Discussions on VT4COVID

We commend Jean-Christophe Richard and colleagues on their excellent investigation of ultra-low tidal volume versus low tidal volume strategy during mechanical ventilation for COVID-19-related acute respiratory distress syndrome (ARDS). What obtained our attention, however, was the use of sedation in their study. The marginal mean dose of midazolam was 8.8 mg/h (SE ±0.6) and of propofol was 60.5 mg/h (±7.1) for the first 14 days after inclusion in the ultra-low tidal volume group. Both of these doses were higher, although not statistically significantly, than the low tidal volume group. The absence of statistical differences between the two groups might not be as noteworthy as the doses received. We cannot ascertain whether the data presented include means for the total number of people taking these medications or only for those who received them during the intervention period (ie, the exposed cohort might have received even higher doses). Regardless, the high and extended exposure to potent sedatives made us question how the depth of sedation interacted with the outcomes presented by the authors.

Outcomes for patients with ARDS can be substantially affected by sedation practices. Data from landmark studies have shown higher survival among patients who received a 50% reduction in the overall amount of sedatives and narcotics than patients who did not receive this reduction, that delirium is an independent predictor of death in critical illness, and that benzodiazepines are independently associated with delirium in the intensive care unit. During the COVID-19 pandemic, the COVID–D study including 14 countries showed changing sedation practices and returning to deep sedation, in which increased use of benzodiazepines was a robust predictor of delirium. The high doses of benzodiazepines and propofol seen in the Article by Richard and colleagues, namely an excess of 150 mg per day of midazolam, are alarming. We invite the authors to further discuss the sedation practices in their trial. We would like to know if this amount of sedation was thought to be required to maintain ventilator synchrony and protocol compliance, and whether such deep sedation could have contributed to the high mortality rates that were seen.

We applaud the work by Richard and colleagues, who provided great knowledge in the optimisation of ventilation strategies and emphasised the interplay between ventilation, sedation, and other encompassing interventions that have established effects on patient outcomes.

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