Correspondence

Discussions on VT4COVID

Authors’ reply

We thank Christina Boncyk and colleagues and Jan De Mey and Pieter Depuydt for their interest in the VT4COVID trial and for their thoughtful remarks.

Regarding the comments by Boncyk and colleagues, we confirm that the sedation and opioid doses presented in the original manuscript are marginal means that were fitted on the whole dataset (ie, including patients who were not receiving one particular drug). We provide additional data for midazolam, propofol, and opioids excluding patients who were untreated (appendix p 2).

We agree with Boncyk and colleagues regarding the association between benzodiazepine use, delirium in the intensive care unit (ICU), and mortality. After the landmark trial by Girard and colleagues, ICU practices have evolved to target light sedation and promote early return to spontaneous breathing in patients under invasive mechanical ventilation. However, light sedation is often difficult to achieve in severe acute respiratory distress syndrome (ARDS). More than 50% of the patients in the control group of the ROSE trial were deeply sedated during the first 4 days after inclusion, despite the per-protocol requirement of the 4 days after inclusion, despite the intervention was unlikely to have caused harm in the majority of patients who were enrolled, in line with the sensitivity analysis on driving pressure at inclusion. We emphasise that none of the patients of the analysis by Goligher and colleagues were ventilated with the aim to achieve ultra-low Vt ventilation.

We strongly agree with the comment from De Mey and Depuydt regarding the need to identify a threshold of driving pressure (or normalised elastance) above which ultra-low Vt ventilation would be beneficial. We are currently running analyses of the trial database to achieve this purpose.

As highlighted by our colleagues, the search for ultraprotective ventilation strategies remains a priority given the high incidence of severe ARDS that have been repeatedly reported in COVID-19 ARDS as a function of normalised elastance (ie, elastance normalised to predicted bodyweight). This analysis identified that the posterior probability of a survival benefit from the lower Vt strategies exceeded 50% in patients with normalised elastance above 1·5 cmH2O/mL per kg of predicted bodyweight. In the VT4COVID trial, normalised elastance at inclusion was 1·86 cmH2O/mL per kg of predicted bodyweight (95% CI 1·51–2·35) in the control group and 1·86 cmH2O/mL per kg of predicted bodyweight (1·61–2·40) in the intervention group. 80 (79%) of 101 patients in the intervention group presented with normalised elastance above 1·5 cmH2O/mL per kg of predicted bodyweight, suggesting that the intervention was unlikely to have caused harm in the majority of patients who were enrolled, in line with the sensitivity analysis on driving pressure at inclusion. We emphasise that none of the patients of the analysis by Goligher and colleagues were ventilated with the aim to achieve ultra-low Vt ventilation.

We strongly agree with the comment from De Mey and Depuydt regarding the need to identify a threshold of driving pressure (or normalised elastance) above which ultra-low Vt ventilation would be beneficial. We are currently running analyses of the trial database to achieve this purpose.

As highlighted by our colleagues, the search for ultraprotective...
ventilation will require, in the future, improved identification of eligible patients and careful protocolisation of co-interventions (eg, sedation) that might negatively affect ARDS prognosis.

Competing interests have not changed since the original VT4COVID Article.

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