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### Brief Academy

## Critical assessment of the evidence<sup>☆</sup>



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### Introduction

The mechanism of barotrauma and volutrauma has been described since the 70s in patients with acute lung injury and acute respiratory distress syndrome receiving high tidal volume ventilation<sup>1</sup> (10–15 ml/kg ideal body weight). This led to the development of controlled clinical trials in an attempt to determine the ideal tidal volume. Different forms of mechanical ventilation were proposed in the 90s using tidal volumes ranging between 3–12 ml/kg of the estimated weight.<sup>2</sup> However, it was only in 2000 when the ARMA study published by the ARDS Network provided recommendations for low-volume mechanical ventilation (6 ml/kg) and airway plateau pressures under 30 cm H<sub>2</sub>O, leading to a significant

reduction in mortality, from 40% down to 31% in patients with ARDS.<sup>3–5</sup> Since then, the protective ventilation strategy has been broadened to include other types of patients, including those taken to elective surgery, although not taking into consideration the large difference in the pathophysiology of ventilation between diseased and healthy lungs, or the different consequences. Despite this, some clinical trials have found the benefit of low tidal volume ventilation in terms of pulmonary infection and, mortality outcomes.<sup>6–10</sup> However, other studies like ours have shown an increase in 30-day mortality.<sup>1,11,12</sup>

### Study objective

The objective of this study was to determine whether low tidal volume with minimal PEEP is associated with lower perioperative morbidity and mortality when compared with high volumes in patients taken to surgery under general anaesthesia.

### Study design

Retrospective observational study.

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## Results of the study

Overall, 29,343 patients taken to elective surgery were included. Patients of cardiac and thoracic surgery, liver transplant, palliative care, and those who had already received anaesthesia were excluded. Also excluded were all patients ventilated with volumes under 250 ml and tidal volumes above 3 or 20 ml per kg, or PEEP above 16.

Variables comprised in the ventilator records were determined: end expiratory volume, respiratory rate, peak intraoperative pressure (PIP), peak expiratory pressure, PEEP, inspired fraction and dynamic compliance, and the primary outcomes were 30-day mortality and length of hospital stay.

Comorbidities were assessed using the APR-DRG system in order to adjust 30-day mortality.<sup>13</sup>

Predictor variables included ASA classification, age, gender, race, body mass index, laparoscopic vs. open surgery, type of surgery, PIP, and dynamic compliance.

Tidal volume was adjusted according to body mass index in order to classify the patients as those ventilated with volumes ranging between 3 and 6, 6 and 8, 10 and 12, and 12 and 20 ml/kg of ideal body weight ( $\text{kg}^{-1}$  IBW), compared to patients ventilated with a tidal volume ranging between 8 and 10 ml/kg of ideal body weight ( $\text{kg}^{-1}$  IBW). In order to determine 30-day mortality and length of stay, simple and adjusted Hazard Ratios were used in order to account for potential confounding variables in a Cox regression model; and in order to diminish selection bias, the propensity index was used to match each of the mechanical ventilation volume categories with the same probability. For probability determinations, variables such as ASA, gender, race, urgent surgery, use of steroids, surgical specialty, laparoscopic surgery, PAR-DRG score, physical fitness, ideal body weight, and body mass index were used.

A 30-day mortality HR of 1.6 [95% CI] [1.25–2.08] was found for the group with volumes of 6–8 ml/kg of ideal body weight. These values were adjusted for pre-operative risk using the comorbidity score APRG DRG, aside from ASA and BMI.

## Level of evidence

Grade IV.<sup>14</sup>

## Comments from the reviewers

The propensity score methodology<sup>15,16</sup> has been used over the past two decades for reducing selection bias in observational studies, and eliminating a large proportion of the underlying differences found between the comparison groups. This is achieved by determining the probability of assigning patients to one or the other therapy as a function of explanatory variables and then comparing the groups in terms of outcomes, taking into consideration similar probability of assignment to each of the groups or therapies. This is a way to simulate a clinical trial despite the limitations of not having considered all the variables that may have influenced assignment to one or another group. In this study, the finding of increased mortality in the group of patients ventilated with 6–8 ml  $\text{kg}^{-1}$  compared with volumes of 8–10 mL  $\text{kg}^{-1}$  does not

reflect a response gradient with smaller volumes, as is to be expected. On the other hand, the mortality outcome is not limited to pneumonia-related mortality. Another limitation of this study is not having determined the plateau pressure, a measurement which would have reflected the true impact on overstretching and would have helped determine whether the anaesthetists could have used that variable to base their decision of adjusting the volume. From the pathophysiological point of view, the ventilation-associated injury will depend on the stress and tension to which the lung parenchyma is subjected as a result of tidal volume, respiratory rate, flow, inspiration time, PEEP, volume and recruitment manoeuvres. To this date, the variable that best evaluates lung overstretching is transpulmonary pressure.<sup>17,18</sup>

Finally, the results of this study are the opposite of those presented in the meta-analysis by Ary Serpa et al., who identified nine studies with 1077 patients which explored the association between low volumes and the mortality outcome and found a RR (95% CI) = 0.64 (0.46–0.86).<sup>19</sup> In the same meta-analysis, no differences were found when clinical trials and observational studies were analysed separately, showing consistency in the results.<sup>8,10,20–25</sup>

## Suggested articles for review

Rocco PR et al.<sup>26</sup>.  
Serpa Neto et al.<sup>27</sup>.  
Hemmes et al.<sup>28</sup>.

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None.

## Conflicts of interest

The authors have no conflicts of interest to declare.

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