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Theoretical Prediction of Lung Hyperinflation (LHI) Due to Asymmetric Pressure－Flow Characteristics of Human Airways During High Frequency Ventilation (HFV)

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The hypothesis of asymmetric resistance to explain the phenomenon of lung hyperinflation (LHI) during high frequency ventilation (HFV) was quantitatively studied. LHI was predicted by modeling the iso-volume pressure-flow (IVPF) data from 5 human subjects using the empirical Rohrer's equation. Non-steadiness during HFV was compensated by employing recently proposed volume-frequency diagram. Tidal volume and ventilation frequency were 100 ml and 20 Hz, respectively. Airflow pattern was a symmetric sinusoid. The prediction results of mean pressure drop across the airways were averaged for those 5 subjects, and compared with zero by one-sided student's t-test. A marginally significant ($P<0.1$) increase in mean pressure drop was observed during HFV at low lung volumes (below FRC), which could increase mean lung volume up to one liter. When the lung volume was above FRC, no significant LHI ($P>0.25$) was resulted. LHI seemed to be inversely related to the lung volume. These results recommend to clinically apply HFV only at lung volumes above FRC.

I. INTRODUCTION

Ventilation patients with a tidal volume smaller than the dead space at a frequency higher than normal called high frequency ventilation (HFV) can provide enough oxygen transport[1,2]. Small tidal volume would reduce alveolar pressure excursion, thus HFV might be applicable to patients with lung trauma. However, recent measurements showed that mean lung volume progressively increased during HFV application in both experimental animals[3] and humans[4]. An increase in mean lung volume reflecting that mean alveolar pressure has been increased could limit the clinical application of HFV, since pressure could be deleteriously high in some parts of the lungs. This phenomenon termed lung hyperinflation (LHI) may be caused by an

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asymmetry between inspiratory and expiratory resistances as hypothesized by simon et al.[5]. The present study modeled this possible resistance asymmetry to predict the degree of LHI during HFV. A theoretical prediction of LHI would help establish clinical guideline for safe HFV application.

Ⅱ. METHODS

(1) Iso-volume pressure-flow curve

At any lung volume level, the pressure drop from the alveoli to the mouth can be formulated by a quadratic equation of airflow known as Rohrer's equation,

$$P_{aw} = K_1 \dot{V} + K_2 \dot{V}^2 \qquad (1)$$

Where P_{aw} is the pressure drop across the airways, $\dot{V}$ is the air flow, and K_1 and K_2 are Rohrer's constants. Bouhuys and Johnson[6] experimentally measured pressure－flow data at various lung volume levels to estimate K_1 and K_2, both of which showed different values between inspiration and expiration. Their estimation results are shown in Table 1. This finding proves an inherent asymmetry in airway pressure－flow characteristics (or resistance defined as the ratio between pressure drop and airflow)between inspiration and expiration. Even for a symmetric airflow pattern, the pressure drop would be different between inspiration and expiration. When the pressure drop is averaged over a ventilation cycle, this asymmetry can result in a higher mean alveolar pressure than the mean pressure at the mouth during HFV. In such case, mean lung volume should increase even with the mean mouth pressure controlled at a constant level, leading to LHI. This mechanism is modeled below.

Table 1 Rohrer's constants estimated in 5 human subjects by Bouhuys and Johnsom[6]

Subject NO	Lung Volume (% VC)		K_{1e} ($cmH_2O/1/sec$)	K_{1i} ($cmH_2O/1/sec$)	K_{2e} ($cmH_2O/1^2/sec^2$)	K_{2i} ($cmH_2O/1^2/sec^2$)
1	high	84	0.77	0.94	0.13	0.13
2		87	0.66	1.11	0.15	0.31
3		85	0.93	0.93	0.12	0.36
4		78	1.20	0.93	0.07	0.10
5		77	1.12	1.10	0.44	0.30
1	medium	38	1.18	1.32	0.16	0.17
2		32	1.84	2.30	0.26	0.09
3		37	1.52	1.13	0.33	0.52
4		27	1.40	1.53	0.80	0.34
5		30	2.35	1.70	0.35	0.54
1	low	22	0.98	1.41	0.48	0.18
2		13	3.80	3.47	1.20	0.26
3		17	1.70	2.95	1.34	0.70
4		16	1.10	2.00	3.67	0.43
5		19	3.02	2.00	0.88	0.62

(2) LHI prediction for a quasi-steady flow pattern

Eq. (1) can be separated during inspiration and expiration as

$$(P_{aw})_i = K_{1i}\dot{V}_i + K_{2i}\dot{V}_i^2 \quad (2a)$$

$$(P_{aw})_e = K_{1e}\dot{V}_e + K_{2e}\dot{V}_e^2 \quad (2b)$$

where the subscripts, i and e, represent inspiration and expiration, respectively. The total mean pressure drop is calculated by taking the difference of the average values of Eqs. (2a and 2b) over a ventilation cycle.

$$\overline{p_{aw}} = \overline{(p_{aw})_e} - \overline{(p_{aw})_i} \quad (3)$$

When the airflow is a symmetric sinusoid, which is a usual airflow pattern during HFV,

$$\dot{V}_e = \dot{V}_i = A \sin 2\pi/Tt \quad (4)$$

where A is the peak flow and T is the ventilation period. Mean flows over a ventilation cycle are

$$\overline{\dot{V}_e} = \overline{\dot{V}_i} = A/T \int_0^{T/2} \sin 2\pi/T\, t\, dt = A/\pi \quad (5)$$

Similarly,

$$\overline{\dot{V}_e^2} = \overline{\dot{V}_i^2} = A^2/4 \quad (6)$$

Since the tidal volume is

$$V_T = \overline{\dot{V}_e}T = AT/\pi \quad (7)$$

the peak flow can be represented as

$$A = \pi f V_T \quad (8)$$

where f is the ventilation frequency (f=1/T). By combining Eqs.(2—8), the mean pressure drop from the alveoli to the mouth (p_{aw}) is obtained.

$$\overline{P_{aw}} = (K_{1e}-K_{1i})fV_T + \pi^2 (K_{2i}) (fV_T)^2/4 \quad (9)$$

A positive $\overline{P_{aw}}$ calculated by Eq.(9) implies that the mean alveolar pressure is raised above the mean mouth pressure during HFV. This would inerease the mean lung volume, leading to LHI. For a given increase in $\overline{P_{aw}}$, the degree of LHI may be different depending on the dynamic compliance of the patient. Thus, $\overline{P_{aw}}$ is a better predictor of LHI than the mean lung volume itself (explained later). Note that Eq.(9) is valid only for a low frequency ventilation (quasi-steady flow), since the iso-volume pressure-flow data are obtained with constant flow tates. As ventilation frequency becomes high enough, non-steadiness is introduced, which significantly modifies the pressure-flow characteristics. Therefore, during HFV, Eq.(9) has to be compensated for the non-steadiness. This procedure is presented below.

(3) High frequency compensation

From the Rohrer's equation, airway resistance is a linear function of airflow.

$$R = K_1 + K_2 \dot{V} \quad (10)$$

where R is the airway resistance. By applying this empirical relationship to HFV,

$$R^H = K_1^H + K_2^H \dot{V} \quad (11)$$

where the superscript, H, represents high frequency. Recent measurements on R^H in human airway model by Isabey et al.[7] showed that R^H was increased at zero flow point and did not change at peak flow point as follows:

$$R^H = rR, \dot{V} = 0 \quad (12a)$$

$$R^H = R, \dot{V} = \Pi f V_T \quad (12b)$$

where r is a constant. From Eqs.(10－12) the Rohrer's constants for HFV is obtained as

$$K_1^H = r\,K_1 \qquad (13a)$$

$$K_2^H = K_2 - (r-1)K_1/(\pi\, f\, V_T) \qquad (13b)$$

By substituting Eq.(13) into Rq.(9) gives

$$(\overline{P_{aw}})^H = (\overline{P_{aw}})^L + (1-\pi/4)\,(r-1) f V_T (K_{1e} - K_{1i}) \qquad (14)$$

where the superscript, L, represents low frequency.

(4) LHI prediction during HFV

LHI was predicted by Eqs.(9) and (14) during HFV. The tidal volume (V_T)and the ventilation frequency (f) were chosen to be 100ml and 20Hz, respectively. At this HFV mode, r would be as long as 6 according to V_T－f diagram proposed by Isabey et al.[7]. To obtain the largest LHI, r=6 was used. The Rohrer's constants data(Table 1) at various lung volumes with the above V_T, f, and r values decided the degree of LHI ($(\overline{P_{aw}})^H$)at those lung volume levels.

Ⅲ. RESULTS

In Bouhuys and Johnson's experiments[6], the Rohrer's constants were estimated at 3 different lung volume levels in each of 5 subjects as shown in Table 1. These 3 lung volumes were selected to provide estimation results for high, medium, and low lung volumes. $(\overline{P_{aw}})^H$ was calculated for each estimation set (K_1 and K_2) shown in Table 1 to provide the degree of LHI. Since the lung volume was divided into 3 ranges, $(\overline{P_{aw}})^H$ values obtained in 5 subjects within the same (high, medium, low)lung volume range were averaged. Mean $(\overline{P_{aw}})^H$ values were compared with no mean pressure drop ($(\overline{P_{aw}})^H=0$) by one-sided student's t-test. The test results are shown in Table 2. At both high and medium lung volumes, mean $(\overline{P_{aw}})^H$ was not significantly different from zero ($P>0.25$). Mean $(\overline{P_{aw}})^H$ showed a lot higher value close to 10 cmH_2O at low lung volume, although it was marginally significant ($P<0.1$).

Table 2 Predicted LHI at high, medium and low lung volumes. Each mean represents an average value of 5 subjects, and was compared with zero by one-sided student's t-test

Lung Volume Range (% VC)	$(P_{aw})^H$ mean+SE (cmH_2O)	P－value
high (77－87)	−0.15+1.07	P>0.25
medium (27－38)	0.73+0.81	P>0.25
low (13－22)	9.59+4.99	P<0.1

Ⅳ. DISCUSSION

During HFV application, Simon et al.[8] suggested that the mean lung volume could increase when less air was expired due to a higher expiratory resistance, resulting in air trapped in the lungs. This hypothesis of asymmetric airway resistantce was generalized in the present study by introducing iso-volume pressure-flow (IVPF) curve to estimate the degree of LHI. Measurements of IVPF data provided the constant values in the empirical Rohrer's equation by least squares estimation [6]. The present study simply took those constants data, and calculated mean pressure drop across the airways for a symmetric sinusoidal flow. Since no other assumption was necessary to make LHI prediction, the present study was, in essence, considering a particular case of Rohrer's equation, which has been widely accepted, empirically. Estimation of Rohrer's constants is

usually performed on the pressure data at constant flows. When LHI is calculated based on these estimation results, quasi-steadiness should be assumed. Trying to evaluate a formula to predict LHI under HFV environments where the airflow is non-steady, the author introduced Isabey et al.'s[7] experimental results on airway resistance change due to HFV in a human airway model. During HFV, different degrees of unsteadiness exist over the same cycle, depending on local acceleration. Near zero flow point (or the flow reversal point), maximum acceleration is introduced, and resistance is larger than that measured under steady flow condition. On the contrary, resistance would not be different at peak flows because of minimum acceleration. This discrepancy was verified by Isabey et al.[7] over a wide range of frequency up to 40 Hz. As a result, the pressure-flow curve should be linearized during HFV. This tendency of linearization has ben predicted[8] and measured[9]. Thus, a second-order polynomial (or Rohrer's equation) should be adequate to describe the pressure-flow curve during HFV, although with different K_1 and K_2 values compared with the steady flow condition[7]. These reasonings were employed to compensate LHI prediction for high frequency note Eqs.(10—12) Therefore, the author believes the present modeling procedure valid.

As can be seen in Eq.(14), the degree of LHI was presented in terms of the increase in mean airway pressure drop (or alveolar pressure) rather than that in mean lung volume. One might say that the mean lung volume should be used for LHI prediction. This speculation is argued for the following reasons. First, the individual difference in lungs and thorax compliance makes it hard to standardize LHI when volume is used. Secondly, the elastic properties do not change during HFV compared with conventional mechanical ventilation as experimentally shown by Weinman dt al.[10], implying that the source of LHI resides the alveolar walls or thorax. Thus, mean airway pressure drop across the airways is a better predictor of LHI.

From Table 2, it is clear that a significant LHI is predicted only at low lung volumes (approximately at 17% VC). Although mean LHI ($(\overline{P_{aw}})^H$) was only marginally significant($P<0.1$) probably due to a large individual variance, the mean values of approximately 10 cmH_2O cna force the mean lung volume to increase by 1 liter, assuming a normal lungs—thorax compliance of $0.1/cmH_2O$, which can create a serious barotrauma on alveolar walls especially in pediatric patients. On the other hand, only a small mean pressure drop is predicted when lung volume is above FRC (above 30%VC). At the high lung volume level, a negative mean pressure drop was calculated, implying that mean lung volume even decreased to a small degree during HFV. Although these changes were not statistically significant ($P>0.25$), a conclusion might be drawn that there exists a significant asymmentric (or nonlinear) behaviour of airways in terms of IVPF curve, which forces lung volume to increase during HFV in a manner varying inversely with results were plotted in Fig. 1. Except in one subject, LHI monotonically decreased with lung volume surrpporting the above observation.

With low lung volume, not only the asymmetry in IVPF curve becomes larger but also the small airways are more potential to collapse, since the airway diameter varies with lung volume. When this happens, local expiratory flow limitation could during HFV if the peak oscillat-

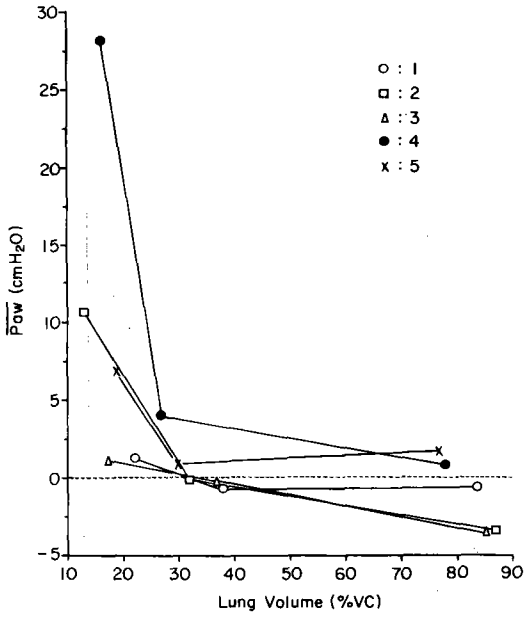

Fig. 1 Individual prediction results of $\overline{P_{aw}}$ in 5 human subjects plotted against lung volume.

ory flow gets close to the limited flow, resulting in a progressive accumulation of air in those parts of the lungs. In this case, local alveolar pressure could increase excessively high with only a small increase in lung volume, which can easily lead to a barotrauma. Therefore, HFV application should be performed with most alveoli open.

V. CONCLUSION

Based on previously measured iso-volume pressure-flow data, the degree of LHI was predicted for a symmetric sinusoidal flow. It was found that only a small LHI was calculated when the lung volume was above FRC, At the lung volume lower than FRC, a significant LHI was predicted. Therefore, it is recommended that lung volume should be kept above FRC during a clinical application of HFV to prevent a barotrauma due to LHI.

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