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## **EDITORIAL**

## Toward lung protective ventilation during general anesthesia: A new challenge



Hacia la ventilación de protección pulmonar durante la anestesia general. Un nuevo desafío

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As Editor-in Chief of Minerva Anestesiologica, the Italian journal devoted to the anesthesiology and critical and intensive care, I wish to congratulate the Revista Española de Anestesiología y Reanimación in its 60 years of dedication to the development of our common medical speciality. We are grateful to be invited to contribute to this celebration.

Lung protective mechanical ventilation refers to the use of low tidal volume (tV) and positive end-expiratory pressure (PEEP) with or without the use of recruitment maneuvers. It has been demonstrated to reduce mortality among patients with the Acute Respiratory Distress Syndrome (ARDS) and currently is considered best practice in the care of critically ill patients.<sup>1,2</sup>

General anesthesia is known to be associated with impairment in lung function, in terms of alterations in respiratory system mechanics and in ventilation/perfusion ratio, promoting the onset of lung atelectasis. The development of atelectasis is very common during general anesthesia and is involved in the pathogenesis of many postoperative pulmonary complications such as Ventilator Induced Lung Injury (VILI), pneumonia and postoperative respiratory failure.

Unfortunately up to now few randomized controlled trials on lung protective ventilation have been conducted during general anesthesia. Recently two meta-analyses have been published and, even considering the limits of the enrolled studies, have demonstrated that lung protective ventilation

in patients without ARDS is associated with better clinical outcomes.  $^{3,4}$ 

Although the lung protective ventilation seems to be beneficial in a broader population with and without ARDS, the use of high tV without PEEP during general anesthesia has been recommended to prevent atelectasis and hypoxemia and represents a commonplace.

A large observational prospective study performed in two thousand patients in French anesthesia units, between January and June 2006, demonstrated that during general anesthesia approximately 20% of patients receive a tV greater than 10 mL kg<sup>-1</sup> of ideal body weight and that the application of PEEP is underutilized, reaching 20%.<sup>5</sup>

Recently, a 5-year observational study of intraoperative lung-protective ventilation, performed from 2006 to 2010, showed that the use of a tV less than  $10\,\mathrm{mL\,kg^{-1}}$  and PEEP levels of  $5\,\mathrm{cmH_2}O$  or greater increased progressively over time, but a considerable percentage of patients continue to receive ventilation that is not lung protective.  $^6$ 

Until 40% of patients undergoing abdominal surgery experiences postoperative pulmonary complications, increasing morbidity and mortality. In this context, Wrigge et al. investigated in two studies the effect of different ventilatory strategies (tV of 12–15 mL kg $^{-1}$  of ideal body weight without PEEP versus tV of 6 mL kg $^{-1}$  and PEEP levels of 10 cmH $_2$ O) on the release of inflammatory mediators, in patients undergoing elective abdominal surgery,  $^{8,9}$  but they did not find differences. Similarly other studies were unable to find any significant differences in the explored outcomes.  $^{10,11}$ 

Differently Weingarten et al. evaluated an open lung strategy with low tidal volume (tV of 6 mL kg<sup>-1</sup> of predicted

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body weight), PEEP of  $12\,\text{cmH}_2O$  plus a recruitment maneuver to minimize atelectasis and the shear stress in lung parenchyma. This open lung strategy compared to a tV of  $10\,\text{mL\,kg}^{-1}$  without PEEP, significantly improved only the intraoperative oxygenation without any difference in the inflammatory response and length of hospital stay. <sup>12</sup>

Severgnini et al. in a large monocentric trial during abdominal surgery found that an open lung strategy with low tV, moderate PEEP levels and gently but repeated recruitment maneuvers improved postoperative respiratory function in terms of dynamic spirometry, oxygenation, and pulmonary complications up to 5 days after surgery, without increasing intraoperative complications. Although a significant difference was not found in the hospital length of stay, 20% of the patients in the treated group as compared with 40% in the control group were in hospital on postoperative day 14.<sup>13</sup>

A recent multicenter randomized clinical trial, the IMPROVE study, found that the lung protective ventilation (tV of  $6-8\,\text{mL\,kg}^{-1}$  of predicted body weight, with PEEP  $6-8\,\text{cmH}_2\text{O}$  and recruitment maneuvers repeated every 30 min compared to non protective ventilation with tV  $10-12\,\text{mL\,kg}^{-1}$  without PEEP) significantly reduced the major pulmonary and extrapulmonary complications from 27.5% to 10.5% and the percentage of patients who required postoperative ventilator assistance from 17% to 5%.14

Differently to previous studies, these two recent intraoperative trials focusing on clinically relevant outcomes (not only lung inflammatory mediators) and enrolling an homogeneous population, with moderate and high preoperative risk of complications, demonstrated that during abdominal surgery a multifaceted protective open lung strategy can prevent the intraoperative alveolar opening and closing that leads to atelectasis and pulmonary complications, and can optimize the health care resources utilization.

Compared to other surgical procedures, thoracic surgery is associated with the highest 30-day mortality rates, ranging from 1% for minor resections to up 12% for pneumonectomies.  $^{15,16}$ 

In the thoracic surgery the ventilation with low tV was traditionally considered to reduce the safety margin against adverse events like hypoxia due to derecruitment or hypoventilation and to decrease the time available for corrective measures in case of sudden respiratory incidents, such as double lumen tube malposition and desaturation.

Schilling et al. in a randomized study in patients scheduled for open thoracic surgery showed that a protective mechanical ventilation (tV  $5\,\mathrm{mL\,kg^{-1}}$  of ideal body weight compared to  $10\,\mathrm{mL\,kg^{-1}}$ ) significantly decreased the postoperative pulmonary inflammatory response. <sup>17</sup>

Moreover, in the Licker's study a multifaceted lung protective ventilation strategy (tV <  $8\,\mathrm{mL\,kg^{-1}}$  with PEEP 4–10 cmH $_2$ O and recruitment maneuvers) significantly reduced the incidence of atelectasis, postoperative acute lung injury, admissions to intensive care and length of hospital stay when compared with a conventional volume target ventilation. This was the first observational study that promoted the implementation of an intraoperative open ventilatory strategy to limit overdistension maintaining functional residual capacity and provided a bundle of scientifically based interventions.

The majority of the studies have demonstrated that during thoracic surgery an intraoperative open lung approach could be beneficial; however, large randomized clinical trials are necessary to generate clinical evidence.

Cardiac surgery is known to induce a variable degree of systemic inflammatory response syndrome, which is severe in 10-35% of cases, and may affect morbidity and mortality. 19 Moreover, despite a widespread use of fast-track protocols, postoperative atelectasis is frequently observed after cardiac surgery and may lead to postoperative pulmonary complications.<sup>20</sup> Many factors contribute in cardiac surgery to the development of decreased lung compliance. pulmonary edema, increased intrapulmonary shunt fraction and decreased functional residual capacity.<sup>20</sup> These factors are mainly related to the surgical procedure: the post pump syndrome, that is a systemic inflammatory response and the ischemia/reperfusion of the heart and the lungs. In this context, an injury through mechanical ventilation could aggravate the primary inflammatory response. Traditionally the ventilator setting in these patients included the use of large tV (10-15 mL kg<sup>-1</sup>), to minimize atelectasis, and minimal levels of PEEP, to reduce hemodynamic consequences, without any lung ventilation during cardiopulmonary bypass period.<sup>19</sup>

Starting from the results of clinical trials in ARDS patients<sup>1,2</sup> some authors hypothesized that mechanical ventilation with lower tV and higher PEEP might attenuate this pulmonary and systemic inflammatory response associated to cardiac surgery. However some authors did not find differences in the plasmatic and pulmonary levels of inflammatory mediators<sup>9,21</sup> comparing low tV with high tV ventilation.

Subsequently, Reis et al. showed that an open lung approach significantly attenuated the inflammatory response, the reduction of postoperative Functional Residual Capacity and the incidence of postoperative hypoxemic events, <sup>19,22</sup> but without finding any difference in ventilation and weaning times. Similarly in other two studies positive effects, in terms of lung compliance and lower reintubation rate, were observed when patients were ventilated with low tidal volume. No difference was found in global extubation time and Intensive Care Unit length of stay.<sup>23,24</sup> Although a little positive evidence results from these studies several confounding factors in cardiac surgery can affect the outcome.

In conclusion, mechanical ventilation is necessary during general anesthesia and even if ventilation is considered a safe and routine procedure, it can be unsafe for the lung, so that in patients affected by pulmonary diseases, comorbidity and in patients subjected to prolonged anesthesia, a lung protective ventilatory approach could be considered.

Further studies with large cohort of patients are needed to confirm this evidence in different types of surgeries; at present, the new challenge is to consider the possibility of a lung protective strategy during general anesthesia, taking into account risks and benefits of this approach.

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