## Commentary

# ICU Cornerstone: High frequency ventilation is here to stay

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#### **Abstract**

With favourable and extensive experience in the neonatal intensive care unit (ICU) and the recent positive experience in the adult ICU, high-frequency ventilation has become a valuable alternative to conventional ventilation in acute lung injury. To arrive at this point, physicians' understanding of the characteristics and kinetics of acute lung injury had to become more distinct, and it was necessary to merge accumulated knowledge from experience with high-frequency ventilation in the neonatal population and that with conventional ventilation in adults. However, this now calls for a better designed clinical trial in the adult population that combines the three most important concepts for lung protection: early intervention (before acute respiratory distress syndrome is established); optimal lung recruitment; and careful avoidance of lung over-distention over the entire period of mechanical ventilation.

Keywords acute lung injury (respiratory distress syndrome, adult), high-frequency ventilation, hypercapnia, respiratory distress syndrome (infant), respiratory physiology

As medical students we were told that mechanical ventilation needs convective gas flow. As residents we learned then that we must normalize gas exchange during mechanical ventilation. We also learned, based on the Radford nomogram published in 1954 [1], that there are some 'normal' respiratory rates and some 'normal' tidal volumes that may be employed to mimic normal physiology.

However, as Henderson and coworkers [2] concluded from their observations in panting dogs almost 90 years ago, adequate alveolar ventilation can be achieved at high respiratory rates and very small tidal volumes at about or below the dead space volume. This could be accomplished using either conventional ventilation at low tidal volumes (3-4 ml/kg) and high rates (above 60/min), with an additional high flow of fresh gas delivered to the patient by a side connector connected to the endotracheal tube (highfrequency positive pressure ventilation), a high-velocity gas jet through a small catheter (high-frequency jet ventilation [HFJV]), a sliding venturi (high-frequency percussive ventilation), or a piston driven oscillator (high-frequency oscillation [HFO]).

Although all of these alternative methods to achieve conventional ventilation are highly effective in eliminating carbon dioxide using low peak airway pressures, the effect on oxygenation is less uniform, and this represents one reason why these newer modes of ventilation (especially HFO) failed to maintain their initial attraction during the subsequent years. Another reason was the publication of the first large multicentre trial (the HiFi trial) in 1989, completed before surfactant became available, that failed to demonstrate better outcomes with HFO than with conventional ventilation in the treatment of respiratory failure in preterm infants [3]. The data from HiFi and a subsequent trial with HFJV [4] indicated an increase in adverse cerebral outcomes in infants assigned to the high-frequency arm. This became another major and persistent concern, although meta-analytic evidence does not support a higher incidence of such outcomes [5]. In contrast to the case with highfrequency ventilation (HFO and HFJV) in the neonatal intensive care unit (ICU), the reduction in ventilator-related movements, which improved operating conditions in airway surgery, ensured that high-frequency positive pressure ventilation and certainly HFJV did find a niche in clinical

practice [6]. High-frequency percussive ventilation has evolved to a standard of burn care in some centres for salvage treatment, and has recently been advocated for patients with acute respiratory distress syndrome (ARDS) too [7,8]. In the adult ICU, HFO was not used until recently, when a new generation of more powerful oscillators (SensorMedics 3100B HFOV, SensorMedics, Yorba Linda, CA, USA) became available.

The increasing recognition that ventilator-induced lung injury exists and that it might to some extent be responsible for multiorgan failure and the high mortality in adult ARDS patients [9] led to the development of lung protective strategies during conventional mechanical ventilation. Recruitment of nonaerated tissue, prevention of lung unit recollapse, and avoidance of over-distention have become the three cornerstones of these concepts of lung protection [10,11]. These goals can best be achieved by using a minimal stress, open lung strategy (i.e. small tidal volumes and high positive end-expiratory pressure [PEEP] levels, which should be high enough to prevent re-collapse of recruited lung units) [11-13]. However, small tidal volume ventilation may cause complications that result from the effects of acute respiratory acidosis on haemodynamics, gas exchange, and oxygen transport or consumption [14-16]. These require increased use of sedatives and often muscle relaxants, and may lead to alveolar instability and lung collapse [17].

Within the context of ventilator-induced lung injury and lung protective strategies, high-frequency ventilation could be considered to be the optimal protective ventilator mode. This is because, by 'design', it provides small tidal volume ventilation (even extremely small) and allows for lung recruitment and maintenance of optimal lung volume without concomitant lung over-distention. 'Side effects' such as acute respiratory acidosis during conventional ventilation do not occur, and spontaneous ventilation, at least in neonates and small children, can easily be maintained, allowing for less sedation and requiring no muscle relaxants. In larger patients, because of higher inspiratory flow demands, spontaneous breathing is not as easily managed, and heavy sedation and/or paralysis may be required.

The success of HFO depends on the ability to recruit lung volume, which is not always easy 'late' in the course of lung disease when substantial ventilator-induced damage is superimposed on a preinjured lung. Unfortunately, the HiFi trial protocol [3], as well as many other studies that examined the efficacy of high-frequency ventilation in neonatal respiratory failure, failed to stress early intervention, volume recruitment manoeuvres and maintenance of high mean airway pressures, as was clearly indicated based on experimental data [18–21]. Recent HFO trials that took care by design to fulfill the condition of 'opening the lung and keeping it open' showed that HFO is efficient and safe for ventilating patients (from neonates to adults) with acute

respiratory failure [22–28]. However, thus far HFO has proved to be better than conventional ventilation in terms of pulmonary outcome only in the neonatal ICU [22,24–26,29] and in one trial in the paediatric ARDS population [23]. The question that rises is whether this can be simply explained by the differences between neonatal and adult respiratory failure and whether these differences preclude direct extrapolation of the neonatal data to adults.

Neonatal respiratory distress syndrome is, like ARDS, an inhomogeneous lung disease [30,31] with dependent (collapsed and fluid filled) and nondependent (aerated) zones. Thus, from the physiological behaviour of the lung, the same concepts (i.e. open the lung and keep it open without over-distending it) can be applied during mechanical ventilation from neonates to adults. However, some difference is evident from the fact that the predominantly surfactant deficient neonatal lung is relatively easy to recruit, at least early after birth before the patient develops significant ventilator-associated lung injury, but in adult ARDS, especially in primary ARDS, the potential for recruitment is lower [11]. However, most patients have at least some recruitable lung but sometimes very high opening pressures are needed.

Interestingly, in a prospective observational study conducted by Mehta and coworkers [32], involving 24 adult patients with severe ARDS (arterial partial oxygen tension/fractional inspired oxygen ratio <100), survivors were on conventional ventilation for a shorter period of time prior to HFO than were non-survivors. Also, in the prospective randomized clinical trial conducted by Derdak and coworkers [28], involving 148 adult patients with established ARDS (arterial partial oxygen tension/fractional inspired oxygen ratio <200, at a PEEP of 10 cmH2O), a prolonged period of conventional ventilation prior to HFO predicted high mortality. Although both studies tested HFO as a rescue mode in established severe ARDS, the time on conventional ventilation previously was still related to outcome. In fact, HFO as an early intervention strategy has only been tested in two clinical trials in infant respiratory distress syndrome, one a non-randomized study by our group [29] and the other a randomized study by Courtney and coworkers [26]. On the other hand, positive results in some of the neonatal HFO trials could be accounted for by inadequacies in terms of lung protective PEEP levels and/or tidal volumes in the conventionally ventilated control groups. Based on experimental data, it could be suggested that using a conventional ventilation strategy for lung recruitment followed by adequate PEEP above closing volume will be as effective as HFO in minimizing lung injury [33], and it is likely that it is much more the strategy than the mode that will make the greatest difference. Therefore, to improve the use of conventional ventilation in the neonatal population and to better define the role of HFO in lung protective ventilation in adult patients, more appropriate trials are still needed.

HFO, if used with the correct strategy, has finally been proven to be at least equivalent to conventional ventilation and it has significant potential to prove to be better than conventional mechanical ventilation, because it offers the optimal technical features that would fulfill all conditions for best lung protection. Unfortunately, there is still a mindset that considers HFO as a rescue rather than a primary mode of therapy. This is in part supported by the hesitation to look into a new mode of ventilation, but once clinicians and nurses get used to the 'philosophy' of HFO, this mode proves to be efficient, safe and simple in its application at bedside. In addition, it allows for excellent carbon dioxide clearance without the need for 'permissive hypercapnia', which may not be always an optimal approach and is certainly not physiological. In fact, HFO allows the clinician to achieve the goals that Radford [1] searched for with his nomogram, and its ongoing use proves that what we were told in medical school on mechanical ventilation was only half the truth.

### Competing interests

None declared.

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