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Comparison of flow and gas washout characteristics between pressure control and high-frequency percussive ventilation using a test lung

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Abstract

Objective—A comparison between flow and gas washout data for high-frequency percussive ventilation (HFPV) and pressure control ventilation (PCV) under similar conditions is currently not available. This bench study aims to compare and describe the flow and gas washout behavior of HFPV and PCV in a newly designed experimental setup and establish a framework for future clinical and animal studies.

Approach—We studied gas washout behavior using a newly designed experimental setup that is motivated by the multi-breath nitrogen washout measurements. In this procedure, a test lung was filled with nitrogen gas before it was connected to a ventilator. Pressure, volume, and oxygen concentrations were recorded under different compliance and resistance conditions. PCV was compared with two settings of HFPV, namely, HFPV-High and HFPV-Low, to simulate the different variations in its clinical application. In the HFPV-Low mode, the peak pressures and drive pressures of HFPV and PCV are matched, whereas in the HFPV-High mode, the mean airway pressures (MAP) are matched.

Main results—HFPV-Low mode delivers smaller tidal volume (V_T) as compared to PCV under all lung conditions, whereas HFPV-High delivers a larger V_T . HFPV-High provides rapid washout as compared to PCV under all lung conditions. HFPV-Low takes a longer time to wash out nitrogen except at a low compliance, where it expedites washout at a smaller V_T and MAP compared to PCV washout.

Significance—Various flow parameters for HFPV and PCV are mathematically defined. A shorter washout time at a small V_T in low compliant test lungs for HFPV could be regarded as a hypothesis for lung protective ventilation for animal or human lungs.

Keywords

high-frequency percussive ventilation; pressure control ventilation; lung protective ventilation; gas washout; tidal volume; peak inspiratory pressure

Introduction

Although conventional pressure-controlled and volume-controlled mechanical ventilation has been adopted worldwide, there is always a risk associated with these types of ventilators due to the potential for ventilator-induced lung injury (VILI), and nosocomial infection (McLuckie 2009). High-frequency percussive ventilation (HFPV) is a hybrid ventilation mode in which a high-frequency pulsatile waveform (more than 150 breaths min^{-1}) is superimposed on a low-frequency conventional time-cycled pressure waveform (Esan *et al* 2012). HFPV delivers high-frequency pulses that stack to form a low-frequency tidal breathing (Allan *et al* 2010). Similar to conventional ventilator modes, the low-frequency tidal breaths or the respiratory rate can be controlled by setting the inspiratory time (I time) and expiratory time (E time). During inspiratory phase, the lung is slowly inflated by the pulsatile flow, and during passive expiration, the lung is allowed to deflate to demand continuous positive airway pressure (dCPAP) that is similar to positive end-expiratory pressure (PEEP) in pressure control ventilation (PCV). High-frequency breaths are also employed during expiration by setting an oscillatory CPAP.

Compared to high-frequency oscillatory ventilation (HFOV), where amplitude and frequency are uncoupled, and expiration is active, HFPV is characterized by passive exhalation and coupled pulsatile amplitude and frequency. A slower pulsatile frequency during HFPV is associated with higher amplitude pulse and used to improve respiratory mucus clearance, and CO_2 clearance and a faster pulsatile frequency (with lower pulsatile amplitude) are used to improve oxygenation. An HFPV device is attached to a patented Venturi device called the 'Phasitron' (Bird 2003a, 2003b). Phasitron interfaces with the patient and the ventilator and entrains additional gas due to a Venturi principle. It automatically adjusts the entrainment volume, depending upon the lung compliance and airway resistance of the patient.

HFPV was initially employed for the treatment of newborns affected by hyaline membrane disease or infant respiratory distress syndrome and the acute respiratory distress syndrome (ARDS) caused by burns and smoke inhalation (Allan *et al* 2010). The usefulness of HFPV has been clinically assessed, particularly in the treatment of post-traumatic respiratory insufficiency (Hurst *et al* 1987), inhalation injury (Cioffi *et al* 1989), acute respiratory infections caused by burns and smoke inhalation (Lentz and Peterson 1996, Reper *et al* 2002), newborns with hyaline membrane disease and/or ARDS (Velmahos *et al* 1999), and surgical bronchial repair in a patient with one lung (Lucangelo *et al* 2006b). Allardet-Servent *et al* (2008) performed randomized controlled studies on rabbits subjected to lung injury and reported that the HFPV provides lung protective ventilation and improves oxygenation and ventilation similar to low-tidal volume (V_T) mechanical ventilation and HFOV. Chung *et al* (2010) performed a randomized controlled trial on 62 severely burned adult patients and suggested that cases of rescue ventilation requirement and barotrauma are significantly lower in HFPV as compared with the low- V_T strategy. Recently, Michaels *et al* (2015) presented clinical data on 39 adult ARDS patients treated with HFPV to enhance recovery and recruitment during extracorporeal membrane oxygenation (ECMO). They showed that the use of HFPV alongside ECMO decreases the length of time on ECMO.

In the last 15 years, only a modest number of scientific research articles have characterized the mechanical behavior of HFPV. For instance, Lucangelo *et al* (2004, 2006a) conducted an experimental study on a test lung model and presented data on mean airway pressure (MAP), peak inspiratory pressure (PIP), positive/negative peak flow rate, and V_T at various compliances and resistances. They measured PIP in the range of 26.68–45.3 cmH₂O and the V_T in the range of 115–465 ml. Lucangelo *et al* (2006a) pointed out a unique gas flow characteristic of HFPV, noting that the high-frequency percussive sub-tidal ‘minibursts’ cause gas wash-in/wash-out during low-frequency inspiration and limit the cumulative tidal volume delivered to the patient. Although they provide very interesting quantitative data on HFPV, no comparison was made with PCV. Allan (2010) also performed *in vitro* measurements using a test lung and reported a mean V_T of 1337 ml. Given that such a high V_T would likely induce volumetric injury, this contrasts with evidence indicating that HFPV confers respiratory protective effects in the clinical setting. Although the ventilator settings and test lung conditions were different in the studies performed by Lucangelo *et al* (2006a) and Allan (2010), the considerable variation in the reported tidal volumes induces skepticism.

The aim of this study is to compare and describe the flow and gas washout behavior of HFPV and PCV in a test lung. Further, the study points to establish standard definitions for HFPV parameters for its clinical applications. The study employs a newly designed experimental setup, to investigate washout measurements of a nitrogen-filled test lung to assess the gas exchange parameters of the both PCV and HFPV under different ventilator settings and simulated respiratory conditions.

Methods

Experimental setup

The experimental setup is presented in figure 1. The Phasitron consists of a sliding Venturi and four ports, namely, an inlet port, entrainment port, exhalation port, and the mouthpiece port as shown in figure 1. The inlet port is connected to the ventilator, and the entrainment port entrains additional air/oxygen due to Bernoulli’s principle of the sliding Venturi mechanism depending on the lung resistance and compliance. The exhalation port has a one-way check valve that is operated by the sliding Venturi and, finally, the mouthpiece port provides the air/oxygen to the lung, which can be directly connected to the buccal cavity of the patient or an endotracheal tube (ETT). For PCV studies, the LTV 950 (Pulmonetic Systems Inc., Medina road suite 100, Minneapolis, MN, USA) was used. The LTV 950 uses a flow control valve and a turbine to provide both pressure controlled and volume controlled breaths. The mouthpiece port from the Phasitron and the compressed nitrogen lines are connected to a test lung (Quicklung, Ingmar Medical, and Pittsburgh, PA, USA) using a Y fitting through two valves, namely valve1 and valve2. The Quicklung provides three simulated resistive loads (5, 20, and 50 cmH₂O/l/s) and three elastic loads (10, 20, and 50 ml/cmH₂O) simulating varied compliance.

Nitrogen washout measurements

The experimental protocol for nitrogen washout measurements starts with keeping the valve2 closed. The valve1 is opened at 15 s and let the test lung filled until 50 s. Once the test lung was inflated, the valve1 was closed, the ventilator was started, and the valve2 was opened (50–55 s). The pressure, flow-rate, and oxygen concentrations were recorded from sampling ports in the ventilator circuit, which are close to the test lung inlet. The pressure and flow-rate data are presented only after nitrogen is completely washed out of the system. The additional dead space (or volume loss) introduced by the oxygen measurement system is ~30 ml during each ventilator cycle (3 s), which is uniform for both PCV and HFPV. Figure 2 shows complete recorded waveforms for pressure, flow rate and oxygen concentration during a nitrogen washout measurement.

Measurement systems

Airway pressure signal was measured using a 16-channel digital pressure sensor array, Scanivalve DSA 3217 (Scanivalve, Liberty Lake, WA, USA), which measures pressure in the range -70 cmH₂O to $+70$ cmH₂O with a full-scale accuracy of 0.1%. Pressure data was recorded using Scantel software at a frequency of 500 Hz. The flow rate was measured using a heated Fleisch type pneumotachograph (Hans Rudolph 3700, Shawnee, KS, USA). The flow meter has a range -160 to $+160$ l min⁻¹ with an accuracy of 2%. The analog signal from the flowmeter was amplified and digitally sampled at 500 Hz. Oxygen concentration was measured using a GA-200B CO₂ and O₂ gas analyzer system (Iworx systems, Dover, NH, USA). The flow rate signal and O₂ signal were recorded into a laptop computer with a data acquisition system (NI 6341, National Instruments, Austin, TX, USA) using LABVIEW 2017 software.

Experimental settings

Since the study focuses on the technological understanding of the two ventilation modalities, the ventilator settings are not limited to any clinical application. The low-frequency of HFPV and respiratory rate of PCV were maintained at the same value of 20 breaths min⁻¹. Moreover, the ratio of the inspiratory time to the expiratory time (I:E ratio) for the two ventilators was set at 1:1. The HFPV was operated at a frequency of 500 cycles min⁻¹, which gives a balance of CO₂ removal and oxygenation. The PCV was set at PIP and PEEP of 30 and 10 cmH₂O respectively. Due to lack of detailed knowledge of flow characteristics and ventilator dynamics, the optimal setting of HFPV often depends on the experience of the respiratory specialists who operate the device. The current study considers two extreme settings of HFPV regarding airway pressure levels and most of the clinical applications set pressures in between these two modes. In the first method (HFPV-High), the average inspiratory pressure, average expiratory pressure and MAP of HFPV were matched with PIP, PEEP, and MAP of PCV. In the second mode (HFPV-Low), the PIP and the dCPAP of HFPV were matched with the PIP and PEEP of PCV. At each ventilator setting, four sets of experiments were performed by varying the compliance ($C = 10$ and 20 ml/cmH₂O) and resistance ($R = 5$ and 20 cmH₂O/l/s) of the test lung. The chosen values of the compliance and resistance represent the physiological state common to clinical conditions, such as ARDS.

Statistical analysis

Each experiment was replicated five times and mean, and standard deviation data for experimental replicates are presented herein (mean $\pm$ SD). PCV was compared with both modes of HFPV across each lung conditions using unpaired t -test. All tests were two-sided, and a p value <0.05 was considered significant.

Definition of flow parameters

Different volumes in HFPV—Description of the HFPV related flow parameters is presented in figure 3. Since the flow-rate signal is bi-directional, a procedure similar to Lucangelo *et al* (2006a) has been followed to decompose instantaneous flow rate $\dot{V}(t)$ signal into its positive and negative parts (figure 3(a)).

The V_T is defined as the maximum volume retained in the lung during inspiration, which can be calculated using cumulative integration of the flow rate signal during inspiration (figure 3(b)).

$$V_T = \int_0^{T_I} \dot{V}(t) dt = \int_0^{T_I} [\dot{V}_{\text{positive}}(t) - \dot{V}_{\text{negative}}(t)] dt. \quad (1)$$

$\dot{V}_{\text{positive}}(t)$ and $\dot{V}_{\text{negative}}(t)$ denote absolute values of the flow rate going into the lung and the flow rate coming out of the lung, respectively. T_I and T_E represent the inspiratory and expiratory times, respectively. The total volume received by the lung during one cycle (V_{TOT}) can be calculated by integrating the positive part of the flow-rate signal.

$$V_{\text{TOT}} = \int_0^{T_I} \dot{V}_{\text{positive}}(t) dt + \int_{T_I}^{T_E} \dot{V}_{\text{positive}}(t) dt. \quad (2)$$

The difference between the V_{TOT} and the V_T is the total available volume that does not contribute to the lung excursion. The present authors termed it as the pulsatile flow volume (V_{PULSE}), which is defined as

$$\begin{aligned} V_{\text{PULSE}} &= V_{\text{TOT}} - V_T \\ &= \int_0^{T_I} \dot{V}_{\text{positive}}(t) dt + \int_{T_I}^{T_E} \dot{V}_{\text{positive}}(t) dt - \int_0^{T_I} [\dot{V}_{\text{positive}}(t) - \dot{V}_{\text{negative}}(t)] dt \\ &= \underbrace{\int_0^{T_I} \dot{V}_{\text{negative}}(t) dt}_{\text{Inspiration}} + \underbrace{\int_{T_I}^{T_E} \dot{V}_{\text{positive}}(t) dt}_{\text{Expiration}}. \end{aligned} \quad (3)$$

For PCV, there is no V_{TOT} and V_{PULSE} and the tidal volume V_T is the integration of instantaneous flow rate $\dot{V}(t)$ during inspiration.

Washout time (t_{wash})—Another variable in our experiments is the nitrogen washout time, or merely the washout time (t_{wash}). It is calculated from the recorded time-varying waveform

for the oxygen concentration (figure 2(c)). t_{wash} can be defined as the time required (in s) to reach end-tidal oxygen concentrations (ETO_2) of 18.9% (90% of the ambient O_2 concentration) during washout. The upper limit of the O_2 concentration, i.e. 18.9%, is selected to avoid the uncertainty in t_{wash} calculation due to the long time to reach 20.9% ETO_2 as a result of the asymptotic ETO_2 distribution.

$$t_{\text{wash}} = t_{18.9} - t_1. \quad (4)$$

Here, $t_{18.9}$ and t_1 represent times (s) corresponding to ETO_2 of 18.9% and 1%, respectively, during washout of nitrogen from the test lung.

Washout efficacy (E_{wash})—To compare the effectiveness of washout between different ventilator modalities, the washout efficacy (E_{wash}) is defined as the washout time per 100 ml tidal volume. E_{wash} characterizes the time required for washout in an idealized situation, where all the ventilation modalities deliver the equal tidal volume of 100 ml. Under similar lung conditions, smaller E_{wash} indicates a more effective washout.

$$E_{\text{wash}} = \frac{t_{\text{wash}} V_T}{100}. \quad (5)$$

Results

Table 1 presents a detailed comparison of various measured and derived quantities between PCV, HFPV-High, and HFPV-Low. Since HFPV-High matches the MAP with that of PCV, the PIP for HFPV-High reaches a higher value as compared to the PIP of PCV. The PIP for HFPV-High was recorded in the range of 48.5 ± 2.2 to 58.8 ± 2.0 cmH₂O. In case of HFPV-Low, the MAP is much smaller and within the range of 7.8 ± 2.1 to 10.8 ± 0.7 cmH₂O as compared to 18.3 ± 5.2 to 20.5 ± 0.9 cmH₂O for PCV.

HFPV-High delivers a higher V_T as compared to PCV for all the resistance and compliance conditions. The maximum V_T is 601.2 ± 201.1 ml for HFPV-High compared to 409.2 ± 3.9 ml ($p < 0.0001$) for PCV when R and C values are 5 cmH₂O/l/s and 20 ml/cmH₂O respectively. Similarly, HFPV-Low delivers consistently smaller volumes as compared to the PCV. At $R = 5$ cmH₂O/l/s and $C = 20$ ml/cmH₂O, V_T for HFPV-Low is $280.6.2 \pm 16.2$ ml. Similarly, at $R = 20$ cmH₂O/l/s and $C = 10$ ml/cmH₂O, PCV delivers 195.8 ± 15.2 ml in comparison to 102.4 ± 12.6 ml delivers by HFPV-Low.

Although V_T is strongly dependent on both the compliance and resistance, V_{TOT} does not significantly vary with compliance for both HFPV-High and HFPV-Low. At $R = 5$ cmH₂O/l/s, V_{TOT} reduces from 1394.3 ± 40.4 ml to 1358.1 ± 77.6 ml due to change in compliance, whereas, it changes from 1000.2 ± 36.7 ml to 996.0 ± 32.9 ml for HFPV-Low. Therefore, with a low compliant lung, more V_{PULSE} is available as compared to a highly

compliant lung under similar settings. Further, as can be seen from the table 1, increasing resistance reduces all the volume (V_T , V_{TOT} , and V_{PULSE}) for HFPV-High and HFPV-Low.

Under all lung conditions, HFPV-High delivers more rapid nitrogen washout as compared to PCV (25.4 ± 3.4 s– 70.8 ± 11.7 s for HFPV-High versus 40.0 ± 4.1 s– 205.2 ± 10.7 s PCV). In general, HFPV-Low takes the larger time to wash out nitrogen as compared to PCV, however, in a low compliant lung, even with a smaller V_T as compared to PCV, HFPV-Low provides a more rapid washout. The washout efficacy, E_{wash} , shows that the HFPV-High is more effective as compared to PCV and overall, HFPV provides more effective washout as compared to PCV especially for low compliant lungs ($R=5$, $C=10$, and $R=20$, $C=10$).

Comparison of waveforms for PCV and HFPV

Figure 4 compares the airway pressure, flow rate and volume waveforms for HFPV-High, HFPV-Low and PCV for one completed ventilation cycle at $R=5$ cmH₂O/l/s, $C=20$ ml/cmH₂O. It shows that both the PCV and HFPV-Low reaches an inspiratory plateau around 0.5–0.8 s. From the time it reaches the inspiratory plateau to the end-inspiratory time, the lung is exposed to the same tidal excursion. HFPV-High does not show any plateau and the breath stacking behavior could be observed until the end of inspiration. As observed the retained volume in the lung was smaller in HFPV-High as compared to PCV at half the inspiration (0.75 s), although at the end of the inspiration, the retained volume in HFPV-High is larger by about 1.5 times. It was observed that the inspiratory plateau reaches much early for both the PCV and HFPV-Low at a small compliance and HFPV-High also reaches an inspiratory plateau (figure not shown for brevity). At a high value of resistance (figure not shown for brevity), the inspiratory plateau reaches much early for HFPV-Low as compared to the PCV. HFPV-High again showed a breath stacking behavior albeit with a lower V_T compared to small resistance conditions. It was also found that the resistance has a stronger impact on the HFPV parameters as compared to PCV.

Effect of resistance and compliance

Figures 5 and 6 present the effects of compliance and resistance on V_T and t_{wash} . As observed in figure 5, compliance has a larger impact on PCV as compared to the HFPV-High and HFPV-Low. At a resistance of 5 cmH₂O/l/s, decreasing compliance from 20 to 10 ml/cmH₂O reduces the V_T by 51.2%, 43.4% and 39.0% for PCV, HFPV-High, and HFPV-Low respectively. Although compliance has a substantial effect on the V_T , it does not significantly change V_{TOT} (table 1). Therefore, at smaller compliances the V_{PULSE} increases (figure not shown for brevity). Resistance does not significantly change the V_T for PCV, however, increasing resistance from 5 to 20 cmH₂O/l/s reduces V_T by 25.5% and 46.8% for HFPV-High and HFPV-Low respectively at a compliance of 20 ml/cmH₂O. Unlike compliance, resistance affects V_{TOT} and reduces it by about 20% when resistance is increased from 5 to 20 cmH₂O/l/s (table 1).

Figure 6 shows that the washout time increases by 5 fold for PCV when compliance decreases from 20 to 10 ml/cmH₂O as compared to about one-fold increase in both HFPV-High and HFPV-Low. As observed from the figures 5 and 6, the effect of resistance on V_T is also reciprocated in the washout times recorded.

Nitrogen washout measurements

Figure 7 presents the time signals of the ETO_2 for PCV, HFPV-High, and HFPV-Low at various lung conditions. Compliance has a much stronger effect on the ETO_2 distribution for PCV as compared to HFPV. A gradual increase of ETO_2 can be observed in figure 7 with PCV for $R=5$, $C=10$ as compared to a steep rise for $R=5$, $C=20$. In contrast, resistance strongly affects HFPV. At $C=10$ and $R=20$, although the recorded V_T are 195.8 ± 15.2 and 102.4 ± 12.6 for PCV and HFPV-Low, respectively, their ETO_2 distributions match and give similar washout times.

Discussion

To our knowledge, this is the first study that assesses the gas exchange parameters in PCV and HFPV by employing nitrogen washout measurements in a test lung. Moreover, the study establishes a standard framework for defining various HFPV flow parameters for clinical applications.

The data suggest that tidal volumes delivered by HFPV-Low are smaller than the PCV; whereas, HFPV-High provides larger tidal volumes as compared to PCV, and a breath-stacking behavior can be observed. Since, the tidal volume is an indicator of the lung excursion, if HFPV is set to close to HFPV-Low settings, it may facilitate lung protective ventilation.

The *in vitro* study revisits conflicting results and interpretations from literature (Lucangelo *et al* 2006a, Allan 2010); through a more comparable and unified experimental design, data acquisition and analysis. The present study reports tidal volumes similar to the ones reported in Lucangelo *et al* (2004, 2006a) in their bench study. The data presented herein does not support the conclusions of Allan (2010), who stated that HFPV delivers injurious V_T under typical settings. The maximum V_T recorded in the current study was 601.2 ml, whereas, Lucangelo *et al* (2006a) and Allan (2010) reported maximum V_T of 465 ml and 3452 ml, respectively. Allan (2010) employed three settings of HFPV with MAP values of 10, 20 and 30 cmH₂O. In the current framework, a MAP of 10 cmH₂O is comparable to HFPV-Low and MAP of 20 cmH₂O corresponds to HFPV-High settings.

Under similar PIP, the low tidal volume delivered with HFPV is due to continuous high-frequency volume washout during inspiration. Continuous washout maintains a small retained volume, although the total volume exchanged (V_{TOT}) is much higher than the volumes delivered by the PCV. Keeping a low tidal volume is necessary for implementing protective ventilation strategies, and V_{PULSE} , which is defined as $V_{TOT} - V_T$, might help remove CO₂ and improve gas exchange through non-convective effects, such as diffusion, pendelluft, and Taylor dispersion. However, present authors observed that the washout rate is correlated with the tidal volume for both PCV and HFPV and did not notice any significant correlation between the washout time and the V_{PULSE} (figure not shown for brevity). However, in a poor compliant lung, we observed that the V_{PULSE} increases considerably and HFPV delivers very effective washout. Future animal studies and computer modeling are needed to understand the effects of V_{PULSE} on oxygenation and CO₂ removal.

HFPV-High provides higher PIPs as compared to the PCV. However, due to the smaller timescales associated with the percussion or minibursts, the pressure is expected to attenuate in actual lung geometry, which will manifest as reduced alveolar pressure. The pressure attenuation phenomenon has been reported in many studies on HFV (Rožánek *et al* 2012, Smallwood *et al* 2016). Under similar PIP, the MAPs recorded by HFPV is much lower as compared to that of PCV due to the shape of the pressure waveform. The low MAP with HFPV-Low may reduce the risk of barotrauma in critically ill patients. However, if a lower MAP (during HFPV-Low) results in de-recruitment and alveolar collapse, it could potentially impair gas exchange and, therefore, further clinical studies are needed.

Data suggests that the resistance affects HFPV more substantially than it affects PCV. This behavior is expected because the Phasitron adjusts the entrainment based upon physical indices of airway resistance. However, how well the orifice type resistance of the test lung represented the actual resistance due to airway contraction, or mucus in patients, is uncertain. Fluid flow with orifice plate is much more complex with the phenomena like flow separation and reattachments.

Nitrogen washout measurements indicate that HFPV-High provides faster washout compared to HFPV-Low and PCV, which is expected given HFPV-High is associated with larger tidal volumes. Surprisingly, HFPV-Low shows a quicker washout as compared to PCV in a low compliance state, with a much reduced tidal volume and MAP. The washout efficacy data shows that the HFPV provides more effective washout for same tidal volume, compared to PCV especially for lungs with poor compliance. These observations suggest a potential for lung protection and improved CO₂ removal using HFPV in critical lung diseases which produce a low compliance state. The results may also explain the clinical data of decreased time on ECMO for ARDS patients when paired with HFPV (Michaels *et al* 2015) since ARDS patients are characterized by poor compliance (Leaver and Evans 2007). Additional *in vivo* animal, and ultimately human data on gas exchange, lung histology (for evidence of VILI), and biomarkers (for evidence of lung biotrauma) is needed to confirm our hypothesis.

Study limitations

As in any *in vitro* study, a test lung can only moderately mimic the respiratory compliance and resistance as compared to a bedside patient. Further, being a passive simulator, the test lung does not emulate the interaction between a patient's breathing pattern and the ventilator. Also, gas washout findings in a sealed circuit (no cuff-leak), single-compartment test lung model will not translate directly to gas exchange in patients with heterogeneous lung injury with regional variation in time constants for alveolar emptying and recruitment.

Conclusion

Under clinical settings for HFPV and PCV, the tidal volume delivered with HFPV can be smaller or larger than the PCV depending on the settings. In a bulk flow model of a low compliant lung, HFPV provides faster nitrogen washout at similar PIPs with a smaller tidal volume and smaller MAP than PCV. Data suggest that the HFPV-Low settings may facilitate

lung protective ventilation and provide effective washout in lungs with poor compliance. Results using one compartment lung models may not be directly translated into clinical practice. However, this study can be used to develop guidelines for the efficient operation of HFPV technology and to design future clinical and animal studies. The newly defined term, pulsatile flow volume, might be an excellent index to be used for evaluating CO₂ removal and oxygenation in an actual lung due to non-convective effects. Future experimental studies using animal models and advanced computational fluid dynamics models that include complex and branched airways will enable rigorous verification and validation to confirm the hypothesis and elucidate new physics (Xing 2015, Dutta and Xing 2017, 2018).

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Figure 1. Schematic of the experimental setup for airway pressure, flow-rate and oxygen concentration measurement using HFPV. For the analyses with PCV, Phasitron and the HFPV are replaced with an LTV 950 unit. Valve1 and Valve2 denote nitrogen tank-flowmeter and ventilator-flowmeter valves respectively.

Figure 2.

Typical recorded waveforms during a washout measurement (HFPV-Low, $R = 5 \text{ cmH}_2\text{O/l/s}$, $C = 20 \text{ ml/cmH}_2\text{O}$): (a) pressure (cmH_2O), (b) flow rate (l min^{-1}), and (c) oxygen concentration (%).

Figure 3. Calculation of various volume (ml) terms in HFPV: (a) decomposition of the flow rate (l/min) waveform into its positive and negative parts during one cycle, and (b) numerical integration on the decomposed positive and negative flow rates during one ventilator cycle.

Figure 4.

Comparison of ventilation waveforms for PCV, HFPV-High and HFPV-Low for one complete ventilation cycle ($R = 5 \text{ cmH}_2\text{O/l/s}$, $C = 20 \text{ ml/cmH}_2\text{O}$): (a) pressure (cmH_2O), (b) flow rate (l min^{-1}), and (c) volume (ml).

Figure 5.

Effect of resistance and compliance on tidal volume (ml): (a) $R = 5$ cmH₂O/l/s and $C = 20$ ml/cmH₂O, (b) $R = 5$ cmH₂O/l/s and $C = 10$ ml/cmH₂O, (c) $R = 20$ cmH₂O/l/s and $C = 20$ ml/cmH₂O, and (d) $R = 20$ cmH₂O/l/s and $C = 10$ ml/cmH₂O.

Figure 6.

Effect of resistance and compliance on washout time (s): (a) $R = 5$ cmH₂O/l/s and $C = 20$ ml/cmH₂O, (b) $R = 5$ cmH₂O/l/s and $C = 10$ ml/cmH₂O, (c) $R = 20$ cmH₂O/l/s and $C = 20$ ml/cmH₂O, and (d) $R = 20$ cmH₂O/l/s and $C = 10$ ml/cmH₂O.

Figure 7.

Comparison of end tidal oxygen concentration distributions between PCV, HFPV-High and HFPV-Low at various lung conditions: (a) $R = 5$ cmH₂O/l/s and $C = 20$ ml/cmH₂O, (b) $R = 5$ cmH₂O/l/s and $C = 10$ ml/cmH₂O, (c) $R = 20$ cmH₂O/l/s and $C = 20$ ml/cmH₂O, and (d) $R = 20$ cmH₂O/l/s and $C = 10$ ml/cmH₂O.

Table 1

Various measured and derived parameters for PCV, HFPV-High, and HFPV-Low under all conditions. All the pressures (PIP, PEEP, and MAP) are in cmH₂O, the volumes (V_T , V_{TOT} , and V_{PULSE}) are in ml, t_{wash} and E_{wash} are in s.

	$R = 5$ and $C = 20$				$R = 5$ and $C = 10$				$R = 20$ and $C = 20$				$R = 20$ and $C = 10$			
	PCV	HFPV-High	HFPV-Low	PCV	HFPV-High	HFPV-Low	PCV	HFPV-High	HFPV-Low	PCV	HFPV-High	HFPV-Low	PCV	HFPV-High	HFPV-Low	HFPV-Low
PIP	30.9 ± 0.8	48.5 ± 2.2 ^a	29.1 ± 2.0	30.9 ± 0.5	49.9 ± 2.5 ^a	29.2 ± 2.0	31.3 ± 0.8	58.2 ± 2.3 ^a	32.7 ± 1.3	32.1 ± 0.9	58.8 ± 2.0 ^a	31.9 ± 1.5	32.1 ± 0.9	58.8 ± 2.0 ^a	31.9 ± 1.5	31.9 ± 1.5
PEEP	10.6 ± 0.5	13.5 ± 3.8	9.9 ± 1.4	10.5 ± 0.5	13.4 ± 4.2	10.1 ± 0.8	10.7 ± 0.8	21.1 ± 1.9 ^a	9.5 ± 1.1	10.6 ± 0.7	19.5 ± 1.3 ^a	10.4 ± 1.3	10.6 ± 0.7	19.5 ± 1.3 ^a	10.4 ± 1.3	10.4 ± 1.3
MAP	20.3 ± 0.5	20.2 ± 1.1	10.8 ± 0.7 ^a	20.3 ± 0.8	20.1 ± 1.2	11.7 ± 2.2 ^a	20.5 ± 0.8	20.9 ± 1.5	8.0 ± 2.1 ^a	20.5 ± 0.9	20.7 ± 1.4	7.8 ± 2.1 ^a	20.5 ± 0.9	20.7 ± 1.4	7.8 ± 2.1 ^a	7.8 ± 2.1 ^a
V_T	409.2 ± 3.9	601.2 ± 20.1 ^a	280.6 ± 16.2 ^a	199.9 ± 6.0	340.2 ± 14.2 ^a	171.2 ± 18.6 ^a	404.1 ± 5.7	447.6 ± 28.2 ^a	149.4 ± 15.4 ^a	195.8 ± 15.2	299.4 ± 18.5 ^a	102.4 ± 12.6 ^a	195.8 ± 15.2	299.4 ± 18.5 ^a	102.4 ± 12.6 ^a	102.4 ± 12.6 ^a
V_{TOT}	—	1394.3 ± 40.4	1000.2 ± 36.7	—	1358.1 ± 77.6	996.0 ± 32.9	—	1196.1 ± 55.0	754.1 ± 41.4	—	1203.2 ± 18.6	778.2 ± 28.6	—	1203.2 ± 18.6	778.2 ± 28.6	778.2 ± 28.6
V_{PULSE}	—	792.8	719.4	—	1017.9	824.8	—	748.4	604.6	—	903.6	675.6	—	903.6	675.6	675.6
t_{wash}	40.0 ± 4.1	25.4 ± 3.4 ^a	60.2 ± 5.7 ^a	205.2 ± 10.7	44.6 ± 8.2 ^a	120.0 ± 12.5 ^a	44.2 ± 1.5	33.2 ± 4.5 ^a	186.4 ± 12.7 ^a	194.1 ± 14.3	70.8 ± 11.7 ^a	211.8 ± 9.3 ^a	194.1 ± 14.3	70.8 ± 11.7 ^a	211.8 ± 9.3 ^a	211.8 ± 9.3 ^a
E_{wash}	163.7	152.7	168.9	410.2	151.7 ^a	205.4 ^a	178.6	148.6 ^a	278.5 ^a	380.0	212.0 ^a	216.9 ^a	380.0	212.0 ^a	216.9 ^a	216.9 ^a

^aSignificant differences ($p < 0.05$) in comparison to PCV.