Tidal Volume Variability During Airway Pressure Release Ventilation: Case Summary and Theoretical Analysis

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Airway pressure-release ventilation (APRV) is used in the management of patients with severe or refractory respiratory failure. In addition to reversal of inspiratory-expiratory ratios, this pressure control mode also allows unrestricted spontaneous breathing. The spontaneous tidal volume (V_T), as well as the V_T resulting from transition between the high and low airway pressures, is uncontrolled. There are limited data on the within-patient variation of actual V_T and the safety of these modes. The authors present a patient with severe ARDS who was managed with biphasic modes (APRV and bi-level positive airway pressure). Serial V_T measurements showed that V_T ranged from 4 to 12 mL/kg predicted body weight. Computed tomography scan images and chest radiographs obtained before and following APRV showed lung parenchyma changes that may be related to ventilator-induced lung injury. We also present a mathematical model that is useful for simulating APRV and demonstrating the issues related to volume delivery for mandatory breaths during the transition between the 2 pressure levels. A key finding of this analysis is the interdependence of release volume, autoPEEP, and the T_{low} time setting. Furthermore, it is virtually impossible to target a specific P_{aCO_2} with a desired level V_T and autoPEEP in a passive model, emphasizing the importance of spontaneous breathing with this mode. This case report suggests caution when using these modes, and that end-inspiratory lung volumes and V_T should be limited to avoid lung injury. The important point of this case study and model analysis is that the application of APRV is more complex than it appears to be. It requires a lot more knowledge and skill than may be apparent from descriptions in the literature. *Key words: airway pressure release ventilation; bi-level; BPAP; mechanical ventilation; ventilator-induced lung injury; ventilator associated lung injury; volutrauma; atelectrauma.* [Respir Care 2012;57(8):1325–1333. © 2012 Daedalus Enterprises]

Introduction

Airway pressure release ventilation (APRV) is a form of pressure control intermittent mandatory ventilation (PC-IMV) typically used in the setting of acute lung injury and severe hypoxemia.[1] During APRV, airway pressure is set at 2 levels, sometimes called P_{high} and P_{low}, for 2 time periods, called T_{high} and T_{low}. These are analogous to inspiratory pressure, PEEP, inspiratory time, and expiratory time, respectively. Two unconventional features of APRV are:

- Extreme inverse inspiratory-expiratory ratio (eg, T_{high} = 4 s and T_{low} = 0.5 s)
- Use of an active exhalation valve that allows unrestricted spontaneous ventilation to occur during T_{high} as well as T_{low}

There are few clinical trials showing that APRV is able to provide improved gas exchange, and it is unclear if APRV results in better clinical outcomes or can worsen lung injury.[2] Particularly, the combination of a pressure control mode and the ability to breathe spontaneously can

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result in unpredictable tidal volume (V_T). Consistently, high V_T has been associated with lung injury and worse outcome in patients with[3] and without[4,5] ALI/ARDS. We report our experience with a patient in whom APRV was used in the setting of severe, refractory hypoxemia, and imaging studies were available before and after the onset of acute illness.

Case Report

A 20-year-old, previously healthy patient, presented to an outside facility with 3 day history of flu like symptoms, including fever, stuffy nose, and cough, with production of purulent sputum. He also reported right upper quadrant pain and vomiting on the day of admission. At admission he was found to have leukocytosis and abnormal liver function tests. Chest computed tomography (CT) scan performed the day following admission showed a small right pleural effusion and infiltrates in the right upper and lower lobes.

The patient was endotracheally intubated on the third day following admission, for laparoscopic surgery. Bronchoscopy performed at that time revealed purulent infiltrates in the right lower lobe. He was extubated following the procedure but developed respiratory distress, and on the day following surgery required endotracheal intubation for mechanical support using pressure control continuous mandatory ventilation (PC-CMV). Respiratory failure progressed rapidly over the next 72 hours, with bilateral diffuse infiltrates evident on radiographs along with severe hypoxia requiring F_{IO_2} of 1.0 and PEEP of 14 cm H_2O to maintain oxygenation. On the third day following intubation for respiratory failure, the patient was transferred to our facility. At that time he was ventilated using PC-CMV (PB 840 ventilator, Covidien, Boulder, Colorado) with an inspiratory pressure (above PEEP) of 24 cm H_2O, PEEP = 14 cm H_2O, and F_{IO_2} = 1.0. The patient was paralyzed using continuous infusion of vecuronium, and sedated with propofol and lorazepam.

During transfer the patient developed a brief period of hypoxemia, to an oxygen saturation of 68%, which responded to manual ventilation. Following arrival at our institution, the patient continued to be hypoxemic, and a decision was made to switch to a non-conventional mode of ventilation, and neuromuscular blockade was discontinued. Bi-level positive airway pressure (BPAP) ventilation (named "BiLevel" on the PB 840 ventilator) was initiated using P_{high} = 35 cm H_2O and P_{low} = 15 cm H_2O (inspiratory pressure[6] = 20 cm H_2O). Spontaneous breaths during P_{high} were not assisted with pressure support. On these ventilator settings, V_T (extracted from the electronic medical record) was documented as varying between approximately 450 mL and 600 mL (7 mL/kg to 9 mL/kg for ideal body weight = 69 kg). This variation in V_T was attributed primarily to the patient's changing inspiratory efforts, which continued throughout the course of mechanical ventilation.

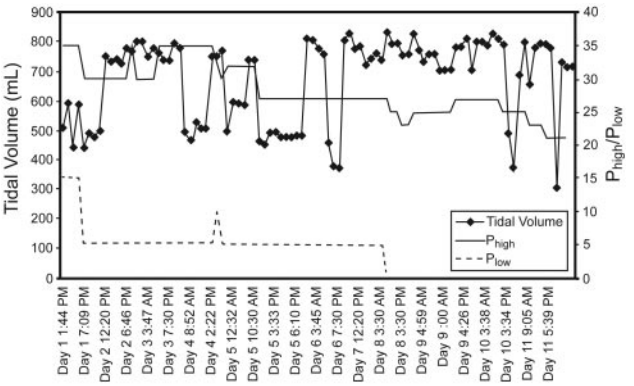

Fig. 1. Time course of mechanical ventilation, showing the tidal volumes that resulted from settings for inspiratory pressure (P_{high}) and end-expiratory pressure (P_{low}).

Within a few hours the BPAP settings were changed to P_{high} = 30 cm H_2O and P_{low} = 5 cm H_2O (inspiratory pressure = 25 cm H_2O). On these ventilator settings, V_T varied between approximately 11 mL/kg and 12 mL/kg from day 2 to day 3. From day 4 to day 8, the V_T variation increased, with values ranging from about 5 mL/kg to 12 mL/kg.

On the 8th day following transfer to our institution, a decision was made to switch to APRV mode, with short

Table 1. Summary of Ventilator Settings and Tidal Volume Ranges

Day	Mode	Tidal Volume, mL/kg	
		P_{low}	P_{high}
1	BPAP	6.4	8.6
1	APRV	6.4	7.1
2	APRV	4.3	11.6
3	APRV	1.4	11.3
4	APRV	5.8	11.2
5	APRV	3.2	11.8
6	APRV	2.2	12.0
7	APRV	1.4	11.3
8	APRV	2.3	12.1
9	APRV	2.3	11.8
10	APRV	2.5	12.0
11	APRV	3.0	11.5

P_{low} = set end-expiratory pressure relative to atmospheric pressure
P_{high} = set peak inspiratory pressure relative to atmospheric pressure
BPAP = bi-level positive airway pressure
APRV = airway pressure release ventilation

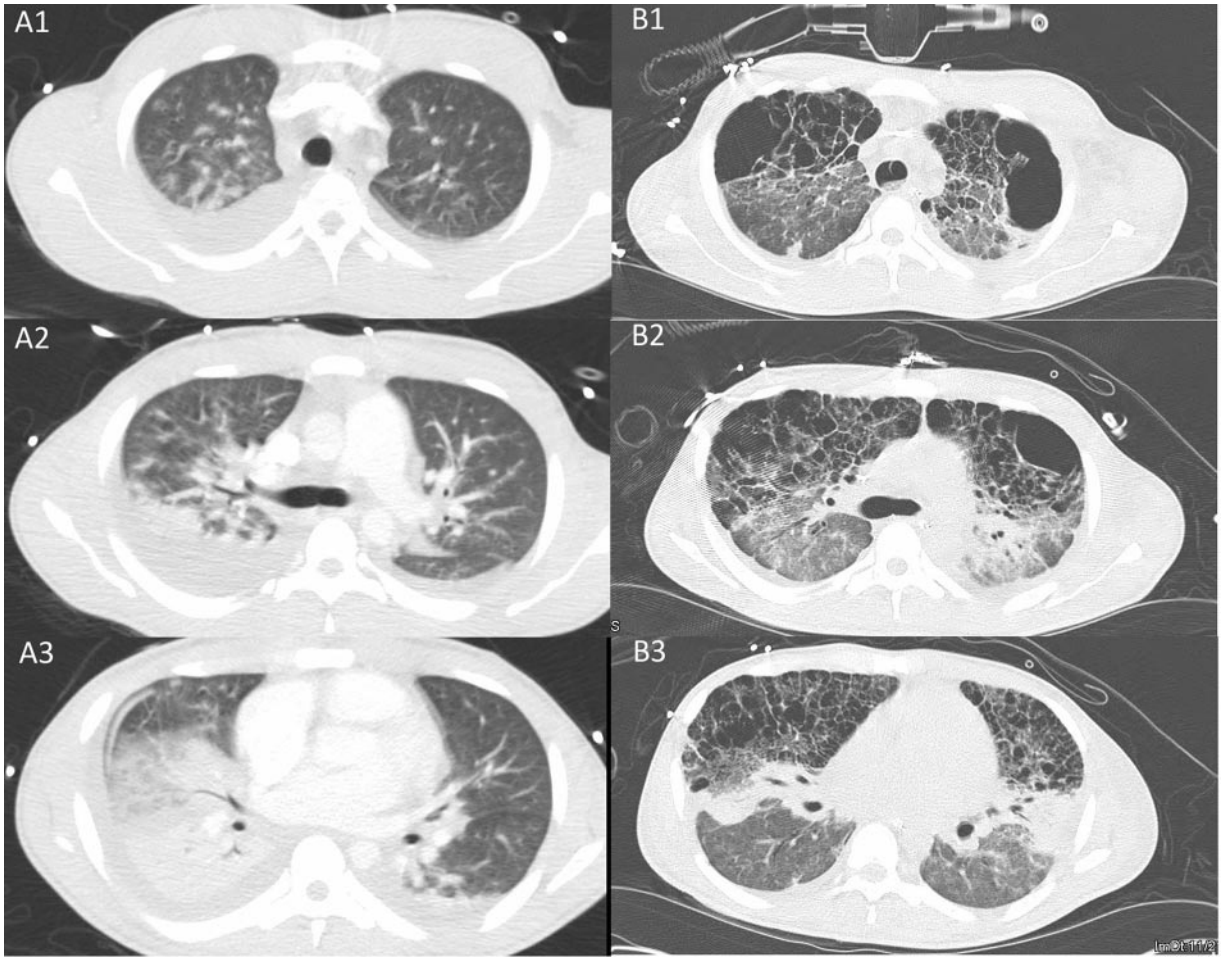

Fig. 2. Representative sections from computerized tomographic images of the chest. Series A1–3 were obtained 2 days after initial onset of flu like symptoms. Series B1–3 were obtained 17 days later. Series A1–3 show typical features of ARDS, with consolidation predominantly in dorsal regions of the lung and bilateral pleural effusions. Seventeen days later, volutrauma is evident, predominantly in the ventral portions of the lung. This suggests that the consolidated portions of the lung were protected from injury due to high volumes.

T_{low} and exhalation to 0 PEEP. Settings were P_{low} = 0 cm H_2O, P_{high} = 25 cm H_2O (inspiratory pressure = 25 cm H_2O), T_{high} = 6.4 s, and T_{low} = 0.3 s, which resulted in a mandatory breath frequency of 9 breaths/min. When the patient was switched to APRV, the V_T ranged from approximately 4 mL/kg to 12 mL/kg).

Figure 1 shows the time course from measured values of V_T and airway pressure. Table 1 summarizes the ventilator modes associated with the V_T observed during the course of mechanical ventilation.

Comparison of CT scans from admission and day 12 shows extensive ventilator-associated lung injury (Fig. 2). Serial chest radiographs show the progression of lung damage (Fig. 3). A week later the patient underwent a tracheostomy procedure and was gradually weaned from mechanical ventilation. Twenty-four days after his transfer, the patient was discharged to a skilled nursing facility for occupational therapy and physical therapy.

Discussion

In the simplest terms, the goals of mechanical ventilation are to promote safety, comfort, and liberation.[7] The goal of safety includes the objectives of optimizing both gas exchange and the pressure-volume relation of the lungs. The latter objective implies that mean lung volume is adjusted such that compliance is maximized. Mean lung volume is a function of both the end-expiratory lung volume (eg, by setting "optimal" PEEP) and V_T. V_T is the only variable shown to directly affect long-term outcomes in mechanically ventilated patients.[8] In particular, for patients with ARDS, the objective should be to keep V_T within approximately 6–8 mL/kg, with larger V_T presumably increasing morbidity and mortality. For this reason, some clinicians prefer volume control modes because V_T is naturally more variable with pressure control modes. As a form of pressure control, both APRV and BPAP involve a

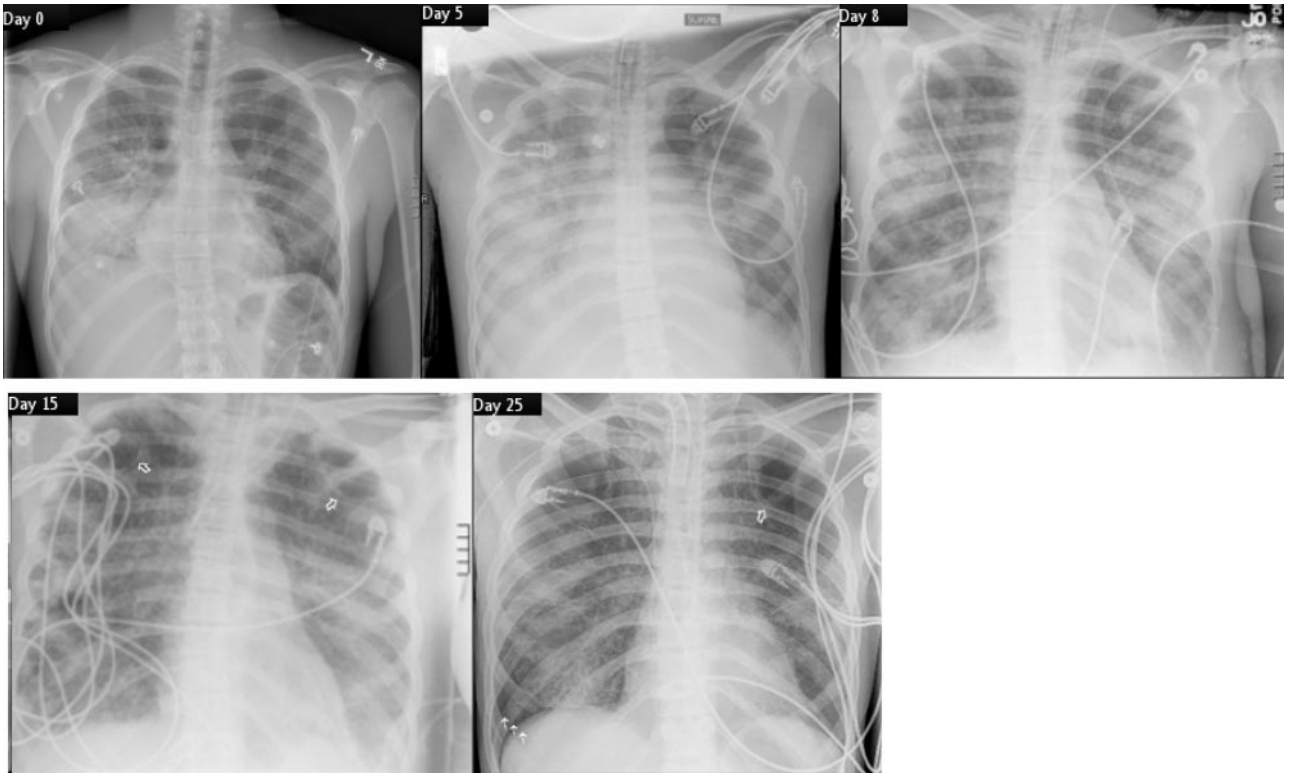

Fig. 3. Representative chest radiographs that show the evolution of ventilator-induced lung injury. On days 0 and 5, when the patient was on pressure control continuous mandatory ventilation, there is no evidence for ventilator-induced lung injury. However, hyperinflation of the left lung is evident. On day 8, after 3 days of ventilation in APRV/BiLevel, areas of hyperlucency are evident on both sides. By day 15, cystic changes are evident (open arrows). Day 25 shows progression of lung injury with pneumothorax on the lower right side (3 arrows).

number of factors that may increase V_T variability, compared to other modes in this category. Indeed, Kallet has observed that "Of the APRV studies that have measured release volumes, mean volumes have been reported between 550 mL to 840 mL and 9 mL/kg by measured body weight, which probably translates into 11 mL/kg predicted body weight. In many studies these values exceeded current lung-protective ventilation targets."[9]

We will now review the factors contributing to V_T variability as they relate to our case study. Some authors assert that "Rather than generating a tidal volume by raising the airway pressure above the set PEEP, release volumes in APRV are generated by briefly releasing airway pressure from P_{high} to P_{low}. Because ventilation with APRV results as airway pressure and lung volume decrease, the risk of over-distention may be reduced."[10] The common description of biphasic modes as "2 levels of CPAP" is misleading, as it obscures the fact that the transition from P_{low} to P_{high} and from P_{high} to P_{low} constitutes a mandatory breath (ie, inspiration is machine triggered and machine cycled[7]), just as in any other form of PC-IMV. We have observed that when clinicians fail to recognize that mandatory breaths are being delivered, they also overlook the associated V_T and tend to focus only on the spontaneous breathing activity of the patient. They also seem to think that because the patient spends the majority of the time at P_{high}, adequate lung volume is being maintained and the brief "pressure releases" are inconsequential in terms of lung derecruitment.

The data from this case study suggest that such ideas are indeed misconceptions. Ventilator-associated lung injury is generally thought to occur both as a result of repetitive collapse and reopening of lung units due to inadequate end-expiratory pressure (atelectrauma) and as the result of stretch injury due to excessive end-inspiratory volumes (volutrauma).[11] APRV in this patient resulted in unknown levels of end-expiratory pressure and V_T that was higher than the generally accepted target of 6 mL/kg for patients with ARDS. The CT scans suggest that severe ventilator-associated lung injury occurred. Representative chest radiographs (see Fig. 3) show the evolution of ventilator-induced lung injury (VILI). There is no evidence for VILI from days 0–5, when the patient was on PC-CMV. However, hyperinflation of the left lung is evident. On day 8, after 3 days of ventilation in APRV/BiLevel, areas of hyperlucency are evident on both sides. Cystic changes are evident by day 18 (open arrows) and progression is evident by day 25, with pneumothorax on the right side.

The culture of the purulent infiltrates obtained from bronchoscopy were negative, with many epithelial cells. While necrotizing pneumonia can present with cavitary lung disease, the CT appearance is very distinctive. Also note that the cystic disease involved the non-consolidated areas of the lung and hence is pathognomonic of VILI. We do not believe that APRV "caused" VILI in this patient: only that it was associated with a large variation in V_T, and that the V_T was large enough to potentially contribute to volutrauma. Although our data cannot be used to imply causation, we can certainly call into question the "lung-protective" features of APRV when no lung-protective parameters (ie, end-expiratory pressure and V_T) are explicitly monitored and managed.

The transpulmonary pressure difference (pressure at the airway opening minus pressure in the pleural space) determines lung volume change and is usually not monitored during mechanical ventilation. Reduced thoracic and abdominal compliance in critically ill patients may require higher airway pressure to achieve the transpulmonary pressure difference that provides acceptable volume change.[12] Spontaneous breathing efforts, however, superimpose marked variability in transpulmonary pressure and therefore V_T. Some ventilators allow the assistance of spontaneous breaths using pressure support. If used, this additional assistance may not only further increase V_T variability but will alter the relationship between APRV settings and expected P_{aCO_2}, because it affects the proportion of work performed by the patient versus the ventilator. Setting APRV pressure targets to predefined arbitrary limits does not guarantee V_T limitation, as documented by our case report. In addition, the fortuitous availability of imaging studies in this patient indicates that the higher V_T resulting from the large transpulmonary pressure differences may not necessarily result in improvement of dependent lung, but, rather, in over-distention and volutrauma.

Practical Implications of Case Study

The term APRV, first described by Stock et al,[1] is used loosely in the literature and often confused with biphasic positive airway pressure (BIPAP), as first described by Baum et al.[13] Both are classified[14] as pressure control intermittent mandatory ventilation (PC-IMV) (ie, mandatory breaths that are time triggered, pressure targeted, and time cycled, with spontaneous breaths possible during and between mandatory breaths). Some adult ventilators (notably those made by Dräger) and almost all infant ventilators have always allowed unrestricted spontaneous breathing during mandatory pressure control breaths, while others have not. Newer ventilators have added APRV capability to their list of modes, under various proprietary names, such as "BiLevel" (Covidien PB 840), "Airway Pressure Release Ventilation" (Dräger Evita XL and Hamilton G5), "Duo Positive Airway Pressure" (Hamilton G5), and "Bi-Vent" on the Maquet Servo-i. Ironically, you can now find within a single ventilator *both* a mode that is PC-IMV with spontaneous *inspiration* (but not expiration) permitted *during* mandatory breaths, and PC-IMV with unrestricted spontaneous breathing (inspiration and expiration) during mandatory breaths (eg, PC-IMV vs BiLevel on Covidien PB 840).

The difference between BIPAP and APRV is in the timing of the upper and lower pressure levels. In BIPAP, T_{high} is usually shorter than T_{low}.[15] Therefore, in order to avoid derecruitment, P_{low} has to be set above zero. Rose et al found that, compared to BIPAP, APRV was described more frequently as extreme inverse inspiratory-expiratory ratio and used rarely with non-inverse ratios. One BIPAP and 8 APRV studies used mild inverse ratio (1:1 to 2:1). There was increased use of 1:1 ratio with BIPAP. In adult studies, the mean P_{high} was 6 cm H_2O greater with APRV than with BIPAP. For both modes, the mean reported P_{low} was 5.5 cm H_2O.[16] To make things even more confusing, the term BiPAP is used on Philips Respironics ventilators to signify pressure control continuous spontaneous ventilation (PC-CSV) (ie, breaths are patient triggered, pressure targeted, and flow cycled, also known as pressure support). We prefer the term "biphasic" as a generic name to distinguish pressure control modes with unrestricted spontaneous breathing during mandatory breaths from conventional PC-IMV and PC-CSV.

Unlike conventional PC-CMV on most adult ventilators (often called "pressure control mode"), APRV accommodates the patient's breathing pattern and allows superimposition of spontaneous breathing on mandatory breaths.[17] Peak airway pressure in APRV does not exceed the set level, and spontaneous breathing efforts augment minute ventilation. One of the important goals of APRV is to promote spontaneous breathing. A theoretical benefit of allowing spontaneous ventilation to occur during mechanical ventilation is to preserve diaphragmatic activity and therefore ventilation to the dependent areas of the lung.[18,19]

Theoretical Analyses Using a Mathematical Lung Model

The practice of setting P_{low} to zero and relying on autoPEEP to maintain end-expiratory lung volume deserves some consideration. Proponents of APRV recommend T_{low} values in the range of 0.2–0.8 seconds[10,12] to achieve adequate autoPEEP, although in practice autoPEEP is virtually impossible to measure when the patient is making active inspiratory efforts. What has not been adequately addressed in the literature is the difficulty of managing ventilatory parameters due to the interdependence of autoPEEP and mandatory breath tidal volumes (ie, the tidal volumes resulting from the transition of P_{low} to P_{high}

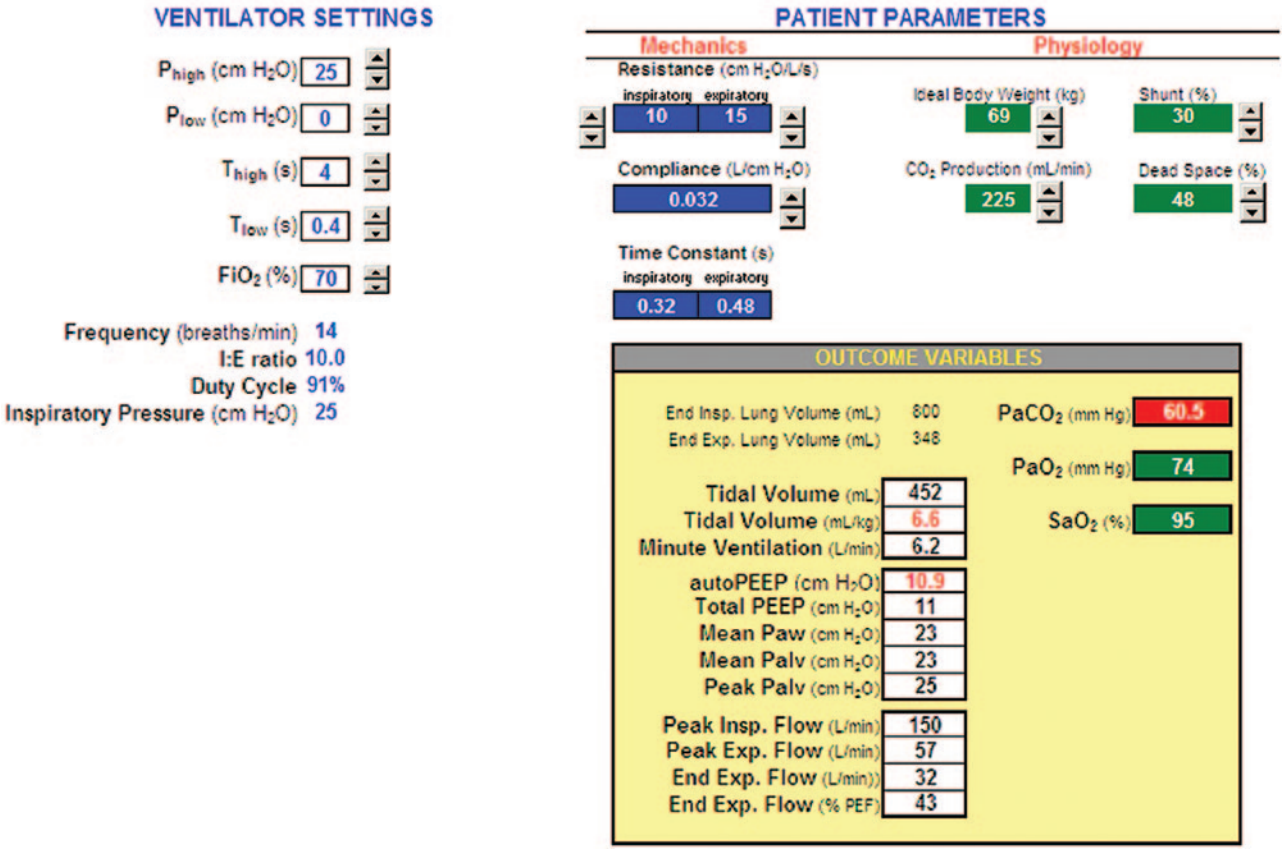

Fig. 4. Patient-ventilator simulator implemented with a spreadsheet (see text for explanation).

Table 2. Equations for Mathematical Model of Pressure Control Ventilation

Symbol	Definition or Equation
C	Respiratory-system compliance, L/cm H_2O
R_I	Inspiratory resistance, cm H_2O/L/s
R_E	Expiratory resistance, cm H_2O/L/s
T_I	Inspiratory time, s
T_E	Expiratory time, s
V_T	Tidal volume, L
k_I	$1/(R_I \cdot C)$
k_E	$1/(R_E \cdot C)$
ΔP	$P_{high} - P_{low}$, cm H_2O
mP_{aw}	Mean airway pressure, cm H_2O
aPEEP	AutoPEEP, end-expiratory pressure above set P_{low}, cm H_2O
PEF	Peak expiratory flow
V_{EE}	End-expiratory volume, L
V_{EI}	End-inspiratory volume, L
V_T	$V_T = [\Delta P \cdot C \cdot (1-e^{-k_I T_I}) \cdot (1-e^{-k_E T_E})]/(1-e^{-k_E T_E} \cdot e^{-k_I T_I})$
V_{EI}	$V_{EI} = V_{EE} + V_T$
V_{EE}	$V_{EE} = V_T \cdot (e^{-k_T T_E})/(1-e^{-k_E T_E}) + (C \cdot P_{low})$
aPEEP	$aPEEP = V_T \cdot e^{-k_E T_E}/[C \cdot (1-e^{-k_E T_E})]$
PEF	$(V_T/C)/R_E$
mP_{aw}	$mP_{aw} = \Delta P \cdot [T_I/(T_I + T_E)] + P_{low}$

and vice versa). To demonstrate this, we developed a spreadsheet based model (Fig. 4, free download available at http://www.mediafire.com/view/?23psqtqhc58pb88) using the equations governing pressure control ventilation developed by Marini et al[20] (Table 2). The model simulated a ventilator with APRV settings connected to a patient with lung mechanics that might be observed in patients with ARDS.[21] The ventilator settings were: P_{high} =

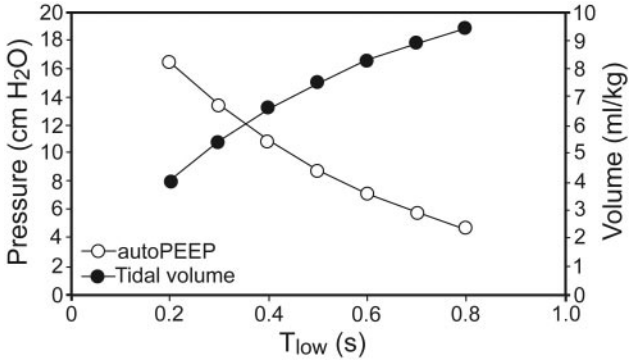

Fig. 5. This figure illustrates the interdependence of autoPEEP, tidal volume, and the T_{low} setting.

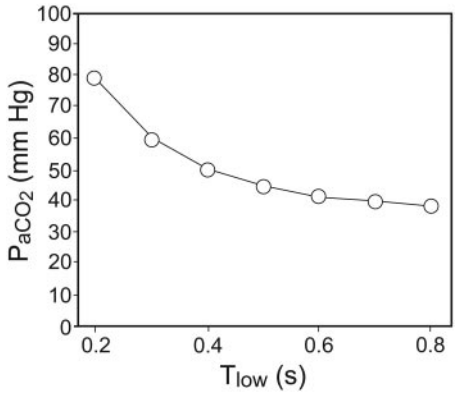

Fig. 6. This figure illustrates the dependence of simulated P_{aCO_2} on the T_{low} setting.

25 cm H_2O, P_{low} = 0 cm H_2O, T_{high} = 4 seconds, T_{low} = 0.2 seconds to 0.8 seconds. The patient (ideal body weight = 69 kg) was modeled by inspiratory resistance = 10 cm H_2O·s/L, expiratory resistance = 15 cm H_2O·s/L, and compliance = 32 mL/cm H_2O, with no inspiratory effort. Dead space as a percentage of V_T was arbitrarily set at 48%. P_{aCO_2} was simulated using the equation[22]:

$$P_{aCO_2} \approx (K \times \dot{V}_{CO_2})/\dot{V}_A$$

where $\dot{V}_{CO_2}$ is carbon dioxide production (set to a normal value[23] of 225 mL/min at standard temperature and pressure dry), $\dot{V}_A$ is alveolar ventilation (in L/min at body temperature and pressure saturated), and K reconciles mL versus L, standard temperature and pressure dry versus body temperature and pressure saturated units, and converts volumetric fraction to partial pressure at sea level ($760 \times 310/273 \times 1/1{,}000 = 0.863$).[24] Note that the model differs from the human state in that air-flow resistance often varies among patients and even within a patient as bronchospasm or retention of secretions occurs. Accordingly, in some patients, autoPEEP can increase to dangerous levels in a patient ventilated using APRV with a very short expiratory time

The calculated values for autoPEEP (equivalent to total PEEP or end-expiratory lung pressure because set PEEP was zero), V_T (from mandatory breaths), and simulated P_{aCO_2} were plotted against values of T_{low}. Figure 5 shows the interdependence of autoPEEP and V_T. AutoPEEP ranged from 4.7 cm H_2O (T_{low} = 0.8 s) to 16.5 cm H_2O (at T_{low} = 0.2 s). Thus, at some T_{low} settings, end-expiratory

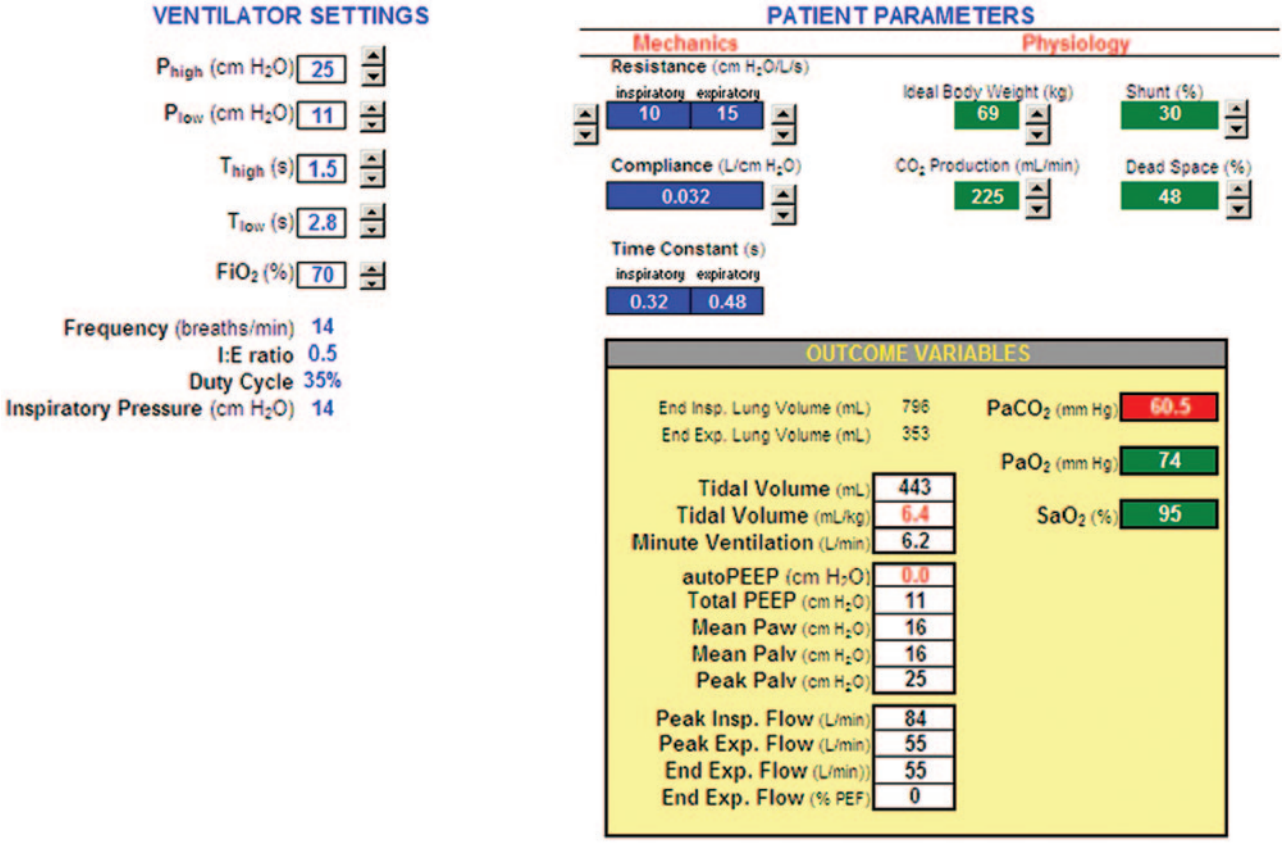

Fig. 7. Simulated ventilator with BIPAP setting (inspiratory-expiratory ratio < 1:1) with the same end-expiratory lung pressure, tidal volume, and alveolar ventilation, but lower mean airway pressure, compared to APRV in Figure 4.

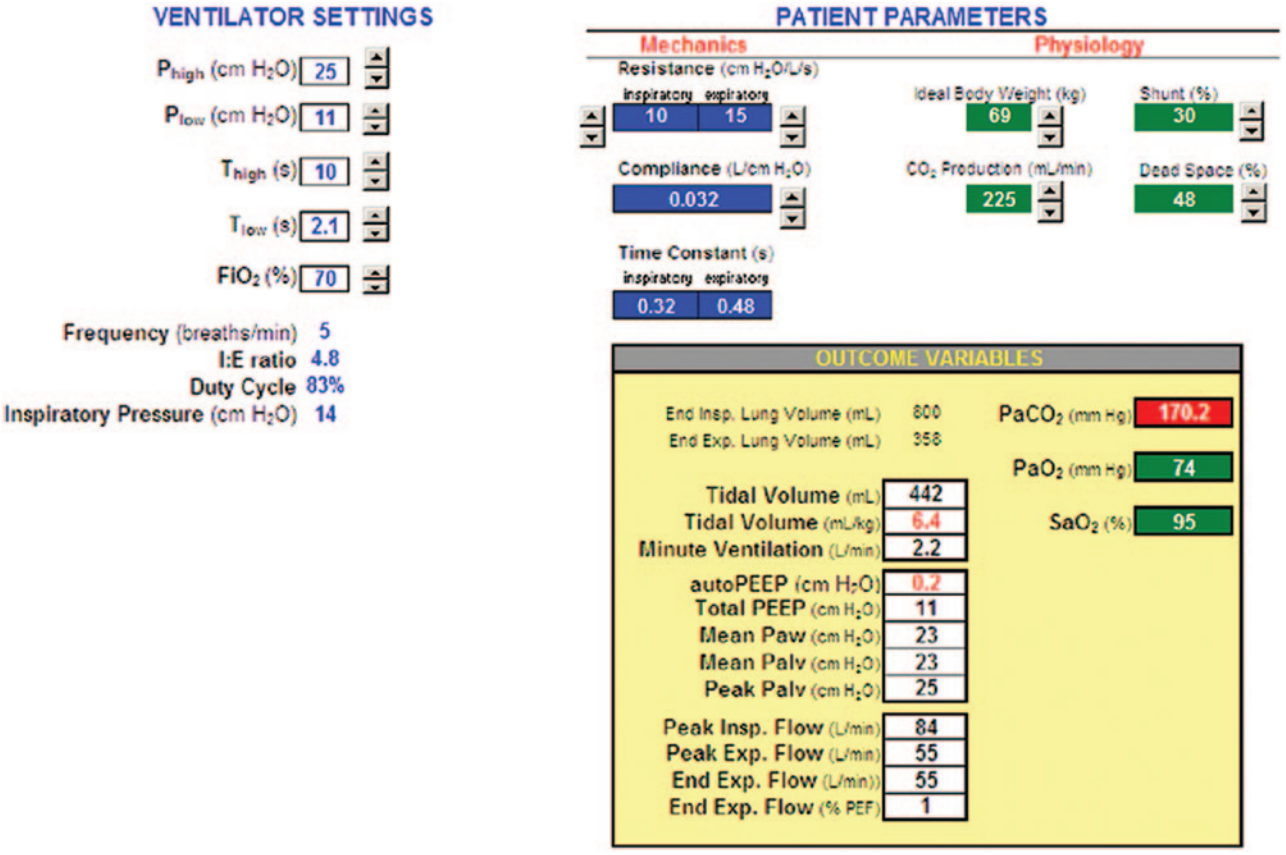

Fig. 8. Simulated ventilator with BIPAP setting (inspiratory-expiratory ratio < 1:1), with the same end-expiratory lung pressure, tidal volume, and mean airway pressure, but lower alveolar ventilation, compared to APRV in Figure 4.

lung pressure is unlikely to provide "optimum PEEP" for a patient with ARDS,[25] particularly given the presumption that the lung is recruitable, and thus it is appropriate for the patient to spend most of his time at a relatively high "CPAP" level (eg, 20–35 cm H_2O).[10,12] We concede that the meaning of "optimum PEEP" is debatable.[26] Consideration of appropriate end-expiratory pressure/lung volume is critical, given the general acceptance of the idea that cyclical alveolar opening and closing is injurious to patients with acute lung injury or ARDS.[27] V_T ranged from 4.0 mL/kg (T_{low} = 0.2 s) to 9.4 mL/kg (T_{low} = 0.8 s). In this simulation, T_{low} values above 0.4 s resulted in V_T greater than the generally accepted safe upper limit of 6 mL/kg.[8] Simulated P_{aCO_2} (Fig. 6) ranged from 46.0 mm Hg (T_{low} = 0.8 s) to 95.9 mm Hg (at T_{low} = 0.2 s). The values expected for P_{aCO_2} in a real patient would be less, depending on how much spontaneous minute ventilation the patient could generate. However, the V_T range would be greater, due to the contribution of inspiratory muscle pressure change to the ventilator's inspiratory driving pressure ($P_{high} - P_{low}$), assuming the use of a ventilator that synchronized mandatory breaths with spontaneous efforts (eg, PB 840 and Evita XL).

This simulation demonstrates the difficulty of applying APRV with zero P_{low}. That is, we find it virtually impossible to target a specific P_{aCO_2} with a desired level V_T and autoPEEP in a passive model. What this implies is that APRV is not a good choice for full ventilatory support. Granted, APRV is intended for partial support, but this exercise indicates the extent to which patients must regulate their own P_{aCO_2} with spontaneous ventilation. Furthermore, the instantaneous values of V_T and autoPEEP are even more unpredictable when factoring in spontaneous breathing efforts and the effect on the total system (ie, patient and ventilator) time constant of the resistance of the ventilator's expiratory manifold. Data from our lab show that there is a wide variance between the expiratory flow curve predicted by a mathematical model and actual flow curves using different ventilators.[28] Furthermore, the patient's time constant changes substantially (by increasing resistance) with accumulation of secretions in the airways. Airway resistance can easily double by the time the patient shows obvious signs of the need for suctioning. Also, the respiratory system time constant is affected by changes in lung and chest wall compliance. In particular, in the absence of paralysis, transient (and unpredictable)

changes in chest/abdominal muscle tension may decrease chest wall compliance, adding further uncertainty to this clinical problem. All of this might argue against APRV (with $P_{low} = 0$) in favor of BIPAP (with P_{low} set to optimal PEEP), because with the latter we can achieve relative independence of V_T from T_{low}, provided that T_{low} is more than about 3 expiratory time constants. Figure 7 shows that by using a BIPAP strategy it is possible to obtain the same level of ventilation with the same V_T and peak inspiratory pressure (as in Fig. 4) as APRV by simply setting P_{low} to the level of autoPEEP and decreasing T_{high}. What you lose is mean airway pressure, which, in this example, decreases from 23 to 14.5 cm H_2O. On the other hand, you can keep the same mean airway pressure by increasing T_{high} (Fig. 8), but now the patient has to make up for the decrease in minute ventilation caused by the reduction in mandatory breath frequency from 14 to 5 breaths/min. So the tradeoff, to simplify, is between safety (predictable V_T and end-expiratory pressure) and comfort (ie, patient work of breathing). Clearly, these issues require further study.

In conclusion, we advise the reader not to draw conclusions regarding causation from a single case report. However, our findings and their theoretical underpinnings should alert users of biphasic modes to their potential complications. The important point of this case study is that the application of biphasic modes requires a lot more knowledge and skill than may be apparent from descriptions in the literature. When patients are mechanically ventilated using pressure control modes of ventilation that encourage superimposed spontaneous ventilation, such as with biphasic modes, we recommend that close attention be paid to V_T, and when possible, autoPEEP. Respiratory drive, and hence spontaneous V_T and autoPEEP levels, may be labile and depend on levels of sedation. This is especially important when ICU protocols implement daily awakening trials into their routine practice.

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