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Reply to Mang *et al.*

From the Authors:

In their letter "Extracorporeal membrane oxygenation transport for severe COVID-19—why we can and should!" Mang and colleagues highlight several important issues related to our recently published work on the association between the availability of extracorporeal membrane oxygenation (ECMO) and mortality during periods of resource limitation during the coronavirus disease (COVID-19) pandemic (1).

We agree that patients most likely to benefit from ECMO are those who are so severely hypoxemic that their transportation from a referring hospital to an ECMO-capable center raises safety concern. Of the 35 patients in our study for whom the health system capacity to provide ECMO at a specialized center was available, 24 patients were cannulated at the referring hospital and transported to the ECMO center that received the referral. Of these, 17 patients (70.8%) survived. The remaining 11 patients were transferred to other regional ECMO centers which lacked the capability to cannulate at the referring center. Of these, 3 patients (27.3%) were cannulated for ECMO after arrival and survived, 5 patients (45.5%) were cannulated for ECMO after arrival and died, and 3 patients (27.3%) died or developed a contraindication to ECMO after transfer but before cannulation. Although confounded by other potential differences in care by center, we agree that these provocative findings suggest the need for future research evaluating the risks and benefits of ECMO cannulation prior to transportation. We also agree with the authors that additional research is needed to identify patients who will derive benefit from the provision of ECMO and to understand the ideal timing of ECMO cannulation. ■

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High-flow Nasal Cannula Oxygen Therapy for Stable Hypercapnic COPD: Just Good Enough?

To the Editor:

High-flow nasal cannula (HFNC) oxygen therapy is being increasingly used to deliver oxygen to patients in the intensive care unit and emergency department, most for acute hypoxemic respiratory failure. The long-term benefit of domiciliary HFNC on patients with stable COPD has also been explored (1–3). In this issue of the *Journal*, Nagata and colleagues (pp. 1326–1335) brought us new insights into long-term home HFNC oxygen therapy (HFNC/LTOT) for patients with COPD with chronic hypercapnic respiratory failure (4). They found that HFNC/LTOT could reduce the frequency of moderate or severe COPD exacerbations. What we can conclude for certain is that HFNC could reduce exacerbations of patients with

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stable COPD compared with LTOT significantly, indicating at least that HFNC could be an alternative to conventional oxygen therapy.

As the first randomized controlled trial of HFNC/LTOT on patients with stable COPD with chronic hypercapnic respiratory failure, the effectiveness of long-term HFNC on hypercapnia should be the main concern. Nagata and colleagues found only a transient improvement of Pa_{CO_2} (at 12 wk) (4). We noticed that another study found that 12-month use of HFNC could stabilize the concentration of CO_2 in patients with COPD with persistent hypoxic and hypercapnic failures (3). The inconsistency reminds us that there leaves much to be elucidated before introducing HFNC to home use for patients with COPD with hypercapnia.

1. The least amount of time patients should spend on HFNC each day to guarantee a therapeutic effect needs to be investigated, as the current studies reported a wide range from 1.6 hours per day to 7.3 hours per day (1, 2, 4).
2. The flow rate of HFNC needs to be titrated both during sleep and daytime. As we know, flow rate relates to the pressure support and the capacity for enhancement of pulmonary function and carbon dioxide removal efficiency. Patients with COPD are more likely to have hypoventilation during the night, indicating the optimal flow rate may be different during the daytime and sleep. Oxygen supplement titration also counts, as the elevated oxygen fraction when HFNC flow remained constant might result in significant increase in Pa_{CO_2} in patients with severe COPD with hypercapnia (5).
3. Explore indicators for the evaluation of good response to HFNC among patients with stable COPD. For example, a significant decrease in dead-space ventilation was correlated with baseline physiologic dead-space fraction, implying the different responses of patients with COPD HFNC (6).
4. The existing device may contribute to sedentary behaviors if used during the daytime. Thus, it needs to develop new devices such as a portable HFNC to enable daily use.
5. The cost-effectiveness of HFNC for patients with stable COPD should also be considered. A cost-effectiveness analysis demonstrated that at threshold values of £20.000–30.000 per quality-adjusted life-year gained, HFNC has an 83–92% probability of being cost-effective compared with usual care in Europe (7). ■

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Erratum: Response to Hypoxia and the Ensuing Dysregulation of Inflammation Impacts *Mycobacterium tuberculosis* Pathogenicity

The article by Bucşan and colleagues (1), published in the July 1, 2022 issue of the *Journal*, includes the wrong set of figures. Because of production errors by the typesetter, the final versions of the six figures were not incorporated in the article; instead, the published article included previous versions of figures that had not been revised. The *Journal* is replacing the online article with one that has been corrected.

Here is a summary of the changes that have been made: in Figure 1H, Figures 2E–I, and Figure 5, the cytokine names and concentrations in pg/ml have been added to the Y axes; in Figures 3D and 3E, labels have been added underneath the pie charts. In addition, the Figure 3B bar graph has been replaced with a dot-plot version of the same data and gene names have been added to the left panel of Figure 6. Finally, Figures 4B–E have been replaced with higher-resolution images. No changes have been made to the underlying data shown in the figures. ■

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