selected in a post hoc manner—a step known to markedly overestimate the accuracy of predictive indexes (3). No conclusions about reliability of a predictive index can be reached without the threshold being prospectively tested with a validation data set.

In addition to methodological problems, there is no justification for judging $P_{0.1}$ 4 cm H$_2$O as a worrisome high value. Such values are seen in patients with stable chronic obstructive pulmonary disease and in patients successfully weaned from mechanical ventilation (4). There is no biological rationale for proposing that this level of respiratory motor output likely causes structural injury of the lung or respiratory muscles. The claim byGattinoni and colleagues that $P_{0.1}$ structural injury of the lung or respiratory muscles. The claim byGattinoni and colleagues that $P_{0.1}$ and $\Delta P_{occ}$ exhibit a coefficient of variation as high as 38% in critically ill patients. Gattinoni and colleagues claim that $P_{0.1}$ and $\Delta P_{occ}$ “correlate well with relatively more precise methods for effort estimation.” On the contrary, $P_{0.1}$ 4 cm H$_2$O is associated with a wide range of pressure–time product: $\approx$110 to $\approx$420 cm H$_2$O $\cdot$ s $\cdot$ min$^{-1}$ (Figure 3H of Reference 5). $P_{0.1}$ 1 cm H$_2$O is associated with a wide range of peak electrical activity of the diaphragm: $\approx$5 to $\approx$20 $\mu$V $\cdot$ s$^{-1}$ (Figure 3B of Reference 5). $\Delta P_{occ}$ of approximately 9 cm H$_2$O is associated with a wide range of pressure–time product: $\approx$2.5 to $\approx$10 cm H$_2$O $\cdot$ s $\cdot$ breath$^{-1}$ (Figure E1 in the online supplement of Reference 6). Investigators excluded 30 of 82 recordings because the ratio of $\Delta P_{occ}$ to change in esophageal pressure fell outside the range of 0.7–1.3. Basing decisions on $P_{0.1}$ and $\Delta P_{occ}$ regarding mechanical ventilation in individual patients is perilous.

Gattinoni and colleagues draw conclusions based on observed rapid shallow breathing index of 49 breaths/min/L. It has been known for decades that measurements of rapid shallow breathing index in the presence of un-estimated levels of respiratory work—inevitable with pressure support ranging between <4 and >11 cm H$_2$O and positive end-expiratory pressure <10 to >14 cm H$_2$O—are uninterpretable (3).

Gattinoni and colleagues continue to claim that the study byTonelli and colleagues supports the existence of P-SILI (7). If inspiratory efforts were causing P-SILI, one would expect a decrease in VT-to-transpulmonary pressure swing ratio—a surrogate of lung compliance; yet, VT-to-transpulmonary pressure swing ratio remained constant across 24 hours of noninvasive ventilation. Chest radiography cannot be linked mechanistically to P-SILI because radiologists were not blinded.

Mechanical ventilation plays a crucial role in the management of patients with COVID-19. Conducting rigorous research is vital to enlighten clinicians at the bedside. A pandemic is no time to engage in speculation and broad generalizations based on dubious interpretations of small data sets. On the contrary, ventilator research in COVID-19 needs to aspire to the highest internal validity.
The Role of Eosinophils during the Withdrawal of Inhaled Corticosteroids in Chronic Obstructive Pulmonary Disease

To the Editor:

We read with great interest a post hoc analysis of the IMPACT trial that investigated the effect of inhaled corticosteroid (ICS) withdrawal in patients with chronic obstructive pulmonary disease (1). Han and colleagues (1) demonstrated that the benefit of fluticasone furoate/umeclidinium/vilanterol combination therapy on exacerbation reduction, lung function, and quality of life was not associated with the abrupt withdrawal of ICSs in the IMPACT trial (1, 2). However, we wonder whether the baseline eosinophil count would play another important role that could impact the effect of ICS withdrawal.

In the European Respiratory Society guideline (3), which is based on the analysis of four studies, COSMIC (4), WISDOM (5), INSTEAD (6), and SUNSET (7), they strongly recommend that ICSs should be continued in patients who have blood eosinophil counts $\geq$300 cells/μl, with or without a history of frequent exacerbations. In this meta-analysis (3), they found that no effect of ICS withdrawal was observed on exacerbation rate (rate ratio [RR], 1.18; 95% confidence interval [95% CI], 0.90–1.18; P = 0.71;}

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

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