Point of view

High frequency oscillatory ventilation tidal volumes: how low can we go?

The publication of the first randomised, controlled trial on high frequency oscillatory ventilation (HFOV) for acute respiratory distress syndrome (ARDS) in adults, from Derdak *et al*,[1] has brought renewed attention in both HFOV and the ideal ventilation strategy for ARDS patients. It represents the possible reintroduction of HFOV as a lung protective approach to the atelectasis-prone lung.

One hundred and forty eight patients with ARDS were randomised to HFOV or conventional ventilation. The thirty-day mortality was 37% in the HFOV group and 52% in the conventional ventilation group ($p = 0.102$), showing a non-significant trend towards reduced mortality. Despite the fact that the study was inadequately powered to compare outcome, it has attracted attention and brought to light some interesting questions regarding HFOV, not least being that it appeared to be as safe and effective as the conventional ventilation mode employed in the control arm.

The publication of the ARDSnet group results,[2] has caused clinicians to focus on the potential harmful effects of mechanical ventilation and highlighted mechanisms to reduce ventilator-induced lung injury (VILI). The ARDSnet study found a statistically significant reduction in the 28-day mortality rates in the low tidal volume group (e.g. 40% in 12 mL/kg group v.s. 31% in the 6 mL/kg group). This has prompted further research into the use of ventilation strategies to limit overdistention and derecruitment of the expanded atelectatic lung.

HFOV is uniquely suited to the goals of limiting overdistention and preventing derecruitment.[3] It uses an oscillating piston to provide active inspiration and expiration of gas, differentiating it from other forms of high frequency ventilation (HFV), and uses very small tidal volumes of 1 - 2 mL/kg at supra physiological rates (3 - 15Hz). The pulmonary influences of arterial oxygenation and carbon dioxide elimination can be separately controlled, as alveolar ventilation and therefore carbon dioxide elimination are dependent on tidal volume and frequency of ventilation, whereas oxygenation is proportional to mean airway pressure and lung volume.[4]

Mechanical ventilation may cause lung injury by a number of mechanisms including overdistention or volutrauma, biotrauma and shear injury or atelectrauma. Volutrauma occurs when high tidal volumes and plateau pressures are applied. In ARDS patients the areas of normal lung are ventilated in preference to the atelectatic areas and are at risk of volutrauma.[5] The pulmonary injury sequence consists of alveolar cell injury and capillary congestion due to endothelial and epithelial damage; this results in further protein leak into alveolar spaces and deactivation of surfactant leading to further microatelectasis.[6] This results in significant reduction in compliance and severe ventilation and perfusion mismatch. Additional data show that a low chest wall compliance is relatively protective against the hazards of high peak airway pressures, suggesting that end expiratory stretch related to transpulmonary pressure is the key factor for this injury.[7] Gattinoni *et al*,[8] with the use of CT scans in adults with ARDS, demonstrated that the dependent lung zones remain consolidated even with significant levels of PEEP. His group described the ARDS lung as a 'baby lung' sitting on top of a consolidated lung, and proposed that tidal volumes of 6 - 10 mL/kg could generate comparatively large tidal volumes of 30 - 50 mL/kg when delivered to a limited number of alveoli.

Dreyfuss *et al*,[9] demonstrated that large tidal volumes were associated with increased protein leak, lung injury and perhaps mortality. In the absence of overt structural damage, the lung responds to mechanical stress/stretch by producing proinflammatory compounds.[10] Also allowing the lung to remain atelectatic may be injurious, because collapsed lung has a propensity to attract polymorph nuclear neutrophils and an assortment of mediators which are not only injurious to the lung but may also induce multiple organ failure (MOF).[11] This effect has been termed biotrauma,[12] with the implication that by decreasing VILI one may be able to avoid further organ failure. HFOV has been shown to produce less histological damage and lower circulating cytokine levels when compared with a high PEEP, low stretch conventional mechanical ventilation strategy.[13,14]

Shearing injury or atelectrauma results from the repetitive opening and closing of lung regions that are forced open with high pressures on inspiration and allowed to close again with low expiratory pressures.[11] HFOV is considered safe in delivering 'super PEEP' with the distending pressure able to be increased up to 45 cmH_2O without large tidal volumes increasing the peak inspiratory pressure above this value. Although the oscillations may cause significant pressure swings in the endotracheal tube, the pressure swings are sufficiently attenuated at the alveolar level.[15,16] The small tidal volumes (1 - 2 mL/kg) delivered at high frequencies are

sufficient to remove carbon dioxide without causing barotrauma and the pressure swings remain low enough to maintain the high distending pressures throughout the respiratory cycle to minimise derecruitment and alveolar collapse.

Clinical studies with HFOV in adults with ARDS are limited to observational studies and case reports in 'rescue' therapy for those patients who have failed with conventional ventilation.[17-20] The only apparent certainty from these reports is the demonstration that HFOV is a safe and effective ventilation technique in adults with severe ARDS who fail conventional ventilation. Because patients who die with ARDS usually die from MOF rather than hypoxaemia, strategies to reduce VILI continue to be employed in an attempt to reduce mortality. The ability of HFOV to maintain an open lung approach using lower peak airway pressures and smaller tidal volumes compared with conventional ventilation may potentially result in less biotrauma, reducing its systemic effect on other organs, and thereby reduce morbidity and mortality.

The optimal mechanical ventilatory parameters in patients with ARDS are changing, but if HFOV is at the extreme end of a low tidal volume ventilation and high PEEP strategy then the question remains, how low can we go with tidal volumes? The technology to measure these tidal volumes is not currently available but respiratory inductive plethysmography is showing promise.[21]

Derdak *et al*, have questioned the use of traditional frequencies in HFOV used in adults and point to the paediatric population where frequencies of 10 - 15 Hz are common.[4] These high frequency/low tidal volume strategies may lead to a more significant trend towards reduced mortality when compared with conventional ventilation. High frequencies with lower tidal volumes would approach an ideal lung protective strategy in the ARDS lung but we are currently constrained by hypercarbia at higher frequencies in adult patients. The main constraint appears to exist with the equipment available, as Sensormedics 3100B is the only adult HFOV machine that is currently marketed. Possibly its inability to clear carbon dioxide at frequencies above 5 - 6 Hz may be related to a reduction in stroke volume and hence tidal volume, because of the under-powering of the oscillator. However, it may also be because we have passed the optimal frequency to clear carbon dioxide in adults and these are the smallest tidal volumes that are of any benefit. No data exists to predict the optimal frequency or inspiratory time to control arterial carbon dioxide in adults; frequencies of 4 - 6 Hz have no scientific basis and are purely empirical. We therefore await further trials to address this issue.

The study by Derdak *et al*,[1] suggests that HFOV should now be considered as another therapeutic method of mechanical ventilation rather than simply 'rescue' therapy.[17,18,20] The early recognition, intervention and minimising of further lung injury by utilising HFOV should become clearer with further studies. Currently, however, valid and reliable data concerning the best parameters for HFOV to protect the lung in ARDS have not yet been published.

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