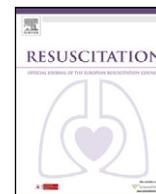




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Simulation and education

A structural model of perfusion and oxygenation in low-flow states[☆]

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ABSTRACT

Background: Recent investigations underscore the critical importance of ventilation strategies on resuscitation outcomes. In low perfusion states, such as cardiac arrest and traumatic shock, the rise in intrathoracic pressure that accompanies positive-pressure ventilation can significantly impede venous return and lead to a decrease in cardiac output. The optimal ventilation strategy in these “low-flow” states remains unclear.

Objective: To create a mathematical model of perfusion and oxygenation to predict the effects of PPV with both normotension and hypotension.

Methods: The lung pressure–volume relationship was modeled using a novel formula allowing manipulation of various lung characteristics. A separate formula was then derived to predict mean intrathoracic pressure (MITP) for specific minute ventilation values using the pressure–volume formula. The addition of positive end-expiratory pressure was also modeled. Finally, a formula was derived to model oxygen absorbance as a function of alveolar surface area and flow based on ventilation rate and MITP.

Results: Mathematical models of the lung pressure–volume relationship, MITP, and absorbance were successfully derived. Manipulation of total lung capacity, compliance, upper and lower inflection points, positive end-expiratory pressure, and minute ventilation allowed prediction of optimal ventilation rate and tidal volume for a normal lung and with various abnormal characteristics to simulate particular disease states, such as acute respiratory distress syndrome (ARDS). For a normal lung, ventilation rates of 4–6 breaths/min with higher tidal volumes (15–20 mL/kg) resulted in the lowest predicted MITP values (5 cm H₂O) and the highest absorbance. The input of lung parameters that would simulate ARDS resulted in optimal ventilation rates of 10–12 breaths/min with lower tidal volumes (8–10 mL/kg) and higher predicted MITP values (10–15 cm H₂O).

Conclusions: A mathematical model of ventilation was successfully derived allowing manipulation of multiple pulmonary physiological variables to predict MITP and potentially identify optimal ventilation strategies. This model suggests the use of lower ventilation rates and larger tidal volumes to minimize the hemodynamic effects of positive pressure ventilation in patients with hypoperfusion but normal lung characteristics.

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1. Introduction

Multiple recent investigations underscore the critical importance of avoiding hyperventilation during resuscitation from traumatic brain injury (TBI), hypovolemic shock, and cardiac arrest.^{1–6} Cerebral perfusion is highly sensitive to even small changes in [CO₂], with hypocapnia leading to the rapid onset of cerebral vasoconstriction and ischemia.^{7–9} In addition, the

mean intrathoracic pressure (MITP) rise that accompanies positive-pressure ventilation can impede venous return and decrease cardiac output, especially in low-perfusion states.^{4–6} Guides to ventilation have generally included the use of either quantitative capnometry in TBI patients or application of prescribed ventilation rates or compression-to-ventilation ratios in cardiac arrest.^{10,11}

Optimal ventilation strategies have been defined for intensive care unit (ICU) patients with acute respiratory distress syndrome (ARDS) to maximize surface area for oxygen absorption and to minimize pulmonary injury due to barotrauma, biotrauma, and atelectrauma.^{12–19} This has led to the widespread application of “lung-protective ventilation” in this patient population, generally resulting in smaller tidal volumes and faster ventilation rates with the use of positive end-expiratory pressure (PEEP). These patients are usually not suffering ongoing hemorrhage, are generally

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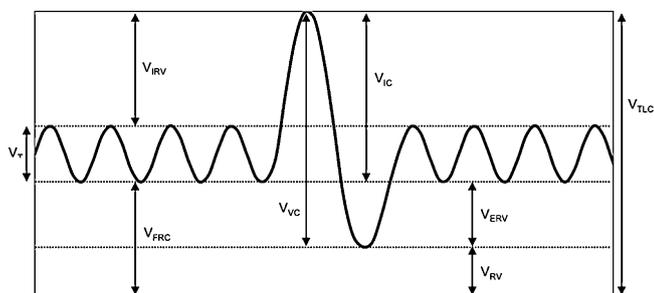


Fig. 1. Pulmonary volumes during normal breathing and with maximal inspiration, and theoretical model of lung function.

euvolemic, and may be on pressor therapy to offset the negative hemodynamic effects of positive-pressure ventilation. These may not be true with acute resuscitation, where absolute or relative hypovolemia may be present.

Optimal tidal volumes and ventilation rates in hypoperfusion states remain poorly defined, potentially involving the dynamic interaction between minute ventilation and pCO₂, the rise in MITP that accompanies positive-pressure ventilation, and changes in alveolar surface area. Here we derive a structural model to predict MITP and oxygen absorption trends with changes in ventilation rate and tidal volume at varying degrees of hypotension. We hypothesized that lower ventilation rates and larger tidal volumes than used in conventional practice would be optimal with regard to both hemodynamics and oxygen absorption in low perfusion states.

2. Methods

2.1. Pulmonary pressure-volume curve

The first objective in deriving a structural model of perfusion and oxygenation was to define the variational relationship between total lung volume (V) and intrapulmonary pressure (P). This relationship was modeled using the nomenclature of Figs. 1–3. Fig. 1 demonstrates normal breathing with a single breath of maximum inhalation followed by maximum exhalation. Fig. 2 defines a sinusoidal curve containing a lower inflection point (LIP) and an upper inflection point (UIP). The LIP represents the transition from the relatively pressure-inefficient phase with initial inflation

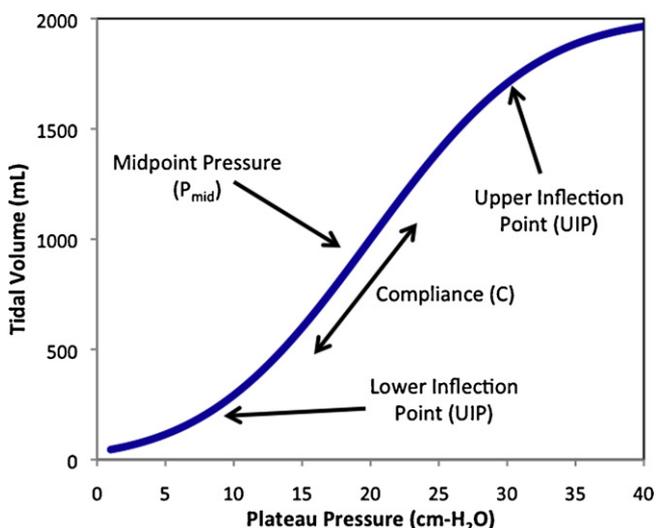


Fig. 2. Intrathoracic pressure versus tidal volume model. This curve uses standard lung parameters (solid; $K = 0.5$, $V_{VC} = 4L$, $P_{mid} = 20$, $C = 9.5$, $PEEP = 0$, $i = 1$, $e = 2$, $V_D = 350$, $Wt = 80$ kg, $VE = 6.4$ L).

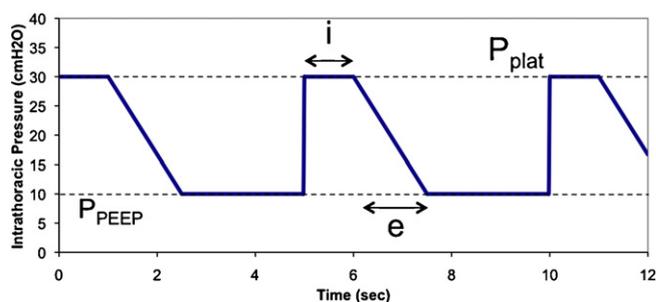


Fig. 3. Pressure-volume cycle over time.

of atelectatic alveoli to more efficient lung volumes. The UIP represents the transition into an “overstretch” zone where relatively small increases in intrapulmonary volume (V) result in a rapid rise in intrathoracic pressures (P). Fig. 3 represents the respiratory/ventilatory cycle over time.

A three-compartment model (dead space, perfused alveoli, and non-perfused alveoli) was used, with relevant terminology defined in Table 1. The relative ratio of perfused to non-perfused lung segments is represented by the term Q, which can be approximated by the ratio of end-tidal to arterial CO₂ (P_{etCO_2}/P_{aCO_2}). The [CO₂], relative volumes, and total CO₂ contribution are displayed in Table 2. Ultimately, these calculations are important in determining the alveolar minute ventilation (VE_{alv}) requirement. Using the equation from Table 1, we can define the relationship between positive-pressure-volume (V_{PPV}) and intrapulmonary pressure (P) by the formula:

$$V_{PPV} = K \cdot V_{VC} \cdot \text{NORMDIST}(P, P_{mid}, C, 1) \quad (1)$$

This formula allows independent manipulation of various lung characteristics. Midpoint pulmonary pressure (P_{mid}) represents the pressure at the midpoint between the LIP and UIP. Compliance (C) is defined as the standard deviation of P around P_{mid} , with lower C values (i.e., steeper slope) representing a more compliant lung. The volumes at which LIP and UIP occur are defined by the input values for K, vital capacity (V_{VC}), and C. The term K allows lowering of the

Table 1
Definitions for derived equations.

<i>General lung equation</i>	
$V = V_R + V_{PPV}$	
<i>Residual volume equations</i>	
$V_R = V_{RD} + V_{Ralv}$	
$V_{Ralv} = V_{RP} + V_{RNP}$	
<i>Positive-pressure ventilation equations</i>	
$V_{PPV} = V_{PEEP} + V_T$	
$V_T = V_{TD} + V_{TAlv}$	
$V_{TAlv} = V_{TP} + V_{TNP}$	
<i>Dead space equation</i>	
$V_D = V_{RD} = V_{TD}$	
<i>Perfusion equations</i>	
$Q = V_{RP}/V_{Ralv} = V_{RP}/(V_{RP} + V_{RNP})$	
$Q = V_{TP}/V_{TAlv} = V_{TP}/(V_{TP} + V_{TNP})$	
$Q = V_{DP}/(V_{DP} + V_{DNP})$	
$Q \approx P_{etCO_2}/P_{aCO_2}$	

V = total lung volume; V_R = residual lung volume; V_{PPV} = lung volume related to positive-pressure ventilation; V_{RD} = residual lung volume in anatomic dead space (nonconducting airways and ventilator circuit); V_{Ralv} = residual lung volume in alveoli; V_{RP} = residual lung volume in perfused alveoli; V_{RNP} = residual lung volume in nonperfused alveoli; V_{PEEP} = lung volume related to positive end-expiratory pressure; V_T = lung volume related to tidal volume ventilation; V_{TD} = tidal volume ventilation that fills anatomic dead space; V_{TAlv} = tidal volume ventilation that fills alveoli; V_{TP} = tidal volume ventilation that fills perfused alveoli; V_{TNP} = tidal volume ventilation that fills nonperfused alveoli; V_D = volume of anatomic dead space; V_{DP} = volume of anatomic dead space that fills perfused alveoli; V_{DNP} = volume of anatomic dead space that fills nonperfused alveoli; P_{aCO_2} = arterial partial pressure of carbon dioxide; P_{etCO_2} = end-tidal partial pressure of carbon dioxide.

Table 2
Definitions used in derived equations at various points in lung cycle.

Ventilation cycle	Lung partition		
	Dead space	Perfused alveoli	Non-perfused alveoli
<i>End expiration</i>			
[CO ₂]	PetCO ₂	PaCO ₂	V _D ·PetCO ₂ /V _T
Volume	V _D	V _{RP}	V _{NP}
Total CO ₂	V _D ·PetCO ₂	V _{RP} ·PaCO ₂	V _{NP} ·V _D ·PetCO ₂ /V _T
<i>End inspiration</i>			
[CO ₂]	0	PaCO ₂	V _D ·PetCO ₂ /V _T
Volume	V _D	V _{RP} + V _{TP} + V _{DP}	V _{RNP} + V _{TNP} + V _{DNP}
Total CO ₂	0	(V _{RP} + V _{TP} + V _{DP})·PaCO ₂	(V _{RNP} + V _{TNP} + V _{DNP})·V _D ·PetCO ₂ /V _T

UIP and LIP values to a physiological range, as the normal human lung displays vertical asymmetry in that UIP values are lower than the vital capacity (V_{VC}). This was acceptable given that our primary interest was to define pulmonary parameters up to the UIP, which already exceeds most tidal volumes used in clinical medicine. These are represented conceptually in Figs. 1–3.

Next, the relationship between alveolar minute ventilation (VE_{alv}) and intrapulmonary pressure was modeled. These equations were based on the following formula:

$$VE_{alv} = f \cdot (V_{TP} + D \cdot V_{DP}) \quad (2)$$

In this model, alveolar minute ventilation is based on the product of ventilation frequency (f) multiplied by the volume of gas without CO₂ entering perfused areas of lung as defined in Table 2. This volume is represented by the sum of each breath entering perfused lung (V_{TP}) and a fraction of the dead space gas that still has CO₂-absorbing capacity (D·V_{DP}). The coefficient D can be defined by the following equation:

$$D = \frac{(PaCO_2 - EtCO_2)}{PaCO_2} \approx 1 - Q \quad (3)$$

We applied the standard formula relating dead space ventilation (V_D), tidal volume (V_T), and measured values for PaCO₂ and EtCO₂:

$$V_D = \frac{V_T \cdot (PaCO_2 - EtCO_2)}{PaCO_2} \quad (4)$$

This would indicate that D = V_D/V_T, resulting in the following derivation of Eq. (2):

$$V_{TP} = \frac{VE_{alv}}{f} - \frac{Q \cdot (V_D)^2}{V_T} \quad (5)$$

2.2. Mean intrathoracic pressure (MITP)

The second objective was to derive a formula to predict MITP based on the following: alveolar minute ventilation (VE_{alv}), intrapulmonary volume (V), ventilation rate (f), and PEEP (P_{PEEP}). The ventilation shape was defined by inspiratory time (i) and expiratory time (e). This is represented graphically in Fig. 3. The following MITP formula was used:

$$MITP = \frac{[f \cdot (P_{Plat} - P_{PEEP}) \cdot (2i + e)]}{120} + P_{PEEP} \quad (6)$$

Plateau pressure (P_{Plat}) was calculated using the following formula, which considers alveolar ventilation (VE_{alv}/f), residual volume (V_{RV}), and the inverse of the approximating cumulative normal distribution (Eq. (1)),

$$P_{Plat} = \text{NORMINV} \left[\frac{V_{PPV}}{K \cdot V_{VC}}, P_{mid}, C, 1 \right] \quad (7)$$

where the volume from positive-pressure ventilation (V_{PPV}) can be defined by the contribution of volume from PEEP added to the tidal volume (V_T). This can be represented by the following formula:

$$V_{PPV} = K \cdot V_{VC} \cdot \text{NORMDIST}(P_{PEEP}, P_{mid}, C, 1) + \frac{VE}{f} \quad (8)$$

2.3. Oxygen absorption

The final objective was to derive a formula to predict oxygen absorption as a function of alveolar surface area and pulmonary blood flow in various perfusion states using the following relationship:

$$O_2 \text{ absorption} \propto \text{alveolar surface area} \times \text{pulmonary blood flow} \quad (9)$$

An equation for alveolar surface area was derived in terms of intrathoracic pressure and dead space via dimensional considerations. Since intrapulmonary volume (V) depends on lung dimensional parameters through a cubic relationship (dimension raised to the 3rd power) and surface area through a square relationship (dimension raised to the 2nd power), alveolar lung surface area should depend on intrathoracic pressure (P) via intrapulmonary volume (V) through Eq. (1), using the formula:

$$\text{Alveolar surface area} \sim (V - V_D)^{2/3} \quad (10)$$

2.4. Dynamic model representation

So far, all of the derived equations have described the structural model representations at any instance in time. The value of the structural model is to provide insights into ventilation characteristics when these relationships are integrated over time with alveolar and pulmonary dynamics.

Oxygenation absorption was modeled using the following general formula:

$$\text{Absorption} \sim \sum [\text{alveolar surface area} \times \text{pulmonary blood flow}],$$

an integration of instantaneous absorption over time. This formula is used to explore variations in absorption with ventilation rate and PAP rather than specific absorption values by calculating an amount of absorbed oxygen accumulated over a sufficient time interval to encompass several cycles of pulmonary dynamics (~15 s). This model calculates alveolar surface area in time increments of 0.02 s. The relationship between pressure and volume is modeled using a formula similar to the prior pressure–volume formula, but with the ability to integrate PEEP, inspiratory time (i), and expiratory time (e) and with values calculated in increments of 0.02 s:

$$V = V_R + [K \cdot V_{VC} \cdot \text{NORMDIST}(P_{PPV}, P_{mid}, C, 1)] \quad (11)$$

In this model, pressure is represented by a “sawtooth” function with lower PEEP bound using a modulo mathematical function (MOD),

the IF function, and the greater-than function with the following formulae:

$$P = \text{IF}(\text{MOD}(\text{time}, \text{vent period}) > e, P_{\text{PEEP}}, \text{IF}(\text{MOD}(\text{time}, \text{vent period}) < i, P_{\text{plat}}, P_{\text{plat}} - (P_{\text{plat}} - P_{\text{PEEP}}) \cdot (\text{MOD}(\text{time}, \text{vent period}) - i) / (e - i))) \quad (12)$$

In this formula, pulmonary plateau pressure (P_{plat}) is determined using Eq. (7).

Finally, this model assumes that incremental pulmonary blood flow is determined primarily by the differential between pulmonary artery pressure (PAP) and pulmonary air pressure (P). Pulmonary blood flow was modeled as a linear function of the differential pressure between pulmonary artery pressure (PAP) and pulmonary pressure (P):

$$g \propto (\text{PAP} - P) \quad (13)$$

The cessation of flow is assumed when pulmonary air pressure exceeds pulmonary artery pressure. Pulmonary artery pressure was

defined by the following formula using time increments of 0.02 s:

$$\text{PAP} = \text{PAP}_{\text{sys}} - (\text{PAP}_{\text{sys}} - \text{PAP}_{\text{dia}}) \cdot \text{MOD} \left[\frac{(\text{time} - \text{Phase}, 60/\text{HR})}{(60/\text{HR})} \right] \quad (14)$$

This allows input of systolic (PAP_{sys}) and diastolic (PAP_{dia}) pulmonary artery pressures as well as heart rate (HR). In addition, pulse phase (Phase) can be modeled, which allows adjustment for phasing between airway and pulmonary arterial pressures. For all calculations, the conversion mmHg = 0.736 cm H₂O was used.

2.5. Model evaluation

The main objective was to explore the hemodynamic and oxygen absorption patterns with various ventilator settings, such as tidal volume (V_T), ventilation rate (f), and PEEP. Our first hypothesis was that larger tidal volumes and slower ventilation rates, without the use of PEEP, would lead to lower MITP values in a normal lung. With lower UIP values, as would be observed with ARDS, the “optimal” ventilator settings would include smaller tidal volumes with faster ventilation rates. Thus, the optimal ventilation profile with regard to minimizing the hemodynamic impact should be defined by the UIP. To explore this hypothesis, MITP was

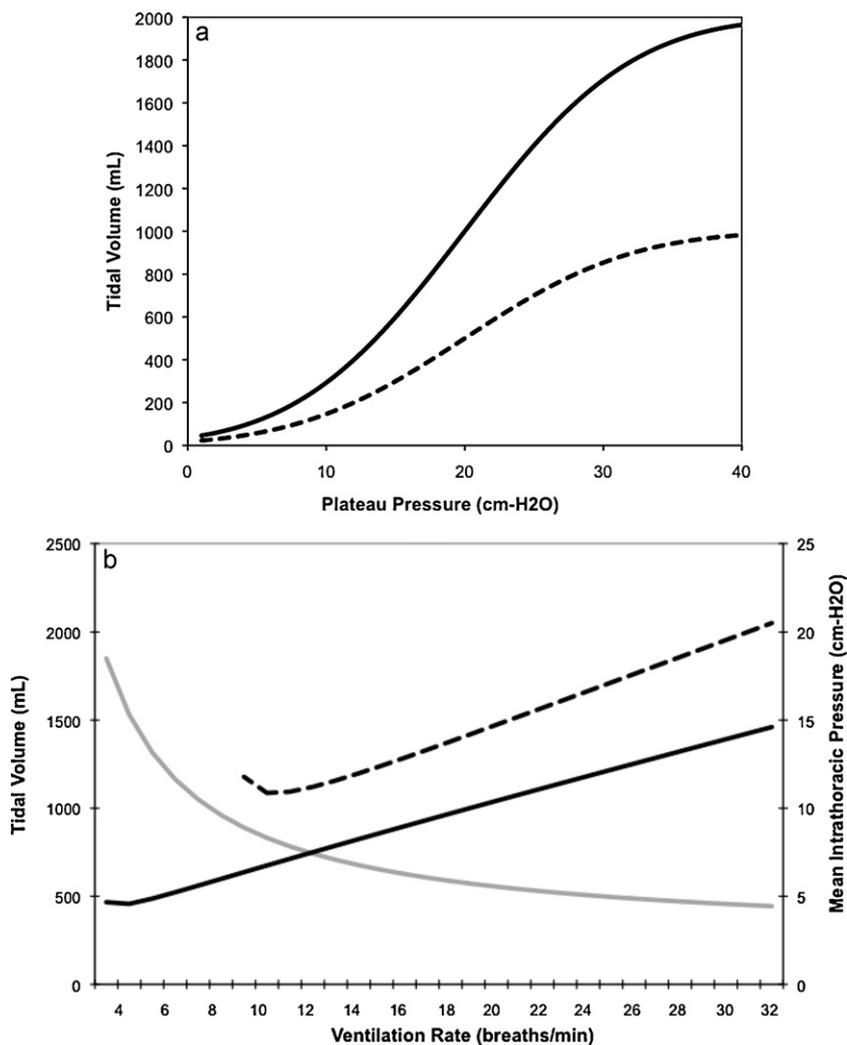


Fig. 4. Standard lung parameters (solid; $K = 0.5$, $V_{\text{VC}} = 4 \text{ L}$, $P_{\text{mid}} = 20$, $C = 9.5$, $\text{PEEP} = 0$, $i = 1$, $e = 2$, $V_D = 350$, $\text{Wt} = 80 \text{ kg}$, $\text{VE} = 6.4 \text{ L}$) vs. lower UIP (dashed; $K = 0.25$, $V_{\text{VC}} = 4 \text{ L}$, $P_{\text{mid}} = 20$, $C = 9.5$, $\text{PEEP} = 0$, $i = 1$, $e = 2$, $V_D = 350$, $\text{Wt} = 80 \text{ kg}$, $\text{VE} = 6.4 \text{ L}$). Note that decreasing the upper inflection point (a), as would be expected with acute respiratory distress syndrome (ARDS) or with extra-pulmonary restriction (tension pneumothorax, burns), results in a higher overall mean intrathoracic pressure (MITP) and a shift to the right with regard to the least hemodynamically intrusive ventilation rate (b).

calculated for various combinations of ventilator settings and lung profiles, with MITP graphed against ventilation rate (f) and plateau volume (V_{plat}).

The second hypothesis concerns ventilation profiles and oxygen absorption. While normal hemodynamic states should result in maximum oxygen absorption with strategies designed to increase surface area, we hypothesized that a threshold pulmonary artery pressure would exist below which the negative impact of ventilation on perfusion would overwhelm the positive impact on surface area. Under these conditions, the optimal ventilation approach with regard to oxygen absorption should again be characterized by larger tidal volumes and slower ventilation rates. In addition, the use of PEEP would be predicted to result in inhibition of pulmonary blood flow and a decrease in oxygen absorption. To explore this hypothesis, various input values for pulmonary artery pressure (PAP), tidal volume (V_T), ventilation rate (f), and PEEP were used to predict oxygen absorption and explored graphically. Constant minute ventilation and FiO_2 1.0 were assumed.

3. Results

The derived pressure-volume formula allows manipulation of various pulmonary mechanical parameters, such as vital capacity (V_{vc}), compliance (C), and midpoint pulmonary pressure

(P_{mid}) to define peak plateau pressure at various inflation volumes (Figs. 1–3). These relationships can then be used to predict MITP for various ventilator settings [tidal volume (V_T), ventilation rate (f), and PEEP (P_{PEEP})], alveolar minute ventilation (VE_{alv}), and dead space (V_D) using the intrathoracic pressure formula.

Assuming normal lung dynamics and ventilation requirements, the model predicts minimal MITP values with larger tidal volumes and slower ventilation rates. Only when the rate is decreased below 5 breaths/min does the resultant tidal volume exceed the UIP, resulting in a rise in MITP (Fig. 4).

If the UIP volume is decreased, as would be observed with ARDS, the model predicts “optimal” ventilator settings (i.e., lowest MITP value) that approach current recommendations for lung-protective ventilation (Fig. 4). Increasing the midpoint pulmonary pressure (P_{mid}) does not change the optimal ventilation rate but changes the slope of MITP (Fig. 5). Similarly, if compliance is decreased, the optimal ventilation rate (i.e., lowest MITP value) does not change, although the rise in MITP becomes steeper to either side of this optimal value (Fig. 6). Adding PEEP increases MITP values but again does not change the optimal ventilation rate (Fig. 7). Lastly, an increase in minute ventilation does not substantially change the pressure-volume curve but does lead to higher tidal volumes – and thus MITP values – at each ventilation rate. This leads to a slight shift in the optimal ventilation rate to the right

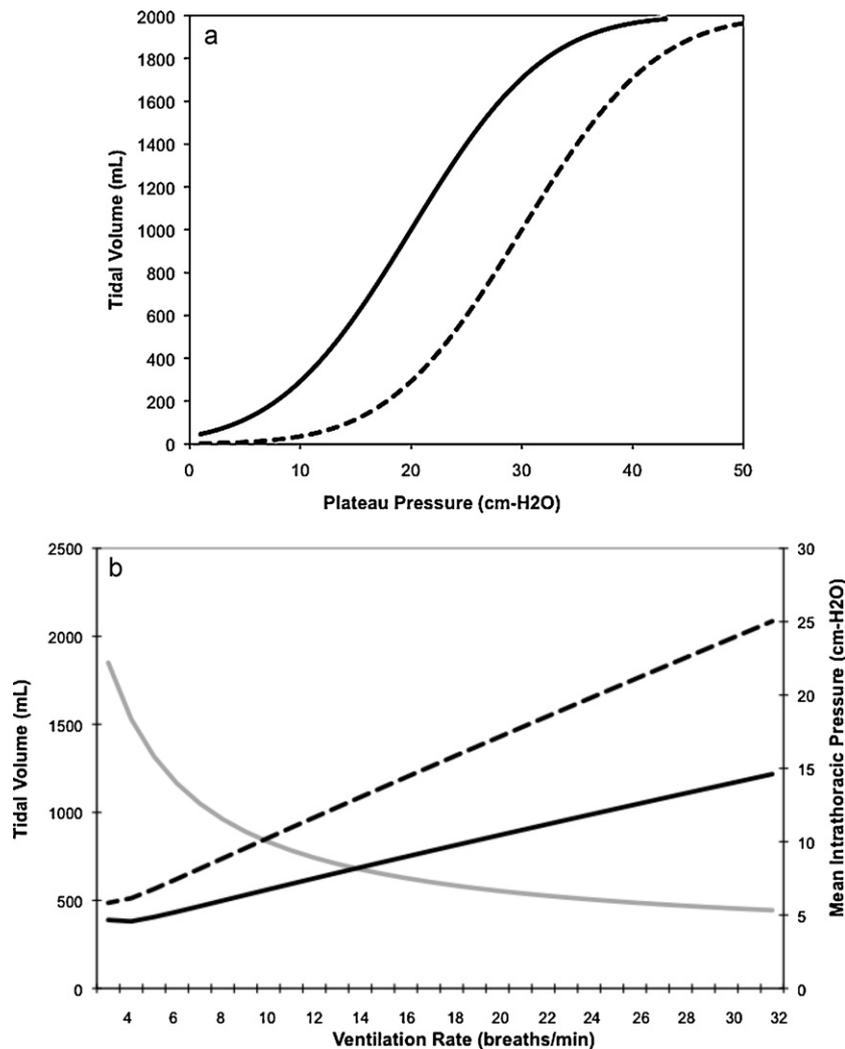


Fig. 5. Standard lung parameters (solid; $K = 0.5$, $V_{vc} = 4$ L, $P_{mid} = 20$, $C = 9.5$, $PEEP = 0$, $i = 1$, $e = 2$, $V_D = 350$, $Wt = 80$ kg, $VE = 6.4$ L) vs. higher P_{mid} (dashed; $K = 0.5$, $V_{vc} = 4$ L, $P_{mid} = 30$, $C = 9.5$, $PEEP = 0$, $i = 1$, $e = 2$, $V_D = 350$, $Wt = 80$ kg, $VE = 6.4$ L). Note that increasing intrinsic intrathoracic pressure by increasing P_{mid} (a) results in higher overall mean intrathoracic pressure (MITP) values but does not shift the least hemodynamically intrusive ventilation rate value (b).

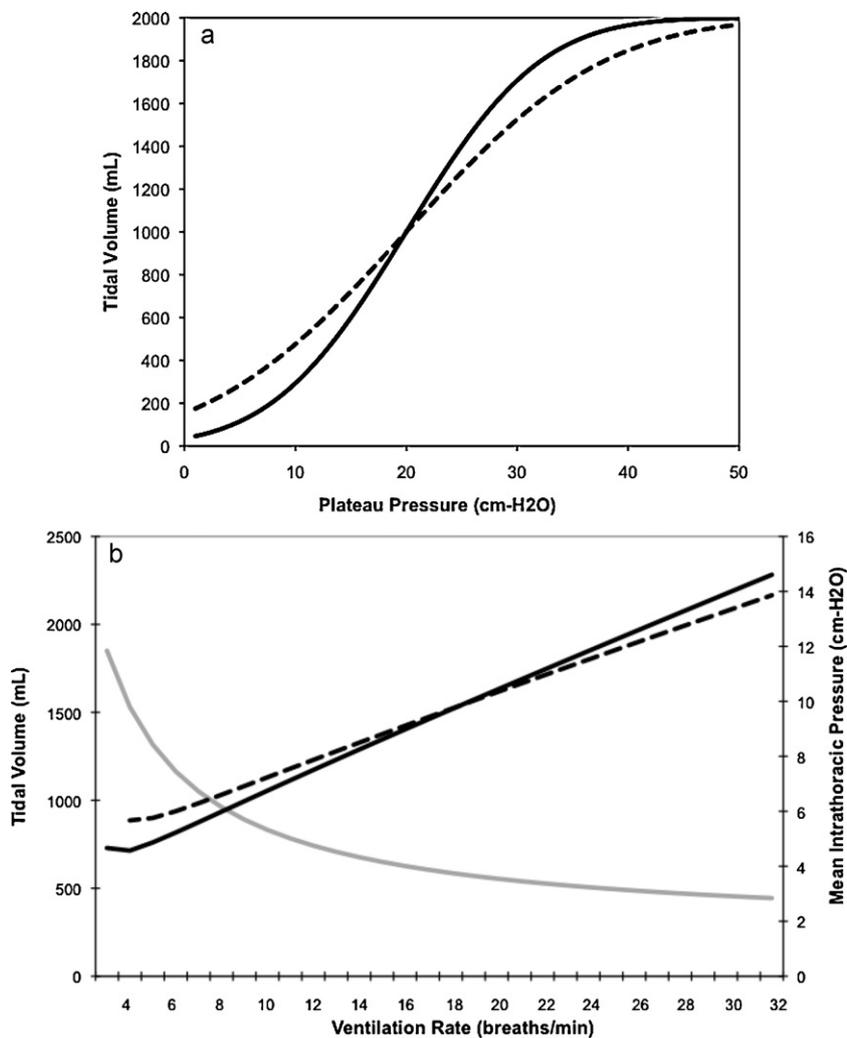


Fig. 6. Standard lung parameters (solid; $K=0.5$, $V_{VC}=4$ L, $P_{mid}=20$, $C=9.5$, $PEEP=0$, $i=1$, $e=2$, $V_D=350$, $Wt=80$ kg, $VE=6.4$ L) vs. lower compliance (dashed; $K=0.5$, $V_{VC}=4$ L, $P_{mid}=20$, $C=14.0$, $PEEP=0$, $i=1$, $e=2$, $V_D=350$, $Wt=80$ kg, $VE=6.4$ L). Note that decreasing pulmonary compliance (a) results in a flatter slope of mean intrathoracic pressure (MITP) versus tidal volume but does not shift the least hemodynamically intrusive ventilation rate value (b).

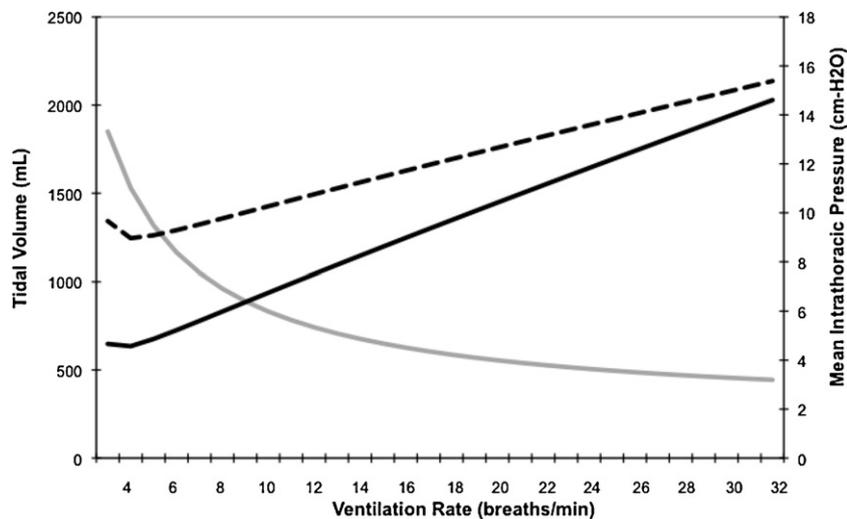


Fig. 7. Standard lung parameters (solid; $K=0.5$, $V_{VC}=4$ L, $P_{mid}=20$, $C=9.5$, $PEEP=0$, $i=1$, $e=2$, $V_D=350$, $Wt=80$ kg, $VE=6.4$ L) vs. higher PEEP (dashed; $K=0.5$, $V_{VC}=4$ L, $P_{mid}=20$, $C=9.5$, $PEEP=10$, $i=1$, $e=2$, $V_D=350$, $Wt=80$ kg, $VE=6.4$ L). Note that adding PEEP increases mean intrathoracic pressure values but does not shift the least hemodynamically intrusive ventilation rate value.

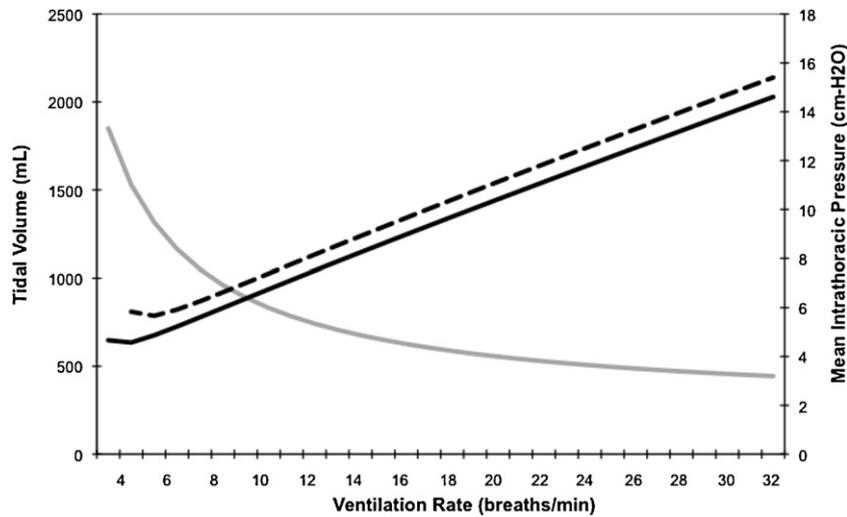


Fig. 8. Standard lung parameters (solid; $K=0.5$, $V_{VC}=4$ L, $P_{mid}=20$, $C=9.5$, $PEEP=0$, $i=1$, $e=2$, $V_D=350$, $Wt=80$ kg, $VE=6.4$ L) vs. higher minute ventilation (dashed; $K=0.5$, $V_{VC}=4$ L, $P_{mid}=20$, $C=9.5$, $PEEP=0$, $i=1$, $e=2$, $V_D=350$, $Wt=80$ kg, $VE=8$ L). Note that increasing minute ventilation increases mean intrathoracic pressure values and shifts the least hemodynamically intrusive ventilation rate value to the right.

(Fig. 8). These data support our hypothesis that the least hemodynamically intrusive ventilation is accomplished with larger, slower breaths until tidal volume exceeds the UIP, at which point additional volume results in a rapid rise in pressure and an increase in MITP. For most lung parameter manipulations, the optimal ventilation rate remains very low. Only with extremely low lung capacities (e.g., ARDS or tension pneumothorax) or with supranormal minute ventilation values does the optimal rate shift to the right.

Modeling oxygen absorption involves a complex relationship between pressure, volume, the fractional concentration of inspired oxygen (FiO_2), and pulmonary blood flow. As a general rule, maximizing surface area – either through larger tidal volumes or the use of PEEP to maintain alveolar surface area during expiration – will result in maximal oxygen absorption. However, input of progressively lower pulmonary artery pressures, as would be observed in hypoperfusion states, reveals a threshold effect where the hemodynamic effects of positive-pressure ventilation limit oxygen absorption by interfering with pulmonary blood flow. In this situation, optimal ventilation to maximize oxygen absorption again favors slower ventilation rates and larger tidal volumes until the UIP is exceeded (Fig. 9).

4. Discussion

Unlike spontaneous ventilation, which enhances cardiac output by augmenting venous return via negative intrathoracic pressure, positive-pressure ventilation may have adverse cardiovascular effects. The clinical impact of these hemodynamic effects has only recently been recognized in low-perfusion states such as hemorrhagic shock and cardiac arrest.^{4-6,20} Here we present a structural model that demonstrates the potential for positive-pressure ventilation to interfere with perfusion and oxygen absorption, especially in the presence of hemodynamic instability.

There are several important implications to these data. This model suggests the optimal ventilation strategy for low-perfusion states includes larger tidal volumes and slower ventilation rates. This approach carries the advantage of minimizing the impact of dead-space ventilation, which results in increased MITP and potential hemodynamic compromise with lower tidal volumes and faster ventilation rates. This effect may be magnified with the additional dead space involved with mechanical ventilation.²¹⁻²³ According to our model, the least hemodynamically intrusive ventilation strategy is defined by tidal volumes that approach the UIP. Tidal

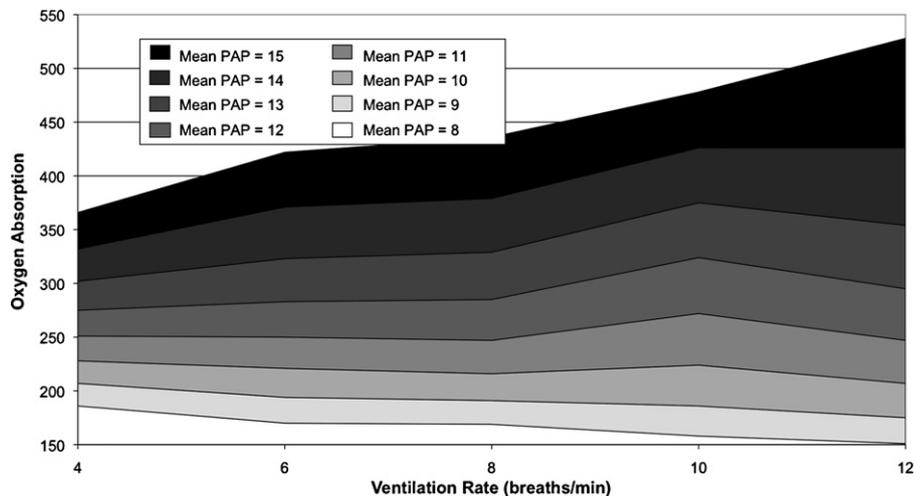


Fig. 9. Oxygen absorption as a function of surface area and pulmonary artery pressure.

volumes that exceed the UIP result in a rapid rise in pulmonary pressure with relatively small increases in volume, exaggerating the hemodynamic effects of positive-pressure ventilation. In addition, overstretch and barotrauma may result at these supratherapeutic tidal volumes. Finally, the routine use of PEEP in low-perfusion states appears to be contraindicated due to the potential for hemodynamic collapse, despite the potential benefits with regard to oxygenation and the avoidance of atelectrauma.^{12–20}

Most clinical data on ventilation has focused on a population of patients with ARDS, where lung-protective ventilation has emerged as the optimal strategy.¹⁴ The primary therapeutic challenge in ARDS is often oxygenation, justifying approaches that maximize alveolar surface area. These include the use of PEEP, increased inspiratory/expiratory ratios, and consideration of ventilation modes such as airway pressure release ventilation (APRV). In ICU patients, intravascular volume and hematocrit have generally been optimized and vasopressor agents can be employed to counteract the hemodynamic effects of positive-pressure ventilation. Interestingly, this model suggests parameters that approach lung-protective ventilation with lower UIP values, as would be observed with ARDS.

The issue of ventilation–perfusion mismatch, which appears to be emerging as an important mediator of lung efficiency during resuscitation, warrants additional discussion.²⁴ The hemodynamic inefficiency of ventilation with smaller tidal volumes and faster rates is related directly to dead space ventilation, which results in excessively high V/Q values. In low-perfusion states, we would anticipate an increase in physiologic dead space, related to ventilation of non-perfused lung units, rather than anatomic dead space, which is related to non-conducting airways or ventilator circuitry.^{21–23} As perfusion status deteriorates, the impact of physiologic dead space ventilation increases, further amplifying the patterns demonstrated here. This could be simulated in this model by increasing the input value for dead space (V_D).

There are multiple limitations to this analysis that warrant additional discussion. Clearly, these data must be validated using *in vivo* animal models and ultimately human data. However, substantial clinical and experimental data support the importance of the hemodynamic effects of positive-pressure ventilation. The balance between the hemodynamic effects and the risk of lung injury due to inflammation and overstretch/barotrauma is almost certainly an individual patient consideration. It is also likely that the risk-benefit ratio with various approaches to ventilation changes as the clinical course evolves. The threshold at which these effects supersede the inflammatory-attenuating effects of lung-protective ventilation as well as the optimal ventilator settings remain to be defined.

This model did not attempt to partition the lung into individual units with regard to the V/Q balance, which appears to be important to both hemodynamic status as well as the impact of various ventilation strategies.²⁴ The effect of oxygen on perfusion to individual lung units and the impact of various pathologies such as ARDS and aspiration, which may affect various lung regions differently, were not addressed. Similarly, oxygen absorption was represented as a predictable, static process but is clearly dynamic, heavily influenced by the health of the underlying alveoli. In addition, the relationship between pressure and volume were simplified for this model but would be expected to be affected by issues related to flow and resistance. For example, we did not attempt to model the upper range of lung volumes above the UIP. However, the model was sufficient to demonstrate a nadir in MITP occurring at the UIP, with additional tidal volume resulting in a rise in MITP. Lastly, the ability of the individual heart to raise pulmonary arterial pressure in hypoperfusion states is highly variable, depending upon the individual patient's cardiac health, volume status, and the underlying disease state. However, there is clearly a threshold below which compensatory mechanisms fail, at which point the principles demonstrated by our model become critically important.

Ultimately, the importance of this structural model is the demonstration of the potential for positive-pressure ventilation to interfere with perfusion and oxygen absorption and to suggest potential strategies to minimize this impact. The model also provides some reassurance that the optimal strategies for ventilation will also enhance rather than interfere with oxygen absorption in low-perfusion states.

5. Conclusions

A structural model was derived to explore the relationship between pulmonary function, ventilation settings, intrathoracic pressure, and oxygen absorption. This model suggests that the least hemodynamically intrusive ventilation strategy involves slower ventilation rates and larger tidal volumes until the upper inflection point of the lung is reached. In addition, the same minimally intrusive ventilation strategy leads to optimal oxygen absorption in low-perfusion states due to the influence of intrathoracic pressure on cardiac output. This model suggests that ICU-derived lung-protective ventilation strategies designed to improve oxygen absorption and minimize barotrauma, biotrauma, and atelectrauma may not be optimal with regard to hemodynamic status during resuscitation.

Conflict of interest statement

No conflict of interest to declare.

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