



## EDITORIAL

# Tidal volume, recruitment and compliance in HFOV: same principles, different frequency

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**T**he widespread clinical introduction of high-frequency oscillatory ventilation (HFOV) for the treatment of respiratory distress syndrome in neonates in the late 1980s and early 1990s heralded a new era of understanding of the optimal approach to lung volume ( $V_L$ ) recruitment, which embraced the concept of open lung ventilation [1]. The promotion of HFOV as a means of independently controlling oxygenation and ventilation contributed to the ease with which it was accepted as a clinical treatment in many neonatal units. Unlike mechanical ventilation at physiological breathing rates where changes in ventilator settings on contemporary ventilators inevitably affect both oxygenation and ventilation, traditional teaching of HFOV promoted changes in mean airway pressure as the means of influencing arterial oxygen tension and alterations to proximal pressure amplitude ( $\Delta P$ ) and frequency ( $f$ ) of the oscillatory waveform as the determinants of arterial carbon dioxide tension ( $P_a\text{CO}_2$ ) [2]. Like any intensive care technology, however, successful and safe application of HFOV is highly dependent on fully understanding the specific nuances of this ventilatory modality.

As recognised previously, there are clear changes in compliance during recruitment of the atelectatic lung [3]. During ventilation at conventional breathing rates, as  $V_L$  is recruited, lung compliance improves and this is accompanied by increased tidal volume ( $V_T$ ) to which the clinical response is normally a reduction in minute volume: in synchronised modes, this is most often achieved *via* a reduction in  $\Delta P$  or targeted  $V_T$  rather than a reduction in respiratory rate.

Changes in compliance [4–7] and lung tissue resistance [5] have also been widely recognised during volume recruitment achieved with HFOV. In this issue of the *European Respiratory Journal*, MIEDEMA *et al.* [8] present an elegant study showing that changes in compliance occurring as a result of  $V_L$  recruitment are reflected in altered delivered  $V_T$ . Their findings provide evidence to support recent clinical findings showing that the  $fV_T^2$  product provides useful clinical feedback during  $V_L$  recruitment manoeuvres. That delivered volume changes with  $V_L$  recruitment during HFOV should not be surprising since the laws governing delivery of volume and pressure to the lung during HFOV should follow the same relationship governing

$V_T$  during pressure-controlled, conventional-rate ventilation:  $V_L$  during inspiration is an exponential function derived from the equation of motion:

$$V_L = CL \cdot \Delta P \cdot (1 - e^{-t/\tau})$$

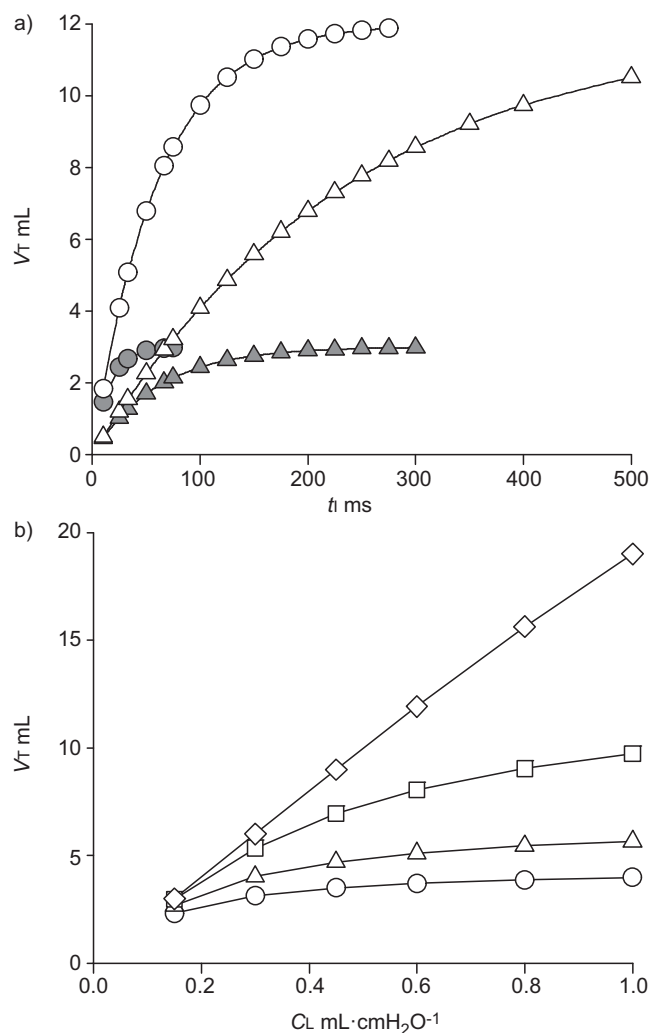
where  $CL$  is lung compliance,  $t$  is the inspiratory time and  $\tau$  is the inspiratory time constant. It should be clear that at a given  $\Delta P$ , the maximum  $V_T$  is predominantly influenced by  $CL$ , whereas the extent and rapidity to which that  $V_T$  is achieved are determined by  $t$  and  $\tau$ , respectively. Thus, as  $CL$  increases in a patient treated with HFOV during  $V_L$  recruitment, we would expect to observe an increase in  $V_T$  (fig. 1a), with resultant increased ventilation efficiency at any given  $f$ .

The key to understanding changes in  $V_T$  changes during HFOV lies more specifically with the  $t$ . During ventilation at normal breathing frequencies, the  $t$  (and, therefore,  $t$ /expiratory time ( $t_E$ ) ratio) is usually adjusted until it is sufficiently long to permit full  $V_T$  delivery. However, during HFOV,  $t/t_E$  is normally held constant regardless of  $f$ . At any given level of  $CL$ ,  $f$  and  $\Delta P$ , the ratio between absolute  $t$  and  $\tau$  determines what proportion of the potential maximum  $V_T$  is actually delivered. The time available to deliver volume to the lung during inspiration decreases as  $f$  increases, resulting in delivery of smaller  $V_T$  at higher  $f$ . By extension, the proportionate increase in  $V_T$  resulting from increased  $CL$  associated with  $V_L$  recruitment will decrease with increasing  $f$  due to shorter  $t$  (fig. 1b). Thus, the differences in  $V_T$  observed in this issue by MIEDEMA *et al.* [8] during HFOV at 10 Hz would be more evident at 5 Hz and may be somewhat less obvious at 15 Hz. At lower  $f$ , rapid shifts in volume as  $CL$  increases may rapidly decrease  $P_a\text{CO}_2$ , but also raise the prospect of inadvertent volutrauma and/or effects on cerebral blood flow with swift  $P_a\text{CO}_2$  flux. Conversely, at higher  $f$ , the fall in  $P_a\text{CO}_2$  observed during the steep (rapid recruitment) phase of the inflation slope may be blunted due to a less marked effect of  $CL$  on delivered volume.

Whereas the change in  $V_T$  at constant oscillatory  $\Delta P$  was shown previously in *in vitro* lung models [9], MIEDEMA *et al.* [8] have demonstrated how this relates to  $V_L$  recruitment *in vivo*. The important detail for clinicians is that the displayed ventilator amplitude does not inform on the changes in cyclic delivered volumes. However, ultimately, the utility of a change in cyclic delivered volumes during  $V_L$  recruitment is only of practical value as a marker of optimal  $CL$  if oscillatory pressure is not altered during the recruitment manoeuvre and if delivered volume is measured. In the clinical setting, oscillatory amplitude is often adjusted continuously during initiation of HFOV in

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**FIGURE 1.** Effect of lung mechanics and inspiratory time on tidal volume (Vt) delivery during high-frequency oscillatory ventilation. a) Maximum potential Vt is determined by lung compliance (CL) and inspiratory time (ti), while the rate of Vt delivery is determined by lung mechanics. Simulation performed assuming a pressure amplitude of 20 cmH<sub>2</sub>O. Each curve is terminated after reaching 99% of the maximum Vt. Open symbols: CL 0.6 mL·cmH<sub>2</sub>O<sup>-1</sup>; closed symbols: CL 0.15 mL·cmH<sub>2</sub>O<sup>-1</sup>; circles: resistance of the respiratory system (Rrs) 100 cmH<sub>2</sub>O·L<sup>-1</sup>·s<sup>-1</sup>; triangles: Rrs 400 cmH<sub>2</sub>O·L<sup>-1</sup>·s<sup>-1</sup>. b) Increasing CL will result in proportionately greater increases in Vt as ti lengthens (or as frequency decreases) at any given ti/inspiratory time ratio. Simulation performed at CL 0.15 mL·cmH<sub>2</sub>O<sup>-1</sup> and Rrs 100 cmH<sub>2</sub>O·mL<sup>-1</sup>. Circles: ti 22 ms; triangles: ti 33 ms; squares: ti 67 ms; diamonds: ti 300 ms.

response to change in chest movement (“wobble”) and the rapidity of change in transcutaneous carbon dioxide, while delivered Vt is not yet routinely measured by all HFOV devices. Newer HFOV devices that offer volume guarantee, with automatic adjustment of  $\Delta P$  alongside enhanced CL, will allow clinicians to use the oscillatory  $\Delta P$  at the airway opening instead of Vt as an indicator of optimal CL during VL recruitment. Nonetheless, given optimal CL during inflation occurs midway along the steep portion of the inflation pressure–volume slope prior to complete VL recruitment, there still remains the question of how Vt (or  $\Delta P$  if operating in a volume-guarantee

mode) can precisely inform the clinician when optimal opening of lung units has been achieved and provide an indication of the best time to commence decreasing mean distending pressure, in order to avoid deleterious overdistension of the fragile immature lung.

Overinflation can be considered in regard to peak alveolar distension ( $D_{alv}$ ), which is the sum of the end-expiratory lung volume ( $V_{EE}$ ) and the cyclic volume change ( $V_t$ ) relative to the total lung capacity (TLC) [10], such that:

$$D_{alv} = (V_{EE} + V_t) / \text{TLC}$$

Given the restricted TLC of the pre-term lung, high Vt superimposed on moderately high distending VL has the potential to impose cyclic overinflation on the lung. Compared with the healthy newborn lung, the lungs of an infant with respiratory distress syndrome have a much lower range of frequencies and mean distending pressures in which ventilation is safely achieved without overdistension. To this end, tools that provide feedback on absolute lung volume and the cyclical distension would enhance management of the infant on HFOV and identification of optimal lung distension. Electrical impedance tomography (EIT), while providing relative rather than absolute VL, does offer potential benefits during acute recruitment procedures. Effective calibration of EIT and easier application at the bedside with real-time bedside feedback will substantially improve the ability of the clinician to appropriately recruit without overdistending the newborn lung. Research needs to continue into other easy bedside measures of VL recruitment. In the interim, clinical approaches that facilitate relatively safe recruitment of the lung and identification of closing volume using markers of oxygenation, such as peripheral oxyhaemoglobin saturation and transcutaneous oxygen tension, have provided guidance for neonatal clinicians without access to research tools [11].

Whereas MIEDEMA *et al.* [8] clearly showed that changes in mean distending pressure have the potential to influence ventilation in addition to VL, it is less clear from their study whether the reverse is true, *i.e.* that changes in oscillatory amplitude influence VL in addition to ventilation. In studying human infants, they were confined to assessing small changes in oscillatory amplitude after completing VL recruitment and achieving clinical stability. Under these conditions, they observed that small changes in oscillatory  $\Delta P$  at 10 Hz had no effect on VL over a short interval. Although this finding may seem intuitive, given the oscillations were occurring around the same mean distending pressure regardless of  $\Delta P$ , it is reasonable to question whether this might always be the case, particularly if the change in  $\Delta P$  was applied over the steep, nonlinear portion of the inflation pressure–volume relationship. Over the last decade, an increasing awareness has developed regarding the potential for variable ventilatory pressures and/or volumes to contribute to lung volume recruitment *via* a phenomenon known as stochastic resonance [12, 13]. Variability in the amplitude of the applied pressure or volume signal (rather than application of a constant  $\Delta P$ ) may promote avalanche airway opening events, resulting in the recruitment of atelectatic airways. The amount of noise (or variability in amplitude) of the applied signal in part determines the extent to which a recruitment effect may be observed [12]. This observation suggests that, in the future, it may also be

possible to fine-tune the oscillatory  $\Delta P$  to achieve maximal affect and to avoid steady loss of distending VL associated with ventilation using small VT.

While MIEDEMA *et al.* [8] did not observe a significant effect of small increments/decrements in oscillatory  $\Delta P$  on VL, the reduction in spontaneous breathing frequency with an increase of only 5 cmH<sub>2</sub>O in oscillatory  $\Delta P$  is worth noting. To date, there has been little work undertaken to define the appropriate spontaneous breathing frequency during HFOV. Spontaneous breathing improves regional lung ventilation distribution during HFOV [14]. However, excessive spontaneous breathing may result in poor patient-ventilation interactions and efficacy of ventilation associated with increased work of breathing [15]. Ablation of spontaneous breathing may contribute to disuse atrophy of the diaphragm (ventilation-induced diaphragmatic dysfunction) [16], with the potential to impede successful weaning from mechanical ventilation. The finding by MIEDEMA *et al.* [8] that relatively small adjustments in oscillatory  $\Delta P$  may have substantial effects on spontaneous breathing frequency along with the marked increase in cyclic delivered volume with increased oscillatory  $\Delta P$  (up to 200%) highlights the need to pay close attention to continuous fine tuning of the ventilation settings during HFOV. Interestingly, oscillatory volume did not return to baseline in a number of patients after the amplitude adjustments suggesting a change to CL, although this was not detected as a change in VL on EIT. The basis for this change warrants further investigation.

Another consideration not explored in the article by MIEDEMA *et al.* [8], but which has important consequences for injury to the airways and the lungs during HFOV, is the extent to which cyclic oscillatory  $\Delta P$  is transmitted from the airway opening to the trachea and the distal lung during VL recruitment. In a seminal analysis of the implications of frequency and pressure selection for HFOV, VENEGAS and FREDBERG [10] showed theoretically that the pressure transmitted to the carina is the critical factor defining the pressure cost of ventilation, and is intimately related to both the mean distending pressure and *f*. These findings were confirmed subsequently by VAN GENDERINGEN *et al.* [7], who used the oscillatory pressure ratio (OPR) derived as the ratio of tracheal to airway opening pressures to define the optimum mean distending pressure on the deflation limb of the pressure-volume relationship. Importantly, the OPR was always lower on the deflation limb than on the inflation limb, highlighting the critical importance of reducing pressure once the lung has been opened. This detail is not immediately apparent if one considers only changes in VT during VL recruitment, underlining the importance of considering all available indices of optimal lung distension in any clinical recruitment protocol.

Although it is now more than two decades since HFOV was widely adopted by clinicians as an alternative and potentially lung protective ventilation modality, the bedside application of optimal lung recruitment principles during HFOV is still not routinely practiced in many clinical units. Suboptimal application of HFOV is due in part to the lack of simple and readily available bedside tools of absolute VL assessments, but also in part due to poor understanding of the consequences of inappropriate strategy for delivery of VT and pressure to the lung. Overall, it becomes apparent that optimal lung volume recruitment is most safely achieved when accompanied by

timely and informed changes in ventilatory settings to avoid both cyclic and static lung under- and overdistension while minimising excessive transmission of oscillatory pressures to the airways and controlling the rate of change of carbon dioxide to avoid rapid flux in cerebral perfusion. The further development and simplification of bedside monitoring tools that can be applied in non-research intensive clinical settings is a vital component of this therapeutic goal.

## STATEMENT OF INTEREST

A statement of interest for J.J. Pillow can be found at [www.ersjournals.com/site/misc/statements.xhtml](http://www.ersjournals.com/site/misc/statements.xhtml)

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