Should our patients with ALI or ARDS be ventilated at higher PEEP levels?

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In patients with the acute respiratory syndrome (ARDS), the lung is atelectatic or consolidated, particularly in dependent regions, so that it cannot participate in gas exchange. During mechanical ventilation, the less affected lung regions must therefore accommodate most of the tidal volume, with the risk of tidal hyperinflation. The ARDS network trial established the importance of hyperinflation by demonstrating that ventilation using lower tidal volumes (6 versus 12 mL/kg) and maintaining a plateau pressure of no more than 30 cm H2O, improves survival [1]. In a second trial of the ARDS network group, the ALVEOLI trial, it was shown that application of higher positive end-expiratory pressure (PEEP) levels improved oxygenation but did not have an impact on survival, suggesting that higher PEEP does not confer additional mortality benefit when low tidal volume ventilation is used [2]. This specific low-tidal-volume strategy has become the standard nowadays and is called ‘protective ventilation’ strategy.

Atelectotrauma (cyclic atelectasis) has been shown to be another important contributor to ventilator-induced lung injury in ARDS. Atelectotrauma may be mitigated by recruitment manoeuvres to open up collapsed alveoli followed by application of high levels of PEEP to prevent further collapse. In theory, ventilation strategies that combine low tidal volumes and high PEEP levels and that prevent atelectotrauma, would be the ideal ventilation strategy for lung protection in ARDS [3]. However, the debate continues as to whether hyperinflation is of more importance than cyclic atelectasis in the development of biotrauma, which is known to induce distal organ dysfunction and, ultimately, multi-organ failure.

Because application of higher PEEP levels may increase the risk of hyperinflation, a compromise must be found between PEEP-induced alveolar recruitment and prevention of hyperinflation. This editorial discusses the results of two studies (both published in the JAMA in February 2008) in which higher PEEP levels were used in patients with acute lung injury (ALI) or ARDS in order to increase alveolar recruitment while avoiding excessive hyperinflation. [4,5]. The first study is called the ‘lung open ventilation’ (LOV) trial and was performed in 30 intensive care units (ICUs) in Canada, Australia, and Saudi Arabia [4]. This was a randomized, controlled trial in 983 patients with ALI or ARDS and the experimental ventilation strategy included: tidal volumes of 6 mL/kg, plateau pressures below 40 cm H2O, recruitment manoeuvres (40-second breath-hold at 40 cm H2O airway pressure), and a table-based PEEP using a scale of PEEP versus FiO2 [4]. The second study called the Expiratory Pressure (ExPress) trial, was performed in 767 patients with ALI and was conducted in 37 ICUs in France [5]. The recruitment strategy consisted of tidal volumes of 6 mL/kg, and PEEP levels were adjusted based on airway pressure and were kept as high as possible without increasing the maximum plateau pressure to above 30 cm H2O [5]. In the ExPress trial, no recruitment manoeuvres were performed. For both studies, the primary outcome was the effect on mortality in comparison with the established low-tidal volume strategy from ARDS network trials.

In both studies, the 28-day mortality rate was 28% in the intervention group and 32% in the controls, but this difference was not significant [4,5]. The intervention group appeared to have improved secondary endpoints in both trials, such as oxygenation and less use of rescue therapies. Moreover, the recruitment ventilation strategy in the ExPress trial resulted in more ventilator-free days and organ failure-free days [5]. In the latter trial, post-hoc analyses based on oxygenation impairment at study enrolment showed that mortality tended to improve and extubation occurred earlier in patients with ARDS, whereas the opposite trend was observed in patients with ALI [5]. Therefore, it was suggested that the strategy of a high level of PEEP and low tidal volume should be used with caution in patients with ALI not reaching the criteria for ARDS.

The outcome of the three trials (ALVEOLI, LOV and ExPress) that applied higher PEEP levels in patients with ALI or ARDS, was comparable for survival but differed in the secondary endpoints [2,4,5]. However, the secondary endpoints were different: all trials showed improved oxygenation but the LOV and ExPress trial also showed less use of rescue therapy and, in addition the ExPress trial resulted in more ventilator-free days and organ failure-free days in the high-PEEP group. The reason for this is not known, but the three trials differed in study design. The ALVEOLI and LOV trials used a scale of PEEP versus FiO2 whereas the ExPress trial applied a PEEP level based on plateau pressure, individually dosed and regardless of its effect on oxygenation.

It has been shown that application of the use of a scale of PEEP vs. FiO2 according to the ARDSnet trial resulted in alveolar hyperinflation (as indicated by the stress index), with impaired cardiac output and increased levels of cytokines (Il-6 and 8) in patients with ARDS [6]. Therefore, it has been suggested that in applying PEEP properly not a universal level of PEEP should be used, but rather the best PEEP level that the individual patient actually needs at a certain time point. This implies constant re-evaluation of the individual ventilator settings, often a difficult task in the hectic ICU environment. However, ignoring the latter monitoring by, for instance, not adjusting PEEP levels when lung function improves or by using a universal high PEEP for all patients, may eventually result in ventilating lungs with pressures higher than necessary and thus causing overdistention. This was probably the case in the ALVEOLI trial because mean PEEP levels on Day 1 were around 15 cm H2O in the intervention group in all three studies, and PEEP was decreased to below 10 cm H2O within one week in the LOV and the ExPress trials, but was still 13 cm H2O in the ALVEOLI trial on Day 7 [2,4,5].

In the LOV trial, a recruitment manoeuvre (40-second breath-hold at 40 cm H2O) was performed in order to open up the lung [4].
Different recruitment manoeuvres have been tested in patients with ARDS and it has become clear that each patient has his own opening pressure. Further, it has been shown that pressures exceeding 60 cm H2O are required to re-open some atelectatic regions [7]. In the LOV trial all patients underwent the same recruitment manoeuvre, and its efficacy on lung function was not monitored. In addition, it is of special importance to use an adequate level of PEEP to prevent re-collapse directly after a recruitment manoeuvre [7]. Again, this is not a universally high level of PEEP based on FiO2, but the PEEP level should be dosed and monitored in order to avoid overdistention. Therefore, it is likely that a significant proportion of patients in the LOV trial who underwent the recruitment manoeuvre failed to ‘open up the lung and keep the lung open’ with the experimental study protocol used.

The PEEP which prevents re-collapse after a recruitment manoeuvre, but avoids overdistention while optimizing lung mechanics, can be defined as the ‘optimal’ PEEP. In practice, what tool should we use to find the ‘optimal’ PEEP? Blood gases have shown to be inappropriate and imaging techniques such as computed tomography (CT) cannot be used as a bedside tool for daily monitoring [8,9]. The stress index, obtained from the shape of the global airway pressure-time curves, can be used to detect tidal recruitment or tidal hyperinflation, but only during controlled constant-flow ventilation [6]. In patients with ARDS, it was shown that adjusting PEEP based on the stress index reduced the risk of alveolar hyperinflation, but data on clinically meaningful outcome is not yet available [6]. Another strategy for individual titration of PEEP could be the simultaneous measurement of dead space and compliance. Recently, Maisch and colleagues [10] performed a recruitment manoeuvre in combination with different levels of PEEP in patients with healthy lungs undergoing general anaesthesia, and found that the ‘optimal’ PEEP was indicated by the highest compliance in combination with the lowest dead space fraction. However, alveolar dead space is not only influenced by alveolar hyperinflation but also by intrapulmonary shunting. The latter is of more importance in patients with ARDS. It therefore still needs to be tested whether assessing dead space is sensitive enough for PEEP dosing in patients with ARDS.

Thus, strategies with higher levels of PEEP appear to be safe and beneficial, especially in patients with ARDS who the sickest. Although the mortality rate did not differ, the higher PEEP strategy resulted in fewer patients with severe hypoxaemia leading to fewer pulmonary deaths, and this could account for the 3 to 4% difference in mortality rate in favour of the higher PEEP group observed in both the LOV and the ExPress trials, in comparison with the low PEEP arm [11]. In addition, Gattinoni et al. [12] have shown that the capacity for opening collapsed lung units varies greatly among patients with ARDS. Thus, ‘optimal’ PEEP can only be achieved by using individual settings that differ from patient to patient and from time to time. Therefore, we are waiting for simple validated bedside tools to better individualize the PEEP levels for our patients with ALI/ARDS.

References