Low intraoperative tidal volume ventilation with minimal PEEP and postoperative morbidity and mortality

Editor—In a retrospective single-centre study including 29,343 adult patients undergoing general non-cardiac surgeries under general anaesthesia, Levin and colleagues showed that intraoperative mechanical ventilation using low tidal volumes with minimal PEEP was associated with worse 30-day mortality and an increased hospital length of stay. The strengths of this study include a large sample of patients and use of multivariable Cox regression and propensity score-matched analyses to adjust for, and reduce, the influences of confounding variables on study end-points. However, the authors recognize that the study included a large number of patients and use of confounding variables that in a non-randomized study may not have been removed completely.

In our view, several important issues in this study are not well addressed. First, health status, types of surgery and comorbidities are important determinants for postoperative morbidity and mortality. In the study by Levin and colleagues, patients’ age, ASA physical status, all patient refined-diagnosis related group (APR-DRG) severity of illness (SOI) and risk of mortality (ROM) scores, and types of surgery are significantly different among patients with various ventilation strategies. In our opinion, no matter how refined the adjustment is for differences in health status, surgery burden, and relevant comorbidities, it is never possible to ensure a complete adjustment for differences among patients with different ventilation strategies, even when propensity score matching is used.

Most importantly, some of the independent risk factors related to postoperative morbidity and mortality are not included in data analysis. For example, preoperative anaemia is common among non-cardiac surgery patients, and low preoperative and postoperative haemoglobin levels are associated independently with increased perioperative mortality, increased postoperative pneumonia, and increased hospital length of stay. Moreover, preoperative use of cardiac medicines such as angiotensin-converting enzyme inhibitors, β-blockers, and statins can also significantly affect hospital and long-term mortality in patients undergoing non-cardiac surgery.

Second, in the study by Levin and colleagues, anaesthetic agent, ventilation mode (volume control or pressure control), ventilator settings, and fraction of inspired oxygen were chosen at the discretion of the attending anaesthetist. Consequently, we cannot exclude the possibility that anaesthetists would have selected anaesthetic and ventilation strategies based on baseline characteristics and pre-existing comorbidities of patients. Furthermore, we are not provided with details of the anaesthetic and intraoperative management. Intraoperative hypoxaemia, blood loss, transfusion, hypotension, tachycardia, and hypertension are associated independently with postoperative morbidity and mortality of non-cardiac surgery patients. We believe that a more persuasive result would have been presented if these data were included in the study design.

Finally, we emphasize that postoperative morbidity and mortality are the results of many perioperative factors and their interaction. To differentiate the effect of one factor on the postoperative adverse outcomes, all of the other factors have to be standardized and controlled in the study design. It is impossible for an observational study to achieve this target. Thus, we agree with the authors that an association between postoperative outcomes and low tidal volume ventilation with minimal PEEP in this study does not prove causality. Moreover, we argue that when making decisions about use of a treatment such as low tidal volume ventilation with PEEP to decrease postoperative morbidity and mortality of surgical patients, we should rely on the large body of robust evidence of efficacy and safety. This high-level evidence comes from a very large number of randomized controlled clinical trials and their meta-analysis, rather than any study using an observational design.

Declaration of interest
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Low tidal volumes during intraoperative ventilation: Beneficial or Harmful?

Editor—Levin and colleagues reviewed the records of 29 343 patients who underwent general anaesthesia with mechanical ventilation to determine an association between intraoperative tidal volume and 30-day mortality. In their centre, the tidal volume used for intraoperative ventilation declined from 9.0 to 8.3 ml kg\(^{-1}\) over the 4-year time span of the study, which confirms global trends in ventilation in intensive care unit patients. Opposite to what Levin and colleagues hypothesized, however, they found an intraoperative tidal volume size of 6–8 ml kg\(^{-1}\) to be associated with an increased mortality. We have several comments and questions.

First of all, Levin and colleagues did not report the mortality rates broken down per tidal volume size, which severely hampers comparisons with other studies on postoperative morbidity and mortality. More important, there was imbalance for ventilation before anaesthetics, ASA categories, emergency procedures, and comorbidity scores in the different cohorts. The authors used the propensity score matching to correct for these imbalances, but while propensity score matching can balance observed baseline covariates between exposure groups, they do nothing to balance unmeasured characteristics and confounders. Hence, as with all observational studies, and unlike randomized controlled trials, propensity score matching analyses have the limitation that some unmeasured confounding may still be present.

Furthermore, it remains obscure why and how the patients died. Since use of lower tidal volumes protects against postoperative pulmonary complications, it is very unlikely that these patients died from pulmonary problems. Mortality in patients who do not develop postoperative complications, however, is very low, 0.5\%, much lower than the overall mortality reported by Levin and colleagues. Finally, we respectfully disagree with the suggestion that anaesthesiologists should use higher levels of PEEP when using lower tidal volumes. The analysis by Levin and colleagues was restricted to the intraoperative tidal volume size, and did not at all consider the level of PEEP. Visual inspection of figure 2C shows that patients received different levels of PEEP. Could we entice the authors to investigate the association between intraoperative levels of PEEP, or different tidal volume size–PEEP combinations, and postoperative mortality? Maybe it will be even more interesting to compare mortality in the patients who were ventilated exactly the same way as in the two arms of the recent randomized trial of protective intraoperative ventilation.

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