in our trial.

We agree with Dr. Mandal et al. that measurement of N-terminal-pro B-type natriuretic peptide can be helpful to evaluate the risk of weaning failure of cardiovascular origin. Unfortunately, we did not measure this parameter as this assessment was beyond the aims of our study. However, all patients included in the trial successfully passed a spontaneous breathing trial with a T-piece or zero positive end-expiratory pressure, which usually unmasks weaning-induced cardiac failure (4).

We fully agree with Dr. Mandal that dyspnea is an important symptom to monitor in patients with acute respiratory failure. In the RINO trial, dyspnea was not systematically assessed except for patients requiring intubation, as this was among the predefined criteria driving the decision to re-intubate patients. In this case, dyspnea was assessed just asking patients if their shortness of breath was very severe or near maximal. This should correspond to values between 7 and 10 in the visual analog scale

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or modified Borg dyspnea scale. As stated in the article, clinical signs suggestive of respiratory muscle fatigue or increased respiratory effort, not dyspnea, were among the criteria used to define the need for rescue noninvasive ventilation. We did not measure and did not report in the paper values of dyspnea in patients receiving rescue noninvasive ventilation.

Dr. Mandal et al. asked for details on gas humidification and patients' comfort with the oxygenation devices used in our study (i.e. Venturi mask and high-flow nasal oxygen). As stated in the manuscript, oxygen was passively humidified (so-called, cold humidification) with the Venturi mask, while a heated humidifier was used with the high-flow nasal oxygen. Although these two techniques of humidification are commonly employed with these devices, they are not comparable in terms of delivered humidity, being the absolute humidity generated by cold humidification half of that delivered by active (heated) humidification, at best (5). We did not measure patients' comfort in our trial. We did it, however, in a previous study where we used the same devices and settings than in the RINO trial (6). In that study, after 24 hours of treatment, patient's comfort related to symptoms of airways dryness was significantly higher with the high-flow nasal oxygen than with the Venturi mask. Similarly, comfort related to the interface (nasal cannula versus face mask) was also significantly higher with the high-flow nasal oxygen from the 12th hour of treatment.

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References

1. Maggiore SM, Jaber S, Grieco DL, Mancebo J, Zakynthinos S, Demoule A, Ricard JD, Navalesi P, Vaschetto R, Hraiech S, Klouche K, Frat JP, Lemiale V, Fanelli V, Chanques G, Natalini D, Ischaki E, Reuter D, Morán I, La Combe B, Longhini F, De Gaetano A, Ranieri VM, Brochard LJ, Antonelli M; RINO trial study group. High-Flow Versus VenturiMask Oxygen Therapy to Prevent Re-Intubation in Hypoxemic Patients After Extubation: A Multicenter, Randomized Clinical Trial. *Am J Respir Crit Care Med* [online ahead of print] 18 Jul 2022; www.atsjournals.org/doi/abs/10.1164/rccm.202201-0065OC.

2. Grieco DL, Maggiore SM, Roca O, Spinelli E, Patel BK, Thille AW, Barbas CS V, de Acilu MG, Cutuli SL, Bongiovanni F, Amato M, Frat J-P, Mauri T, Kress JP, Mancebo J, Antonelli M. Non-invasive ventilatory support and high-flow nasal oxygen as first-line treatment of acute hypoxemic respiratory failure and ARDS. *Intensive Care Med* 2021;47:851–866.

3. Maggiore SM, Battilana M, Serano L, Petrini F. Ventilatory support after extubation in critically ill patients. *Lancet Respir Med* 2018;6:948–962.

4. McConville JF, Kress JP. Weaning patients from the ventilator. *N Engl J Med* 2012;367:2233–9.

5. Chanques G, Constantin J-M, Sauter M, Jung B, Sebbane M, Verzilli D, Lefrant J-Y, Jaber S. Discomfort associated with underhumidified high-flow oxygen therapy in critically ill patients. *Intensive Care Med* 2009;35:996–1003.

6. Maggiore SM, Idone FA, Vaschetto R, Festa R, Cataldo A, Antonicelli F, Montini L, De Gaetano A, Navalesi P, Antonelli M. Nasal high-flow versus Venturi mask oxygen therapy after extubation. Effects on oxygenation, comfort, and clinical outcome. *Am J Respir Crit Care Med* 2014;190:282–8.

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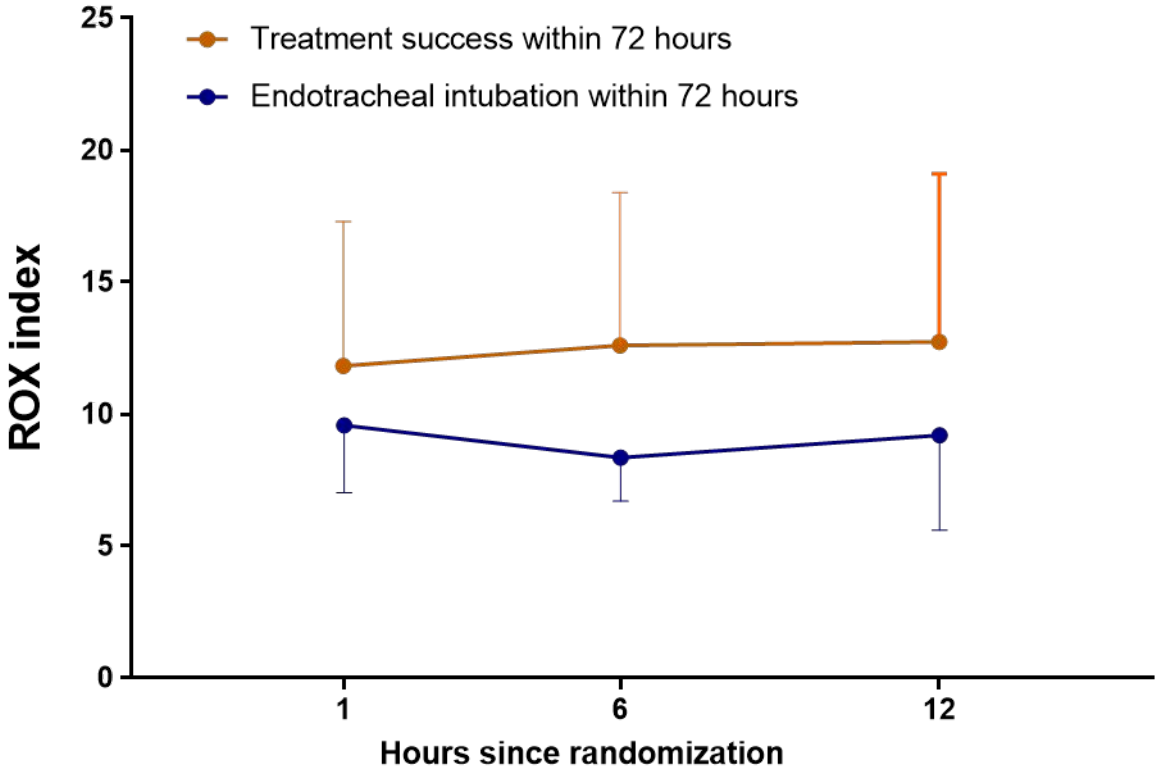
Figure 1.

Values of ROX index in patients undergoing high-flow nasal oxygen in the RINO trial, classified according to the subsequent need for endotracheal intubation within 72 hours from treatment start. Data are expressed as mean and standard deviation.



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