Editorial

Driving pressure in obese patients with acute respiratory distress syndrome: one size fits all?

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The acute respiratory distress syndrome (ARDS) is an acute and diffuse inflammatory condition of the lungs, characterized by hypoxemia and bilateral pulmonary infiltrates (1). Its treatment remains mainly supportive with most of the patients requiring mechanical ventilation, that can worsen lung injury (2,3). The lungs of ARDS patients are particularly prone to overdistension since their size are reduced by the presence of non-aerated areas (4), thus, the goal of therapy nowadays is to prevent the occurrence of the so-called ventilator induced lung injury (VILI) instead of acquiring normalization of arterial blood gases (3). Previous studies have shown that VILI is strictly associated to high tidal volume ventilation, since animals ventilated with high airway pressures but low tidal volume did not develop lung damage (5), suggesting that volutrauma instead of barotrauma is the most important driver for VILI. The clinical importance of avoiding volutrauma was confirmed in the classic ARDSNet trial, where ventilation with low tidal volume reduced the mortality and increased the number of ventilator-free days in patients with ARDS when compared to ventilation using high tidal volume (6).

The tidal opening and closing of lung units is another important mechanism of VILI, named atelectrauma (3). Higher levels of positive end-expiratory pressure (PEEP) are expected to mitigate atelectrauma by keeping lung units opened during all respiratory cycle (3,7). However, three randomized controlled trials (RCT) failed to show a mortality benefit of higher levels of PEEP in ARDS patients compared to lower levels of PEEP (8-10). Opposite, a recent meta-analysis showed that an open lung strategy, consisting of recruitment maneuvers and use of higher levels of PEEP, reduced mortality in ARDS (11). However, a new multicenter and well-powered RCT evaluating the effect of an open lung strategy consisting of recruitment maneuvers followed by PEEP titration in patients with ARDS found a higher mortality rate, lower number of ventilator-free days and higher incidence of barotrauma with high levels of PEEP when compared to the ARDSNet strategy (12).

According to the phenomenon of lung hysteresis, at each exhalation the lungs return less energy than they had absorbed in the previous inspiration (13). In other words, at each breath there is an energy dissipation in the respiratory system that probably generates heat and lung injury (14). Also, there is a linear relationship among the area of hysteresis, which bears close relation to VILI, and the driving pressure (i.e., the difference between plateau pressure and PEEP) (14). In addition, the total energy delivered by the ventilator is proportional to the product of the compliance of the respiratory system and the square of the driving pressure. Thus, driving pressure is an important driver of the energy delivered by the mechanical ventilator at each breath and have attained special interest in recent years.

Another important aspect of the driving pressure is its relation to tidal volume and the reduced size of the "baby lung". A classical study has shown that the compliance of the respiratory system in patients with ARDS is related

to the volume of normally aerated lung area and not to the volume of non-aerated areas (15). The formula of the static compliance of the respiratory system dictates that the driving pressure is determined by the quotient of the tidal volume and the respiratory system compliance. Since in ARDS the compliance is related to the volume of normal lung tissue, the driving pressure indicates whether the tidal volume is adequate according to the functional residual capacity (FRC) of the lung (16). As the FRC in ARDS patients can be highly variable, pursuing an adequate driving pressure would be a way of matching tidal volume to the baby lung size (4,16).

The driving pressure can also be used as a surrogate of transpulmonary driving pressure in patients without elevated chest wall elastance (16). In conditions of elevated chest wall elastance, such as increased abdominal pressure, the driving pressure no more reflects transpulmonary driving pressure, as the esophageal pressures are higher than expected. Increasing abdominal pressure tends to increase inspiratory esophageal pressure disproportionally more than expiratory esophageal pressure, the net effect being a decrease in transpulmonary driving pressure (17). Thus, in patients with elevated chest wall elastance the transpulmonary driving pressure may better reflect lung stress (16).

The best clinical evidence of the impact of the driving pressure in outcomes of ARDS patients comes from an individual patient meta-analysis (18). By using multilevel mediation analysis of 3,562 patients from nine RCT, the investigators assessed the independent impact of the driving pressure in the mortality rate of patients with ARDS. The purpose of a mediation analysis is to determine whether a variable deeply affected by treatment allocation can explain partly or completely the treatment effect. In this investigation, it was found that high plateau pressure was linked to higher mortality only in patients with high driving pressure. Also, higher levels of PEEP conferred benefit only when associated with decrease in the driving pressure. In addition, reduction of driving pressure after randomization was associated with increased survival, and, a further decrease in driving pressure was associated with increased survival even in patients already receiving lung-protective ventilation. Finally, neither tidal volume nor PEEP were significant mediators of better survival in this group of patients. Indeed, the relationship between driving pressure and mortality has been confirmed by several studies (16) and, even in patients receiving extracorporeal membrane oxygenation, the driving pressure is significantly associated with mortality (19).

Does the lung protective strategy of ventilation apply for all subgroups of patients with ARDS? It is true that the importance of the driving pressure in the overall population of patients with ARDS has been widely discussed. However, there is a lack of evidence concerning obese patients specifically, since the possible increase in chest wall elastance may modify the effects of the driving pressure on lung stress (20). Obesity is an epidemic disease, and is associated with risk factors for cardiovascular diseases, such as hypertension, stroke and diabetes (21). In a meta-analysis including 24 observational studies, obesity was associated with significant increased risk for ARDS, however, obese patients with ARDS had lower mortality compared to eutrophic patients (22). Nevertheless, the impact of different strategies of ventilation in the group of obese patients with ARDS, which could explain the differences in the outcomes, is still under investigation.

In this context, Jong *et al.* published a study assessing the relationship between driving pressure during the first day of ventilation and 90-day mortality in obese patients with ARDS (23). The authors conducted a retrospective analysis of 100 obese patients (body mass index ≥30 kg/m^2) and 262 non-obese patients with ARDS. In a multivariate Cox proportional hazard model, the driving pressure was independently associated with 90-day mortality but only in non-obese patients. In obese patients, the driving pressure in the first day of ventilation was not different between survivors and non-survivors (14±5 *vs.* 13±4 cmH_2O; P=0.408), while in eutrophic patients it was significantly lower in survivors than in non-survivors (12±4 *vs.* 15±5 cmH_2O; P<0.001). The authors concluded that, contrary to non-obese ARDS patients, driving pressure was not associated with mortality in obese ARDS patients (23).

The study was well conducted and produce new evidence in the field, however, it has some limitations. It is a retrospective and single center study, and the results may not be generalizable. Also, the obesity criteria was determined based on body mass index, which cannot reflect the body fat and free fat mass distribution or the presence of abdominal obesity, which seems to be relevant for the changes in lung function observed in obese patients. Despite the limitations, the role of driving pressure could be different in obese patients, and the question is: does the answer rely into the mechanics of the chest wall of obese patients?

Obese patients usually have a higher elastance of the chest wall, lower pulmonary compliance and, consequently, low to negative values of transpulmonary pressure

(20,24). Thus, due to these changes in the chest wall elastance, the driving pressure, as it is calculated today, does not necessarily reflects the true transpulmonary driving pressure, which is the difference between the end-inspiratory transpulmonary pressure and the end-expiratory transpulmonary pressure (24) and, in theory, the transpulmonary driving pressure monitoring should be more reliable in this scenario.

The study also suggests that the interaction among obesity and ventilatory mechanics in patients with ARDS must be different from non-obese patients. Considering different physiologic and anatomic patterns of the individuals, some patients may benefit from a classical driving pressure monitoring to predict VILI. However, other group of patients, like the obese patients, may benefit from a transpulmonary driving pressure monitoring strategy. Indeed, these findings suggest that an individualized approach is needed and, for ARDS patients, one size does not fit all.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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