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Editorial

Open the lungs, keep them open and... take a break?

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In both critically ill patients with acute respiratory distress syndrome (ARDS) and patients undergoing major surgery, the reduction in tidal volume (V_T) delivered through mechanical ventilation has been associated with improved clinical outcomes, including reduced mortality after ARDS, and decreased postoperative complications [1,2]. Although the concept of permissive hypercapnia emerged in severe ARDS patients [3], the need to ensure sufficient carbon dioxide clearance while delivering lower V_T prompted the use of more physiological parameters during controlled mechanical ventilation, such as maintenance of adequate expiration times.

Currently, it is recognised that the inspiration-to-expiration (I:E) ratio – within a respiratory cycle – of 1:2 or less (e.g., 1:3–1:5) favours carbon dioxide clearance and limits the risks of breath stacking and "residual" auto-positive end-expiratory pressure (auto-PEEP) [4]. Historically, however, I:E time ratios greater than 1 have been suggested to improve oxygenation through an increase in mean airway pressure without any increase in tidal volume [5]. In this way, recruiting newly aerated lung regions and increasing the total compliance of the respiratory system (C_{RS}) may be possible. However, the clinical benefit of such an approach has not been confirmed [6–8].

With the current practice of controlled mechanical ventilation with I:E $\leq$ 1:2 to limit auto-PEEP, applying an end-inspiratory pause also allows the dynamic measurement of end-inspiratory plateau pressure (Pplat), which is a major (yet not sole) determinant of the risk of ventilator-induced lung injury. Monitoring the Pplat is critical to the evaluation of driving pressure (Pplat-PEEP), which is a prognostic variable in ARDS and surgical patients and serves as a surrogate for the adequation between V_T and C_{RS} (driving pressure = V_T/C_{RS}). Altogether, these variables can better individualise intraoperative ventilatory settings, including PEEP adjustment [9–11]. Even with a 1:2 ratio setting, increasing the duration of an end-inspiratory pause may have physiological benefits, such as a reduction in airway dead space, by prolonging the mean distribution time, which is the time given to inspired gas for distribution and diffusion within the lungs [12].

In an article published in this issue of *Anaesthesia, Critical Care & Pain Medicine*, Lopez-Herrera Rodriguez et al. investigated the effects of the duration of the end-inspiratory pause on parameters of respiratory function and mechanics in major abdominal surgery patients under volume-controlled ventilation (V_T, 7 mL.kg^{-1} predicted body weight). The authors applied an elegant design with crossover assignment to two end-inspiratory pause durations (10% vs. 30% of the total inspiratory phase, while keeping the I:E ratio of 1:2 unchanged) combined with an "open-lung" approach (schematically, a stepwise alveolar recruitment manoeuvre with PEEP titration based on C_{RS} optimisation). Measures of respiratory mechanics, such as the C_{RS} (primary endpoint), driving pressure, Pplat, mean airway pressure and the level of PEEP, of gas exchange (oxygenation, carbon dioxide) and of lung aeration (dynamic tidal gas distribution in electrical impedance tomography) were serially assessed.

The main finding of the study is that, in surgical patients without a preexisting lung injury, an end-inspiratory pause of 30%, compared with a pause of 10%, increases the C_{RS} while decreasing the driving pressure, mean airway pressure and tailored PEEP level. These results were reported before and after application of the open-lung approach. However, the moderate yet significant increase in arterial oxygenation observed with an end-inspiratory pause of 30% before the open-lung approach was not found when ventilation was tailored using the above-mentioned approach.

In addition, prolonging the end-inspiratory pause to 30% did not affect arterial carbon dioxide or lung aeration, even when measured before the open-lung approach. Unsurprisingly, the study also confirmed that the open-lung approach was itself associated with more homogeneous distribution of lung aeration, independent of the duration of the end-inspiratory pause. The investigators should be commended for employing very controlled and granular experimental conditions, such as study population, ventilator settings, depth of anaesthesia, analgesia, paralysis and haemodynamic monitoring, and rigorous design with prior statistical power calculation, among other strengths. These conditions increased the confidence in the results from this study.

There are, however, some limitations inherent to the work design. First, the experimental procedures were performed in patients anaesthetised for major abdominal surgery, but before surgery effectively started. Whether the effects of extending the duration of the end-inspiratory pause remain true in settings in which C_{RS} is itself constrained, such as during pneumoperitoneum insufflation or Trendelenburg positioning, warrants further inves-

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tigation. Second, there was no strict evaluation of the *time x randomisation group* interaction, as often performed in crossover trials [13], which limits the interpretability of the effects of the sequence order (an end-inspiratory pause of 30% and then a pause of 10% vs. an end-inspiratory pause of 10% and then a pause of 30%), and the wash-out of 5 minutes between the two crossover sequences may have been too short to remove the effects of the first sequence. Last, the small sample size (32 patients) and single-centre design prompt future validation studies.

Importantly, these findings also highlight multiple issues for future research. Here, the effects of the duration of the end-inspiratory pause were assessed in surgical patients without pre-existing, moderate-to-severe (acute or chronic) lung disease, thereby accounting for rather low driving, plateau or mean pressures and high C_{RS} after application of an open-lung approach. Similar effects of prolonging the end-inspiratory pause were reported in a small single-centre study of patients with ARDS [14]; however, the increase in C_{RS} and driving pressure were attributable, at least in part, to the reduced V_T in this latter study, as unchanged levels of arterial carbon dioxide were targeted throughout the experimental procedure. The amount of recruitable lung available, which is often greater in patients with severe ARDS, may influence the response to an increased duration of end-inspiratory pause, and their potential effects on increased alveolar recruitment may substantially vary [3,15]. In both surgical and ARDS scenarios, it remains unknown to what extent such a recruitment (as hypothesised globally from an increased C_{RS}) might also be associated with concurrent distension in some lung regions, especially in patients in whom C_{RS} is substantially influenced by its parietal component, such as in obese patients [3,16]. Strict translation of the current findings out of the open-lung approach and/or to clinical benefits, such as reduced postoperative pulmonary complications after major surgery, is an exciting research field that warrants further investigation.

As smartly executed in the study by Lopez-Herrera Rodriguez et al., research on lung-protective mechanical ventilation is addressing increasingly precise aspects of ventilator settings in patients with or without lung injury. In this domain, as in many others, taking a (longer) pause might be a good idea.

Disclosure of interest

The authors declare that they have no competing interest.

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