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A Mathematical Model of Mean Airway Pressure Based Upon Positive End-Expiratory Pressure, *I*:*E* Ratio, and Plateau Pressure

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A mathematical model of mean airway pressure (P_{mean}) has been derived which is based upon positive end-expiratory pressure (P_{peep}) and I:E ratio (I:E). Plateau pressure (P_{PL}) is also utilized:

$$P_{mean}/P_{PL} = [(I:E) + \mathbf{R}]/[(I:E) + 1]$$

where **R** is defined as: $\mathbf{R} = P_{peep}/P_{PL}$. Based upon this model, it can be shown that (1) increasing I:E ratio will increase P_{mean}/P_{PL} in a self-limiting logarithmic manner; (2) P_{mean}/P_{PL} is a linear function with respect to **R**; (3) increases in R are associated with a diminished effect of I:E ratio on P_{mean}/P_{PL}; (4) similarly, increases in I:E ratio are associated with a diminished effect of R on P_{mean}/P_{PL}; (5) overall, changes in P_{mean}/P_{PL} will consistently be effected more by changes in **R** than by changes in I:E ratio. This model illustrates the interrelationship between plateau pressure, PEEP, and I:E ratio as they affect mean airway pressure. Furthermore, it appears to be useful in explaining the clinically reported discrepancies regarding the efficacy of inverse ratio ventilation (IRV), especially when simultaneously applied with varying levels of PEEP. In addition, for a given plateau pressure, it is also possible to mathematically optimize PEEP and I:E ratio combinations so as to avoid excessive amounts of either.

Key words: mean airway pressure; i:e ratio; positive end-expiratory pressure; plateau pressure.

INTRODUCTION

Mean airway pressure, P_{mean}, has been used to clinically assess mean alveolar pressure (Boros, 1979). Increases in P_{mean} are generally associated with an increase in the amount of alveolar recruitment (Huang *et al.*, 2001). The benefits of using a relatively high inspiratory time, and consequently a larger mean airway pressure, may be useful for those patients with acute respiratory distress syndrome (ARDS), diffusion abnormalities, or other pulmonary diseases (Yanos *et al.*, 1998). Clinically, this benefit can frequently be life saving. Immediate increases, in the arterial partial pressure of oxygen, can be achieved with maneuvers such as this which increase alveolar recruitment. However, excessive inspiratory times may lead to "air trapping" in which there is an inadequate amount of expiratory time. This can result in an excessive mean and/or peak airway pressure as well as hypoventilation (Mercat *et al.*, 2001). It should be noted that inspiratory time and expiratory time are usually described as a dimensionless ratio that is clinically referred to as I:E ratio: $I{:}E = \frac{\text{inspiratory time}}{\text{expiratory time}}$.

Furthermore, most anesthesia and intensive care unit (ICU) ventilators have variable I:E settings that may be used to an advantage for management of patients with the above-mentioned adverse pulmonary conditions.

Inverse ratio ventilation (IRV), in which inspiratory time exceeds expiratory time, has been investigated as a potentially useful ventilatory strategy. Multiple studies have shown IRV to be helpful in ARDS management (Gore, 1998). However, other studies have shown IRV to be ineffective (Lessard *et al.*, 1994).

Positive end-expiratory pressure (PEEP) is frequently used to facilitate oxygenation in ARDS and similar conditions. PEEP appears to function by keeping the alveoli from collapsing during expiration. PEEP will also increase mean airway pressure as well as peak airway pressure. Thus, increasing PEEP is also a means of increasing alveolar recruitment (Armstrong and MacIntyre, 1995).

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It should also be noted that excessive mean and/or peak airway pressure may be associated with barotrauma or pressure-induced pulmonary injury. In addition, excessive mean airway pressure may also cause decreases in cardiac output and subsequent tissue hypoperfusion. Pneumonthorax, a potentially acute life-threatening condition, may also result from an excessive mean and/or peak airway pressure.

As stated, excessive mean and/or peak airway pressures may result from excessive PEEP as well as an insufficient expiratory time. In addition, inordinately large tidal volumes, especially when delivered to patients with decreased pulmonary compliance, may also yield high mean and/or peak airway pressures.

Thus, the purpose of this paper is to examine a model of mean airway pressure based upon $I{:}E$ ratio, PEEP, and plateau pressure. It should be noted that plateau pressure refers to the distending pressure that generates the tidal volume, delivered by the ventilator, during inspiration.

This model illustrates the interrelationship between $I{:}E$ ratio, PEEP, and plateau pressure as they affect mean airway pressure. The understanding of this interrelationship may offer clinicians significant advantages in the management of patients with complex pulmonary diseases.

Furthermore, it appears that the combination of PEEP and $I{:}E$ ratio can be mathematically optimized. This strategy results in obtaining a desired or "target" mean airway pressure while simultaneously avoiding excessive PEEP or inspiratory time.

MODELING MEAN AIRWAY PRESSURE AS A FUNCTION OF *I*:*E* RATIO AND PLATEAU PRESSURE

On the basis of Fig. 1, the relationship between $I{:}E$ ratio and mean airway pressure P_{mean} can be mathematically modeled:

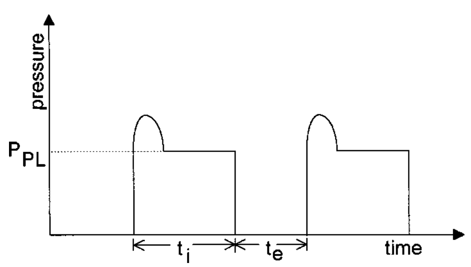

Figure 1. Airway pressure as a function of time. P_{PL} refers to plateau pressure whereas t_i and t_e are the absolute inspiratory and expiratory times respectively.

$$P_{\text{mean}} = \frac{1}{(t_i + t_e)} \cdot \int_0^{(t_i+t_e)} P(t)dt \approx \frac{P_{\text{PL}} \cdot t_i}{(t_i + t_e)} \qquad (1)$$

where t_i and t_e are inspiratory and expiratory times, respectively. P_{PL} is plateau pressure. Note that $P(t) = 0$ during t_e. This only applies to situations in which PEEP $= 0$.

Dividing the right hand side of Eq. (1) by $\frac{1}{t_e}$ and substituting $I{:}E = \frac{t_i}{t_e}$ yields:

$$P_{\text{mean}} \approx \frac{P_{\text{PL}} \cdot \left(\frac{t_i}{t_e}\right)}{\left(\frac{t_i}{t_e} + 1\right)} = \frac{P_{\text{PL}} \cdot (I{:}E)}{[(I{:}E) + 1]} \qquad (2)$$

Rearranging Eq. (2) shows that $\frac{P_{\text{mean}}}{P_{\text{PL}}}$ can be expressed solely as a function of the $I{:}E$ ratio:

$$\frac{P_{\text{mean}}}{P_{\text{PL}}} = \frac{(I{:}E)}{[(I{:}E) + 1]} \qquad (3)$$

Figure 2 summarizes $\frac{P_{\text{mean}}}{P_{\text{PL}}}$ for a range of $I{:}E$ ratios. The logarithmic shape of this curve should be noted as increases in $\frac{P_{\text{mean}}}{P_{\text{PL}}}$ are less pronounced as $I{:}E$ ratio increases. Therefore, the benefits of IRV, with inspiratory time exceeding expiratory time, would appear to be self-limiting in nature. This can be quantified by examining $\frac{d(\frac{P_{\text{mean}}}{P_{\text{PL}}})}{d(I{:}E)}$:

$$\frac{d\left(\frac{P_{\text{mean}}}{P_{\text{PL}}}\right)}{d(I{:}E)} = \frac{1}{[(I{:}E) + 1]} \cdot \left[1 - \frac{(I{:}E)}{[(I{:}E) + 1]}\right] \qquad (4)$$

Substituting Eq. (3) into Eq. (4):

$$\frac{d\left(\frac{P_{\text{mean}}}{P_{\text{PL}}}\right)}{d(I{:}E)} = \frac{1}{[(I{:}E) + 1]} \cdot \left[1 - \frac{P_{\text{mean}}}{P_{\text{PL}}}\right] \qquad (5)$$

Note that

$$\lim_{\frac{P_{\text{mean}}}{P_{\text{PL}}} \to 1} \frac{d\left(\frac{P_{\text{mean}}}{P_{\text{PL}}}\right)}{d(I{:}E)} = 0 \quad \text{and} \quad \lim_{(I:E) \to \infty} \frac{d\left(\frac{P_{\text{mean}}}{P_{\text{PL}}}\right)}{d(I{:}E)} = 0.$$

Therefore, the "flattening" in the right hand side of Fig. 2 is a function of increasing $I{:}E$ ratio and/or increases in $\frac{P_{\text{mean}}}{P_{\text{PL}}}$. As shown in the following section, PEEP will increase $\frac{P_{\text{mean}}}{P_{\text{PL}}}$ and will also decrease the effect of increases in $I{:}E$ ratio on $\frac{P_{\text{mean}}}{P_{\text{PL}}}$.

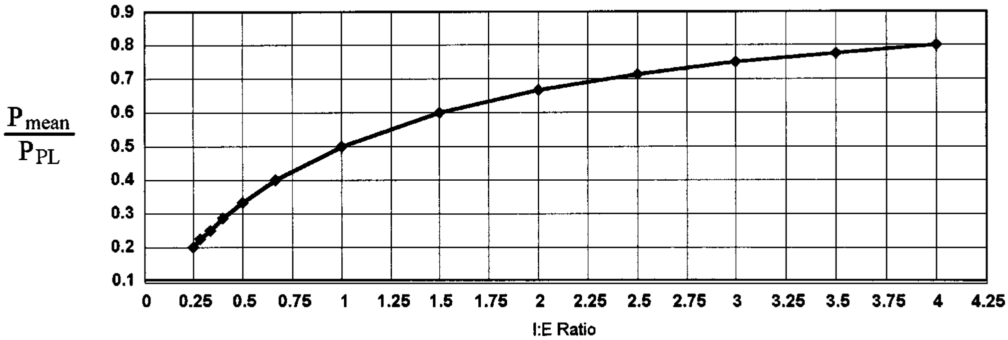

Figure 2. $\frac{P_{mean}}{P_{PL}}$ is a logarithmic function of $I{:}E$ ratio. Notice that increases in $I{:}E$ ratio are self-limiting in their effect on $\frac{P_{mean}}{P_{PL}}$.

MODELING POSITIVE END-EXPIRATORY PRESSURE AS AN ADDITIONAL COMPONENT OF MEAN AIRWAY PRESSURE

Using the definition of P_{mean} from Eq. (1), the above model of $\frac{P_{mean}}{P_{PL}}$ can be modified to include PEEP:

$$P_{mean} = \frac{1}{(t_i + t_e)} \cdot \int_0^{(t_i+t_e)} P(t)dt \approx \frac{1}{(t_i + t_e)} \cdot [P_{PL} \cdot (t_i) + P_{peep} \cdot (t_e)] \quad (6)$$

The effect of PEEP, generating pressure during expiration, is demonstrated in Fig. 3. Thus, $P(t) > 0$ during t_e. For the purposes of this model, this pressure, P_{peep}, will be defined as a fraction of the plateau pressure, P_{PL}:

$$P_{peep} = \mathbf{R} \cdot P_{PL} \quad (7)$$

Thus, **R** represents the ratio of P_{peep} to P_{PL} or $\mathbf{R} = \frac{P_{peep}}{P_{PL}}$. By defining **R** in this manner, both R and $I{:}E$ ratio are dimensionless ratios with approximately the same magnitude. This will be useful in comparing their relative contributions to $\frac{P_{peep}}{P_{PL}}$.

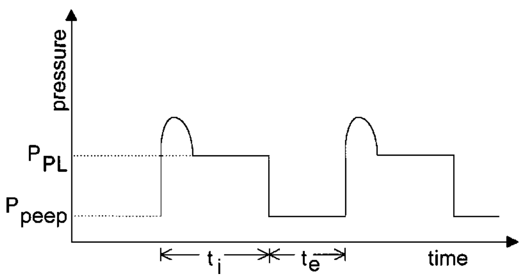

Figure 3. Airway pressure with the application of positive end-expiratory pressure (PEEP)

Furthermore, for the purposes of this model, it should be noted that the addition of P_{peep} does not affect P_{PL}. Therefore, P_{PL} remains independent from the addition of P_{peep}.

Equation (7) can be substituted into Eq. (6):

$$P_{mean} = \frac{P_{PL} \cdot t_i}{(t_i + t_e)} + \frac{\mathbf{R} \cdot P_{PL} \cdot t_e}{(t_i + t_e)} \quad (8)$$

Dividing both right hand terms of Eq. (1) by $\frac{1}{t_e}$ and substituting $I{:}E = \frac{t_i}{t_e}$ yields:

$$P_{mean} = \frac{P_{PL} \cdot (I{:}E)}{[(I{:}E) + 1]} + \frac{\mathbf{R} \cdot P_{PL}}{[(I{:}E) + 1]} \quad (9)$$

Rearranging Eq. (9) shows that $\frac{P_{mean}}{P_{PL}}$ can now be expressed as a function of $I{:}E$ ratio and **R**:

$$\frac{P_{mean}}{P_{PL}} = \frac{[(I{:}E) + \mathbf{R}]}{[(I{:}E) + 1]} \quad (10)$$

Notice that Eq. (10) reduces to Eq. (3) when PEEP $= 0$ so that $\mathbf{R} = 0$.

Figure 4 shows $\frac{P_{mean}}{P_{PL}}$ graphically for different values of **R** over a range of $I{:}E$ ratios. It can be readily observed that increasing **R** diminishes the effect of $I{:}E$ ratio on $\frac{P_{mean}}{P_{PL}}$. Furthermore, increases in $I{:}E$ ratio are associated with a diminished increase in $\frac{P_{mean}}{P_{PL}}$ from an increased **R**.

It should also be noticed that $I{:}E$ ratio changes will increase $\frac{P_{mean}}{P_{PL}}$ the most under conditions of little to no **R** or $\frac{P_{peep}}{P_{PL}}$. Therefore, at low levels of **R**, $I{:}E$ ratio increases may have a significant "PEEP-sparing" influence with respect to increases in mean airway pressure.

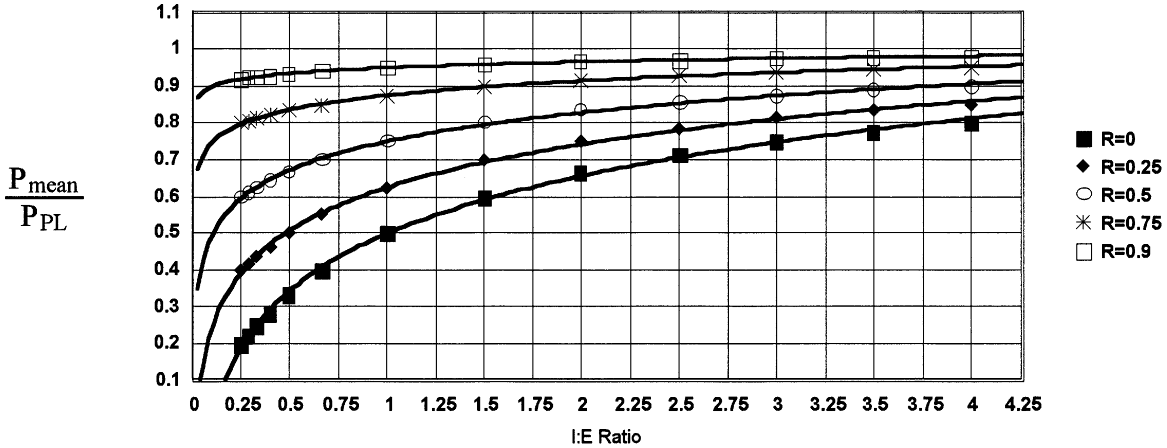

Figure 4. $\frac{P_{\text{mean}}}{P_{\text{PL}}}$ as a function of $I{:}E$ ratio with different levels of **R**. Note that **R** represents $\frac{P_{\text{PEEP}}}{P_{\text{PL}}}$. From this graph it is apparent that increasing $I{:}E$ ratio has its greatest influence, on $\frac{P_{\text{mean}}}{P_{\text{PL}}}$, with low levels of **R**. In addition, with large $I{:}E$ ratios, increases in **R** have less of an effect on $\frac{P_{\text{mean}}}{P_{\text{PL}}}$.

$P_{\text{mean}}/P_{\text{PL}}$ IS A LINEAR FUNCTION OF R AND LOGARITHMIC FUNCTION OF $I{:}E$ RATIO

When $I{:}E$ ratio is assumed to be constant, then Eq. (10) can be simply expressed as a linear function of $\mathbf{R}$: $\frac{P_{\text{mean}}}{P_{\text{PL}}} = I{:}E/(I{:}E + 1) + \mathbf{R}/(I{:}E + 1)$. Furthermore, Eq. (10) can also be approximated as follows: $\frac{P_{\text{mean}}}{P_{\text{PL}}} = 0.5 \cdot (1 + \mathbf{R}) + 0.225 \cdot (1 - \mathbf{R}) \cdot \ln(I{:}E)$. So that, for a constant **R**, $\frac{P_{\text{mean}}}{P_{\text{PL}}}$ can be thought of as a logarthmic function of $I{:}E$ ratio.

ASSESSING CHANGES IN $P_{\text{mean}}/P_{\text{PL}}$ FROM CHANGES IN R AND $I{:}E$ RATIO

The individual contributions of $I{:}E$ ratio and **R**, on $\frac{P_{\text{mean}}}{P_{\text{PL}}}$, can be assessed by examining

$$\frac{\partial\left(\frac{P_{\text{mean}}}{P_{\text{PL}}}\right)}{\partial(I{:}E)} \quad \text{and} \quad \frac{\partial\left(\frac{P_{\text{mean}}}{P_{\text{PL}}}\right)}{\partial \mathbf{R}}.$$

These partial first derivatives of Eq. (10) are shown, in their most simplified form, as Eqs. (13) and (14).

$$\frac{\partial\left(\frac{P_{\text{mean}}}{P_{\text{PL}}}\right)}{\partial(I{:}E)} = \frac{1}{[(I{:}E)+1]} \cdot \left[1 - \frac{(I{:}E)}{[(I{:}E)+1]} - \frac{\mathbf{R}}{[(I{:}E)+1]}\right] \tag{11}$$

Combining both right-hand terms yield:

$$\frac{\partial\left(\frac{P_{\text{mean}}}{P_{\text{PL}}}\right)}{\partial(I{:}E)} = \frac{1}{[(I{:}E)+1]} \cdot \left[1 - \frac{[(I{:}E)+\mathbf{R}]}{[(I{:}E)+1]}\right] \tag{12}$$

Substituting Eq. (10) into Eq. (12) yields Eq. (13) which is identical to Eq. (5):

$$\frac{\partial\left(\frac{P_{\text{mean}}}{P_{\text{PL}}}\right)}{\partial(I{:}E)} = \frac{1}{[(I{:}E)+1]} \cdot \left[1 - \frac{P_{\text{mean}}}{P_{\text{PL}}}\right] \tag{13}$$

Note that:

$$\lim_{\mathbf{R}\to 1} \frac{\partial\left(\frac{P_{\text{mean}}}{P_{\text{PL}}}\right)}{\partial(I{:}E)} = 0 \quad \text{and} \quad \lim_{(I:E)\to\infty} \frac{\partial\left(\frac{P_{\text{mean}}}{P_{\text{PL}}}\right)}{\partial(I{:}E)} = 0$$

$$\text{and} \quad \lim_{\frac{P_{\text{mean}}}{P_{\text{PL}}}\to 1} \frac{d\left(\frac{P_{\text{mean}}}{P_{\text{PL}}}\right)}{d(I{:}E)} = 0.$$

The clinical implications of this are: As **R** increase, $I{:}E$ ratio changes will affect $\frac{P_{\text{mean}}}{P_{\text{PL}}}$ less. Just as in the former model, Eqs. (3) through (5), $I{:}E$ ratio increases are still self-limiting as they affect $\frac{P_{\text{mean}}}{P_{\text{PL}}}$.

In addition, increases in $\frac{P_{\text{mean}}}{P_{\text{PL}}}$, from an increase in **R**, will result in a decrease in the effect of $I{:}E$ ratio on $\frac{P_{\text{mean}}}{P_{\text{PL}}}$. This change in $\frac{P_{\text{mean}}}{P_{\text{PL}}}$, as a function of **R**, can be readily demonstrated as:

$$\frac{\partial\left(\frac{P_{\text{mean}}}{P_{\text{PL}}}\right)}{\partial \mathbf{R}} = \frac{1}{[(I:E)+1]} \tag{14}$$

Thus,

$$\lim_{(I:E)\to\infty} \frac{\partial\left(\frac{P_{\text{mean}}}{P_{\text{PL}}}\right)}{\partial \mathbf{R}} = 0.$$

Summarizing, increases in **R** will be less effective at increasing $\frac{P_{\text{mean}}}{P_{\text{PL}}}$ as $I:E$ ratio increases. This is illustrated in Fig. 4.

COMPARING CHANGES IN $P_{\text{mean}}/P_{\text{PL}}$ FROM CHANGES IN R AND $I:E$ RATIO

Comparing

$$\frac{\partial\left(\frac{P_{\text{mean}}}{P_{\text{PL}}}\right)}{\partial \mathbf{R}} \quad \text{to} \quad \frac{\partial\left(\frac{P_{\text{mean}}}{P_{\text{PL}}}\right)}{\partial (I:E)}.$$

can be accomplished by dividing Eq. (14) by Eq. (13):

$$\frac{\left(\frac{\partial\left(\frac{P_{\text{mean}}}{P_{\text{PL}}}\right)}{\partial \mathbf{R}}\right)}{\left(\frac{\partial\left(\frac{P_{\text{mean}}}{P_{\text{PL}}}\right)}{\partial (I:E)}\right)} = \frac{\frac{1}{[(I:E)+1]}}{\frac{1}{[(I:E)+1]}\cdot\left[1-\frac{P_{\text{mean}}}{P_{\text{PL}}}\right]} \tag{15}$$

Simplifying Eq. (15) yields:

$$\frac{\left(\frac{\partial\left(\frac{P_{\text{mean}}}{P_{\text{PL}}}\right)}{\partial \mathbf{R}}\right)}{\left(\frac{\partial\left(\frac{P_{\text{mean}}}{P_{\text{PL}}}\right)}{\partial (I:E)}\right)} = \frac{1}{\left[1-\frac{P_{\text{mean}}}{P_{\text{PL}}}\right]} \tag{16}$$

Since

$$0 < \frac{P_{\text{mean}}}{P_{\text{PL}}} < 1, \text{ then}$$

$$\frac{\partial\left(\frac{P_{\text{mean}}}{P_{\text{PL}}}\right)}{\partial \mathbf{R}} \text{ will always be greater than } \frac{\partial\left(\frac{P_{\text{mean}}}{P_{\text{PL}}}\right)}{\partial (I:E)}.$$

This is illustrated in Fig. 5. Therefore, changes in **R** will always affect $\frac{P_{\text{mean}}}{P_{\text{PL}}}$ more than changes in the $I:E$ ratio.

MEAN AIRWAY PRESSURE OPTIMIZATION USING LAGRANGE MULTIPLIERS

Using the *Method of Lagrange Multipliers*, it is possible to determine the optimum combination, of **R** and $I:E$ ratio, for a given $\frac{P_{\text{mean}}}{P_{\text{PL}}}$. Thus, a combination of **R** and $I:E$ ratio, yielding a maximum product of **R** and $I:E$ ratio, can be determined for a desired $\frac{P_{\text{mean}}}{P_{\text{PL}}}$. This strategy would theoretically result in an "ideal amount" of both inspiratory time and PEEP without an excessive quantity of either (See Appendix).

It should be emphasized that this represents the maximization of the product of $(I:E)\bullet\mathbf{R}$. If a lesser amount of PEEP is desired, in achieving a target $\frac{P_{\text{mean}}}{P_{\text{PL}}}$, then an excessive amount of inspiratory time may result. This could result in an insufficient amount of expiratory time. Likewise, if a decreased amount of inspiratory time is required to achieve a target $\frac{P_{\text{mean}}}{P_{\text{PL}}}$, then an excessive amount of PEEP may be needed. This could result in an excessive peak airway pressure. Thus, by maximizing the $(I:E)\bullet\mathbf{R}$ product, theoretically optimum quantities of both the $I:E$ ratio and PEEP could be achieved.

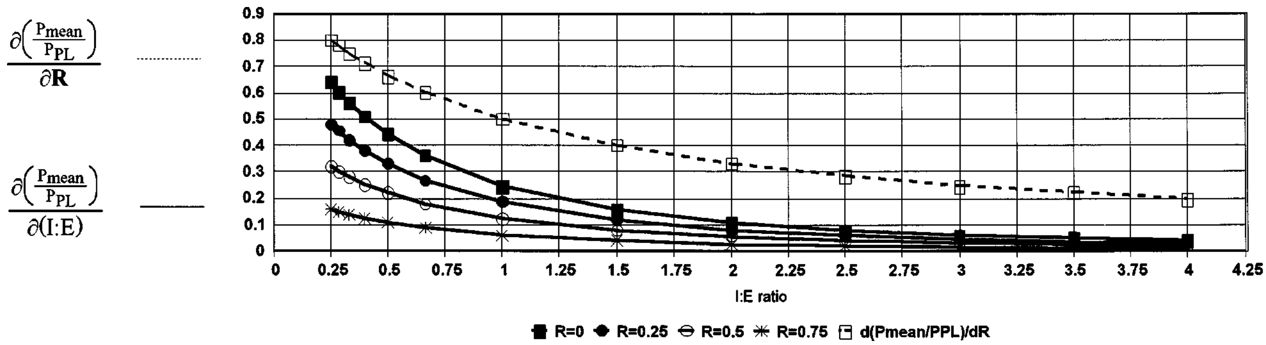

Figure 5. Changes in $\frac{P_{\text{mean}}}{P_{\text{PL}}}$ are consistently effected more by changes in **R** than by changes in $I:E$ ratio.

Initially, a function **F** is defined as:

$$\mathbf{F}(\mathbf{R}, I{:}E, \lambda) = \left[\frac{1}{[(I{:}E)\cdot\mathbf{R}]} + \lambda\cdot\left\{\frac{[(I{:}E)+\mathbf{R}]}{[(I{:}E)+1]} - \frac{P_{\text{mean}}}{P_{\text{PL}}}\right\}\right] \quad (17)$$

The following partial differential equations (18), (19), and (20) are then solved simultaneously:

$$\frac{\partial \mathrm{F}}{\partial \mathbf{R}} = \frac{-1}{(I{:}E)\cdot\mathbf{R}^2} + \frac{\lambda}{[(I{:}E)+1]} = 0 \quad (18)$$

$$\frac{\partial \mathrm{F}}{\partial (I{:}E)} = \frac{-1}{(I{:}E^2)\cdot\mathbf{R}} + \lambda\cdot\left\{\frac{1}{[(I{:}E)+1]} - \frac{[(I{:}E)+\mathbf{R}]}{[(I{:}E)+1]^2}\right\} = 0 \quad (19)$$

$$\frac{\partial \mathrm{F}}{\partial \lambda} = \frac{[(I{:}E)+\mathbf{R}]}{[(I{:}E)+1]} - \frac{P_{\text{mean}}}{P_{\text{PL}}} = 0 \quad (20)$$

The solution, to this set of equations, yields expressions for values of **R** and $I{:}E$ ratio which produce a maximum $(I{:}E)\cdot\mathbf{R}$ product and nevertheless attain the desired $\frac{P_{\text{mean}}}{P_{\text{PL}}}$:

$$\mathbf{R} = \frac{1}{2}\cdot\frac{P_{\text{mean}}}{P_{\text{PL}}} \quad (21A)$$

$$I{:}E = \frac{-1}{2}\cdot\frac{\left[\frac{P_{\text{mean}}}{P_{\text{PL}}}\right]}{\left[-1+\frac{P_{\text{mean}}}{P_{\text{PL}}}\right]} \quad (21B)$$

$$\lambda = -4\cdot\frac{\left[\frac{P_{\text{mean}}}{P_{\text{PL}}}-2\right]}{\left[\frac{P_{\text{mean}}}{P_{\text{PL}}}\right]^3} \quad (21C)$$

This would potentially allow for optimizing ventilator $I{:}E$ ratio and PEEP settings in achieving a "target" $\frac{P_{\text{mean}}}{P_{\text{PL}}}$. Thus, for a given plateau pressure, a desired mean airway pressure could be attained without excessive quantities of either PEEP or inspiratory time. It should be noted that λ is used for calculation purposes only and has no clinical utility.

MEAN AIRWAY PRESSURE OPTIMIZATION USING SUBSTITUTION

It is also possible to derive these optimization equations by substitution. Rearranging Eq. (10), so as to solve for **R**, yields:

$$\mathbf{R} = \left(\frac{P_{\text{mean}}}{P_{\text{PL}}} - 1\right)\cdot(I{:}E) + \frac{P_{\text{mean}}}{P_{\text{PL}}} \quad (22)$$

This straight line is a solution set of **R** and $I{:}E$ ratio combinations for the "target" $\frac{P_{\text{mean}}}{P_{\text{PL}}}$. This is illustrated in Fig. 6.

The $(I{:}E)\cdot\mathbf{R}$ product is a parabolic-shaped function and is also shown in Fig. 6:

$$\mathbf{R}\cdot(I{:}E) = \left(\frac{P_{\text{mean}}}{P_{\text{PL}}} - 1\right)\cdot(I{:}E)^2 + \frac{P_{\text{mean}}}{P_{\text{PL}}}\cdot(I{:}E) \quad (23)$$

The maximum of this function is determined by setting the first derivative of the above equation equal to zero and solving for $I{:}E$ ratio:

$$\frac{d[\mathbf{R}\cdot(I{:}E)]}{d(I{:}E)} = 2\cdot\left(\frac{P_{\text{mean}}}{P_{\text{PL}}} - 1\right)\cdot(I{:}E) + \frac{P_{\text{mean}}}{P_{\text{PL}}} = 0 \quad (24)$$

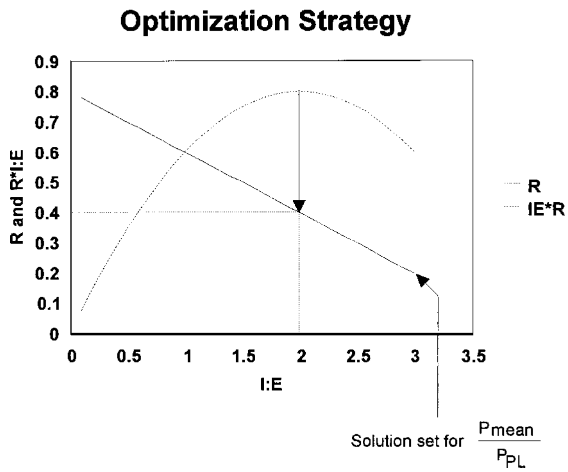

Figure 6. The solution set, of **R** and $I{:}E$ ratio combinations, for a target $\frac{P_{\text{mean}}}{P_{\text{PL}}} = 0.8$, is graphically represented with the solid straight line. The dashed parabola represents all $(I{:}E)\cdot\mathbf{R}$ products. The greatest point on this parabola represents the optimum combination of $I{:}E$ ratio and **R** to achieve this desired $\frac{P_{\text{mean}}}{P_{\text{PL}}}$. Deviations, from this point, would generate either an excessive PEEP, or an excessive inspiratory time, for the desired $\frac{P_{\text{mean}}}{P_{\text{PL}}}$. (This particular example is from Table 1 case **D**. The target $\frac{P_{\text{mean}}}{P_{\text{PL}}} = 0.8$ and the optimum combination is an $I{:}E$ ratio $= 2.0$ with $\mathbf{R} = 0.4$ where $\mathbf{R} = \frac{P_{\text{PEEP}}}{P_{\text{PL}}}$.)

The resultant expression for $I{:}E$ ratio is identical to Eq. (21B):

$$I{:}E = \frac{-1}{2} \cdot \frac{\left[\frac{P_{\text{mean}}}{P_{\text{PL}}}\right]}{\left[-1 + \frac{P_{\text{mean}}}{P_{\text{PL}}}\right]} \tag{25}$$

Substituting this expression for $I{:}E$ ratio back into Eq. (22) yields an expression for **R**:

$$\mathbf{R} = \left(\frac{P_{\text{mean}}}{P_{\text{PL}}} - 1\right) \cdot \left(\frac{-1}{2} \cdot \frac{\left[\frac{P_{\text{mean}}}{P_{\text{PL}}}\right]}{\left[-1 + \frac{P_{\text{mean}}}{P_{\text{PL}}}\right]}\right) + \frac{P_{\text{mean}}}{\text{PL}} \tag{26}$$

Simplifying the above formula results in an expression for **R** which is identical to Eq. (21A):

$$\mathbf{R} = \frac{1}{2} \cdot \frac{P_{\text{mean}}}{P_{\text{PL}}} \tag{27}$$

APPLYING THE OPTIMIZATION STRATEGY

Table 1 numerically illustrates the application of this strategy in several theoretical clinical scenarios. Obviously, individual patient management demands would result in modifications in its implementation.

Case **A** represents a patient with chronic obstructive pulmonary disease (COPD). These patients frequently have extremely "delicate" alveoli with bulleous emphysema. Ideally, they should have both low mean and peak airway pressures. These patients will also frequently exhibit "airtrapping" and may therefore need significant expiratory times. Thus, by using a low "target" mean airway pressure, for a given plateau pressure, the optimization strategy yields a solution with both a large expiratory time and a relatively small amount of PEEP. Note that peak airway pressure is the sum of plateau pressure and PEEP.

Had an $I{:}E$ ratio of 1:2 been used, with a PEEP = 2.5 cm H_2O and P_{PL} = 20 cm H_2O, then a calculated mean airway pressure, using Eq. (10), would be 8.33 cm H_2O. This represents a 66.7% increase in mean airway pressure from that of the optimization strategy.

Had PEEP = 0, then, using Eq. (3), an $I{:}E$ ratio of 1:3 would be required to achieve a mean airway pressure of 5 cm H_2O. This represents half the expiratory time as compared to the optimization model. Air trapping could result.

If an $I{:}E$ ratio of 1:8 had been used, then, using Eq. 10, PEEP would have to equal 3.125 cm H_2O to achieve a mean airway pressure of 5 cm H_2O. This would result in a higher peak airway pressure than that of the model. This would increase the risk of barotrauma.

Case **B** represents values for a normal patient. Notice that the optimization strategy yields typical ventilatory parameters which are commonly used in clinical practice.

Case **C** is a patient with acute respiratory distress syndrome (ARDS). Notice that the optimization strategy resulted in a relatively low PEEP of 7.5 cm H_2O used in conjunction with IRV. The resultant $I{:}E$ ratio in this case is 1.5:1.

Had an $I{:}E$ ratio of 1:2 been used, PEEP would have to be 12.5 cm H_2O to achieve the desired mean airway pressure. This would have resulted in a higher peak airway pressure.

Case **D** represents a patient with more severe ARDS than in case **C**. Note again that inspiratory time and PEEP are both increased, to yield a larger mean airway pressure, without an excessive quantity of either.

Clinically, controlling $I{:}E$ ratio may require excessive amounts of anesthetics which can be undesirable

Table 1. Clinical Scenarios Using the Mean Airway Pressure Optimization Strategy

Case	Target $\frac{P_{\text{mean}}}{P_{\text{PL}}}$	**R**	$I{:}E$ ratio	Clinical scenario[a]	Peak inspiratory pressure[b]
A	$\frac{1}{4}$	$\frac{1}{8}$	$\frac{1}{6}$	Severe chronic obstructive pulmonary disease (COPD) with "air trapping." If $P_{\text{PL}} = 20$ then $P_{\text{mean}} = 5$ and PEEP = 2.5	22.5
B	$\frac{1}{2}$	$\frac{1}{4}$	$\frac{1}{2}$	Normal patient. If $P_{\text{PL}} = 20$ then $P_{\text{mean}} = 10$ and PEEP = 5	25
C	$\frac{3}{4}$	$\frac{3}{8}$	$\frac{3}{2}$	Acute respiratory distress syndrome (ARDS). If $P_{\text{PL}} = 20$ then $P_{\text{mean}} = 15$ and PEEP = 7.5. Note the use of inverse ratio ventilation (IRV) with $I{:}E = 1.5{:}1$	27.5
D	$\frac{4}{5}$	$\frac{2}{5}$	$\frac{2}{1}$	Severe ARDS. If $P_{\text{PL}} = 20$ then $P_{\text{mean}} = 16$ and PEEP = 8. Note the use of inverse ratio ventilation (IRV) with $I{:}E = 2{:}1$	28

[a] Pressure is expressed with units of cm H_2O.
[b] Peak insiratory pressure is defined as: P_{PL} + PEEP.

especially on a long-term basis. In addition, it is not currently customary for clinicians to set mean airway pressure as a “target.” Rather, the adjustment of ventilatory parameters is based upon arterial blood gas partial pressures, pulse oximetry, and end-tidal CO_2. This strategy reinforces that inspiratory time and PEEP are complementary in raising mean airway pressure and thus recruiting alveoli.

Furthermore, this strategy emphasizes the role of mean airway pressure as a global measure of alveolar recruitment. In addition, it illustrates the interactive and synergistic role of PEEP, I:E ratio, and plateau pressure on mean airway pressure.

Currently, it is not common to clinically think of I:E ratio and PEEP “combined” in the recruitment of alveoli. This model, as well as the optimization strategy, illustrates how these parameters interact.

Additional clinical observation would be necessary to validate and refine this strategy. It may be that individual disease states would require uniquely different optimization techniques (Naik *et al*., 1998).

DISCUSSION

Clinically, any increase in mean airway pressure, such as increasing tidal volume, positive end-expiratory pressure, or increases in I:E ratio, may lead to such complications as air trapping or pneumothorax. Hypotension and hypoperfusion, secondary to decreased venous return, can also occur. This develops from an increased intrathoracic pressure resulting in a decreased preload. Cardiac output is therefore reduced.

Furthermore, an insufficient expiratory time can also lead to hypoventilation and an associated respiratory acidosis. However, respiratory acidosis is frequently well-tolerated for patients with life-threatening ARDS. These patients have been shown to benefit from “low-stretch” or “protective” ventilatory strategies which are based upon a reduced tidal volume (Wang and Wei, 2002).

Clinically, increases in I:E ratio may be seen as a useful means of increasing mean airway pressure when little or no PEEP is needed or wanted. This has been observed clinically (Yanos *et al*., 1998).

In addition, increases in PEEP will increase peak airway pressure, which can increase barotrauma. Whereas increases in I:E ratio may avoid this. However, the addition of PEEP has been shown to yield dramatic improvements in patients with severe lung injury from ARDS and similiar conditions (Nelson, 1996).

In general, the demands of individual clinical situations will dictate allowable values of **R**, I:E ratio, as well as mean, plateau, and peak airway pressures, so as to optimize patient-based ventilator management. Typically, arterial blood gas analysis, pulse oximetry, and capnography are utilized to ascertain adequacy of ventilatory management.

Mean airway pressure has been suggested as a useful tool for practicing clinicians to assess the overall contributions of plateau pressure, I:E ratio, and PEEP in alveolar recruitment. This model may be useful as a guide in understanding how these parameters interact in contributing to mean airway pressure.

Specifically, as I:E ratio increases, for a given plateau pressure, mean airway pressure increases. Yet, as PEEP is added, the benefit of increasing inspiratory time is less apparent.

In addition, the model illustrates how PEEP consistently contributes to the increase in mean airway pressure more so than increases in I:E ratio.

Thus, the benefits of increasing inspiratory time or I:E ratio, on mean airway pressure, are more apparent at zero or low levels of PEEP.

Utilizing the optimization strategy, PEEP and I:E ratio can be combined in a way to yield a desired or “target” mean airway pressure. Furthermore, the use of this method may avoid using excessive quantities of either PEEP or inspiratory time.

CONCLUSION

The interrelationship between I:E ratio, PEEP, and plateau pressure, as they affect mean airway pressure, has been modeled. The benefits of increasing inspiratory time and/or PEEP have been shown in clinical studies. Yet, the practicing clinician may not appreciate how these parameters may interact.

Thus, in the absence of air trapping, it may be helpful to use as great an inspiratory time as possible. This would result in a higher mean airway pressure without increasing peak airway pressure. Increasing I:E ratio has a considerable ability to raise mean airway pressure and recruit alveoli. On the basis of this model, this contribution appears to be significant at low levels of PEEP. In addition, it appears that at high levels of PEEP, I:E ratio will not raise mean airway pressure notably.

This interaction may explain why the potentially beneficial effects of I:E ratio increases, and even IRV, may not be consistently apparent in clinical practice.

A strategy to optimize ventilator management, based upon "targeting" mean airway pressures, has also been presented. Using this method, it may be possible to utilize a maximum combination of PEEP and $I{:}E$ ratio and possibly avoid potential complications associated with excessive peak airway pressures or excessive inspiratory times.

APPENDIX

Method of Lagrange Multipliers

It should be noted that the solution set, for the partial first derivatives of $\mathbf{F}(\mathbf{R}, I{:}E, \lambda) = 0$, produces a maximum of the product $(I{:}E)\cdot \mathbf{R}$ by determining the minimum of $\frac{1}{[(I:E)\cdot\mathbf{R}]}$. This is subject to the constraint that the values of $I{:}E$ ratio and $\mathbf{R}$ are also a solution to Eq. (10):

$$\mathbf{F}(\mathbf{R}, I{:}E, \lambda) = \left[\frac{1}{[(I{:}E)\cdot\mathbf{R}]} + \lambda\cdot\left\{\frac{[(I{:}E)+R]}{[(I{:}E)+1]} - \frac{P_{\text{mean}}}{P_{\text{PL}}}\right\}\right]. \tag{1A}$$

The establishment of the minimum can be verified by assessing the partial second derivatives:

$$\frac{\partial F}{\partial \mathbf{R}} = \frac{-1}{(I{:}E)\cdot R^2} + \frac{\lambda}{[(I{:}E)+1]} \quad \text{thus}$$
$$\frac{\partial^2 F}{\partial \mathbf{R}^2} = \frac{2}{I{:}E\cdot\mathbf{R}^3}. \tag{2A}$$

Since $I{:}E > 0$ and $\mathbf{R} > 0$ then $\frac{\partial^2 F}{\partial \mathbf{R}^2} > 0$ and

$$\frac{\partial F}{\partial (I{:}E)} = \frac{-1}{(I{:}E)^2\cdot\mathbf{R}} + \lambda\cdot\left\{\frac{1}{[(I{:}E)+1]} - \frac{[(I{:}E)+\mathbf{R}]}{[(I{:}E)+1]^2}\right\} \quad \text{thus}$$
$$\frac{\partial^2 F}{\partial (I{:}E)^2} = \frac{2}{(I{:}E)^3\cdot\mathbf{R}} + \lambda\cdot\left\{\frac{-2}{[(I{:}E)+1]^2} + 2\cdot\frac{[(I{:}E)+\mathbf{R}]}{[(I{:}E)+1]^3}\right\}. \tag{3A}$$

Note that

$$[(I{:}E)+\mathbf{R}] \cong [(I{:}E)+1] \quad \text{then}$$
$$\frac{\partial^2 F}{\partial (I{:}E)^2} \cong \frac{2}{(I{:}E)^3\cdot\mathbf{R}}. \tag{4A}$$

Again, since $I{:}E > 0$ and $\mathbf{R} > 0$ then $\frac{\partial^2 F}{\partial (I:E)^2} > 0$.

With both partial second derivatives greater than zero, when the solution set to the partial first derivatives is obtained from Eq. (18) to (20), the result is a minimum value for $\frac{1}{[(I:E)\cdot\mathbf{R}]}$ and a maximum value for the $(I{:}E)\cdot\mathbf{R}$ product.

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