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Increase In Mean Alveolar Pressure Due To Asymmetric Airway Geometry During High Frequency Ventilation

=**Abstract**=

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During high frequency ventilation (HFV), mean alveolar pressure has been measured to increase with mean airway opening pressure controlled at a constant level in both humans and experimental animals. Since this phenomenon could potentiate barotrauma limiting advantages of HFV, the present study theoretically predicted the difference between mean alveolar and airway opening pressures (MP_{alv}). In a Weibel's trumpet airway model, approximated formula for MP_{alv} was derived based on momentum conservation assuming a uniform velocity profile. The prediction, equation was a function of gas density(ρ), mean flow rate(Q), and diameter of the airway opening where the pressure measurement was made(D_0): $MP_{alv}=4\rho(Q/D_0^2)^2$.

This was a result of the difference in cross-sectional area between the alveoli and the airway opening. A simple aireway model experiment was performed and the results well fitted to the prediction, which demonstrated the validity of the present analysis. Previously reported MP_{alv} data from anesthetized dogs in supine position were comparable to the predicted values, indicating that the observed dissociation between mean alveolar and airway opening pressures during HFV can be explained by this innate geometric (or cross-sectional area) asymmetry of the airways. In lateral position, however, the prediction substantially underestimated the measurements suggesting involvement of other important physiological mechanisms.

Key Words : Lung hyperinflation, High frequency ventilation, and Airway asymmetry.

1. INTRODUCTION

High frequency ventilation(HFV) as a mode of artificial respriation offers the promise of lower barotrauma[1] as well as other clinical advantages [2-5]. Mean lung volume has been observed to increase during HFV in both patients[6,7] and experimental animals[8,9]. One might expect that mean alveolar pressure could be underestimated by the mean pressure at airway opening, resulting in a concommitant rise in lung volume, which has been experimentally demonstrated in dogs[10]. This could limit clinical advantages of HFV, since mean pressure could be deleteriously high in some parts of the lung despite a small pressure swing even when mean pressure at airway opening is at a safe controlled level.

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Cha et al.[11] observed this phenomenon in excised dog lungs implying a purely mechanical characteristics of airways, since all neural and humoral pathways were not operating. They introduced an asymmetry in lumped airway parameters (resistance and gas inertance) between inspiration and expiration for an explanation. However, they neither reached an accurate quantitative estimation nor proposed any clear sources of this asymmetry. Dichotomous or trichotomous branching results in a much larger cross-sectional area near alveoli than at airway opening. The present study analyzed, based on momentum conservation, how this innate asymmetric structure could lead to an increaed mean alveolar pressure during HFV. Mathematical prediction was made to compare with an airway model experiment and with the previously reported data from animal experiments.

2. MATHEMATICAL FORMULATION

Airways can be considered as a solid tube, the cross-sectional area of which increases with axial distance from the entrance, so called Weibel's trumpet model[12]. Assuming one-dimensional fluid velocity parallel to the axis and having a uniform profile on a given cross-sectional plane,

$$u(x,t) = \frac{\dot{V}(x,t)}{A_x} \tag{1}$$

where u(x, t) and $\dot{V}(x,t)$ are velocity, and respectively, flow rate at distance, x, and time, t, and A_x represents cross-sectional area of the corresponding plane. Since flow rate must not change with distance (incompressible fluid), u(x, t) is rewritten as

$$u(x, t) = G_x \cdot \dot{V}(t) \tag{2}$$

where G_x is the inverse of A_x. Momentum conservation is achieved by applying one-dimensional Navier-Stokes equation on Equation (2) as

$$\frac{\partial u}{\partial t} + u\frac{\partial u}{\partial x} = -\frac{1}{\rho}\frac{\partial p}{\partial x} + \frac{4\mu}{3\rho}\frac{\partial^2 u}{\partial x^2} \tag{3}$$

where P is the static pressure at distance, x, and time, t, and ρ and μ are density and dynamic viscosity of the fluid, respectively. Inserting Equation (2) into (3) gives

$$-\frac{1}{\rho}\frac{\partial p}{\partial x} = Gx\frac{dGx}{dx}\dot{V}^2(t) + Gx\frac{d\dot{V}}{dt} - \frac{4\mu}{3\rho}\frac{d^2Gx}{dx^2}\dot{V}(t) \tag{4}$$

To obtain the pressure difference between alveoli (x = L) and airway opening (x = O), the left side of Equation (4) is first intergrated over x = O~L.

$$\begin{aligned}\int_0^L \left(-\frac{1}{\rho}\frac{\partial p}{\partial x}\right)dx &= -\frac{1}{\rho}\int_0^L \partial p \\ &= -\frac{P(L, t)-P(O, t)}{\rho} \\ &= -\frac{p_{alv}(t)}{\rho}\end{aligned} \tag{5}$$

Note in Equation (5) that $P_{alv}(t)$ represents the increase in alveolar pressure at time, t, relative to the airway opening. The right side of Equation (4) is also integrated, and by combining with Equation (5),

$$P_{alv}(t) = \rho(G_0^2 - GL^2)\frac{\dot{V}^2(t)}{2} - \rho(I_1-I_2) \tag{6}$$

where

$$I_1 = \frac{d\dot{V}}{dt}\int_0^L Gx\,dx \tag{7}$$

and

$$I_2 = \frac{4\mu}{3\rho}\dot{V}(t)\int_0^L \frac{d^2Gx}{dx^2}\,dx \tag{8}$$

For a periodic $\dot{V}(t)$ as in HFV, the time average of $P_{alv}(t)$ is calculated by integrating over a period, T, than dividing it by T. When $\dot{V}(t)$ is an odd function, time averages of both I_1 and I_2 are reduced to zero since both $d\dot{V}/dt$ and $\dot{V}$ are also odd functions of time. Thus, the mean alveolar pressure increase (MP_{alv}) becomes

$$MP_{alv} = \frac{1}{T}\int_0^T P_{alv}\,dt \tag{9}$$

$$= \frac{\rho}{2}\left(\frac{1}{A_0^2} - \frac{1}{A_L^2}\right)E(\dot{V}^2) \tag{10}$$

where

$$E(\dot{V}^2) = \frac{1}{T}\int_0^T \dot{V}^2(t)\,dt \tag{11}$$

since $G_0 = 1/A_0$ and $G_L = 1/A_L$ as previously defined. Note in Equation (10) that MP_{alv} is resulted from the cross-sectional area differecnce between the alveoli and the airway opening in conjunction withe the time average of the squared flow shape. Since A is much larger than A_0 in Weibel's model,

Equation (10) can be approximated to

$$MP_{alv} \approx \frac{\rho}{2A_0^2} E(\dot{V})^2 \quad (12)$$

When $\dot{V}(t)$ is a pure sinusoid,

$$\dot{V}(t) = \pi f V_T \sin 2\pi ft \quad (13)$$

where f and V_T are ventilation frequency and stroke volume, respectively. From Equations (11-13),

$$MP_{alv} = 4\rho \left[\frac{Q}{D_0^2} \right]^2 \quad (14)$$

where Q and D_0 are mean flow rate ($Q = fV_T$) during HFV and diameter of the airway opening, respectively. Equation (14) provides a prediction formula of the mean alveolar pressure increase during a symmetric sinusoidal HFV characterized by mean flow rate, Q, and density, ρ, of the gas used.

3. AIRWAY MODEL EXPERIMENT

A simple experiment was performed to test the validity of the above theoretical prediction using an airway model. The model used was a hollow Zavala lung model (Meditech, Watertown, MA). It was made of silicone rubber molded around a solid airway not a real cast. In spite of general flexibillity, it had a negligible compliance. The same model has been previously used to study steady and unsteady pressure-flow relationships in central airways[13]. The model was enclosed by a balloon with a compliance of 0.2 $1/cmH_2O$ and placed inside a sealed box. HFV was generated using a rubber bellows driven by a linear motor, power amplifier and sinusoidal generator. The experimental set-up is shown in Fig. 1. Stroke volume was measured using a pressure transducer (Valydine, MP45,±5cmH_2O) connected to the box with a tygon tubing (5 mmID). The tracheal cannula was extended out of the box with a silastic tubing and connected to the bellows. Tracheal pressure was measured through a side tap located near the proximal end of the trachea. The inner diameter where tracheal pressure was meaured was D_0 = 1.4cm. Mean flow rate of HFV was adjusted to be 700-1100 m l /sec with a 100 ml/sec increment by varying tidal volume with the frequency set at 20Hz. Another side tap was connected to a

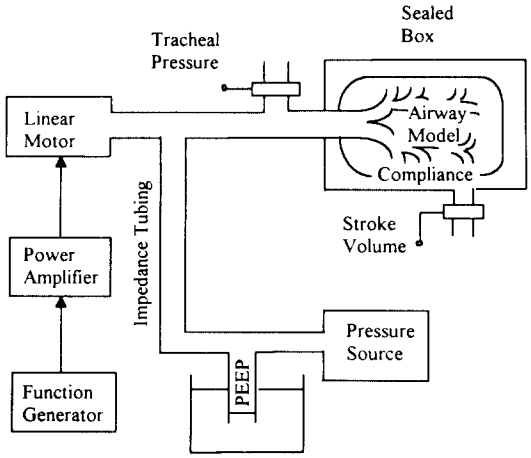

Fig. 1 The experimental set-up of the present airway model experiment. See text for detailed description

glass cylinder (4cm ID, 20cm long), which was surrounded by a column of water, and through which compressed air was flowed. This combination of a high-pressure air tank and a water column operated as a hydraulic mean pressure controller. During HFV application, mean tracheal pressure was maintained constant (3 - 5 cmH_2O). Static tracheal pressure was measured following occlusion in approximately one-minute HFV application during each run. The change in mean tracheal pressure after occlusion represents the degree of dissociation between alveolar and tracheal pressures due to HFV. Occlusion pressure was measured at a few random points in the oscillation cycle and the results averaged for each run to minimize phasic influences. The same technique has been successfully employed in dogs previously[10].

For a given mean flow rate(Q), the occulsion pressure mesurements were highly reproducible with a negligible variance, and the mean value was taken as a representative increase in mean alveolar pressure (MP_{alv}) in repeated runs. These values were compared with the prediction made by Equation (14). Since Equation (14) can be characterized as a linear relationship between MP_{alv} and $(Q/D_0^2)^2$

intersecting the origin with a unique slope, 4ρ, for a given gas (air), linear regression analysis with zero intercept was performed on the measured data with $(Q/D_0^2)^2$ as the independent variable. The estimated slope, 4.47×10^{-6}, was not significantly different ($P>1.0$) from the predicted value, 4.61×10^{-6}, with a significant correlation coefficient of 0.985($P<0.005$), which validated the present analysis. This comparision is presented in Fig. 2.

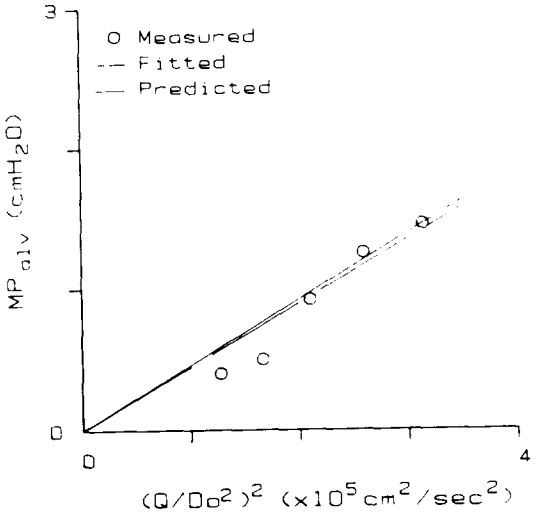

Fig. 2 MP_{alv} measurements made from the airway model experiment. Open circles represent the measured data with the predicted line drawn. The broken line is the results of fitting the measurement data points by linear regression analysis with no constant

4. COMPARISON WITH IN-VIVO DATA

Simon et al.[10] measured differences between mean airway and alveolar pressures during HFV in anesthetized dogs varying mean airway pressure and body posture. They employed the occlusion technique for pressure measurements as in the present study. Although mean flow rate ranged 750-2250 ml/sec, which was almost twice wider, a larger diameter at the airway opening (D_0 = 2cm) resulted in a $(Q/D_0^2)^2$ range comparable to our model experiment. MP_{alv} values at a given mean flow rate were averaged over all animals in supine position regardless of mean airway opening pressure, since the present analysis did not take into account any effects of the difference in absolute mean airway opening pressure level. This would also enable a general comparison with inter-individual variance minimized. The results are presented in Fig. 3. When the slope characterizing the relationship between MP_{alv} and $(Q/D_0^2)^2$ was estimated by linear regression, it was not significantly different from the predicted value ($P>0.25$) with a correlation coefficient of 0.894($P<0.05$). For a closer comparison, averaged MP_{alv} at each Q was statistically compared with zero and also with the predicted value by a student's t-test. At all Q values, MP_{alv}'s were significantly larger than zero, verifying statistically meaningful measurements. On the other hand, comparision of each MP_{alv} with the corresponding predicted value showed no significant dif-

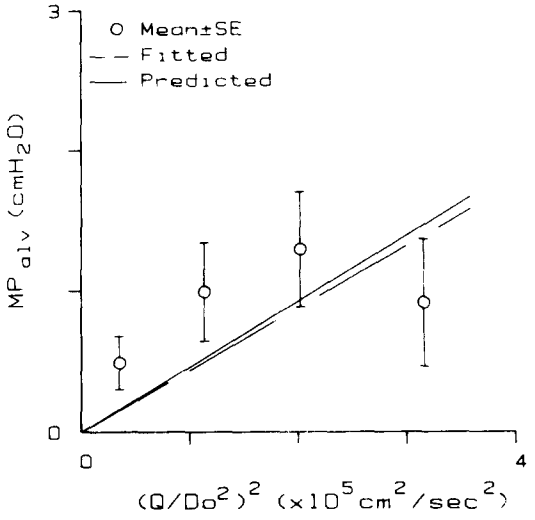

Fig. 3 Comparison of MP_{alv} between the data from anesthetized dogs in suine position(Simon et al., 1984) and the predicted line. Open circles and bars represent the mean±SE of the experimental data. The broken line is the results of fitting the supine data points by linear regression analysis with no constant

ference, demonstrating a quantitatively appropriate prediction. These results are summarized in Table 1.

Table 1 Comparison of measured MP_{alv} with zero and predicted values. P values are summarized for comparisons with both zero and predicted values using student's t-test at different flow rates(Q). MP_{alv} data are presented in mean±SE with the number of data points of 16 at all Q values. Note that the measured MP_{alv}'s are significantly larger than zero while no significant difference is found when compared with the predicted values

Q(ml/sec)	MP_{alv} measured (cmH_2O)	Comparison with zero	Comparison with predicted value
750	0.49±0.19	P<0.01	P>0.2
1350	0.99±0.36	P<0.01	P>0.2
1800	0.29±0.44	P<0.005	P>0.2
2250	0.91±0.46	P<0.05	P>0.2

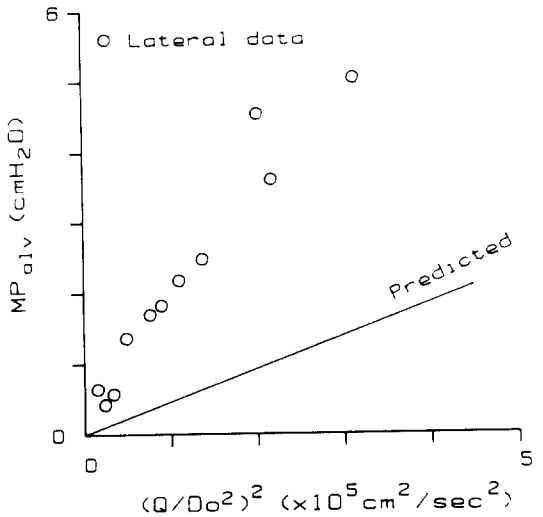

Fig. 4 Comparison of MP_{alv} between the data from anesthetized dogs in lateral position(Simon et al., 1984) and the predicted line. Open circles represent the experimental data in one dog. Note the substantial deviation from the predicted line. See text for detailed discussion

Effects of different body posture on MP_{alv} were also examined by Simon et al.[10]. In general, mean alveolar pressure was more dissociated in lateral position than supine position. Since the present analysis did not include this effect, it is obvious that the present prediction would not fit the measurement. Such an example is shown in Fig 4. In this particular animal, who showed the biggest dissociation, measured MP_{alv} values were 3 to 4 times of the predicted values. This is discussed later.

5. DISCUSSION

The present theoretical analysis is based on two basic assumptions. One is that airways were considered a single-unit tapered solid tube. This well-known trumpet model of Weible[12] is often used to evaluate an overall mechanical behaviour of complicated airway structure. Since this model provides a well defined cross-sectional area at each airway generation, it would be appropriate for the present work in which major focus was on the difference on cross-sectional area between two arbitrary locations of the airway. The other assumpution was that the fluid velocity was one-dimensional parallel to the axis with a uniform profile at any airway location at a given time. With a large enough cross-sectional area, a significant radial velocity component may exist.

However, as complex branching proceeds, the diameter of each airway becomes smaller in spite of the large total cross-sectional area of that particular generation, thus radial velocity component may not be significant. A uniform velocity profile also simplified the analysis to a great degree. Under an oscillatory flow condition where unsteadiness exists [14], it is extremely difficult to obtain a well-defined analytical velocity profile. It may very not only through a particular diameter taken on the same cross-sectional plane but also through the distance from the airway opening. In such case, estimation of any global variable such as mean pressure, an integrated result of local velocity or ener-

gy, is almost impossible. When velocity profile was measured in a larynx and central airway model, it generally had a shape close to a flat profile[15] supporting a uniform velocity profile. Based on the above discussion, we consider our assumptions reasonable.

The validity of our analysis was further explored by performing a simple experiment on an airway model. Since this model was manufactured on a human airway cast, it could reflect a branching structure up to 5-th generation identical to the real human airways. Minimal compliance of the model guaraunteed the solidity assumed in the analysis. Therefore, measurements on this model should verify the assumputions described above. The results, as shown in Fig. 2, well fitted to a predicted curve, which clearly demonstrated that the present analysis was capable of estimating an accurate MP_{alv}.

According to Equation (14), MP_{alv} is expected to vary quadratically with mean flow rate (Q) during HFV. This property has been previously reported in both patients [7] and experimental animals [10]. Data from Simon et al.'s[10] well-conditioned experiment on anesthetized dogs in supine position fitted reasonably well with the prediction curve as shown in Fig. 3. In this comparision, we took an average of MP_{alv} measurements regardless of the mean pressure level controlled at the airway opening, since the present analysis did not take this effect into account. Although there existed a large variance depending on the mean pressure level at the airway opening even whithin a same subject, the averaged MP_{alv} values were comparable with the prediction.

Statistical test also did not show any significant deviation from the predicted values(Table 1). Individual difference was also ignored for a general comparison, since there was no substantial inter-individual variance. Although not presented here in detail, one particular animal(#4)'s data fell on the predicted curve almost perfectly. Therefore, it is clear that our analysis can explain their experimental observation made in supine dogs.

In lateral position, however, they observed a generally larger MP_{alv}. Since effects of different body posture were not included, it is obvious that our prediction should underestimate the measurement. This is shown in Fig. 4. As expected, a large difference was found in that the measurement reached 3-4 times of the prediction. This result suggests that other important mechanisms were involved. The present analysis is simply based on a characteristic of airway geometry, i.e., asymmetry in cross-sectional area between the inlet(airway opening) and the outlet(alveoli), thus the prediction results reflect a purely mechanical behaviour of airways. In addition to this mechanical characteristic. other physiologic mechanisms may also cause MP_{alv} to rise during HFV. One possibility is discussed below.

Increase in mean lung volume during HFV, termed lung hyperinflation(LHI), has been suggested to be mediated by expiratory flow limitation[16]. With the expiratory flow limited, respiratory gas can be accumulated in those parts of the lung where oscillatory flow is limited during expiratory phase, resulting in an increase in mean lung volume, and consequently, alveolar pressure. This mechanism would become more significant under a condition which airways are potent to collapse. When the subject is in lateral position, weight of one lung on top would press the other on bottom, the airways of which might be more easily collapsed. In this case, expiratory flow limitation could play a major role for LHI in addition to the present asymmetric geometry. However, the fact that supine data well fitted to the prediction implies that subjects under a usual condition does not require any other physiological mechanism, instead purely mechanical characteristics of airway can explain the observed increase in alveolar pressure during HFV.

Simon et al.[10] paid a special attention, in their experimental design, to the airway pressure measurement to minimize the contribution of kinetic energy component. They performed a simple calculation based on mean velocity of sinusoidal flow at the measuring site to demonstrate a negligible dy-

namic pressure component when the lateral pressure was measured with a large enough diameter(2.0cm). However, using mean velocity of a sinusoidal flow may invalidate their estimation. Our analysis is in essence equivalent to a direct mathematical evaluation of this dynamic pressure effect while keeping the time varying property of velocity, which should provide a more accurate estimate. Since the supine data were explainable in this way, we attribute their results to this technical limitation (or the asymmetric nature of airway structure in terms of cross-sectional area), but not to any other physiological mechanisms.

In lateral position, however, it is quite possible that an important physiological mechanism such as expiratory flow limitation was involved as previously discussed.

Equation (14) predicts linear dependence of MP_{alv} on respiratory gas density. Robertson et al.[8] reported a larger increase in functional residual capacity with a denser gas. Simultaneous measurements of small airway pressure were also made by a "distal" catheter. This ranged 0-2, 3-5, and 4-7 cmH_2O for gases of 20% O_2 balanced with He, N_2, and 6.1 cmH_2O, respectively. Note that these values are well within the measurement range for each gas. Thus, the observed gas density dependency was also well predicted by the present analysis.

It is common to apply HFV with the mean pressure at airway opening controlled to a desired level. Due to a limited diameter where the pressure is controlled and a consequently different contribution of kinetic energy from that in the alveoli having a much larger cross-sectional area, alveolar pressure may be dissociated with airway opening pressure. This is fundamental in any mechanical structure having a similar asymmetry. Oscillatory flow during HFV makes it difficult to accurately estimate this dissociation. The present work enlightens a way of accurate estimation based on a few reasonable assumptions. A much larger cross-sectional area near alveoli compared to that of airway opening enabled to derive an approximated formula [Equation (14)] in which all parameters (ρ,Q,D_0) were easy to evaluate at the airway opening. As far as the behaviour of an airway during HFV does not show a significantly different characteristic from the assumputions made here, Equation (14) should accurately predict an elevated mean alveolar pressure, since the present analysis is simply based on a physical principle, i.e., momentum conservation. This is particularly important when a narrow extension has to be connected with the airway opening. According to Equation (14), a 10% decrease in diameter would increase MP_{alv} by approximately 50%. Therefore, a special care must be taken where HFV is monitored and/or controlled. A clinical application can be made by lowering the controlled mean pressure at airway opening to a degree estimated by Equation (14) to maintain mean alveolar pressure at a desired level.

6. CONCLUSION

We estimated the observed underestimation of mean alveolar pressure by the mean pressure at airway opening during HFV. A well-known Weibel's trumpet airway model was employed to derive an approximated prediction formula based on momentum conservation. This was a result of an inherent asymmetry in cross-sectional area between airway opening and the alveoli. The prediction results were comparable with data from both human airway model and animal experiments. Validity and limitations of the present analysis were discussed.

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