Reply to Mandal *et al.*

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From the Authors:

We thank Dr. Mandal and colleagues for their letter regarding our study (1).

They asked if we used the ratio of percutaneous oxygen saturation (Sp_{O_2}) over $F_{I_{O_2}}$, divided by the respiratory rate (ROX index) to monitor patients randomized to receive high-flow nasal oxygen in our trial. Although we collected data on Sp_{O_2}, $F_{I_{O_2}}$, 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 was the ROX index 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. The mean ROX index during the initial 12 hours of treatment was 9.98 in patients who needed endotracheal intubation within 72 hours versus 12.30 in patients who did not (mean difference, 2.31 [95% confidence interval, 0.44–4.19]; repeated measures ANOVA $P = 0.016$). Values of the 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 postextubation respiratory failure (2, 3), and this may explain the higher ROX values in our trial.

We agree with Dr. Mandal and colleagues that measurement of N-terminal pro–B-type natriuretic peptide can be helpful in evaluating 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. This 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 Reintubation Rate after Oxygen Therapy (RINO) trial, dyspnea was not systematically assessed except for patients requiring intubation, as this was among the predefined criteria driving the decision to reintubate patients. In this case, dyspnea was assessed just by 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 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.

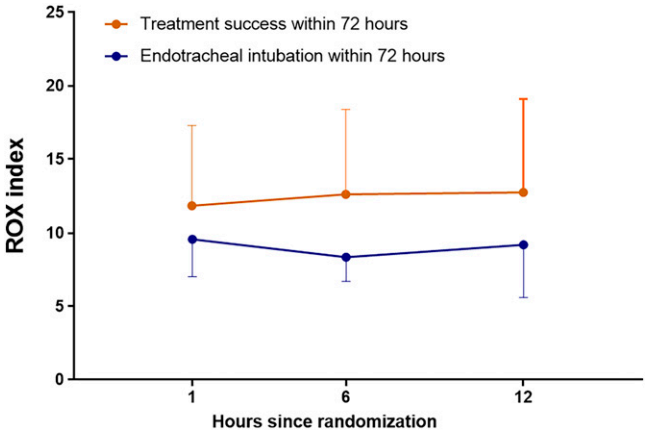

Figure 1. Values of the ROX index in patients undergoing high-flow nasal oxygen in the Reintubation Rate after Oxygen Therapy (RINO) trial, classified according to the subsequent need for endotracheal intubation within 72 hours from treatment start. Data are expressed as mean and standard deviation. ROX = ratio of Sp_{O_2} over $F_{I_{O_2}}$, divided by the respiratory rate.

Dr. Mandal and colleagues asked for details on gas humidification and patient 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, whereas a heated humidifier was used with 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 patient comfort in our trial. We did measure it, however, in a previous study in which we used the same devices and settings as in the RINO trial (6). In that study, after 24 hours of treatment, patient comfort related to symptoms of airway dryness was significantly higher with the high-flow nasal oxygen than with the Venturi mask. Similarly, comfort related to the interface (nasal cannula vs. face mask) was also significantly higher with the hgh-flow nasal oxygen from the 12th hour of treatment. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

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Originally Published in Press as DOI: 10.1164/rccm.202212-2201LE on December 15, 2022

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Positive- and Negative-Pressure Ventilation Characterized by Local and Global Pulmonary Mechanics

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To the Editor:

Although negative pressure ventilation (NPV) is more physiological, positive pressure ventilation is more commonly used for treating respiratory failure. Sattari and colleagues should be commended for their good work in resolving the question of whether the different modes of ventilation produce different ramifications (1). However, there are still a few issues related to the interpretation of the findings of this experiment. Lung mechanics can be partitioned into the airway and parenchymal tissue components. In this study, they were just concerned with the global and parenchymal tissue components without the airways. Dong and colleagues found the airways, especially smaller airways (diameters less than 3.5 mm), were significantly greater at high negative inflation pressures compared with those at high positive inflation pressures with computed tomography scanning; this suggests that NPV is more effective in distending the peripheral airways (2). According to the evidence from Sattari and colleagues and Dong and colleagues, we could clarify that NPV may be a better option for maintaining sufficient peripheral lung ventilation with better oxygenation and less lung injury. This, of course, is premised on the assumption that the findings of the present studies can be applied to diseased lungs. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

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Reply to Dong *et al.*

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From the Authors:

We thank Dong and colleagues for their interest and commendation of our study by Sattari and colleagues recently published in the *Journal* (1). We are pleased the authors drew parallels between our conclusions and that of published work by Dong and colleagues in the *American Journal of Physiology–Lung Cellular and Molecular Physiology* (2), and we appreciate the opportunity to further elucidate the complex interplay between global pressures and local strains as explored in our examination of positive-pressure ventilation (PPV) versus negative-pressure ventilation (NPV) through a novel application of digital image correlation interfaced with our custom-designed electromechanical ventilation system.

Supported by the National Natural Science Foundation of China (82104510) and Xing-Lin Scholar Enhanced Scholar Project of Chengdu University of TCM (YYZX2021002).

Originally Published in Press as DOI: 10.1164/rccm.202211-2044LE on November 17, 2022

Originally Published in Press as DOI: 10.1164/rccm.202211-2108LE on November 17, 2022