Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

References

1. Luo L, Luo X, Chen W, et al. Consistency analysis of programmed death-ligand 1 expression between primary and metastatic non-small cell lung cancer: a retrospective study. *J Cancer*. 2020;11(4):974-982.
2. Saito Y, Horiuchi S, Morooka H, et al. Inter-tumor heterogeneity of PD-L1 expression in non-small cell lung cancer. *J Thorac Dis*. 2019;11(12):4982-4991.
3. Verocq C, Decaestecker C, Rocq L, et al. The daily practice reality of PD-L1 (CD274) evaluation in non-small cell lung cancer: a retrospective study. *Oncol Lett*. 2020;19(5):3400-3410.
4. Tsao MS, Kerr KM, Kockx M, et al. PD-L1 immunohistochemistry comparability study in real-life clinical samples: results of Blueprint Phase 2 Project. *J Thorac Oncol*. 2018;13(9):1302-1311.
5. Hong L, Negrao MV, Dibaj SS, et al. Programmed death-ligand 1 heterogeneity and its impact on benefit from immune checkpoint inhibitors in NSCLC. *J Thorac Oncol*. 2020;15(9):1449-1459.
6. Perrotta F, Nankivell M, Adizie B, et al. Endobronchial ultrasound-guided transbronchial needle aspiration for PD-L1 testing in non-small cell lung cancer. *Chest*. 2020;158(3):1230-1239.
7. US Food and Drug Administration. FDA approves pembrolizumab for adults and children with TMB-H solid tumors. https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-pembrolizumab-adults-and-children-tmb-h-solid-tumors. Accessed June 29, 2020.

Improving the Safety of High-Flow Therapies in the Management of Patients With COVID-19

To the Editor:

The use of high-flow therapies and noninvasive ventilation in the management of respiratory failure developed in many patients with coronavirus disease 2019 (COVID-19) represents a great challenge for health-care workers because these respiratory support procedures could increase virus aerosolization. They can be considered as independent risk factors for the spread of infection.[1,2] Several measures are supposed to be taken while treating patients with COVID-19 with ventilation modalities, such as patient isolation in adequately ventilated or negative pressure rooms, limiting the number of individuals in the isolation room, and wearing protective respirators by health-care workers.[3,4] Also, using a properly fitted patient interface with minimal air leaks is highly suggested to increase the safety of such procedures. The study presented by Leonard et al[5] in a recent issue of *CHEST* (September 2020) gives a clear vision on how a surgical mask placed over the face during the use of high-flow therapy can participate in reducing the velocity of the gas exhaled and the dispersion of aerosol droplets into the surrounding environment through the use of a computational fluid dynamic technique. This technique enables the simulation of design and off-design conditions and accident scenarios of any engineered system.[6] The present trial represents a great step toward achieving the optimal control of aerosol generation during high-flow therapies, especially in patients with COVID-19 with early stages of respiratory failure where gas flow rates $>$ 6 L/min are required with keeping other safety precautions. Leonard et al[5] best answered three important questions in this trial: (1) how the added mask affects the velocity of the delivered gas, (2) how the leakage either intentional or unintentional around the mask affects the extent of particles capture, and (3) what are the consequences of adding that mask on one of the important physiological benefits of high-flow therapy (eg, nasopharyngeal dead space washout). However, a fully comprehensive study is needed to test the impact of adding a surgical mask on all clinical benefits of high-flow therapy, besides the tolerability of the patient to such adjustment in the well-known procedure. Only one high gas flow of 40 L/min was tested here, but what about flows higher than that level, which is likely to be needed in certain patient conditions? Other high flow is needed to be tested to know whether these flows will show similar behavior as that of 40 L/min or not, especially with the recommendation of the authors to use flows $>$ 40 L/min to overcome the reduction in CO_2 flushing in a patient with increased work of breathing.

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References

1. Lucchini A, Giani M, Isgrò S, Rona R, Foti G. The "helmet bundle" in COVID-19 patients undergoing noninvasive ventilation. *Intensive Crit Care Nurs*. 2020;58:102859.
2. Cheung JC-H, Ho LT, Cheng JV, Kwan Cham EY, Lam KN. Staff safety during emergency airway management for COVID-19 in Hong Kong. *Lancet Respir Med*. 2020;8(4):e19.
3. Hui DS, Chow BK, Lo T, et al. Exhaled air dispersion during high-flow nasal cannula therapy versus CPAP via different masks. *Eur Respir J*. 2019;53(4):1802339.
4. World Health Organization. Infection prevention, and control during health care when COVID-19 is suspected: interim guidance. World Health Organization; 2020.
5. Leonard S, Atwood CW Jr, Walsh BK, et al. Preliminary findings on control of dispersion of aerosols and droplets during high-velocity nasal insufflation therapy using a simple surgical mask: implications for the high-flow nasal cannula. *Chest*. 2020;158(3):1046-1049.
6. Oberkampf WL, Trucano TG. Verification and validation in computational fluid dynamics. *Progress in Aerospace Sciences*. 2002;38(3):209-272.

Response

To the Editor:

The coronavirus 2 pandemic has created an unprecedented rapid production of new information in the scientific literature. Translating experimental data into clinical practice remains a challenge that requires care and thoughtful validation. We greatly appreciate the commentary from Madney et al and agree with their primary conclusion that a more comprehensive study is needed to test the impact of implementation. Ultimately, careful monitoring of nosocomial transmission, especially to clinical staff, must be reported and that information considered in the risk-benefit calculation of any management paradigm. Madney et al ask a very reasonable question regarding the model—the selection of a peak flow of 40 L/min for the simulation. The communication is a short format, and the mechanistic considerations of the therapy tested could not be fully articulated.

The therapy simulated in our paper[1] evaluates a therapy classified as high-velocity nasal insufflation (HVNI). HVNI is mechanistically different from high-flow nasal cannula (HFNC) therapy, while sharing some important characteristics. Both provide supraphysiological flow of conditioned, oxygen-rich gas to the patient using an open interface.[2] HVNI is in a separate Food and Drug Administration classification because it imparts higher velocities to the high flows of gas to facilitate the rapid clearance of the extrathoracic dead space. This provides the ability to manage respiratory distress in spontaneously breathing patients at volumetric flow rates typically well below 40 L/min. The clinical impact of this compared with other forms of HFNC has not yet been fully defined. In a trial of 204 adult patients presenting in the ED with undifferentiated respiratory failure requiring noninvasive ventilatory support, Doshi et al[3] demonstrated noninferiority to noninvasive positive pressure therapy with initial flow rates of 35 L/min and final titrated flow rates of 30 $\pm$ 6 L/min. Higher flow rates are commonly seen when using conventional HFNC therapy,[4] and such higher mass flow of gas leaving the nose and mouth may impact the overall particle dispersal and subsequent transmission. However, experimental evidence from Hui et al[5] suggests that a surgical mask over conventional forms of high-flow therapies likely reduce the risk of aerosol dispersion from them as well. All experimental evidence to date, although limited, suggests these therapies are safe and have limited risk for nosocomial or health-care provider infection when mitigated by use of a surgical mask on the patient.

The higher mass flow quantities generated with conventional HFNC were not evaluated in this report, and as such, the impact on the ventilatory effect of dead space washout for such therapy was not determined in this study and may be an interesting topic for future study. The current analysis demonstrated that the washout of the accessible extrathoracic dead space modeled in this simulation, with the virtual mask in place, still provided significant elimination of rebreathed CO_2, and that reduction was amenable to adjustment in the flow rate of the high velocity gas entrained into the nose of the patient.

We greatly appreciate these suggestions for addition in our ongoing evaluation of mitigation methods being considered for patient management.

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