## "Established" Respiratory Treatment in Acute Respiratory Distress Syndrome: Scientific Rigor or a Square Peg in a Round Hole?

*To the Editor*:

Dr. Hardin, in his editorial (1), surmises that there is nothing new under the sun, particularly that established ventilatory approaches should also be applied to coronavirus disease (COVID-19) acute respiratory distress syndrome (ARDS) (C-ARDS). We know of only two trials in unselected ("average") ARDS that provide significant results: one establishing that 6 ml/kg is better than 12 ml/kg and the other establishing that positive end-expiratory pressure (PEEP) higher than 15 cm $H_2O$ increases mortality. Further advances in ARDS treatment were only proved or suggested in subgroups: prone position if $Pa_{O_2}/F_{I_{O_2}}$ ratio is below 150 mm Hg and higher PEEP in hyperinflammatory phenotypes. Therefore, subgroups deviate from the average ARDS behavior and require modification of standard management.

Like many, we are not so certain that all patients benefit from 6 ml/kg predicted body weight $V_T$—or tolerate the suggested entries of a PEEP–$F_{I_{O_2}}$ table. Outcomes from intermediate $V_T$ may be, on average, equivalent to a lower $V_T$ (2). Many clinicians seem to have already figured this out; $V_T$ in all groups of the Panwar study (3) was set in the 7–8 ml/kg range, which is similar to those in the quoted article by Hager and colleagues (4).

Lung protection is linked to repetitive excessive "strain;" consequently, $V_T$ is ideally set individually in relation to gas volume or compliance (i.e., driving pressure) rather than predicted body weight. In patients with relatively preserved lung gas volumes (e.g., many with early-stage COVID-19), very low $V_T$s may lead to dyspnea or asynchronies, adversely affecting the outcome. Conversely, even $V_T$ of 6 ml/kg may be excessive for some patients with very severe ARDS. In this context, it does not seem a paradox that in LUNG-SAFE (Large Observational Study to Understand the Global Impact of Severe Acute Respiratory Failure), patients with better compliance had a larger $V_T$, and we do not think it reasonable to presume that these patients would have necessarily benefited from lower $V_T$ (1).

Just as one $V_T$ does not translate into the same strain, a higher PEEP may improve oxygenation and outcome (i.e., if there is extensive recruitable lung tissue), or overstretch compliant airspaces.

That some small minority of patients with broadly defined ARDS might be found that resemble some stage of the evolving C-ARDS physiology is hardly surprising. What is different, however, is that unexpectedly high gas volumes and compliance occur routinely despite infiltrates and impressive hypoxemia in the early stages of C-ARDS (5). Therefore, why infer that considering respiratory mechanics and recruitability when choosing $V_T$ and PEEP is somehow heretical, advocating a strategy "the same as it ever was"? Patients with C-ARDS are not your "average" ARDS. ■

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

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## Reply to Camporota *et al.*

*From the Editorialist*:

Acute respiratory distress syndrome (ARDS) is a heterogeneous syndrome. Given this heterogeneity, there have been many efforts to define subgroups of patients with ARDS: by etiology, by respiratory mechanics, by the distribution of radiographic abnormalities, by the severity of gas exchange abnormality, or by biomarkers. In their response to the editorial "Novel Phenotypes in Respiratory Failure: Same as It Ever Was" (1), Dr. Camporota, Dr. Gattinoni, and Dr. Marini articulate the plausible and widely held hypothesis that such subgroups would benefit from distinct treatment strategies. Indeed, this hypothesis has animated much of the recent research literature on ARDS. To date, however, it has proven surprisingly difficult to prospectively demonstrate a mortality benefit from any particular tailored approach. Prone ventilation has proven



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