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Adaptive support ventilation with and without end-tidal CO_2 closed loop control versus conventional ventilation

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Abstract *Purpose:* Our aim was to compare adaptive support ventilation with and without closed loop control by end tidal CO_2 ($ASVCO_2$, ASV) with pressure (PC) and volume control ventilation (VC) during simulated clinical scenarios [normal lungs (N), COPD, ARDS, brain injury (BI)]. *Methods:* A lung model was used to simulate representative compliance (mL/cmH_2O): resistance (cmH_2O/L/s) combinations, 45:5 for N and BI, 60:7.7 for COPD, 15:7.7 and 35:7.7 for ARDS. Two levels of PEEP (cmH_2O) were used for each scenario, 12/16 for ARDS, and 5/10 for others. The CO_2 productions of 2, 3, 4 and 5 mL/kg predicted body weight/min were simulated. Tidal volume was set to 6 mL/kg during VC and PC. Outcomes of interest were end tidal CO_2 ($etCO_2$) and plateau pressure (P_{Plat}).
Results: $EtCO_2$ levels in N and BI and COPD were similar for all modes. In ARDS, $etCO_2$ was higher in $ASVCO_2$ than in other modes ($p < 0.001$). Under all mechanical conditions $ASVCO_2$ revealed a narrower range of $etCO_2$. P_{Plat} was similar for all modes in all scenarios but ARDS where P_{Plat} in ASV and $ASVCO_2$ were lower than in VC ($p = 0.001$). When P_{Plat} was $\geq$28 cmH_2O, P_{plat} in ASV and $ASVCO_2$ were lower than in VC and PC ($p = 0.024$). *Conclusion:* All modes performed similarly in most cases. Minor differences observed were in favor of the closed loop modes. Overall, $ASVCO_2$ maintained tighter CO_2 control. The $ASVCO_2$ had the greatest impact during ARDS allowing $etCO_2$ to increase and protecting against hypocapnia evident with other modes while ensuring lower P_{plat} and tidal volumes.

Keywords Mechanical ventilation · Adaptive support ventilation · Closed loop control · ARDS · COPD · Brain injury

Introduction

Adaptive support ventilation (ASV) is a form of pressure targeted closed loop ventilation, designed to optimize the relationship between tidal volume and respiratory frequency based on lung mechanics as predicted by Otis [1]. Adaptive support ventilation provides a ventilatory pattern that minimizes the work of breathing (WOB) and auto positive end expiratory pressure (autoPEEP or intrinsic PEEP) while limiting peak airway pressure. ASV automatically determines the tidal volume (V_T) and respiratory rate (RR) that best maintains the peak pressure below the target level and minimal WOB [2].

Recently we demonstrated in a lung model that ASV was better able to maintain plateau pressures (P_{Plat}) <28 cmH_2O than a fixed tidal volume of 6 mL/kg during volume controlled ventilation (VC) [3]. In that evaluation ASV varied V_T between 2.9 and 9.0 mL/kg, however, when V_T fell below its lower limit of 4.3 mL/kg the ventilator alarmed notifying us of the marked reduction. The algorithm used by the ASV mode considered lung mechanics in its adjustment; no reference to gas exchange was incorporated. Recently, a new algorithm for ASV has added closed loop control of $etCO_2$ in parallel to the current closed loop control by lung mechanics ($ASVCO_2$).

In this study, our aim was to compare the performance of ASV and $ASVCO_2$ to that of pressure control ventilation (PC) and VC during simulated normal lungs, ARDS, COPD, and brain injury scenarios and to compare the ability of all modes to maintain P_{Plat} below a set target as respiratory mechanics and CO_2 production varied. Our hypothesis was that $ASVCO_2$ would maintain $etCO_2$ within a normal range predefined for specific conditions compared to levels achieved using other ventilator modalities, delivering clinically acceptable tidal volumes whilst avoiding clinically significant hypocapnia or hypercapnia across a range of respiratory mechanics, PEEP, minute ventilation and CO_2 production levels. Further, that $ASVCO_2$ will achieve this outcome with peak pressure plateaus less than a target pressure of 28 cmH_2O. This pressure was chosen based on the recommended maximum plateau pressure in the ARDSnet protocol [4].

Materials and methods

Experimental setup

The Michigan Instruments Dual Adult Training/Test Lung (Model 1600 Michigan Instruments Inc., MI, USA) with CO_2 titrated into one of the test lung chambers was utilized throughout the study. The Galileo Ventilator (Galileo) (Hamilton Medical, Bonaduz, Switzerland) was used for ASV, VC and PC modes and a modified Hamilton G5 Ventilator (G5) (Hamilton Medical, Bonaduz, Switzerland) was used for $ASVCO_2$. Disease specific algorithms in the G5 were used for the specific simulated lung mechanics scenarios. These algorithms included 'Normal Lungs', 'ARDS', 'COPD', and 'Brain Injury' states. One chamber of the Michigan Instruments test lung was passively ventilated during all modes. The Hamilton Medical standard adult circuit was used with both ventilators. The study was conducted without the inclusion of an active humidifier to avoid water contamination in the lung model. The lung model was directly connected to the circuit wye; no endotracheal tube was included.

Ventilation strategies

In all ventilator modes inspiratory time was set at 0.8 s. The target minute volume (MV) was set either to 100, 150 or 200 % of predicted healthy normal MV of 0.1 L/kg predicted body weight (PBW) [5] for a 70 kg PBW individual during ASV, VC and PC (Table 1). The flow waveform in VC was square and peak flow was set to insure that active delivery of the V_T occurred over the entire inspiratory time. In PC, the ventilating pressure was set to result in a V_T of 6 mL/kg. ASV determined the respiratory rate and tidal volume based on its algorithms. The pressure limit alarm was set at 38 cmH_2O (10 cmH_2O higher than the desired peak pressure) in ASV and $ASVCO_2$ to insure that peak pressure was maintained $\leq$28 cmH_2O. The ventilators maintained a 10 cmH_2O window of pressure above the target pressure where alarms were activated if pressure exceeds the target level.

Lung model settings

Measurements were obtained during simulation of four different clinical scenarios for mechanical ventilation including the normal lung, ARDS, COPD and brain injury. For each scenario, combinations of lung model compliance, resistance, target minute volume, PEEP, and CO_2 production rate were applied as defined in Table 1. Compliance and resistance settings were based on typical lung mechanics reported in normal lung conditions, patients with severe ARDS/acute lung injury and with COPD [4, 6–11]. For VC, PC and ASV, this approach resulted in 16 unique testing conditions for the normal lung and COPD, and 32 unique testing conditions for the ARDS scenarios. During $ASVCO_2$, MV was auto-adjusted by the ventilator according to the scenario-specific algorithm and the $etCO_2$. Therefore, in this mode, there were eight unique testing modes for the normal lung and COPD, and 16 unique combinations for the ARDS scenarios. For the brain injury scenario, ventilatory settings and conditions were those of a normal lung. Therefore, simulations were only performed for eight unique conditions during $ASVCO_2$ using the brain-injury algorithm.

Variables evaluated

The following variables were recorded during all modes of ventilation: P_{Plat}, RR, V_T, MV, $etCO_2$ and autoPEEP. RR, V_T, and MV, all were obtained directly from the ventilator display. The P_{Plat} was assumed equal to end inspiratory pressure during ASV, $ASVCO_2$ and PC and determined by establishing a >1.0 s end inspiratory pause during VC for a single breath after steady state was established. The P_{Plat} was obtained directly from the ventilator display. AutoPEEP was read directly off the

Table 1 Lung mechanics and ventilatory settings used for simulation of different clinical scenarios

	Compliance (mL/cmH_2O)	Resistance ($cmH_2O/L/s$)	PEEP (cmH_2O)	MV[a] (%) (ASV, PC, VC only)	RR (breaths/min) (PC, VC only)[a]	CO_2 titrated into the lung chamber (ml/kg/min)[b]
Normal	45	5	5/10	100/150	16/25	2/3/4/5
Brain injury	45	5	5/10	100/150	16/25	2/3/4/5
$ARDS_1$	35	7.7	12/16	150/200	25/33	2/3/4/5
$ARDS_2$	15	7.7	12/16	150/200	25/33	2/3/4/5
COPD	60	7.7	5/10	100/150	16/25	2/3/4/5

ARDS adult respiratory distress syndrome, *COPD* chronic obstructive pulmonary disease, *PEEP* positive end expiratory pressure, *MV* minute volume, *RR* respiratory rate, *ASV* adaptive support ventilation, *PC* pressure control ventilation, *VC* volume control ventilation

[a] Respiratory rate and set minute volume were paired, to target a 6 mL/kg tidal volume for VC and PC

[b] Predicted body weight was defined as '70 kg' for all test scenarios

ventilator and verified by observing the lung model end expiratory pressure. The primary performance variable used to compare modes was $etCO_2$ and the secondary performance variables were the number of test scenarios in which the P_{Plat} was $\geq$28 cmH_2O, the V_T was outside of the 4–8 mL/kg range and the development of autoPEEP.

Data analysis and statistics

Data were expressed as median (25–75th percentile) or mean (±SD). Statistical analyses were performed with the Kruskal–Wallis or ANOVA tests depending on the data distribution using SPSS software (Statistical Package for the Social Sciences, version 15.0; SPSS Inc.; Chicago, IL). Post hoc analyses were performed using Bonferoni correction. The test of homogeneity of variances (Levene's test) was used to compare group variances. A p value < 0.05 was considered statistically significant.

Results

Normal lung and brain injury scenarios

In normal lung (N) and brain injury (BI) settings, V_T in ASV and $ASVCO_2$ were higher than in VC and PC ($p < 0.001$) (Table 2). P_{Plat}, $etCO_2$ (both variables presented in figures—online resources 1 and 2) and RR (Table 3) were similar for all modes, but the $etCO_2$ levels in $ASVCO_2$ demonstrated a narrower distribution (interquartile range: 3 for N and 1.75 for BI settings, $p \leq 0.01$) compared to the greater variance in other modes (interquartile ranges: 22.75, 22, 21.75 for ASV, VC, PC) (Online resources 1 and 2). No P_{Plat} $\geq$28 cmH_2O were detected and PEEP did not affect results.

ARDS scenarios

In $ASVCO_2$ $etCO_2$ was higher than in other modes ($p < 0.001$) (Fig. 1). V_T was higher in VC than in PC ($p < 0.001$) (Table 2). P_{Plat} was higher in low compliance than high compliance within each ventilation mode ($p < 0.01$) (Fig. 1). In low compliance, P_{Plat} was significantly higher in VC and PC when compared to $ASVCO_2$ and ASV ($p < 0.001$). Across all evaluations, RR was similar in all modes, however, for $ASVCO_2$ and ASV modes (Table 3), RR in low compliance scenarios was higher than RR in high compliance scenarios ($p < 0.001$).

ARDS scenarios where $P_{Plat} \geq 28$ cmH_2O

When P_{Plat} was $\geq$28 cmH_2O $etCO_2$ in $ASVCO_2$ was higher than in VC and PC ($p < 0.001$) (Fig. 2). The V_T in VC was higher than V_T in other ventilation modes ($p < 0.05$) (Table 2). In low compliance, V_T in ASV and $ASVCO_2$ were lower than V_T in VC and PC ($p < 0.001$) and V_T in VC was lower than in PC ($p < 0.001$) (Table 2). P_{Plat} in ASV and $ASVCO_2$ were lower than in PC ($p < 0.05$) (Fig. 2). In addition, P_{Plat} in ASV was lower than in VC ($p < 0.05$). P_{Plat} in $ASVCO_2$ also trended to be lower than in VC but this was not a statistically significant difference ($p = 0.055$). With low compliance, P_{Plat} in $ASVCO_2$ was the lowest and P_{Plat} in VC was the highest ($p < 0.01$). The RR (breaths/min) was higher in ASV when compared to VC and PC ($p = 0.008$) (Table 3). For $ASVCO_2$ and ASV modes, RR in low compliance was higher than RR in high compliance. In low compliance, RR in ASV was higher than both VC and PC ($p < 0.001$). In high compliance, RR in $ASVCO_2$ was lower than both VC and PC ($p = 0.002$).

COPD scenarios

In all ventilation modes $etCO_2$ were similar, although $etCO_2$ in $ASVCO_2$ tended to be higher than in other modes (Fig. 3). The V_T in ASV and $ASVCO_2$ were higher than VC and PC ($p < 0.001$) (Table 2). The V_T in ASV and $ASVCO_2$ were higher than VC and PC for both PEEP levels (Table 2). The P_{Plat} was similar for all modes. No P_{Plat} $\geq$28 cmH_2O were detected in any scenario (Fig. 3).

Table 2 Tidal volume levels (mL/kg PBW) in different disease settings under changing conditions; low and high PEEP (5 and 10 cmH_2O for normal, brain injury and COPD scenarios, 12 and 16 cmH_2O for ARDS scenarios) and compliance levels (15 and 35 mL/cmH_2O)

	Tidal volume levels (mL/kg PBW)							
	$ASVCO_2$		ASV		VC		PC	
	Low	High	Low	High	Low	High	Low	High
PEEP effect (low/high, cmH_2O)								
Normal (low: 5, high: 10)	7.3 ± 0.8	7.4 ± 0.7	7.2 ± 0.4	7.2 ± 0.4	6.4 ± 0.2*	6.4 ± 0.1*	6.3 ± 0.4*	6.3 ± 0.2*
Brain injury (low: 5, high: 10)	7.5 ± 0.8	7.5 ± 0.7	Same as above					
COPD (low: 5, high: 10)	7.4 ± 0.7	7.5 ± 0.6	7.6 ± 0.5	7.7 ± 0.5	6.2 ± 0.1*	6.3 ± 0.2*	6.6 ± 0.4*	6.7 ± 0.3*
ARDS (low: 12, high: 16)	5.5 ± 1.6	5.0 ± 2.0	5.9 ± 1.6	5.3 ± 2.0	6.3 ± 0.2	6.3 ± 0.2	6.0 ± 0.2	6.0 ± 0.2
ARDS P_{Plat} ≥28 (low: 12, high: 16)	4.1 ± 0.1	5.0 ± 2.0	4.4 ± 0.1	5.3 ± 2.0	6.4 ± 0.1*	6.3 ± 0.2	5.9 ± 0.1	6.0 ± 0.2
Compliance effect (low/high, mL/cmH_2O)								
ARDS (low: 15, high: 35)	3.7 ± 0.5^	6.9 ± 0.6	3.9 ± 0.5^	7.4 ± 0.3$^{\$}$	6.4 ± 0.1*	6.2 ± 0.1*	5.9 ± 0.1*	6.1 ± 0.1*
ARDS P_{Plat} ≥28 (low: 15, high: 35)	3.7 ± 0.5^	6.8 ± 0.6	3.9 ± 0.5^	7.3 ± 0.6†	6.4 ± 0.1*$^{,\#}$	6.2 ± 0.1	5.9 ± 0.1*	6.2 ± 0.1

ASVCO₂ adaptive support ventilation with closed loop CO_2 control, *ASV* adaptive support ventilation, *VC* volume control ventilation, *PC* pressure control ventilation, *COPD* chronic obstructive pulmonary disease, *ARDS* adult respiratory distress syndrome, *PBW* predicted body weight, P_{Plat} plateau pressure, *PEEP* positive end expiratory pressure

* $p < 0.05$ versus tidal volume in $ASVCO_2$ and ASV
† $p < 0.05$ versus tidal volume in VC and PC
# $p < 0.05$ versus tidal volume in PC
$ $p < 0.05$ versus tidal volume in $ASVCO_2$
^ $p < 0.05$ versus tidal volume in the high compliance scenarios with the corresponding mode

Table 3 Respiratory rates (breath/minute) in different disease settings under changing conditions; low and high PEEP (5 and 10 cmH_2O for normal, brain injury and COPD scenarios, 12 and 16 cmH_2O for ARDS scenarios) and compliance levels (15 and 35 mL/cmH_2O)

	Respiratory rates (breaths/min)							
	$ASVCO_2$		ASV		VC		PC	
	Low	High	Low	High	Low	High	Low	High
PEEP effect (low/high, cmH_2O)								
Normal (low: 5, high: 10)	17.8 ± 4.6	17.8 ± 4.6	17.9 ± 2.6	17.9 ± 2.9	20.5 ± 4.8	20.5 ± 4.8	20.5 ± 4.8	20.5 ± 4.8
Brain injury (low:5, high: 10)	18.8 ± 4.8	18.0 ± 4.7	Same as above					
COPD (low: 5, high: 10)	14 ± 3.4*	14.3 ± 3.5*	16.8 ± 2.4	16.8 ± 2.4	20.5 ± 4.8	20.5 ± 4.8	20.5 ± 4.8	20.5 ± 4.8
ARDS (low: 12, high: 16)	24.5 ± 9.6	27.4 ± 13.8	30.4 ± 7.4	31.6 ± 9.3	29 ± 4.1	29 ± 4.1	29 ± 4.1	29 ± 4.1
ARDS P_{Plat} ≥28 (low: 12, high: 16)	30.5 ± 10.1	27.4 ± 13.8	36.9 ± 3.9	30.0 ± 9.3	29.0 ± 4.3	29 ± 4.3	29.0 ± 4.3	29 ± 4.3
Compliance effect (low/high, mL/cmH_2O)								
ARDS (low: 15, high: 35)	34.6 ± 10.1^	17.3 ± 3.8	38.2 ± 5^	23.8 ± 2.6	29 ± 4.1	29 ± 4.1	29 ± 4.1	29 ± 4.1
ARDS P_{Plat} ≥28 (low: 15, high: 35)	34.6 ± 10.1^	16 ± 3.4*	38.2 ± 5^,*	23.6 ± 2.6	29 ± 4.1	29 ± 4.3	29 ± 4.1	29 ± 4.3

ASVCO₂ adaptive support ventilation with closed loop CO_2 control, *ASV* adaptive support ventilation, *VC* volume control ventilation, *PC* pressure control ventilation, *COPD* chronic obstructive pulmonary disease, *ARDS* adult respiratory distress syndrome, P_{Plat} plateau pressure, *PEEP* positive end expiratory pressure

* $p < 0.05$ versus respiratory rates in VC, PC
^ $p < 0.05$ versus respiratory rates in the high compliance scenarios with the corresponding mode

The RR in $ASVCO_2$ were lower than in VC and PC ($p = 0.003$) (Table 3).

AutoPEEP levels were similar among all modes not exceeding 0.5 cmH_2O in COPD, 1 cmH_2O in normal and brain injury and 2 cmH_2O in ARDS scenarios.

Discussion

Our findings can be summarized as follows: (1) In normal lung and brain injury, ASV, $ASVCO_2$, VC and PC performed similarly. (2) In COPD scenarios, V_T were higher and RR lower in ASV and $ASVCO_2$ compared to VC and PC. (3) In ARDS scenarios, $etCO_2$ in $ASVCO_2$ was higher than in other modes and V_T and P_{Plat} were lower than other modes. (4) The $ASVCO_2$ performed as expected but seemed to only have a major effect when compared specifically to ASV in ARDS scenarios.

The new algorithm for adaptive support ventilation ($ASVCO_2$; currently available as IntelliVent® in Europe) is designed to keep $etCO_2$ in a defined range by adjusting target MV based on input from the user and measured parameters [12]. Total RR and $etCO_2$ are measured and

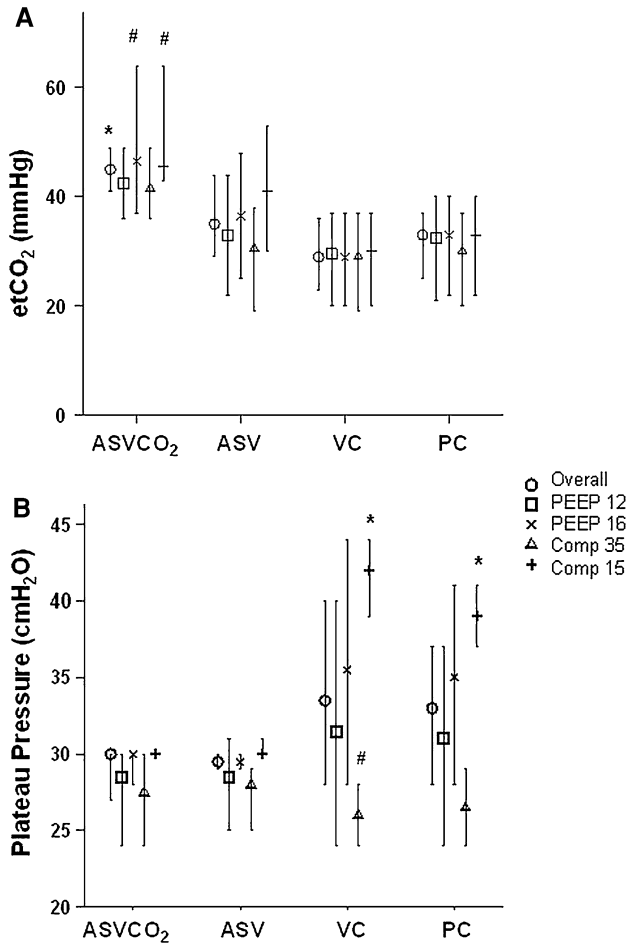

Fig. 1 End tidal CO_2 (**a**) and plateau pressure (**b**) levels in ARDS settings. *ARDS* acute respiratory distress syndrome, *ASVCO*$_2$ adaptive support ventilation with closed loop CO_2 control, *ASV* adaptive support ventilation, *VC* volume control ventilation, *PC* pressure control ventilation *et CO*$_2$ end tidal carbon dioxide, P_{Plat} plateau pressure. **a** $^{*}p < 0.05$ versus $etCO_2$ in ASV, VC, PC, $^{\#}p < 0.05$ versus $etCO_2$ in VC, PC. **b** $^{*}p < 0.05$ versus P_{Plat} in $ASVCO_2$, ASV, $^{\#}p < 0.05$ versus P_{Plat} in ASV

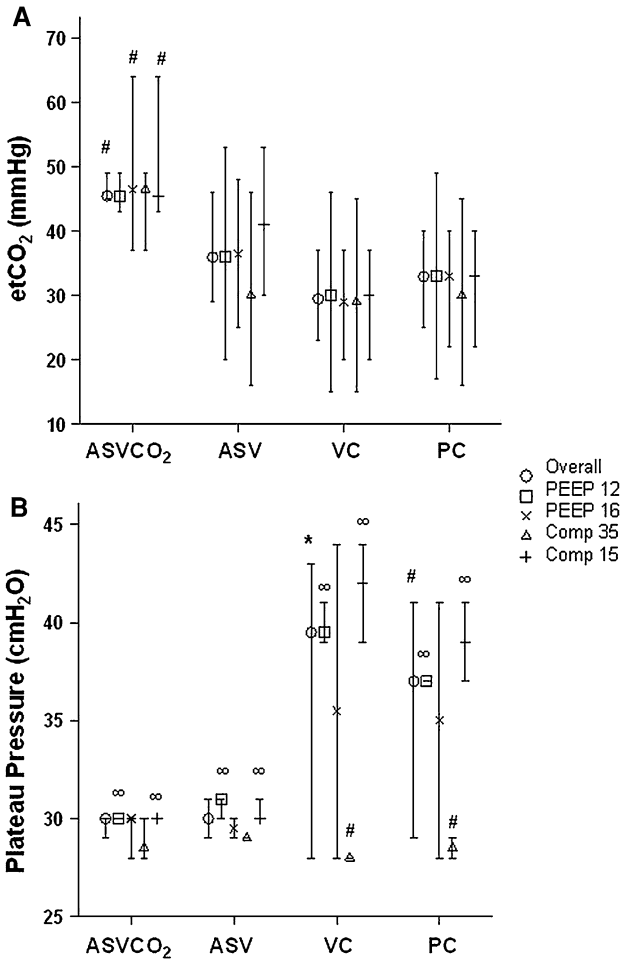

Fig. 2 End tidal CO_2 (**a**) and plateau pressure (**b**) levels in ARDS settings where plateau pressures were equal or greater than 28 cmH_2O. *ARDS* acute respiratory distress syndrome, *ASVCO*$_2$ adaptive support ventilation with closed loop CO_2 control, *ASV* adaptive support ventilation, *VC* volume control ventilation, *PC* pressure control ventilation, *etCO*$_2$ end tidal carbon dioxide, P_{Plat} plateau pressure. **a** $^{\#}p < 0.05$ versus $etCO_2$ in VC, PC. **b** $^{*}p < 0.05$ versus P_{Plat} in ASV, $^{\#}p < 0.05$ versus P_{Plat} in ASV and $ASVCO_2$, $^{\infty}p < 0.05$ versus P_{Plat} in other modes

patient gender, height, type of lung disease, the presence of brain injury, severity of lung injury and pressure limit are set by the user. Based on these factors, a target MV is calculated by the CO_2 controller. Using the minimal work of breathing principle (Otis Equation) [1], a target V_T and RR are then determined by the ASV controller. Acceptable $etCO_2$ ranges depend on patient's lung disease state, calculated as $2 \times [Pinsp(cmH_2O) + PEEP(cmH_2O)]$ and treatment options. That is, if the patient has severe lung injury, permissive hypercapnia is allowed; if the patient is at the weaning stage limits are increased by 5 mmHg; if the patient has chronic hypercapnia, ranges are shifted by +10 mmHg; if the patient has brain injury the limits are 33 mmHg (minimum) and 38 mmHg (maximum) regardless of the lung conditions. The key to the optimal performance of this algorithm is does the $etCO_2$ accurately reflect $PaCO_2$ in the specific patient? This must be determined in clinical trials. In addition, very low V_T in ARDS can lead to progressive atelectasis, as a result, careful adjustment of applied PEEP to stabilize the lung and avoid tidal recruitment is required.

To our knowledge, this study is the first to evaluate performance of the $ASVCO_2$ algorithm in different disease settings and to compare it with ASV, PC and VC. In normal lungs with or without brain injury, all modes performed similarly. The brain injury algorithm [12] ensures strict low normocapnia while limiting airway pressures but did not alter the ventilatory parameters compared with other modes due to the normal lung settings. We cannot, however, predict the combined effects of head injury plus ARDS. The

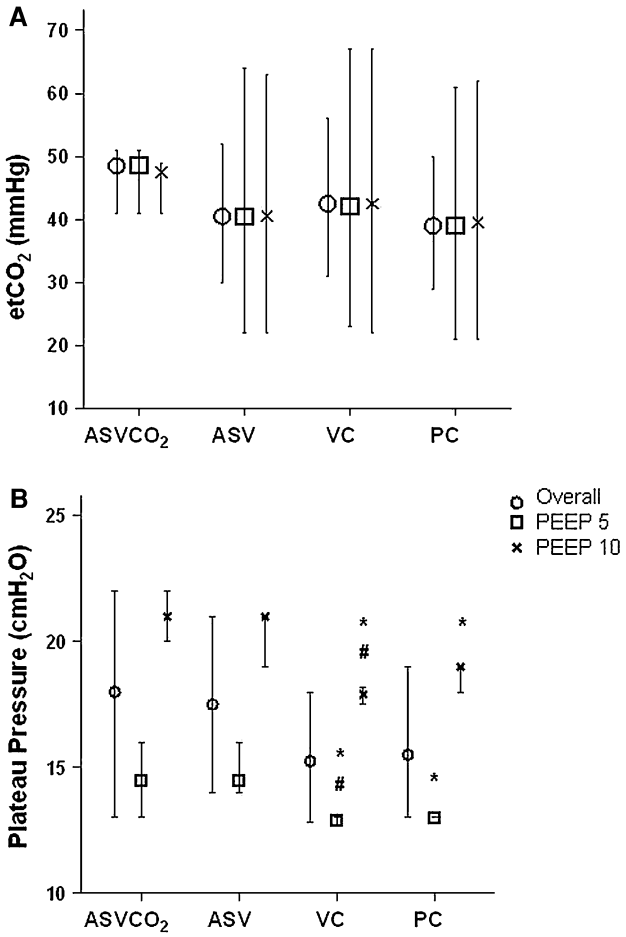

Fig. 3 End tidal CO_2 (**a**) and plateau pressure (**b**) levels were similar across all ventilation modes in COPD settings. *COPD* chronic obstructive pulmonary disease, *ASVCO*$_2$ adaptive support ventilation with closed loop CO_2 control, *ASV* adaptive support ventilation, *VC* volume control ventilation, *PC* pressure control ventilation, *etCO*$_2$ end tidal carbon dioxide, P_{Plat} plateau pressure. *$p < 0.05$ versus P_{Plat} in ASV and ASVCO$_2$. $^{\#}p < 0.05$ versus P_{Plat} in PC

manufacturer indicates the brain injury algorithm overrides all other disease algorithms.

In COPD scenarios, ASVCO$_2$ kept the etCO$_2$ level at 47 ± 3.8 mmHg while other modes averaged around 39–42 mmHg with larger standard deviations (12–14 mmHg). Although this tendency did not show a statistically significant difference, it may be of importance when considered for clinical use in patients with chronic hypercapnia. As P_{Plat} remained similar in all modes, V_T was higher in ASV and ASVCO$_2$. This finding for ASV was consistent with previous laboratory and observational clinical studies [13–16], howeve, the maximum tidal volume we found was 8.1 mL/kg for ASVCO$_2$ and 8.25 mL/kg for ASV as opposed to much higher values (10–22 mL/kg) observed in previous studies [15, 16]. Large V_T in COPD were attributed to the longer expiratory time constant. In our study, the V_Ts were very similar to those of normal lungs (*C*: 45 mL/cmH$_2$O, *R*: 5 cmH$_2$O/L/s). This finding is partly because we used only one set of lung mechanics for COPD (*C*: 60 mL/cmH$_2$O, *R*: 7.7 cmH$_2$O/L/s).

In ARDS scenarios, the ASVCO$_2$ algorithm resulted in permissive hypercapnia as recommended by many to maintain a lung protective ventilation strategy [4, 6, 17–19]. Permissive hypercapnia although not a desired outcome during ventilatory support does allow a decrease in V_T and P_{Plat} as well as a shifting of the oxyhemoglobin dissociation curve to the right unloading more oxygen to the tissue. In addition, at least laboratory data indicates cell survival is enhanced during hypercarbia versus normocarbia [20]. Most importantly it does not cause any adverse response provided it is achieved gradually and the patient does not have significant heart or kidney disease or a metabolic acidosis [4, 6, 17–19]. Overall, tidal volumes in all modes were comparable to the NIH ARDSnet protocol [4] (4–8 mL/kg) except for the few scenarios where the P_{Plat} exceeded 28 cmH$_2$O. Theoretically, the lower limit for tidal volume in ASV and ASVCO$_2$ is 4.4 mL/kg which equals two times the anatomical dead space (2.2 mL/kg), however when the P_{Plat} limit was reached (28 cmH$_2$O) V_T decreased further. Since we used a lung model and not a live animal model or patients, we were unable to evaluate the effect that proper setting of PEEP would have on the operation of ASVCO$_2$ or ASV. If the lung was recruited and PEEP set to avoid derecruitment, it is reasonable to expect that compliance would improve and the decrease in V_T may have been minimized [21]. Proper PEEP adjustment would also minimize the increase in P_{Plat} noted in VC and PC.

P_{Plat} were significantly higher in PC and VC than in ASVCO$_2$ and ASV with ARDS. In cases where the P_{Plat} was ≥28 cmH$_2$O, V_T in ASVCO$_2$ and ASV ranged between 3.2 and 6.5 mL/kg (median: 4.2) and 3.4–7.3 mL/kg (median: 4.4), respectively. The number of scenarios where the V_T was lower than 4 mL/kg was 4 (50 %) in ASVCO$_2$ and 8 (50 %) in ASV (Table 4). In these settings alarms identified the low V_T. The overriding goal of ASVCO$_2$ or ASV in ARDS is to minimize the development of lung injury (volutrauma or barotrauma) [4, 22]. This goal is accomplished by attempting to maintain ventilation within the ARDSnet defined tidal volume and P_{Plat} targets [4]. As described in the ARDSnet protocol as P_{Plat} increases the tidal volume needs to be decreased.

The findings of this study highlight the potential benefit of closed loop ventilatory control. This potential benefit may be directly related to the ability of ASVCO$_2$ and ASV to allow variability in MV, RR and V_T which normally occurs as lung mechanics changes. We may

Table 4 Frequency distribution table for tidal volumes and plateau pressures for each ventilation mode in ARDS scenarios

Compliance	15 mL/cmH_2O				35 mL/cmH_2O			
Vent mode	$ASVCO_2$	ASV	VC	PC	$ASVCO_2$	ASV	VC	PC
VT (ml/kg)								
3	4	8						
4	4	7						
5		1						
6			12	16	2		16	16
7			4		5	12		
8					1	4		
P_{plat} (cmH_2O)								
24-27					4	8	8	8
28-31	8	16			4	8	8	8
32-35								
36-39			4	8				
40-43			8	8				
44-47			4					

ARDS adult respiratory distress syndrome, *ASVCO2* adaptive support ventilation with closed loop CO_2 control, *ASV* adaptive support ventilation, *VC* volume control ventilation, *PC* pressure control ventilation, *VT* tidal volume, P_{Plat} plateau pressure

discover soon that this variability may be one of the most important benefits of these types of modes of ventilation [23].

Limitations

There are a number of limitations to the current study: (1) this is a simulation study, thus the data obtained from this study can not be directly extrapolated to patients. However the use of a simulator allowed us to precisely define the lung mechanics for each disease setting and identify the precise responses for each ventilation mode and algorithm. (2) A one compartment lung model was used which does not reflect the complexities of a multi-compartmental lung. (3) As only passive ventilation was simulated, we can not predict how these modes will work during active ventilation. (4) The complete range of lung mechanism settings in COPD and ARDS was not evaluated; there are many different *C*:*R* combinations for these specific conditions. As a result we cannot be sure how these algorithms will respond under all possible scenarios. (5) In $ASVCO_2$ the CO_2 algorithm overrides lung mechanics. The impact of this in brain injury and COPD or ARDS is not defined by this study. (6) We did not directly measure P_{Plat} during $ASVCO_2$, ASV and PC but used the end inspiratory pressure as a reflection of P_{Plat}. In scenarios where flow did not return to zero at the end of the breath, P_{Plat}. was overestimated. However, in most scenarios flow was close to zero at the termination of these pressure targeted breaths. (7) The lung model was directly connected to the wye connection of the circuit without an endotracheal tube. Therefore the resistance of an endotracheal tube may have affected the delivery of the tidal volume in PC, ASV and $ASVCO_2$ modes.

Conclusion

$ASVCO_2$, ASV, PC and VC performed similarly in most cases. The minor differences observed were in favor of the closed loop mechanisms. Overall, $ASVCO_2$ maintained tighter CO_2 control in all scenarios. $ASVCO_2$ had the greatest impact during ARDS; $ASVCO_2$ allows $etCO_2$ to increase, resulting in greater hypercapnia and lower V_T and plateau pressure than ASV, VC or PC.

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