selected patients, such as patients with severe hypoxemia but at low risk for rapid progression to IMV.

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The authors reply:

We thank Laserna et al (1) for their interest in our study (2) and their insights. Although the rate-oxygenation index (ROX) index did perform poorly in predicting progression to invasive mechanical ventilation in our cohort of high-flow nasal cannula (HFNC) patients, a

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TABLE 1.
Variables in Model Predicting Time to Ventilation or Death

Variables	Adjusted Hazards (*p*)
Rate-oxygenation index < 3.85	0.50 (< 0.001)
Do-not-resuscitate/do-not-intubate order	0.52 (< 0.001)
Spo_2/Fio_2 ratio	0.76 (< 0.001)
Alanine transaminase	0.79 (0.02)
Estimated glomerular filtration rate	0.79 (0.001)
Systolic blood pressure	0.84 (0.03)
Hemoglobin	0.87 (0.07)
Albumin	0.93 (0.32)
C-reactive protein	0.96 (0.52)
Temperature	1.21 (0.007)
White race	1.24 (0.017)
Pulse	1.31 (< 0.001)

These variables were selected from a larger pool of variables using the least absolute shrinkage and selection operator regularization method. The complete list of variables considered also included age, sex, Charlson comorbidity index, body mass index, diastolic blood pressure, respiratory rate, absolute lymphocyte count, D-dimer, and ferritin.

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TABLE 2.
Additional Differences Between Groups

Outcomes	Matched High-Flow Nasal Cannula	Matched Control	*p*
Duration of mechanical ventilation (mean [SD])	14.4 d (14.6 d)	16.6 d (13.9 d)	0.199
Duration of mechanical ventilation among survivors (mean [SD])	15.1 d (14.0 d)	17.4 d (13.4 d)	0.223
Number requiring tracheostomy (mean)	32 (7.6%)	32 (7.6%)	0.572
Number treated with tocilizumab (mean)	49 (11.6%)	30 (7.1%)	0.025

model including a number of demographic, clinical, and laboratory variables in addition to the ROX index performed better at predicting ventilation or death by days 1 and 7 with area-under-the-curves (AUCs) of 0.73 and 0.71, respectively. Among the large group of variables, we collected, least absolute shrinkage and selection operator regularization methods (3) identified the following variables to use in our predictive model in order of most to least significant: ROX less than 3.85, do-not-resuscitate (DNR)/do-not-intubate (DNI) order, pulse, Spo_2/Fio_2 ratio, White race, glomerular filtration rate, alanine transaminase, temperature, systolic blood pressure, hemoglobin, albumin, and C-reactive protein (**Table 1**). We suspect that DNR/DNI status may have been a proxy for frailty and overall health status.

Due to the rapid creation and closing of new ICU and stepdown units during the time period of the study, it was difficult for us to extract and validate data regarding ICU length of stay (LOS), ICU mortality, neuromuscular blockade, and prone positioning. We suspect, however, that the use of prone positioning or neuromuscular blockade would not have been different according to whether a patient received HFNC prior to intubation. However, we agree that future analyses will be more robust with the inclusion of neuromuscular blockade and both awake and postintubation prone positioning.

There was no difference between the groups in percentage of patients who underwent tracheostomy. There was a nonstatistically significant trend toward reduced duration of mechanical ventilation among HFNC patients (both overall and among survivors) compared with controls (**Table 2**). As these differences were not statistically significant, we are hesitant to draw conclusions from them. On the other hand, tocilizumab use was modestly higher in the HFNC versus the control group (11.6% vs 7.1%; $p = 0.025$), which may have been due to a greater opportunity to use this therapy prior to intubation.

We agree that secular trends are difficult to completely control for as practice continues to evolve throughout the course of the pandemic. Thus, despite our best efforts, the hazard ratio associated with HFNC use may have not been stable throughout the time period studied. For instance, HFNC may have not been employed to its full effect early in the pandemic in which patients tended to be intubated earlier in their course. We find it reassuring, however, that a recent randomized controlled trial found decreased need for invasive mechanical ventilation as well as a trend toward lower mortality among patients treated with HFNC versus standard supplemental oxygen therapy (4). These findings along with those from our own analysis support the use of HFNC for pneumonia and ARDS in appropriately selected patients.

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Noninvasive Method of Measuring of Tidal Volume: A Promising Novel Tool?

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To the Editor:

We read with great interest a recently published study by Le Moigne et al (1) in *Critical Care Medicine*, in which the authors introduce the concept using time-of-flight (TOF) technology to noninvasively measure tidal volumes in healthy volunteers using high-flow nasal cannula (HFNC). The authors establish a design and model for estimating tidal volume measurements in patients on HFNC, with the objective of establishing a noninvasive method to measure tidal volume that may be useful in the prevention of self-induced lung injury secondary to volutrauma.

Overall, the study by Le Moigne et al (1) shows promise that noninvasive TOF technology can measure tidal volume and additionally has the added benefit of tracking changes in tidal volume and respiratory rate, which would have important implications in monitoring for self-induced lung injury.

We consider an adequate design of the established means model, but we consider that there are some controversial points that should be taken into account. The authors describe a relationship between tidal volume and respiratory pattern. This relationship is not well established because there is no measurement of other aspects such as patient compliance or resistance, which are determining factors in the tidal volume during respiratory work of breathing and during acute illness (2). The authors also acknowledge the limitations of their study, which are the use of healthy subjects and small sample size. Thus, the use of TOF in a more diverse setting is still unclear if patients with obstructive and/or restrictive lung disease would benefit from this type of monitoring. For instance, considerations of patients with comorbidities of chronic obstructive pulmonary disease, hyperinflation, obesity, or in conditions in which paradoxical breathing pattern is present may obscure accurate measurements as they are based on the movement of the rise and fall of the chest wall. Additionally, because TOF tidal volume is a calculated average over 1 minute, it may not be accurate in patients who are breathing irregularly (i.e., Cheyne-Stokes). Other clinical considerations are agitation or delirium,

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