The Effects of Pressure Control Versus Volume Control Assisted Ventilation on Patient Work of Breathing in Acute Lung Injury and Acute Respiratory Distress Syndrome

Richard H Kallet MS RRT, Andre R Campbell MD, James A Alonso RRT, Diane J Morabito MPH RN, and Robert C Mackersie MD

BACKGROUND: Patient work of breathing (WOB) during assisted ventilation is reduced when inspiratory flow ($\dot{V}_I$) from the ventilator exceeds patient flow demand. Patients in acute respiratory failure often have unstable breathing patterns and their requirements for $\dot{V}_I$ may change from breath to breath. Volume control ventilation (VCV) traditionally incorporates a pre-set ventilator $\dot{V}_I$ that remains constant even under conditions of changing patient flow demand. In contrast, pressure control ventilation (PCV) incorporates a variable decelerating flow wave form with a high ventilator $\dot{V}_I$ as inspiration commences. We compared the effects of flow patterns on assisted WOB during VCV and PCV. METHODS: WOB was measured with a BICORE CP-100 monitor (incorporating a Campbell Diagram) in a prospective, randomized cross-over study of 18 mechanically ventilated adult patients with acute lung injury (ALI) or acute respiratory distress syndrome (ARDS). Tidal volume, inspiratory time, and mean ventilator $\dot{V}_I$ were constant in each mode. RESULTS: At comparable levels of respiratory drive and minute ventilation, patient WOB was significantly lower with PCV than with VCV (0.59 ± 0.42 J/L vs 0.70 ± 0.58 J/L, respectively, $p < 0.05$). Ventilator peak $\dot{V}_I$ was significantly higher with PCV than with VCV (103.2 ± 22.8 L/min vs 43.8 L/min, respectively, $p < 0.01$). CONCLUSIONS: In the setting of ALI and ARDS, PCV significantly reduced patient WOB relative to VCV. The decrease in patient WOB was attributed to the higher ventilator peak $\dot{V}_I$ of PCV. *Key words: acute lung injury, acute respiratory distress syndrome, assisted mechanical ventilation, central respiratory drive, constant flow pattern, decelerating flow pattern, inspiratory flow rate, pressure-time product, pressure control ventilation, volume control ventilation, work of breathing.* [Respir Care 2000;45(9):1085–1096]

Background

Patient work of breathing (WOB) during assisted ventilation is reduced when inspiratory flow ($\dot{V}_I$) from the ventilator exceeds patient flow demand.[1–4] Because patient flow demand reflects inspiratory muscle contractile velocity,[5,6] the ventilator will impose resistive work whenever patient flow demand exceeds ventilator $\dot{V}_I$. Also, during acute lung injury (ALI) and acute respiratory distress syndrome (ARDS), elastic WOB increases because the inspiratory muscles strain against poorly compliant lungs and chest wall.[7,8] Therefore, high ventilator $\dot{V}_I$ delivery also may lessen a patient's elastic WOB by displacing the chest faster than can be achieved by the inspiratory muscles straining under high elastic loads.

Because patients in acute respiratory failure often have unstable breathing patterns, their requirements for tidal volume (V_T) and flow can change from breath to breath.[9]

Richard H Kallet MS RRT and James A Alonso RRT are affiliated with Respiratory Care Services, Department of Anesthesia, University of California, San Francisco, at San Francisco General Hospital, San Francisco, California. Andre R Campbell MD, RRT, Diane J Morabito MPH RN, and Robert C Mackersie MD are affiliated with the Department of Surgery, University of California, San Francisco, at San Francisco General Hospital, San Francisco, California.

A version of this paper was presented at the Society for Critical Care Medicine Symposium, San Diego, California, February 7, 1997.

Funding for this study was provided by the Departments of Anesthesia and Surgery, University of California, San Francisco, at San Francisco General Hospital, and by the San Francisco Trauma Foundation.

Correspondence: Richard H Kallet MS RRT, Respiratory Care Services, Department of Anesthesia, San Francisco General Hospital, NH: GA-2, 1001 Potrero Avenue, San Francisco CA 94110. E-mail: richkallet@earthlink.net.

Volume control ventilation (VCV) traditionally delivers a breath with a pre-set ventilator $\dot{V}_I$ that remains constant (ie, a rectangular flow waveform),[10] even under conditions of changing patient flow demand. During pressure control ventilation (PCV), peak airway pressure is sustained by a variable, decelerating flow wave form with a high ventilator $\dot{V}_I$ as inspiration commences.[10] Because PCV regulates ventilator $\dot{V}_I$ to maintain a set airway pressure, transmitted negative pressure from patient effort should cause the ventilator $\dot{V}_I$ to increase and to be sustained when patient effort is prolonged. Therefore, the ability of PCV to produce a high, variable, and sustained $\dot{V}_I$ should adapt better to changes in patient flow and V_T requirements. Furthermore, the high $\dot{V}_I$ and decelerating flow pattern of PCV cause a larger portion of the V_T to be delivered earlier during inspiration.[10] This may also reduce the elastic WOB by displacing the chest faster than can be achieved by the inspiratory muscles. Based on those attributes we predicted that PCV would reduce patient WOB during assisted ventilation more than constant flow VCV in patients with ALI and ARDS.

Materials and Methods

Study Subjects

A convenience sample of 18 nonconsecutive ventilator-dependent patients on the medical, general surgery, and trauma surgery services were entered into the study. Signed, informed consent was obtained from either the patient or a relative. The Committee on Human Research at the University of California, San Francisco, approved the study. Patients were either clinically stable, or in the recovery phase of illness when weaning from mechanical ventilation was taking place. Entrance criteria were: minute ventilation ($\dot{V}_E$) $\geq$ 10 L/min, static respiratory system compliance $\leq$ 50 mL/cm H_2O, and meeting the North American-European Consensus Conference definition for either ALI or ARDS.[11] Patients with primary respiratory failure from ALI or ARDS who had an underlying component of chronic obstructive pulmonary disease or asthma also were entered into the study.

Study Protocol

The study incorporated a random presentation of breathing modes in a short, time-series, cross-over design. A blind envelope pull was used to prevent presentation bias. Nine patients were randomized to each presentation order (VCV to PCV and PCV to VCV). Ten minutes were allowed for adaptation and stabilization of breathing pattern between modes. Data collection required approximately 30 minutes in each mode. Afterwards, patients with a positive end-expiratory pressure (PEEP) of $\leq$ 10 cm H_2O were given a short trial of spontaneous breathing on 100% oxygen through a modified Jackson-Reese circuit. Depending on patient tolerance, data were collected once or twice over 1–2 minutes. Tolerance was defined as $<$ 20% change in either heart rate or blood pressure from study conditions and arterial oxygen saturation (as measured via pulse oximetry [S_{pO_2}]) of $\geq$ 95%. This data provided an approximation of patient WOB, $\dot{V}_I$, V_T, and inspiratory time (T_I) in order to compare ventilator settings during assisted ventilation with patients' spontaneous breathing patterns.

Procedures

Upon enrollment into the study, a Smart Cath (Thermo Respiratory Group, Palm Springs, California) nasogastric tube with an esophageal balloon was placed in the lower third of the esophagus. We manipulated the positon of the balloon while inspecting the synchrony of the peak esophageal pressure (ΔP_{ES}) and airway pressure deflections at moderately low trigger sensitivity settings (–5 cm H_2O). When cardiac artifact was minimized, an occlusion test was performed for position confirmation using the method described by Baydur.[12] All patients were studied in the semi-recumbent position. Maximum inspiratory pressure (MIP) was measured using the "Method 1" described by Marini et al, in which the airway is occluded at end-expiration, allowing no movement of air in either an inspiratory or expiratory direction.[13] This method was chosen in order to measure muscle strength from approximately functional residual capacity.

Prior to data collection, relaxed chest wall compliance (C_{CW}) curves were constructed using an analysis of 2–5 breaths during a short period of controlled ventilation. This was achieved following additional sedation with a 100–200 μg dose of Fentanyl (in 50 μg doses) to suppress spontaneous respiratory activity. C_{CW} curves were constructed from esophageal pressure-volume tracings with a counterclockwise movement, a narrow loop and a rightward rotation of the axis (Fig. 1).[14] In 3 patients, controlled ventilation could not be achieved and a normal C_{CW} line was used (200 mL/cm H_2O). After patients recovered and began to trigger the ventilator, central respiratory drive and patient effort were monitored until the presedation baseline had been achieved.

Equipment

Two ventilators were used for this study: the Siemens Servo 900C (Siemens Medical Systems Inc, Danvers, Massachusetts) and the Hamilton Veolar (Hamilton Medical Inc, Reno, Nevada). Each ventilator was calibrated prior to the study. The ventilator was set to achieve a T_I of 1.0 second. This was verified by measurement from the scalar $\dot{V}_I$ wave form. The control rate (f) on the ventilator was set between 10 and 12 breaths per minute and was held con-

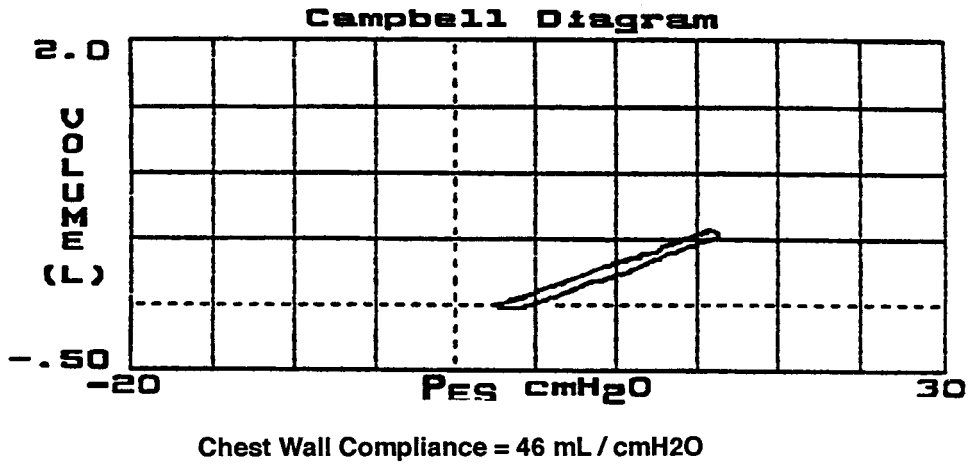


Fig. 1. Campbell diagram for calculation of passive chest wall compliance. Relaxed chest wall compliance is calculated from the esophageal pressure-volume loop. This pressure-volume loop was taken from Patient 2, who suffered from acute respiratory distress syndrome, chronic pleural effusions, and chronic pleural thickening. The severe rightward shift in the slope reflects the low compliance of the chest wall. P_{ES} = esophageal pressure.

stant across treatments. This allowed all patients to consistently trigger breaths during the study period. V_T was set at the level prescribed for patient care. During PCV, the prescribed V_T usually was achieved by setting the pressure control level to the plateau pressure for the same V_T during VCV. By setting T_I at 1.0 second and maintaining a constant V_T, mean ventilator $\dot{V}_I$ was constant for each mode. Fractional concentration of inspired oxygen and PEEP were kept at the level prescribed by the managing physician. No patient care activities took place during the study period.

Measurements

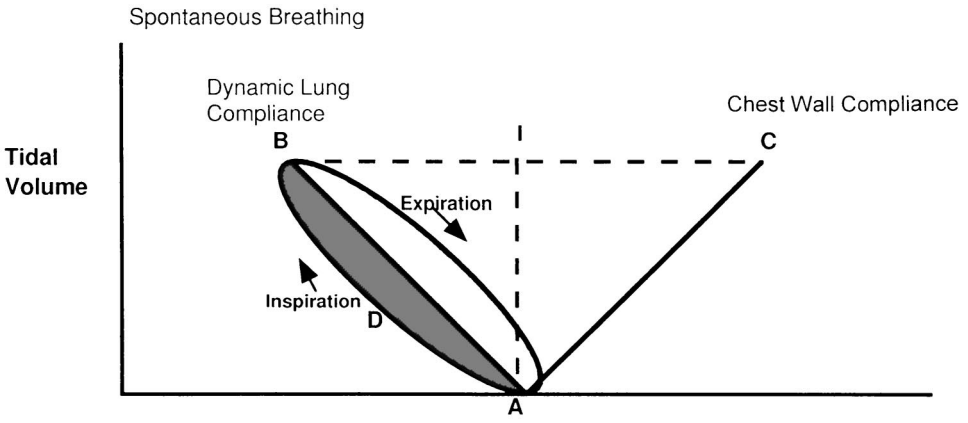
Patient and ventilator variables were measured with a pulmonary mechanics monitor incorporating a Campbell diagram (BICORE CP-100, Thermo Respiratory Group, Palm Springs, California). The precision and accuracy of this monitor has been previously validated.[15,16] The monitor and transducers were calibrated prior to each study. The Var-Flex (Thermo Respiratory Group, Palm Springs, California) airway pressure/flow transducer was placed at the patient Y adapter so that all reported volumes excluded compressible circuit volume. Data collection included f, inspired V_T, peak ventilator $\dot{V}_I$, intrinsic PEEP ($PEEP_I$), the fraction of T_I to total respiratory cycle time (ie, the duty cycle, calculated as T_I/T_{TOT}), and pressure-time product (PTP). Central respiratory drive was measured as the esophageal pressure at 100 milliseconds ($P_{0.1}$) after the onset of effort. Campbell diagram software was used to measure ΔP_{ES} and patient WOB in joules per liter (Fig. 2).[15] ΔP_{ES} was measured as the change in esophageal pressure from the X intercept of the chest wall compliance line from the Campbell diagram to the most negative point on the esophageal pressure-volume curve. $PEEP_I$ was measured as the difference in esophageal pressure between the X intercepts of the chest wall line (end-expiratory plateau) and lung compliance line (onset of inspiratory flow) from the Campbell diagram, minus the trigger sensitivity level measured at the airway (the lowest airway pressure change from baseline at the onset of flow). The mechanics monitor calculated PTP using the method described by Sassoon et al[17] as the integral of the negative change in P_{ES} over T_I, taking into account C_{CW}. However, the monitor is programmed to use a normal chest wall compliance value (200 mL/cm H_2O) in order to calculate PTP. Therefore, reported calculated values of PTP probably underestimate the true PTP as C_{CW} is often abnormal during ALI and ARDS.[18] The lung injury score was calculated using the method described by Murray et al.[19]

Fifteen to 20 assisted breaths were selected for analysis (Figs. 2–4). The criterion used for breath selection was a patient-triggered breath in which the P_{ES} remained below baseline after the onset of volume change. In one case (patient 5), respiratory drive was unstable, making it difficult to distinguish between well synchronized assisted ventilation and diminished drive. Therefore, we excluded all breaths from analysis when the WOB markedly fellbelow normal (< 0.08 J/L) in either mode. Dyssynchronous breaths associated with coughing and gross agitation, likewise, were excluded.

Calculations

The following formulas were used for calculation of the derived variables:

$$\dot{V}_E = V_T \times \text{total f (L/min)} \quad (1)$$



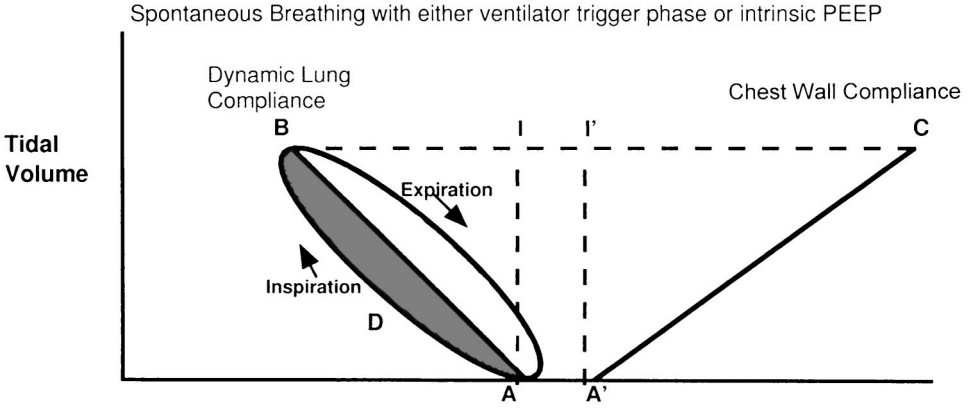


Fig. 2. A schematic drawing of a Campbell diagram in which line AB represents the lung compliance constructed dynamically during spontaneous breathing. Line AC represents the chest wall compliance constructed during passive ventilation and fitted to the end-expiratory pressure. The ellipse ADBA is the esophageal (or pleural) pressure-volume loop. The shaded area of the ellipse represents the flow-resistive work of breathing (WOB) performed by the patient. The area enclosed by ABCA represents the elastic WOB performed on the lungs and chest wall. Line AI bisects the elastic WOB so that area ABIA represents the elastic work performed on the lungs, whereas area AICA represents the elastic work performed on the chest wall. The unshaded portion of the ellipse represents passive expiration. Expiratory work is provided by the energy released during elastic recoil of the lungs to functional residual capacity. Spontaneous breathing through a ventilator's demand-flow system causes a trigger-phase so that a separation occurs between the lung and chest wall compliance lines. This signifies that the onset of effort (Point A′) does not correspond to the onset of inspiratory flow (Point A). This separation between effort and flow also occurs in the presence of intrinsic positive end-expiratory pressure ($PEEP_I$). The increase in area ABCA′A is caused by rectangle AII′A′, which represents the increased elastic work imposed by the trigger function of the ventilator and/or the presence of $PEEP_I$.

Respiratory muscle power in joules/minute

$$(\dot{W}) = \dot{V}_E \text{ (L/min)} \times \text{WOB (J/L)} \quad (2)$$

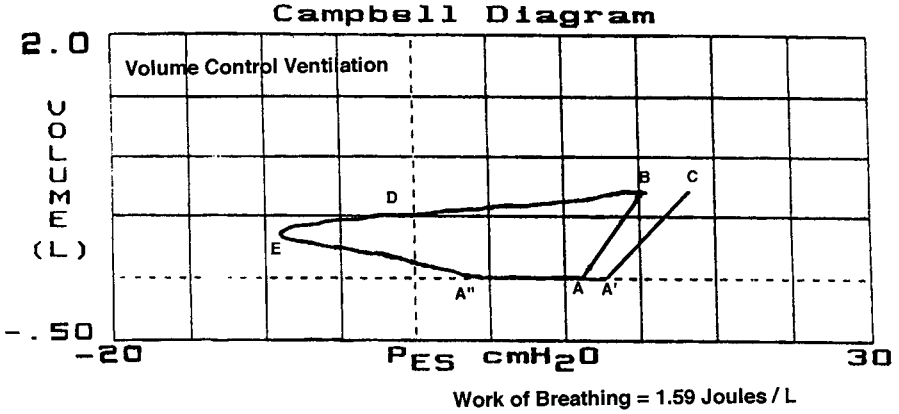
Spontaneous inspiratory time

$$= \text{spontaneous f} \times T_I/T_{TOT} \text{ (s)} \quad (3)$$

$$\text{Pressure time index (PTI)} = \Delta P_{ES}/MIP \times T_I/T_{TOT} \quad (4)$$

Data Analysis

Descriptive statistics are reported as means and standard deviations. The small sample size and non-normal data dis-



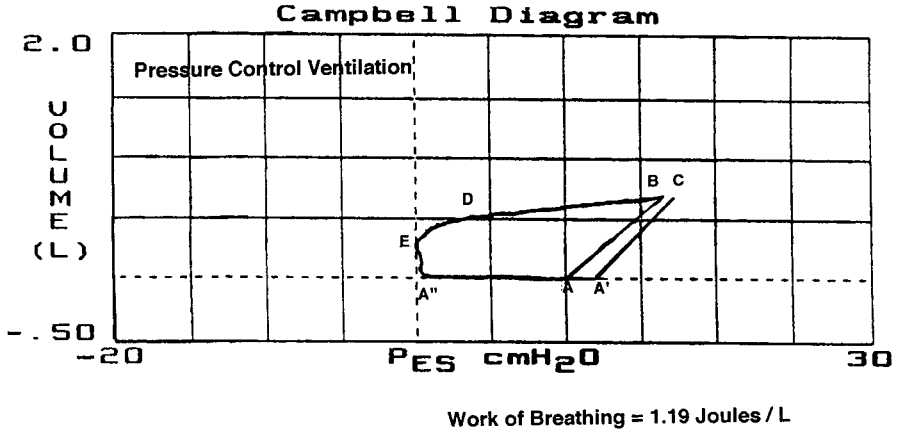


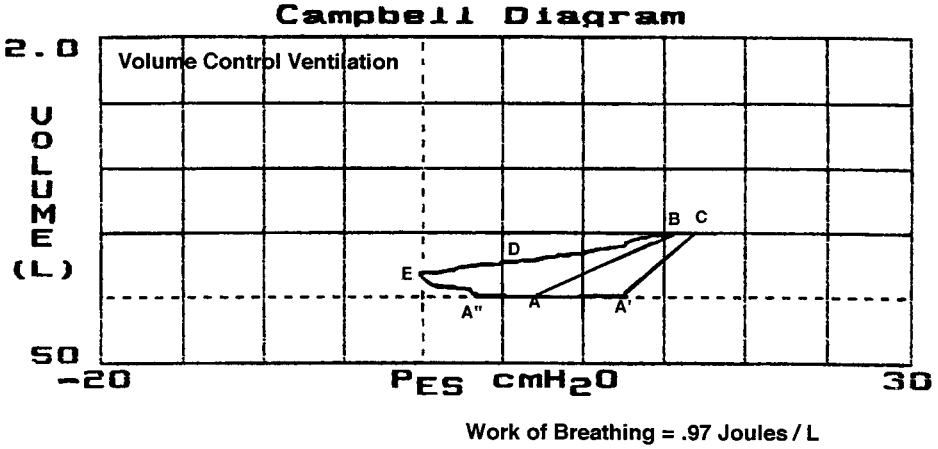
Fig. 3. Campbell diagram peak esophageal pressure vs tidal volume (P_{ES}-V_T) loops comparing high levels of assisted work of breathing (WOB) between volume control ventilation (VCV) and pressure control ventilation (PCV). The morphology of the pressure-volume loop is altered by the effect of positive pressure ventilation. A, B, C, D, and A′ are as defined in the legend for Figure 2. Point A″ is added to denote the post-trigger drop in P_{ES}, which represents the amount of effort exerted by the patient until there is sufficient flow delivery to cause a change in volume. Point E is added to denote peak negative P_{ES}, and the horizontal distance between A′ and E represents peak esophageal pressure (ΔP_{ES}). The horizontal distance AE represents the portion of the ΔP_{ES} associated with the post-trigger phase. The differences in the magnitude of AE between VCV and PCV represents the effects of each flow pattern on the resistive WOB. The loops were matched for $\dot{V}_I$ and approximate agreement in baseline pressure (Point A′). The dynamic lung compliance line AB is not an accurate representation of lung compliance because of the contribution of positive airway pressure during the breath.

tribution required inferential statistical analyses using a Wilcoxon signed-rank test for paired comparisons between modes. Spearman's rank-order test was used to assess correlation (rho). Results were considered significant if $p < 0.05$. Data were analyzed using Stat View (Abacus Concepts, Berkeley, California).

Results

All 18 patients met either ALI or ARDS criteria at the time of study enrollment. One patient, recovering from ALI, had an improvement in his ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (P_{aO_2}/F_{IO_2}) to > 300 after enrollment. The mean Murray[19] lung injury score revealed a moderate degree of damage (Table 1). Only 7 patients had scores indicative of severe injury (≥ 2.5) at the time of study.[19] The mean PEEP level was 6.7 ± 2.8 cm H_2O and the mean F_{IO_2} was 0.46 ± 0.08. Respiratory system compliance was in the range reported for ARDS (see Table 1).[7]

PCV was associated with significantly lower patient WOB, ΔP_{ES}, and $\dot{V}_I$ than was VCV (Table 2). PTP was



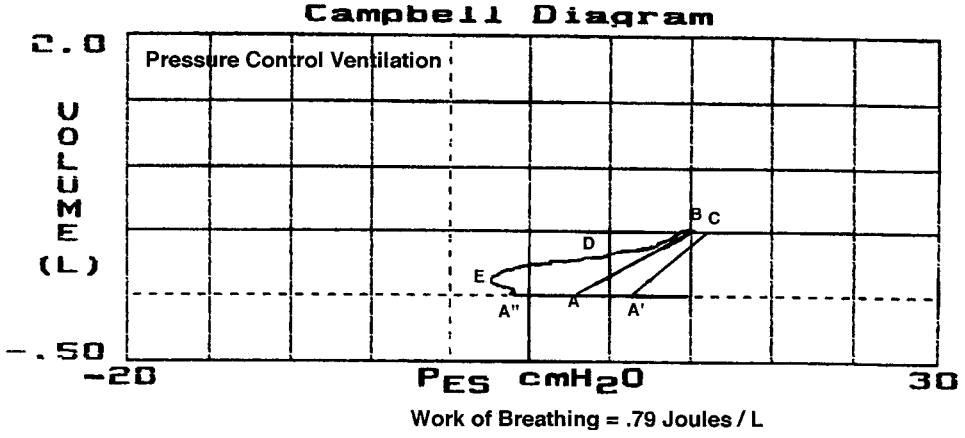


Fig. 4. Campbell diagram peak esophageal pressure vs tidal volume (P_{ES}-V_T) loops comparing moderate levels of assisted work of breathing (WOB) between volume control ventilation (VCV) and pressure control ventilation (PCV). The characteristic differences in the contour of the pressure-volume loops seen between VCV and PCV at high levels of work and effort also are present at moderate levels of work and effort. A, B, C, D, E, A′ and A″ are as defined in the legends for Figures 2 and 3.

lower during PCV, but the difference was not statistically significant. Central respiratory drive, or $P_{0.1}$, was the same between modes and was in the range reported for ARDS patients at 50% of total ventilator support.[4,20] Ventilator conditions were successfully maintained at constant levels between ventilator treatments (Table 3). V_T, total f, mean ventilator $\dot{V}_I$, and $\dot{V}_E$ were not different between assisted VCV and PCV. S_{pO_2} was monitored continuously and S_{pO_2} values were always $\geq$ 95% during data collection, in each mode. The pressure control level needed to maintain V_T was greater than the plateau pressure measured during VCV (32.7 $\pm$ 6.4 cm H_20 vs 29.7 $\pm$ 7.6 cm H_2O, respectively). Peak ventilator $\dot{V}_I$ was significantly greater during PCV. However, mean ventilator $\dot{V}_I$ was low relative to general practice (41 L/min vs 60 L/min).[21] Mean V_T as a function of body size was 10.0 $\pm$ 2.5 mL/kg.

We were able to measure inspiratory muscle strength at the beginning of the study in all patients. The MIP revealed a moderately strong inspiratory muscle force reserve (see Table 1). Our results were similar to those reported by Marini et al for critically ill patients, using the same measurement technique.[13] In addition, we were able to assess the breathing pattern and WOB during brief periods of spontaneous ventilation in 16 of 18 patients at the end of the study (Table 4). The peak $\dot{V}_I$, mean $\dot{V}_I$, and V_T that could be generated during spontaneous breathing was lower than the respective values measured during VCV and PCV. Mean patient T_I was close to ventilator T_I (0.9 s vs 1.0 s,

Table 1. Patient Demographics at Entrance into Study

Case	Sex	Age	Diagnosis	C_{RS} (mL/cm H_2O)	C_{CW} (mL/cm H_2O)	PEEP (cm H_2O)	LIS	MIP (cm H_2O)
1	M	47	Pneumonia, ALI	50	143	5	0.75	14
2	F	57	ARDS, ESLD, chronic pleural effusion/ pleural thickening	16	46	8	2.75	26
3	M	19	Smoke inhalation, resolving ARDS	28	109	5	1.75	75
4	F	33	Hypovolemic shock, ascites, ARDS	21	90	15	2.5	39
5	F	65	Blunt chest trauma, pulmonary contusion, pneumonia, ALI	41	146	5	1.75	44
6	M	44	Abdominal abscesses, pleural effusion, resolving ALI	45	175	5	1.00	53
7	F	49	Blunt chest trauma, flail chest, ALI, aspiration pneumonia	40	256	7	2.00	27
8	M	38	Blunt chest trauma, pulmonary contusion, flail chest, ALI	50	262	5	1.50	32
9	M	70	Sepsis, ALI, COPD	39	*	5	1.33	71
10	M	61	Pneumonia, ALI, sepsis	33	129	5	2.67	56
11	F	33	Resolving ARDS, sepsis	25	205	5	1.33	63
12	F	39	Pneumonia, ARDS, ESLD	35	200	5	1.75	45
13	M	38	Blunt chest trauma, ARDS	23	*	5	2.50	60
14	F	51	Pancreatitis, ESLD, sepsis, ARDS	24	126	10	3.00	57
15	M	66	Pneumonia, sepsis, ALI	38	131	5	1.50	23
16	M	39	Multiple stab wounds to chest/abdomen, ARDS	21	39	10	2.75	23
17	M	76	Pneumonia, ARDS, COPD	28	*	5	1.75	29
18	F	42	Necrotizing faciitis, ARDS, sepsis	26	164	10	2.50	57
Mean ± SD		48.2 ± 15.0		32 ± 11	137 ± 70	6.7 ± 2.8	1.95 ± .66	44.1 ± 18.3

C_{RS} = respiratory system compliance. C_{CW} = chest wall compliance. PEEP = positive end-expiratory pressure. LIS = lung injury score (ARDS Score).[19] MIP = maximal inspiratory pressure (esophageal). ALI = acute lung injury. ARDS = acute respiratory distress syndrome. ESLD = end-stage liver disease. COPD = chronic obstructive pulmonary disease. * = data unobtainable.

Table 2. Patient Variables Between VCV and PCV During Assisted Ventilation

Variable	VCV	PCV
$P_{0.1}$ (cm H_2O)	4.17 ± 5.14	4.05 ± 4.38
ΔP_{ES} (cm H_2O)	9.14 ± 5.48	7.45 ± 5.65*
PTP (cm $H_2O \cdot s \cdot min$)	95.7 ± 59.3	83.2 ± 53.8
WOB (J/L)	0.70 ± 0.58	0.59 ± 0.42†
$\dot{W}$ (J/min)	8.22 ± 4.42	6.92 ± 4.36*

Values are reported as mean ± standard deviation.
VCV = volume control ventilation.
PCV = pressure control ventilation.
$P_{0.1}$ = esophageal pressure in the first 100 miliseconds.
ΔP_{ES} = peak esophageal pressure.
PTP = pressure-time product.
WOB = work of breathing.
$\dot{W}$ = power output of the inspiratory muscles.
*$p < 0.01$.
†$p < 0.05$.

Table 3. Ventilator Variables Between VCV and PCV During Assisted Ventilation

Variable	VCV	PCV
V_T (mL/breath)	674 ± 88	685 ± 97
Total f (breaths/min)	18.2 ± 3.3	18.1 ± 3.3
Peak $\dot{V}_I$ (L/min)	43.8 ± 8.4	103.2 ± 22.8*
Peak P_{AW}	40.7 ± 8.4	32.7 ± 6.4†
Mean $\dot{V}_I$ (L/min)	40.7 ± 5.3	41.1 ± 5.8
$\dot{V}_E$ (L/min)	12.4 ± 2.9	12.5 ± 3.3

Values are reported as mean ± standard deviation.
VCV = volume control ventilation.
PCV = pressure control ventilation.
V_T = tidal volume.
f = respiratory frequency.
$\dot{V}_I$ = inspiratory flow rate.
P_{AW} = airway pressure.
$\dot{V}_E$ = minute ventilation.
*$p < 0.001$.
†$p < 0.05$.

respectively). Measurements of WOB, $\dot{V}_I$, pressure-time index, PTP, and the rapid-shallow breathing index (f/V_T) made during spontaneous breathing exceeded the levels thought to induce (or indicate) respiratory muscle fatigue and weaning intolerance. Therefore, our sample generally appeared to be ventilator-dependent.

A confounding variable ($PEEP_I$) was detected in 4 of 18 patients. In 3 cases (patients 3, 4, and 17) $PEEP_I$ was slightly higher during PCV than during VCV (3.03 cm H_2O vs 1.03 cm H_2O). However, WOB was less during PCV than VCV (0.73 J/L vs 0.82 J/L). All three of these

Table 4. Spontaneous Breathing Variables Measured in 16 Patients

Variable	Mean ± SD	Weaning Threshold
V_T (mL/breath)[23]	300 ± 120	≥ 400
f (breaths/min)[24]	30.1 ± 10.4	< 35
$\dot{V}_E$ (L/min)[25]	9.00 ± 4.99	< 10.0
f/V_T[26]	115.9 ± 58.9	< 105
Peak $\dot{V}_I$ (L/min)	33.0 ± 10.8	
Mean $\dot{V}_I$ (L/min)	20 ± 8.1	
ΔP_{ES} (cm H_2O)	14.2 ± 5.9	
ΔP_{ES}/MIP[27]	0.39 ± 0.16	< 0.40
WOB (J/L)[28]	1.40 ± 0.77	< 0.95
$\dot{W}$ (J/min)[29]	12.37 ± 9.93	< 10.0
T_I/T_{TOT}	0.41 ± 0.09	
T_I	0.89 ± 0.33	
PTI[30]	0.16 ± 0.06	0.15
PTP (cm $H_2O \cdot s \cdot min$)[17]	279.5 ± 127.3	< 150

V_T = tidal volume.
f = respiratory rate.
$\dot{V}_E$ = minute ventilation.
f/V_T = rapid shallow breathing index.
$\dot{V}_I$ = inspiratory flow rate.
ΔPES = peak esophageal pressure.
ΔP_{ES}/MIP = ΔPES as a fraction of maximal inspiratory esophageal pressure.
WOB = inspiratory work per liter of ventilation.
$\dot{W}$ = inspiratory muscle power output.
T_I/T_{TOT} = inspiratory time fraction.
T_I = inspiratory time.
PTI = pressure-time index.
PTP = pressure-time product.

Table 5. Differences in Dependent Measures Between VCV and PCV During Assisted Ventilation After Excluding Patients with $PEEP_I$

Variable	VCV	PCV
$P_{0.1}$ (cm H_2O)	4.54 ± 5.81	4.09 ± 4.94
ΔP_{ES} (cm H_2O)	6.78 ± 5.75	5.63 ± 5.84
PTP (cm $H_2O \cdot s \cdot min$)	90.45 ± 62.21	66.2 ± 39.70*
WOB (J/L)	0.56 ± 0.56	0.49 ± 0.34†
$\dot{W}$ (J/min)	7.23 ± 4.45	6.10 ± 4.61‡
V_T (mL/breath)	680 ± 80	690 ± 90
$\dot{V}_E$ (L/min)	12.44 ± 2.46	12.26 ± 2.94

Values are reported as mean ± standard deviation.
VCV = volume control ventilation.
PCV = pressure control ventilation.
$P_{0.1}$ = esophageal pressure in the first 100 milliseconds.
ΔPES = peak esophageal pressure.
PTP = pressure-time product.
WOB = work of breathing.
$\dot{W}$ = power output of the inspiratory muscles.
V_T = tidal volume.
$\dot{V}_E$ = minute ventilation.
*$p < 0.01$.
†$p < 0.05$.
‡$p < 0.001$.

patients had an underlying component of chronic obstructive pulmonary disease or asthma. Expiratory activity was minimal in either mode. In the remaining case (patient 10) $PEEP_I$ varied greatly between modes (5.1 cm H_20 vs 12.3 cm H_2O for PCV and VCV, respectively) as did WOB (1.68 J/L and 2.28 J/L for PCV and VCV, respectively). Active expiratory effort was prominent during VCV. We suspected that $PEEP_I$ was attributable to mild dynamic hyperinflation in the first 3 patients and active expiration in patient 10.[22,31] When the data were reanalyzed after excluding all cases with $PEEP_I$, PTP was significantly lower during PCV ($p < 0.05$) (Table 5). All other significant results of dependent variables from the main data pool remained significant during reanalysis. V_T, total f, $\dot{V}_I$, and $P_{0.1}$ were not different between modes when all cases with $PEEP_I$ were removed.

Discussion

The main finding of our study was that PCV was more effective than VCV in reducing patient WOB, ΔP_{ES}, and $\dot{W}_I$ during assisted ventilation at a constant mean ventilator $\dot{V}_I$. When $PEEP_I$ was controlled for in the analysis, PTP also was significantly less with PCV. Both PTP and $\dot{V}_I$ are mechanical correlates of respiratory muscle oxygen consumption.[32] We believe that the attributes of PCV (a high peak ventilator $\dot{V}_I$, demand-responsive changes in peak ventilator $\dot{V}_I$, and a sustained high $\dot{V}_I$ when patient effort is prolonged) were responsible for the lower patient WOB with PCV, relative to VCV. The most important factor probably was the peak ventilator $\dot{V}_I$, which was significantly higher during PCV than during VCV. The demand-responsive changes in peak ventilator $\dot{V}_I$ and a sustained high $\dot{V}_I$ were assessed by the variability in both peak ventilator $\dot{V}_I$ and V_T, respectively. We calculated the standard deviation in the breaths used for analysis in individual subjects in each mode. We found that the mean standard deviation for peak ventilator $\dot{V}_I$ was over two and one half times higher during PCV than during VCV (9.6 L/min and 3.6 L/min, respectively). In each patient, V_T variability was not different between the modes. Therefore, the ability of PCV to vary peak ventilator $\dot{V}_I$ on a breath-to-breath basis (and not variability in V_T size) also may have contributed to reducing patient WOB during PCV.

We hypothesized that PCV would diminish both the elastic and resistive components of work. The Campbell diagram is used to assess the total mechanical WOB by accounting for the elastic load contributed by the chest wall.[33] Although the Campbell diagram also can be used to differentiate elastic from resistive work during spontaneous breathing[33] and weaning,[14,34] its use is not valid during high levels of assisted ventilation.[14] However, inspection of the P_{ES}-V_T curves generated during assisted ventilation may provide some insight into the nature of the total work

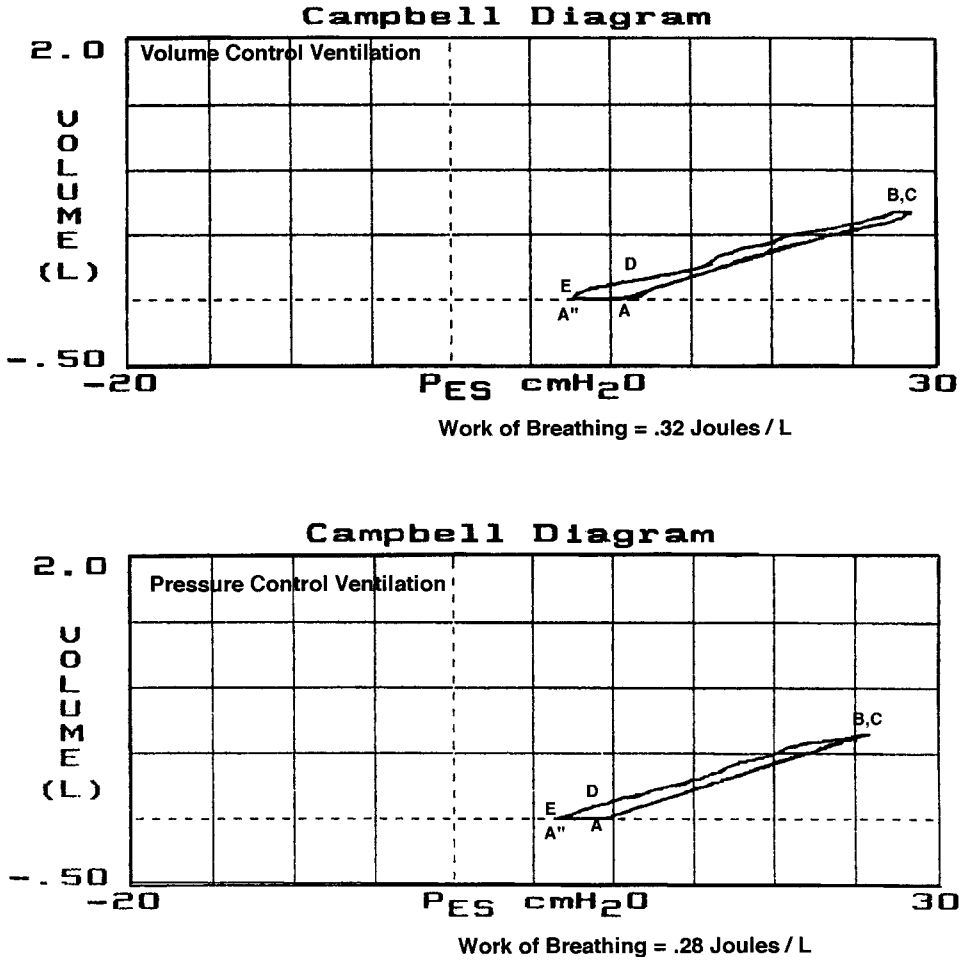


Fig. 5. Campbell diagram peak esophageal pressure vs tidal volume (P_{ES}-V_T) loops comparing low levels of assisted work of breathing (WOB) between volume control ventilation (VCV) and pressure control ventilation (PCV). The loops were matched for V_T and approximate agreement in baseline pressure. A, B, C, D, E, A′ and A″ are as defined in the legends for Figures 2 and 3. The contour of the pressure-volume loops are almost indistinguishable between VCV and PCV. These tracings suggest the equivalence in WOB reduction between modes at low levels of effort.

performed by patients in each mode. The P_{ES}-V_T curves from assisted VCV and PCV (Figs. 3–5) were characteristic of the differences in waveform morphology found across the sample between modes. At both high and moderate levels of patient work, P_{ES} continued to move in a negative direction despite constant volume change during VCV (see Figs. 3 and 4). We interpreted this as indicating the presence of imposed resistive WOB. Furthermore, P_{ES} often remained below the end-expiratory (baseline) pressure at end-inspiration. This indicated to us that the volume control breath did not reduce the elastic WOB associated with lung inflation and chest wall displacement. During PCV, P_{ES} tended to change in a positive direction at a lower volume (see Fig. 3). This tendency supports the concept that PCV's rapid ventilator $\dot{V}_I$ and V_T delivery may exceed the contractile velocity of the inspiratory muscles, thereby arresting the drop in muscle pressure and thus reducing both the resistive and elastic WOB. At low levels of patient effort the P_{ES}-V_T curves were almost indistinguishable, with minimal differences in work (see Fig. 5). This suggests that patient WOB is not different between modes at low effort.

To our knowledge, only Cinnella et al[35] have directly compared patient WOB between assisted VCV and PCV. They reported no differences in patient WOB at 12 mL/kg V_T but significantly less work during PCV at 8 mL/kg V_T. As in our study, Cinnella et al kept V_T and mean ventilator $\dot{V}_I$ constant between modes. In our study V_T was kept at the level used for clinical management (10.0 ± 2.5 mL/kg). We found no relationship between V_T size and patient WOB in either mode (rho = 0.09). We believe the differences in results between studies are explained by peak ventilator $\dot{V}_I$ performance during PCV. Peak ventilator $\dot{V}_I$ during VCV was comparable to our study (43.8 L/min vs

43.2 L/min, respectively) and the pre-set T_I in each mode was the same as in our study (1 s). However, the peak ventilator $\dot{V}_I$ during PCV reported by Cinnella et al[35] was much lower than in our study (54.6 L/min vs 103.2 L/min, respectively). The small differences in peak ventilator $\dot{V}_I$ between modes reported by Cinnella et al[35] were probably due to the fact that many of their subjects had severe obstructive lung disease with high inspiratory resistance. High inspiratory resistance decreases peak ventilator $\dot{V}_I$ in PCV because less flow is needed to achieve the target airway pressure.[36] In addition, high inspiratory resistance during PCV causes ventilator $\dot{V}_I$ to taper off slowly (because of the slower rate-rise in alveolar pressure)[36] so that the flow waveform was transformed in the Cinnella study from an exponential decelerating to a quasirectangular pattern (L Brochard, Henri Mondor Hospital at the University of Paris, 2000, personal communication). The differences in WOB at 8 mL/kg V_T for the entire sample were probably due to the larger differences in peak ventilator $\dot{V}_I$ between VCV and PCV in the subset of patients without obstructive lung disease (45 L/min vs 67 L/min, respectively).[35]

Two related studies compared the effects of variable versus constant flow wave forms on WOB. Haas et al[37] compared VCV to volume-assured pressure support ventilation (VAPS). During VAPS, peak ventilator $\dot{V}_I$ was higher (63 L/min) than during VCV (54 L/min), although mean ventilator $\dot{V}_I$ appears to have been the same as in our study. The differences in patient WOB between VAPS and VCV was similar to ours (0.43 J/L vs 0.52 J/L, respectively). However, VAPS does not function the same as PCV. In VAPS both peak airway pressure and minimum V_T are set so that the ventilator controls $\dot{V}_I$ according to two algorithms. The ventilator $\dot{V}_I$ wave form of VAPS was a hybrid resembling a half-sine wave during early inspiration and a constant flow pattern in the later part of inspiration.[37]

MacIntyre et al[38] compared the effectiveness of treating patient-ventilator flow-dyssynchrony either by increasing ventilator $\dot{V}_I$ during VCV (by shortening T_I) or by adding a "pressure-limiting feature" to the breathing pattern. This latter approach appeared to alter peak ventilator $\dot{V}_I$ by incorporating a decelerating flow pattern. PTP (in cm H_2O) rather than WOB (in J/L) was measured. Although there was an improvement in PTP during the pressure-limited breath delivery, the difference was not statistically significant.[38] Comparing our study to that of MacIntyre et al[38] is difficult. In their study, differences in V_T, T_I, and f occurred between treatments and the resulting differences in both peak and mean ventilator $\dot{V}_I$ across treatments were not reported.

MacIntyre et al[38] treated ventilator $\dot{V}_I$ dyssynchrony with VCV by reducing T_I to approximately 0.5 second (compared to approximately 1 s during the pressure-limited breaths) in order to achieve comparable levels of work reduction.[38] Depending on ventilator design, shortening T_I may have a significant clinical impact. The Siemens 900C cannot set T_I independently of the control f. In addition, V_T is determined by both the control f and the pre-set $\dot{V}_E$. Therefore, in ventilators designed like the Siemens 900C, treating ventilator $\dot{V}_I$ dyssynchrony by shortening T_I (at a constant V_T) requires a higher f and pre-set $\dot{V}_E$. This may exceed both the f and $\dot{V}_E$ requirements of the patient, resulting in hypocapnia and complete suppression of spontaneous effort. Also, preliminary evidence suggests that using a high mean ventilator $\dot{V}_I$ may inadvertently increase respiratory drive and may cause dyssynchrony between the patient and ventilator.[39]

Our study did not address whether raising peak ventilator $\dot{V}_I$ during VCV to equal that achieved during PCV accomplishes the same reduction in WOB. To approach the peak ventilator $\dot{V}_I$ achieved during PCV (103.2 L/min) with VCV would have required a pre-set $\dot{V}_I$ that exceeded patient demand. It is of interest to note that our study, as well as the studies by Cinella et al[35] and Hass et al,[37] all set VCV with a mean ventilator $\dot{V}_I$ significantly less than 60 L/min. However, when MacIntyre et al[38] used a mean ventilator $\dot{V}_I$ of 76 L/min to treat $\dot{V}_I$ dyssynchrony, PTP was not significantly different. In fact, PTP was higher during VCV than during pressure-limited breaths at a more appropriate T_I.[38] Several recent studies have all reported that high ventilator $\dot{V}_I$ delivered with a rectangular wave causes respiratory center excitation manifested by increased *f*.[39–42] Bshouty and Georgopoulos[43] found that high mean ventilator $\dot{V}_I$, rather than peak ventilator $\dot{V}_I$, may be responsible for the respiratory center excitation. Therefore, a high peak ventilator $\dot{V}_I$ with VCV may lessen patient WOB, but at a certain point this may be countered by the effects of high mean ventilator $\dot{V}_I$ on respiratory drive. In addition, our study did not address the issue of whether using VCV with a decelerating flow wave form would have produced the same results. We think it is reasonable to predict that VCV with a decelerating flow wave form would reduce WOB more than VCV with a constant or rectangular flow wave form. However, peak ventilator $\dot{V}_I$ would remain fixed and would not necessarily be adequate in situations where patient flow demand was both vigorous and fluctuating.

Conclusions

In conclusion, PCV may help in the management of critically ill patients with ALI and ARDS by reducing patient WOB, $\dot{W}$, and PTP. We attributed these reductions to the characteristic high, variable ventilator $\dot{V}_I$ and faster V_T delivery of PCV. In addition, in ventilators where T_I cannot be set independently of control f, PCV allows for

better flow matching without the necessity of setting backup f and $\dot{V}_E$ in excess of patient demand.

REFERENCES

1. Marini JJ, Capps JS, Culver BH. The inspiratory work of breathing during assisted mechanical ventilation. Chest 1985;87:612–618.
2. Marini JJ, Rodriguez M, Lamb V. The inspiratory workload of patient-initiated mechanical ventilation. Am Rev Respir Dis 1986;134: 902–909.
3. Ward ME, Corbeil C, Gibbons W, Newman S, Macklem PT. Optimization of respiratory muscle relaxation during mechanical ventilation. Anesthesiology 1988;69:29–35.
4. Sassoon CSH, Mahutte CK, Te TT, Simmons DH, Light RW. Work of breathing and airway occlusion pressure during assist-mode mechanical ventilation. Chest 1988;93:571–576.
5. Derenne JPH, Macklem PT, Roussos CH. The respiratory muscles: mechanics, control and pathophysiology. Am Rev Respir Dis 1978; 118:119–133.
6. Silverman L, Lee G, Plotkin T, Sawyers LA, Yancey AR. Air flow measurements on human subjects with and without respiratory resistance at several work rates. Arch Ind Hyg Occup Med 1951;3: 461–478.
7. Bernasconi M, Ploysongsang Y, Gottfried SB, Milic-Emili J, Rossi A. Respiratory compliance and resistance in mechanically ventilated patients with acute respiratory failure. Intensive Care Med 1988;14: 547–553.
8. Katz JA, Zinn SE, Ozanne GM, Fairley HB. Pulmonary, chest wall, and lung-thorax elastances in acute respiratory failure. Chest 1981; 80:304–311.
9. Marini JJ. The role of the inspiratory circuit in the work of breathing during mechanical ventilation. Respir Care 1987;32:419–427; discussion 427–430.
10. Kallet R. The effects of flow patterns on pulmonary gas exchange, lung-thorax mechanics, and circulation. Respir Care 1996;41:611–624.
11. Bernard GR, Artigas A, Brigham KL, Carlet J, Falke K, Hudson L, et al. The American-European Consensus Conference on ARDS: Definitions, mechanisms, relevant outcomes and clinical trial coordination. Am J Respir Crit Care Med 1994;149:818–824.
12. Baydur A, Behrakis PK, Zin WA, Jaeger M, Milic-Emili J. A simple method for assessing the validity of the esophageal balloon technique. Am Rev Respir Dis 1982;126(5):788–791.
13. Marini JJ, Smith TC, Lamb V. Estimation of inspiratory muscle strength in mechanically ventilated patients: The measurement of P_{Imax}. J Crit Care 1986;1:32–38.
14. Van de Graaff WB, Gordey K, Dornseif SE, Dries DJ, Kleinman BS, Kumar P, Mathru M. Pressure support: changes in ventilatory pattern and components of the work of breathing. Chest 1991;100:1082–1089.
15. Blanch PB, Banner MJ. A new respiratory monitor that enables accurate measurements of work of breathing: a validation study. Respir Care 1994;39:897–905.
16. Petros AJ, Lamond CT, Bennett D. The Bicore pulmonary monitor: a device to access the work of breathing while weaning from mechanical ventilation. Anaesthesia 1993;48:985–988.
17. Sassoon CSH, Light RW, Lodia R, Sieck GC, Mahutte CK. Pressure-time product during continuous positive airway pressure, pressure support ventilation, and T-piece during weaning from mechanical ventilation. Am Rev Respir Dis 1991;143:469–475.
18. Pelosi P, Cereda M, Foti G, Giacomini M, Pesenti A. Alterations of lung and chest wall mechanics in patients with acute lung injury: effects of positive end-expiratory pressure. Am J Respir Crit Care Med 1995;152:531–537.
19. Murray JF, Matthay MA, Luce JM, Flick MR. An expanded definition of the adult respiratory distress syndrome. Am Rev Respir Dis 1988;138:720–723.
20. Alberti A, Gallo F, Fongaro A, Valenti S, Rossi A. $P_{0.1}$ is a useful parameter in setting the level of pressure support ventilation. Intensive Care Med 1995:21:547–553.
21. Hubmayr RD. Setting the ventilator. In: Tobin MJ, editor. Principles and practice of mechanical ventilation. New York: McGraw-Hill; 1994: 191–206.
22. Marini JJ. Monitoring during mechanical ventilation. Clin Chest Med 1988;9:73–100.
23. Morganroth ML, Morganroth JL, Nett LM, Petty TL. Criteria for weaning from prolonged mechanical ventilation. Arch Intern Med 1984;144:1012–1016.
24. Lemaire F. Difficult weaning. Intensive Care Med 1993;19:S69–S73.
25. Sahn SA, Lakshminarayan S. Bedside criteria for discontinuation of mechanical ventilation. Chest 1973;63:1002–1005.
26. Yang KL, Tobin MJ. A prospective study of indexes predicting the outcome of trials of weaning from mechanical ventilation. N Engl J Med 1991;324:1445–1450.
27. Roussos C, Macklem PT. Diaphragmatic fatigue in man. J Appl Physiol 1977;43:189–197.
28. Levy MM, Miyasaki A, Langston D. Work of breathing as a weaning parameter in mechanically ventilated patients. Chest 1995;108:1018–1020.
29. Henning RJ, Shubin H, Weil MH. The measurement of the work of breathing for clinical assessment of ventilator dependence. Crit Care Med 1977;5:264–268.
30. Bellemere F, Grassino A. Effect of pressure and timing of contraction on human diaphragm fatigue. J Appl Physiol 1982;53:1190–1195.
31. Petrof BJ, Legare M, Goldberg P, Milic-Emili J, Gottfried SB. Continuous positive airway pressure reduces work of breathing and dyspnea during weaning from mechanical ventilation in severe chronic obstructive pulmonary disease. Am Rev Respir Dis 1990;141:281–289.
32. Collett PW, Perry C, Engel LA. Pressure-time product, flow and oxygen cost of resisitve breathing in humans. J Appl Physiol 1985; 58:1263–1272.
33. Campbell EJM. The respiratory muscles and the mechanics of breathing. Chicago: Year Book Publishers; 1958: 83–87.
34. Banner MJ, Kirby RR, Gabrielli A, Blanch PB, Layon AJ. Partially and totally unloading respiratory muscles based on real-time measurements of work of breathing: a clinical approach. Chest 1994; 106:1835–1842.
35. Cinnella G, Conti G, Lofaso F, Lorino H, Harf A, Lemaire F, Brochard L. Effects of assisted ventilation on the work of breathing: volume-controlled versus pressure-controlled ventilation. Am J Respir Crit Care Med 1996;153:1025–1033.
36. Blanch PB, Jones M, Layon AJ, Camner N. Pressure-present ventilation. Part 1: Physiologic and mechanical considerations. Chest 1993; 104:590–599.
37. Haas CF, Branson RD, Folk LM, Campbell RS, Wise CR, Davis K, et al. Patient-determined inspiratory flow during assisted mechanical ventilation. Respir Care 1995;40:716–721.
38. MacIntyre NR, McConnell R, Cheng KCG, Sane A. Patient-ventilator flow dyssynchrony: flow-limited versus pressure-limited breaths. Crit Care Med 1997;25:1671–1677.
39. Fernandez R, Mendez M, Younes M. Effect of ventilator flow rate in the volume-cycled mode on neural inspiratory duration (TIN) in normal subjects (abstract). Am J Respir Crit Care Med 1997;155: A83.

40. Puddy A, Younes M. Effect of inspiratory flow rate on respiratory output in normal subjects. Am Rev Respir Dis 1992;146:787–789.
41. Hawryluck L, Georgopoulos D, Bshouty Z. Interaction between peak inspiratory flow and mechanical inspiratory time (TIM) and their effect on respiratory output (abstract). Am J Respir Crit Care Med 1997;155:A363.
42. Leevers AM. The effects of varying inspiratory flow rate during assisted ventilation on respiratory output (abstract). Am J Respir Crit Care Med 1997;155:A365.
43. Bshouty Z, Georgopoulos D. The effect of mean versus peak inspiratory flow on respiratory output (abstract). Am J Respir Crit Care Med 1997;155:A365.