

Response of Ventilator-dependent Patients to Different Levels of Pressure Support and Proportional Assist

ELENI GIANNOULI, KIM WEBSTER, DAN ROBERTS, and MAGDY YOUNES

Sections of Respiratory and Critical Care Medicine, Department of Medicine, University of Manitoba, Winnipeg, Manitoba, Canada

The ventilator's response to the patient's effort is quite different in proportional assist ventilation (PAV) and pressure support ventilation (PSV). We wished to determine whether this results in different ventilatory and breathing pattern responses to alterations in level of support and, if so, whether there are any gas exchange consequences. Fourteen patients were studied. Average elastance (E) was 22.8 (range, 14–36) cm H₂O/L and average resistance (R) was 15.7 (range, 9–21) cm H₂O/L/s. The highest PSV support (PSVmax) was that associated with a tidal volume (V_T) of 10 ml/kg (20.4 ± 3.2 cm H₂O), and the highest level of PAV assist (PAVmax) was 78 ± 7% of E and 76 ± 7% of R. Level of assist was decreased in steps to the lowest tolerable level (PSVmin, PAVmin). Minute ventilation, V_T, ventilator rate (RRvent), and arterial gas tensions were measured at each level. We also determined the patient's respiratory rate (RRpat) by adding the number of ineffective efforts (ΔRR) to RRvent. There was no difference between PSVmin and PAVmin in any of the variables. At PSVmax, V_T was significantly higher (0.90 ± 0.30 versus 0.51 ± 0.16 L) and RRvent was significantly lower (13.2 ± 3.9 versus 27.6 ± 10.5 min⁻¹) than at PAVmax. The difference in RRvent was largely related to a progressive increase in ineffective efforts on PSV as level increased (ΔRR 12.1 ± 10.1 vs 1.4 ± 2.1 with PAVmax); there was no significant difference in RRpat. The differences in breathing pattern had no consequence on arterial blood gas tensions. We conclude that substantial differences in breathing pattern may occur between PSV and PAV and that these are largely artifactual and related to different patient-ventilator interactions. Giannouli E, Webster K, Roberts D, Younes M. Response of ventilator-dependent patients to different levels of pressure support and proportional assist.

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Pressure support ventilation (PSV) (1, 2) and proportional assist ventilation (PAV) (3–5) differ fundamentally in the relation between timing and pressure amplitude of ventilator cycle on one hand, and timing and pressure amplitude of the patient's inspiratory effort on the other hand. Because with PAV ventilator pressure output (airway pressure [Paw]) is proportional to instantaneous patient effort (Pmus), there is automatic synchrony between the ends of the patient's effort and ventilator cycle. Furthermore, because Paw remains proportional to Pmus at all levels of assist, the total pressure applied (Paw and Pmus), and hence tidal volume (V_T), remain under the control of the patient, even at the highest assist levels (3).

By contrast, with PSV there is no automatic linkage between the end of the patient's effort and the end of the ventilator cycle. The timing of one relative to the other is governed

in a complex way by many factors, the most important of these being the patient's respiratory mechanics, the flow level used to cycle the ventilator off, and the magnitude of set PSV relative to Pmus (2, 6, 7). Apart from the issue of synchrony, the fact that Paw is independent of Pmus renders V_T more controlled by the ventilator, since at least one of the major V_T determining forces (i.e., Paw) is independently controlled by the operator.

Because of these differences, it may be suspected that the response of V_T and respiratory rate (RR) to changes in level of assist may differ in the two modes. In the present study we compare the response of ventilation, breathing pattern, and gas exchange to different levels of PAV and PSV in a group of ventilator-dependent patients with assorted pathology.

METHODS

Clinical Studies

We studied 14 patients who were placed on mechanical ventilation for a variety of disorders (Table 1). The study was done 2–7 d after intubation at a time when the clinical condition was stable (no need for vaso-pressors and no significant hemodynamic events or arrhythmias in the preceding 24 h). The protocol was approved by the Institutional Review Board and informed consent was obtained from patient or next of kin. All patients were ventilated on PSV prior to the study. The levels used and associated breathing pattern and blood gas tensions are

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Correspondence and requests for reprints should be addressed to Dr. M. Younes, Respiratory Hospital, RS 315, 810 Sherbrook St., Winnipeg, MB, R3A 1R8 Canada.

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TABLE 1
PATIENT CHARACTERISTICS AND BASELINE DATA

Patient No.	Age	Weight (kg)	E	R _T	F _I O ₂	PaO ₂	PaCO ₂	pH	ET	PEEP	PSV	V _T	RR	Diagnosis
1	74	75	33	17	0.40	89	42	7.46	8	5.0	6	0.36	33	CABG, post-op bleeding, pneumonia
2	68	88	16	19	0.50	78	49	7.38	7.5	7.5	14	0.70	28	Severe COPD, pneumonia
3	62	85	26	18	0.40	99	34	7.51	8	4.0	20	0.80	22	Meningitis, septic shock, acute tubular necrosis
4	62	89	34	10	0.40	118	35	7.27	8	4.0	20	0.90	12	Pneumonia, CHF
5	73	65	26	12	0.40	83	41	7.35	8	5.0	12	0.30	23	ARDS, lymphoma, nephrotic syndrome
6	46	71	26	15	0.40	99	28	7.51	8	5.0	20	0.60	24	MVA, intracranial bleeding, pneumonia
7	78	92	14	15	0.50	99	43	7.42	8	5.0	9	0.50	40	Repaired AAA
8	85	97	14	13	0.60	70	60	7.38	8	5.0	15	0.60	12	CVA, aspiration pneumonia
9	53	74	36	21	0.55	94	49	7.4	8	5.0	15	0.80	18	Mesenteric thrombosis
10	67	108	16	18	0.50	99	45	7.31	8	5.0	10	0.80	23	CVA, COPD, CRF
11	55	99	15	16	0.50	106	46	7.46	8	5.0	15	0.70	17	MVA, flail chest, hemopneumothorax
12	73	70	18	20	0.45	124	53	7.37	8	7.5	15	0.8	13	Pneumonia, respiratory failure
13	81	82	23	9	0.50	70	51	7.34	8	10.0	12	0.52	22	Pneumonia, COPD exacerbation
14	81	84	22	15	0.40	139	40	7.41	7	5.0	10	0.38	37	CHF, muscle weakness, CVA
Mean	68.4	84.2	22.8	15.7	0.46	98	44	7.40	7.9	5.6	13.8	0.63	23.1	
SD	11.6	12.4	7.7	3.7	0.07	20	8.4	0.07	0.3	1.6	4.3	0.19	8.8	

Definition of abbreviations: AAA = abdominal aortic aneurysm; ARDS = adult respiratory distress syndrome; CABG = coronary artery bypass; CHF = congestive heart failure; CRF = chronic renal failure; CVA = cerebrovascular accident; E = elastance in cm H₂O/L; ET = endotracheal tube size; MVA = motor vehicle accident; PEEP = positive end-expiratory pressure (cm H₂O); PSV = pressure level during pressure support ventilation; RR = respiratory rate counted from ventilator cycles; R_T = total resistance in cm H₂O/L/s flow; V_T = tidal volume.

shown in Table 1. All patients were ventilator-dependent as evidenced by development of respiratory distress upon attempts to reduce PSV.

Apparatus. A heated pneumotachograph was inserted between the endotracheal tube and the Y connector to measure respired flow and volume. Paw was monitored at the Y connector. The exhalation valve was connected to a 10-L mixing chamber, and the P_{CO₂} in the chamber (P_{eCO₂}) was monitored with a capnograph (Normocap 200; DATEX, Helsinki, Finland). The flow, volume, Paw, and P_{eCO₂} were recorded on a computer disk.

In three patients (Patients 12–14) a fluid-filled esophageal catheter was inserted for direct monitoring of the patient's efforts. The catheter was connected to a fluid-filled transducer (CDX press 3; COBE, Lakewood, CO). Saline was injected at a constant rate of 3 ml/h. The catheter was advanced so that the side hole was 35 cm from the nose. In each case there were strong cardiac oscillations and rhythmic negative respiratory efforts. The catheter was then moved slightly up or down to the level associated with minimal cardiac artifacts.

We used the Winnipeg ventilator. It has been described in detail earlier (4). Briefly, it is a piston-based ventilator that can provide PAV, PSV, and volume-cycled ventilation. Positive end-expiratory pressure (PEEP) is applied by attaching a PEEP valve to the exhalation valve and pressurizing the piston during expiration to a comparable level using an external control. In this fashion inspiratory flow begins as soon as Paw decreases below PEEP. The inspiratory cycle is flow-triggered, with the flow triggering level being externally adjustable. In the current experiments trigger sensitivity was set to the lowest level not associated with false triggering (≤ 0.1 L/s).

In the PSV mode, the adjustable rate of rise of pressure (attack rate) was set to a time constant of 200 ms. The flow at which cycling off occurred was set to a fixed level of 0.1 L/s. In the PAV mode the levels of flow assist (FA) and volume assist (VA) were independently controlled using adjustable external analog dials.

Protocol. The Winnipeg ventilator was initially set in the PSV mode at identical fraction of inspired oxygen (F_IO₂), PEEP, and PSV levels to those used previously. After a few minutes to allow the patient to adjust to the new ventilator, the mode was switched to AC in the volume cycled mode to measure respiratory elastance (E) and resistance (R). V_T was set to the level observed on PSV or to 8 ml/kg,

whichever was higher. Flow was set at 1.0 L/s. Back-up rate was increased until no triggering efforts were visible and the pressure waveform was reproducible (controlled mechanical ventilation [CMV]). Single-breath inspiratory hold maneuvers were carried out. A rough calculation of E and R was made at the bedside ($R = [(peak\ pressure - plateau\ pressure)/\dot{V}]$ and $E = [(plateau\ pressure - PEEP)/V_T]$). The relevant values were read off a needle meter on the face of the ventilator. More precise determinations of E and R were made at the end of the study from the computer stored data (*see below*).

Different levels of PSV and PAV were then studied. The order of testing (PSV first or PAV first) was randomized. The highest level of support was initially tested. For PSV, this was the level producing a V_T of approximately 10 ml/kg, which, according to MacIntyre and colleagues (8, 9), is associated with minimal work of breathing. For PAV the highest level was initially 80% of E and R, as determined in the CMV mode. After switching to PAV, end-inspiratory occlusions were repeated and E on PAV was recomputed (5). Subsequently the value of E obtained on PAV was used to set the high level of VA (80% of E).^{*} The high assist level was maintained for 10–15 min. With each mode, the level of assist was subsequently reduced in steps of 20% of the initial setting. Each step was maintained for 10–15 min. Decrements continued until a level was reached where some distress (accessory muscles use, chest wall indrawing, or paradox) became evident. At this point assist was increased to the highest level and this was maintained for 20–30

^{*} We used the value of E obtained during PAV (as opposed to that obtained during CMV), since it is the relevant elastance during breathing on PAV. Although on average E on PAV and on CMV are similar, there is some scatter, with some patients displaying higher E on CMV, and vice versa. In a systematic comparison in 48 patients, with a range of elastance between 13 and 83 on CMV, the correlation (r) between E on PAV and on AC was 0.93, with a slope of 0.97 and intercept of 2.2 (not different from zero). The SD of the difference between the two measurements was 14% of the CMV value (for preliminary report, see Reference 27). Differences between E on PAV and on CMV in individual patients can be due to differences in V_T in the face of nonlinear elastic behavior, differences in T_i in the face of important viscoelastic behavior (28), or to differences in volume at the beginning of inspiration due to differences in degree of DH or to use of expiratory muscles during PAV (28).

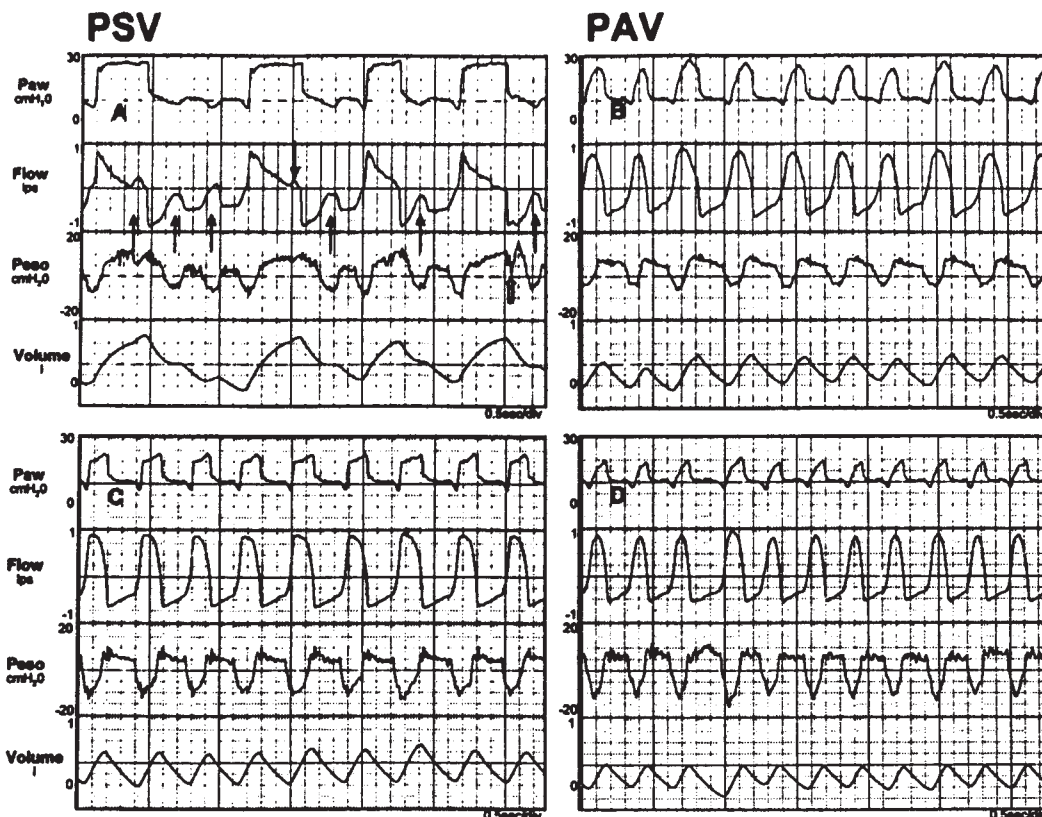


Figure 1. Airway pressure (Paw), flow, esophageal pressure (Pes), and volume tracings from patient 12 at two levels of PSV (A and C) and two levels of PAV (B and D). (A) PSV = 18 cm H₂O; (B) high PAV (actual % assist = 75%); (C) PSV = 12; (D) low PAV (actual % assist = 37%). (A) Upward pointing solid arrows represent transients in the flow and Paw tracings that were identified as ineffective efforts (see Footnote¹). Downward pointing solid arrow indicates a flow transient that was questionable. Open arrow denotes an ineffective inspiratory effort (from Pes tracing) that was not identified from the flow and Paw tracing. Note that breathing patterns at the two PSV levels are substantially different (slow and deep in [A], rapid and shallow in [B]) despite similar patient's respiratory rate (RRpat) (compare Pes tracing), and RRpat is similar in all four conditions despite different levels and types of support and different magnitude of inspiratory effort.

min. The procedure was then repeated for the other mode. The step during which distress occurred was not used for analysis.

Computer data were collected the last 3–5 min at each step. In 11 patients (Patients 1–11), an arterial blood sample was analyzed for PaO₂, PaCO₂, and pH at each step.

Analysis. The last 2 min of the computer-stored data were analyzed at each step to obtain average V_T, ventilator respiratory rate (RRvent), inspiratory time of the ventilator cycle (T_i) calculated from triggering to the point of resetting of pressure, respiratory duty cycle (T_i/T_{tot}), V_E, peak inspiratory pressure, and PEEP. CO₂ production (V̇CO₂) was computed from minute ventilation (V̇_E) and mixed expired CO₂ concentration. The computer data were also used to obtain the following:

1. **Actual respiratory rate of the patient (RRpat).** The Paw and ventilation (V̇) tracings at each step were examined for evidence of ineffective inspiratory efforts. At times during PSV the inflation cycle spanned more than one breath (Figure 1, top). The occurrence of a second inspiration during the same inflation cycle was defined as the occurrence of a secondary increase in inspiratory flow that is clearly distinguishable from signal noise (6, 7), lasting at least 0.3 s and associated with no increase (usually there is a small decrease) in Paw.² Ineffective efforts occurring during the ventilator's expiratory phase were counted when there was an unambiguous (i.e., clearly distinguishable from noise) transient reduction in expiratory flow associated with reduction in Paw and lasting at least 0.3 s (Figure 1, top) (6, 7). These dips were distinguished from artifacts by their duration and their occurrence at fairly regular intervals

¹ The criteria used to define ineffective efforts were based on the following considerations: To the extent that flow during the inspiratory phase is determined by (Paw – Palv)/R, a secondary increase in inspiratory flow during the inflation phase, despite the same or lower Paw, can only result if alveolar pressure (Palv) decreased or R transiently decreased. Changes in R due to changes in bronchomotor tone or to accumulation of thick secretions take place over a completely different time scale. Less viscid secretions can cause quick changes in R due to bubbling. The pattern, however, is readily recognizable. A decrease in Palv during an ongoing inflation, with progressively increasing volume (and hence, transpulmonary pressure), can only mean that pleural pressure (Ppl) decreased even more. It follows that a secondary increase in inspiratory flow, at similar or lower Paw, must be the result of a secondary reduction in Ppl. Likewise, transient departure of expiratory flow, in an inspiratory direction, from the flow trajectory established earlier during expiration can result either from a negative deviation in Palv, and hence Ppl, from its established trajectory or to an increase in R upstream or downstream from the Paw port. Changes in R upstream are subject to the same qualifications mentioned earlier. Changes in R of the expiratory tubing are excluded as the cause if Paw also decreases during the transient; an increase in external expiratory resistance would decrease flow but with an increase in Paw. It follows that a transient reduction in expiratory flow along with reduction in Paw can only result from a transient reduction in Palv, and hence Ppl. The additional constraints used with both inspiratory and expiratory transients, of a minimum duration of 0.3 s and occurrence at fairly regular intervals consistent with respiratory rhythm, help eliminate other sources of nonrespiratory reductions in Ppl (e.g., flow transients related to cardiac artifacts, movement, etc.). In addition, these constraints help exclude transients related to physical changes in bronchial or endotracheal tube secretions.

consistent with respiratory rhythm (Figure 1A) (*see* footnote on preceding page). The average number/min of these ineffective efforts was computed at each step (ΔRR) and this was added to RRvent to arrive at true RR of the patient (RRpat). In the three patients in whom an esophageal catheter was inserted, RRpat was determined separately from the flow/Paw signals (as above) and from the esophageal pressure (Pes) signal. To avoid bias, the Pes signal was not displayed on the screen during determinations from flow/Paw, and vice versa.

2. *Recalculation of respiratory mechanics.* Bedside measurements of E and R were obtained from rapidly changing needle display and were not precise. The computer data were used to precisely calculate R and E on CMV and E on PAV. The values of E and R obtained in this fashion during CMV are reported in Table 1.
3. *Calculation of FA and VA actually delivered during PAV.* The external analog dials for FA and VA on the Winnipeg ventilator do not offer optimal resolution or accuracy. For these reasons we determined the actual assist delivered as opposed to relying on the dial position at the time of data collection. The actual FA and VA at each PAV step were computed by sampling Paw, \dot{V} , and inspired volume at two points during randomly selected breaths. In these breaths one point was selected at peak flow while the other was selected near end inspiration, where inspired volume is high and flow is relatively low. The two sets of values were used to solve for the two unknowns (FA and VA) in the PAV assist equation: $Paw - PEEP = FA \cdot \dot{V} + VA \cdot V$.

The values of FA and VA so obtained were expressed as percentage of R and E, respectively. For E we took the value of E-obtained PAV (*see* footnote on page 1717). For R, we took the value obtained during CMV, since there is no reliable way to non-invasively measure R on PAV. V_D/V_T was calculated at each assist level from Pa_{CO_2} and $P\bar{e}_{CO_2}$: $V_D/V_T = (Pa_{CO_2} - P\bar{e}_{CO_2})/Pa_{CO_2}$.

Statistical Analysis

There were three to five steps tested in different patients with either mode. To facilitate comparisons, we elected to divide the data into four levels of assist in each mode. When only four steps were tested, the actual data in the four steps were used. Where three or five steps were tested, we used the data obtained at the minimum and maximal levels and used the intermediate one or three steps to generate two intermediate levels by interpolation. Comparisons between different

levels of assist and at comparable levels of PAV and PSV were made by two-way ANOVA for repeated measures. When the F value was significant, Tukey's test was used to identify the specific differences that were significant (*i.e.*, $p < 0.05$).

Computer Simulation

In order to better define the role of patient-ventilator interactions in mediating the observed differences in the specific patient population studied, we utilized a computer simulation routine described in detail previously (10-12) and used extensively in the past to model ventilatory output under various physiologic and pathologic conditions (13, 14), including patient-ventilator interactions (6, 7). In the latter application, applied pressure consists of a ventilator-generated component (Paw) and a patient-generated component (Pmus). For PSV, Paw follows a function specified by rise time, PSV level, and a cycling off flow level. For PAV, FA and VA are specified. Pmus waveform consists of a rising phase with a specified duration (neural T_i) and peak level and an expiratory duration of a specified amount. The passive elastic and resistive properties are also specified. Iteration begins in the first cycle at a default volume representing passive FRC. Volume at the end of the first cycle is used as the starting volume for the next cycle. Iteration continues until a steady state is reached where end-expiratory lung volume and ventilatory output do not change in consecutive cycles. Where no steady state could be reached, iteration continues for 50 cycles and the results are examined to identify the pattern of breathing in this sequence.

For the present application model, parameters were set to reflect the different levels of assist used, the specific features of PSV used (time constant of rising phase = 200 m and flow for cycling off = 0.1 L/s) and the average mechanical properties in this patient population ($Rrs = 16$ cm H₂O/L/s and Ers in the operating range of 23 cm H₂O/L) (Table 1). An average patient respiratory rate (RRpat) of 24 min⁻¹ with a T_i/T_{tot} ratio of 0.4 was used. V_T , mechanical T_i , and relationship between RRpat and RRvent were computed at different levels of peak Pmus and assist.

RESULTS

Table 1 shows patient characteristics and baseline data on the PSV level patients were on prior to the study. The mechani-

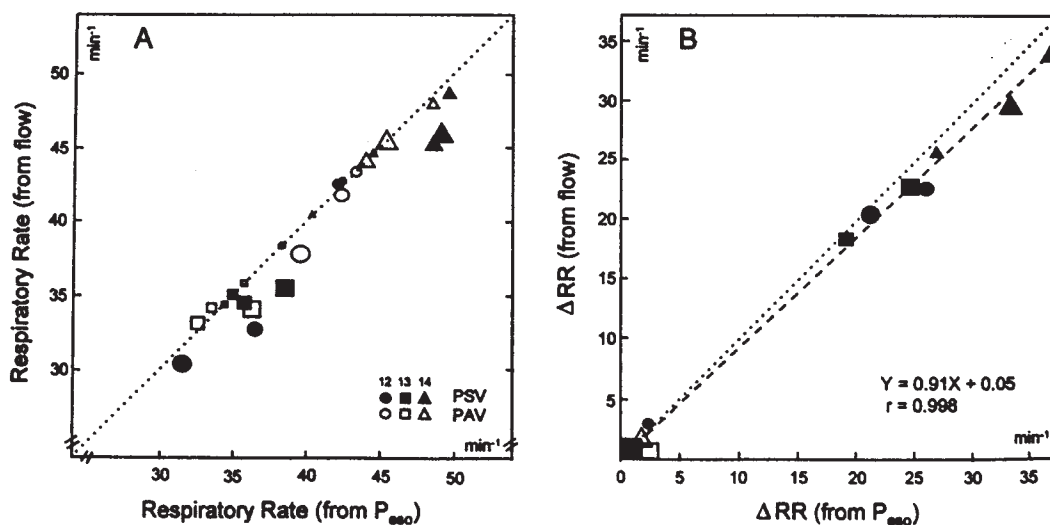


Figure 2. (A) Relation between actual patient respiratory rate determined from esophageal pressure (Pes) and rate estimated noninvasively from the flow signal in three patients (different symbols, patient number identified in insert). Size of symbol in each case denotes magnitude of assist: *largest closed symbol* is PSVmax; *largest open symbol* is PAVmax. Note good agreement in all three patients under all conditions. (B) Estimates of ineffective efforts (ΔRR) determined from Pes and from flow. Same symbol designations as in (A). All points showing no ineffective efforts with both techniques ($\Delta RR < 1.0$) are represented by the *solid square* near the origin. Note the excellent agreement between estimates made by the two methods.

cal abnormalities were mixed. All patients had abnormal gas exchange with a PaO₂/F_iO₂ ratio of 116 to 295 (mean ± SD = 206 ± 48).

Figure 2A shows the relationship between the patient's respiratory rate (RR_{pat}) determined from Pes and from the flow/Paw tracings in three patients in whom Pes was monitored. Most points fell very close to the line of identity. Figure 2B compares estimates of ineffective efforts (ΔRR) using the two techniques. In most cases (virtually all PAV data and during the lowest one or two PSV levels) there were no ineffective efforts (< 1/min) with either technique. Large ΔRR values (up to 37/min) were obtained during higher PSV levels. Here, there was good agreement between the estimates of the two techniques (r = 0.998). There was a tendency for ineffective efforts to be slightly underestimated when flow/Paw was used (slope = 0.91). ΔRR determined from flow/Paw did not exceed ΔRR from Pes in any case.

Table 2 shows the results of some ventilatory and Paw data. The PSV level required to produce a V_T of approximately 10 ml/kg was 20.4 ± 3.2 cm H₂O. The actual V_T during PSVmax was 10.2 ± 2.2 ml/kg. The lowest tolerated PSV level (PSVmin) was 8.7 ± 3.0 cm H₂O. For PAV, the highest VA was 78 ± 7% of elastance and the highest FA was 76 ± 7% of resistance. At this level, ΔPaw was 16.2 ± 4.8 cm H₂O. At the lowest tolerated level delivered VA was calculated to be 31 ± 3.6% of E and FA was 55 ± 5% of R. Given the prevailing flow and V_T, as well as the values of R and E, we estimate that at PAVmin the percent unloading was approximately halfway between the FA and VA delivered, or about 43% of the total work. At PAVmin, ΔPaw was 11.1 ± 4.2 cm H₂O (Table 2).

TABLE 2
VENTILATORY* AND PRESSURE VARIABLES AT DIFFERENT LEVELS OF PSV AND PAV (n = 14)

	Mode	Level			
		Min 1	2	3	Max 4
ΔPaw, cm H ₂ O	PSV	8.7 (3.0)	12.6 [†] (2.7)	16.4 [†] (2.7)	20.4 ^{††} (3.2)
	PAV	11.1 (4.2)	12.7 [†] (4.1)	14.0 [†] (4.4)	16.2 [†] (4.8)
PEEP, cm H ₂ O	PSV	6.1 (3.1)	6.1 (3.1)	6.0 (3.0)	6.0 (3.0)
	PAV	6.2 (2.8)	6.0 (2.9)	6.0 (2.9)	6.1 (3.0)
V _E , L/min	PSV	12.6 (4.0)	12.2 (4.1)	11.0 (3.5)	10.9 (2.4)
	PAV	13.6 (4.1)	12.8 (4.0)	12.9 (3.8)	12.9 (3.6)
T _i , s	PSV	0.9 (0.2)	1.2 (0.4)	1.7 ^{††} (0.4)	2.1 ^{††} (0.4)
	PAV	0.8 (0.3)	0.9 (0.3)	0.9 [†] (0.3)	1.1 [†] (0.3)
T _E , s	PSV	1.4 (0.9)	1.6 (1.1)	2.5 (1.5)	3.2 ^{††} (2.4)
	PAV	1.4 (0.9)	1.5 (1.0)	1.5 (1.1)	1.6 (1.3)
T _i /T _{tot}	PSV	0.41 (0.08)	0.45 (0.09)	0.45 (0.13)	0.43 (0.11)
	PAV	0.40 (0.06)	0.41 (0.07)	0.42 (0.08)	0.43 (0.08)

All values represent mean (± SD).

ΔPaw = differences between peak airway pressure during inspiration and positive end-expiratory pressure (PEEP). T_i, T_E, and T_i/T_{tot} refer to ventilator's inspiratory and expiratory times and the inspiratory duty cycle. All statistical comparisons are results of two-way ANOVA for repeated measures with two-way interaction.

* Other ventilatory variables are shown in Figure 3.

[†] Significantly different from level 1 in the same mode.

^{††} Significantly different from same level of PAV.

At the lowest level of assist there was no significant difference between PSV and PAV in V_T, RR_{vent}, RR_{pat}, or in ΔRR (Figure 3). V_E and ventilator T_i, expiratory time (T_E), and T_i/T_{tot} were also not different between the two modes (Table 2). At higher levels of support V_T increased much more with PSV than with PAV (Figure 3). The increase in V_T with PAV was slight and reached significance only at PAVmax (Figure 3). At PAVmax, V_T ranged from 0.33 to 0.84 L. V_T was significantly higher during PSV than during PAV at the two highest levels (Figure 3). Ventilator rate decreased much less with PAV than with PSV, and the difference between the two modes became significant at the two higher levels (Figure 3). The difference in response of RR_{vent} was largely the result of occurrence of ineffective inspiratory efforts (ΔRR), an example of which is shown in Figure 1. ΔRR increased progressively with level of support in the PSV mode (Figure 3). ΔRR was minimal at all levels of PAV (Figure 3). The changes in true patient rate (RR_{pat}) were relatively small in both modes, and the differences between PAV and PSV were not significant (Figure 3).

Figure 4 shows individual responses in RR_{vent} and RR_{pat} as level of assist was changed between maximum and minimum. At low level of support, the data points (solid dots) fall near the line of identity in both modes. With high-level PSV the data points (open circles) deviate from the line of identity in all but two patients. The deviation is greatest in patients with the highest intrinsic rates (i.e., RR_{pat}). In all patients

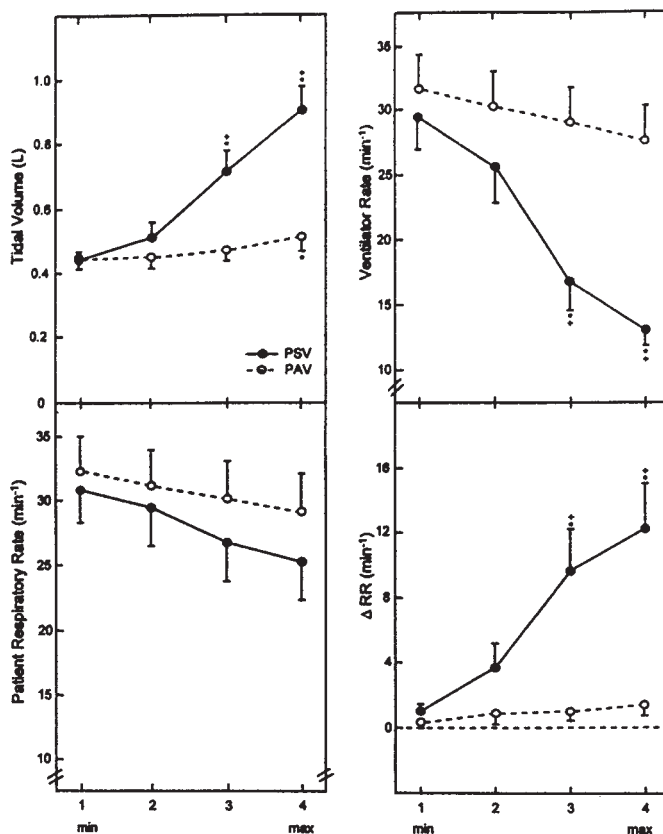


Figure 3. Average responses of tidal volume (V_T), ventilator rate (RR_{vent}), patient's respiratory rate (RR_{pat}), and number of ineffective efforts (ΔRR) at different levels of PSV and PAV. Bars are SEM. *Significantly different from value during minimum support with the same mode. [†]Significantly different from comparable support level with PAV.

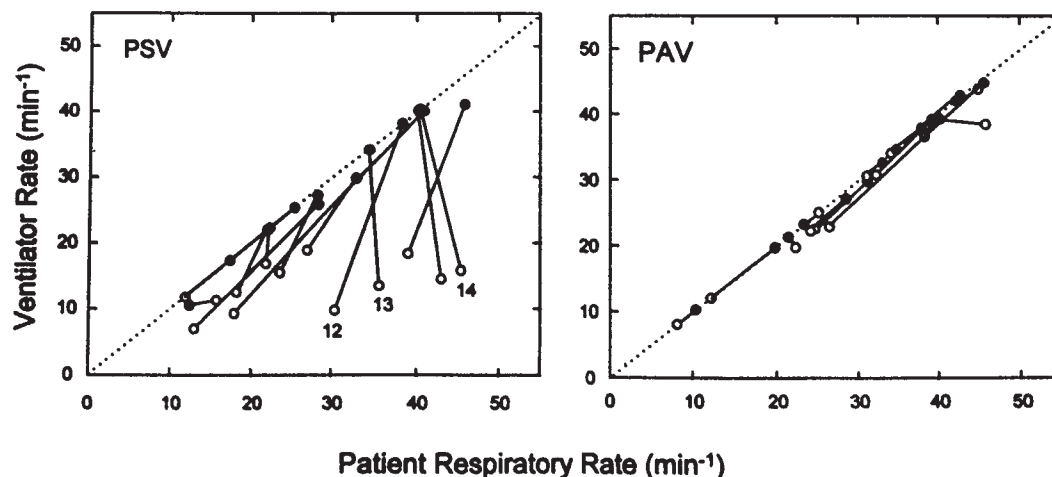


Figure 4. Relationship between patient respiratory rate (RR_{pat}) and ventilator rate (RR_{vent}) at two levels of pressure support (*left panel*) and proportional assist (PAV). Note that at the lowest level of support (*solid circles*) the data points are close to the line of identity in both modes. With high support, ventilator rate deviates substantially from the patient's rate during PSV but relatively much less so with PAV. Note also that three patients with RR_{pat} greater than 40 at the lowest assist level in both modes failed to reduce their rates (RR_{pat}) appreciably at the highest support level. Numbers 12, 13, and 14 in PSV panel denote the three patients in whom RR_{pat} was determined from esophageal pressure.

RR_{vent} decreased below 20/min, but the range of RR_{pat} was still quite large (12 to 46/min). With PAV, with one exception where Δ RR was 7.0/min, the data points remained very close to the line of identity.

Ventilator inspiratory time (T_i) increased progressively with level of PSV, with T_i exceeding 2.0 s in seven patients. T_i increased only slightly with PAV level. The difference in T_i response between PSV and PAV was significant at the higher two levels (Table 2). T_E showed corresponding changes, increasing markedly with PSV but not with PAV. There was no change in T_i/T_{tot} as a function of mode or support level. Minute ventilation did not show consistent changes with level of assist or with mode (Table 3).

Changes in Pa_{O₂}, Pa_{CO₂} and pH with assist level in the two modes were comparable (Table 3). V_D/V_T decreased with

level of assist in both modes. The decrease was more pronounced in PSV. V̇_{CO₂} did not change with mode or level of support (Table 3).

Computer Simulation Results

In both panels of Figure 5, the diagonal line marked zero represents the relationship between peak P_{mus} and V_T in the absence of assist. With PAV, as percent of assist increased, the slope of the relation increased. In all cases a stable solution was reached with RR_{pat}:RR_{vent} ratio of 1:1 and the ventilator cycle terminating within 0.1 s of the end of inspiratory effort.

In the PSV mode the relation was variable and was affected by PSV level and intensity of effort. At PSV 5, the assist simply caused a parallel upward shift and the RR_{pat}:RR_{vent} ratio remained 1:1. At higher levels the response displayed three

TABLE 3
GAS EXCHANGE VARIABLES AT DIFFERENT LEVELS OF PSV AND PAV (n = 11)

	Mode	Level			
		Min 1	2	3	Max 4
V̇ _E , L/min	PSV	12.2 (4.5)	11.4 (4.0)	10.7 (3.1)	10.8 (2.6)
	PAV	13.4 (4.7)	12.6 (4.5)	12.5 (4.2)	12.6 (4.0)
F _I O ₂	PSV	0.47 (0.07)	0.47 (0.07)	0.47 (0.07)	0.47 (0.07)
	PAV	0.46 (0.07)	0.46 (0.07)	0.46 (0.07)	0.46 (0.07)
Pa _{O₂} , mm Hg	PSV	97 (19)	99 (18)	100 (22)	107 (21)
	PAV	96 (19)	99 (18)	100 (20)	103 (19)
Pa _{CO₂} , mm Hg	PSV	43.5 (8.1)	41.6 (9.7)	40.8 (10.2)	39.7 (9.7)
	PAV	42.3 (7.4)	40.7 (8.0)	41.8 (8.1)	39.5 (5.5)
pH	PSV	7.40 (0.08)	7.40 (0.07)	7.42 (0.03)	7.43 (0.07)
	PAV	7.40 (0.07)	7.41 (0.07)	7.41 (0.07)	7.42 (0.09)
V̇ _{CO₂} , ml/min	PSV	305 (89)	289 (79)	293 (73)	299 (50)
	PAV	304 (63)	290 (63)	295 (66)	299 (63)
V _D /V _T	PSV	0.56 (0.07)	0.53 (0.10)	0.49 (0.07)*†	0.45 (0.03)*†
	PAV	0.58 (0.07)	0.55 (0.07)	0.56 (0.07)	0.53 (0.10)*

All values represent mean (± SD). V̇_{CO₂} = rate of CO₂ production.

* Significantly different from level 1 in the same mode.

† Significantly different from same level in PAV, two-way ANOVA for repeated measures with two-way interaction.

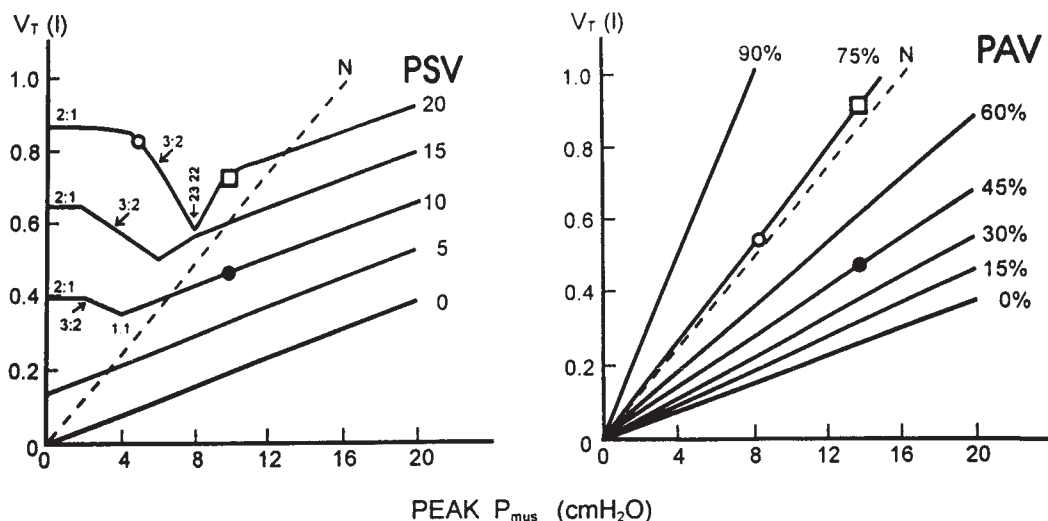


Figure 5. Results of computer simulation of the relationship between peak inspiratory muscle effort (peak P_{mus}) and tidal volume (V_T) at different levels of support with pressure support (PSV) and proportional assist (PAV). Patient's characteristics (resistance and elastance) were similar to those of the average patient in this study (Table 1). Numbers to the right of different isopleths in the PSV panel denote PSV level, while corresponding numbers in the PAV panel denote the percent of elastance and resistance used for volume assist and flow assist, respectively. Dashed line marked "N" is the relation in a subject with normal mechanics ($R = 4.0$ cm $H_2O/L/s$, $E = 11.0$ cm H_2O/L). Solid dots: relation pertaining to results at PSVmin and PAVmin observed in the current study. Open square: expected V_T as assist level is increased to PSVmax or PAVmax without downregulation of patient's effort. Open circle: final steady-state response to the change from minimum to maximum assist. Ratios in the PSV panel denote the relation between patient's rate and ventilator rate at the relevant points. When no ratio is indicated in either panel, it is 1:1. To generate data at peak $P_{mus} = 0$ (i.e., Y intercepts), very brief efforts (0.1 s) were simulated.

phases. At high peak P_{mus} there was a vertical shift and a continued RRpat:RRvent ratio of 1:1. As peak P_{mus} decreased to a critical level, which was higher at higher PSV levels, a transitional zone developed where the relation between P_{mus} and V_T was biphasic; V_T decreased sharply as P_{mus} decreased, followed by a rapid increase as P_{mus} decreased further. At the beginning of this transitional zone, ventilator cycle began extending progressively more into neural expiration, reducing the time available for emptying and resulting in progressively more dynamic hyperinflation (DH). Initially, efforts continued to be able to trigger the Paw cycle, and RRpat:RRvent ratio remained 1:1. However, V_T decreased sharply as DH increased. At slightly lower levels of peak P_{mus} in this transitional phase a steady state was not reached; with successive neural cycles, ventilator cycle extended progressively more into neural TE and end-expiratory volume progressively increased. After a number of cycles, one effort fails to trigger PSV, allowing volume to return to passive FRC. The sequence then repeats (notice 23:22 ratio at the trough in the PSV 20 line). As P_{mus} decreased further, within this transitional zone, mechanical T_i increased further and a larger fraction of breaths failed to trigger PSV. In this region average V_T increased (as P_{mus} decreased), in part because more breaths started near passive FRC (less DH) as a result of preceding nontriggered efforts and in part because of the longer mechanical T_i . Beyond this transitional zone, V_T reached a constant level that was independent of P_{mus} with a stable 2:1 rhythm. Here, every triggered breath begins near passive FRC and mechanical T_i is long enough to permit equilibration between applied pressure and elastic recoil. V_T equals PSV/Ers.

Whereas Figure 5 shows the result for the case where the patient's RR and mechanics are similar to the average patient in this study, other simulations (not shown) using different pa-

tient characteristics show that a higher RRpat and a longer time constant (Rrs/Ers) cause the transitional zone to occur at relatively higher P_{mus} and the RRpat:RRvent ratio at minimal P_{mus} to be greater (e.g., 3:1, 4:1, etc.), and vice versa.

DISCUSSION

The present study shows that the breathing pattern responses to different levels of PSV and PAV are substantially different and that these differences are largely artifactual, reflecting the manner in which the ventilator responds to changes in patient effort in the two modes.

Technical Considerations

Use of flow to estimate ineffective efforts. Our use of flow and Paw to identify ineffective efforts requires justification. The criteria used were based on straightforward physical principles and practical consideration of the features of other possible causes of such flow transients.² We therefore feel that with the criteria used here there is little possibility that ineffective effort will be wrongly identified. This was borne out by the results in the three patients in whom efforts were also directly identified from Pes; in no case did the number of ineffective efforts identified from flow exceed the number identified from Pes. Difficulties may arise where the magnitude of the flow transient is very small or its duration is borderline (e.g., transient marked by downward pointing arrow, Figure 1A). These features, however, reflect feeble and/or very brief negative transients in intrapleural pressure (Ppl) (see corresponding Pes tracing, Figure 1A). Such transients would be questionable regardless of whether one uses flow or Ppl.

Whereas overestimation of ineffective efforts using the current criteria would be quite unlikely, underestimation is possi-

ble under two circumstances. First, if an inspiratory effort occurs at the very beginning of the ventilator's expiratory phase, before a clear expiratory flow trajectory has been established, it may simply truncate the peak of the expiratory flow and not be clearly recognized as an independent flow transient (e.g. effort marked by *open arrow*, Figure 1A). Second, where expiratory flow limitation exists and Ppl is in excess of the value required to generate maximum flow, reduction in Ppl may not result in reduction in expiratory flow. The three patients in whom ineffective efforts were identified independently by the two techniques represent extreme examples of dyssynchrony with PSV. The results in these patients (Figure 2B) suggest that underestimation of ineffective efforts by the flow method is acceptably small.

Comparability of level of assist with PSV and PAV. The choice of the lowest level of assist was based on a clinical judgment by the experimenters (E.G. and K.W.) that the patient could not sustain a further reduction in support. This is admittedly subjective. However, since no difference was identified in any variable at minimum assist, the issue of whether the assist level was comparable is moot. The situation is, however, different at the higher levels of assist where substantial differences in breathing pattern and ΔRR were observed. It may be argued that the observed differences in breathing pattern and ΔRR were related to a relatively lower level of assist with PAV. We believe this to be highly unlikely for the following reasons:

1. Arterial P_{O_2} , P_{CO_2} , and pH were virtually identical at level 4 (Table 3). To the extent that these are important (if not the most important) determinants of inspiratory effort, there is no reason to believe that patients had a higher respiratory drive with PAV.
2. Although the operational target for PAVmax was 80% of E and R, the actual assist delivered, determined posthoc, ranged from 65 to 95%. There was no evidence that increasing PAV in the range from 80 to 95% resulted in a different response to PAV. In fact, in three patients in whom percent of assist exceeded 90%, the differences in V_T between PAVmax and PAVmin were zero, 0.06, and 0.05 L, not any greater than the average increase in V_T (0.06) (Figure 3) and in each of these patients ΔRR was zero. This suggests that using a higher PAVmax would not have altered the results.
3. Although ΔP_{aw} at PAVmax was only 80% of ΔP_{aw} at PSVmax (16.2 ± 4.8 versus 20.4 ± 3.2 cm H₂O) (Table 2), the pressure assist with PAV was delivered more than twice as often ($RR_{vent} = 27.6 \pm 10.5$ with PAVmax versus 13.2 ± 3.9 with PSVmax) (Figure 3). The product $\Delta P_{aw} RR_{vent}$ at PAVmax was 167% of the corresponding value at PSVmax.
4. Breathing pattern at PSV 3 remained different from PAVmax where ΔP_{aw} was similar (16.2 ± 4.8 versus 16.4 ± 2.7 cm H₂O) (Table 2). Thus, at PSV 3, V_T was larger ($p < 0.02$), RR_{vent} was lower ($p < 0.005$) and ΔRR was greater ($p < 0.005$) than at PAVmax.

Responses to Different Levels of PSV and PAV

The results observed during PAV are very similar to those reported previously (15); the changes in V_T and respiratory rate are quite small over a wide range of assist in the tolerable range. The response to different levels of PSV in the current study is also similar to earlier findings (1, 16–19); V_T progressively increases and ventilator rate progressively decreases as PSV level is increased. The advantage of the present study is that both modes were used in the same patients, thereby allowing us to determine whether the different responses are ar-

tifactual or represent differences in respiratory control with the two modes.

Differences in respiratory rate. The responses of ventilator rate to different levels of PSV and PAV were substantially different; the decrease in RR_{vent} with PSV was nearly four times greater than with PAV (29.6 to 13.7 with PSV versus 31.9 to 27.6 with PAV) (Figure 3). These differences, however, were largely artifactual; the responses of RR_{pat} were substantially smaller in absolute terms and not significantly different between the two modes (Figure 3). The decrease in RR_{vent} with PSV was predominantly related to a progressively greater number of ineffective efforts (ΔRR) (Figure 3).

That discrepancies between RR_{vent} and RR_{pat} are likely to occur with PSV was theoretically predicted earlier (6, 7) and was well demonstrated in practice in several recent studies (20–22). It was also predicted that PAV would be less likely to result in such discrepancies (6, 7). The present study confirms this prediction. As shown by computer simulation of the two modes (6, 7, current study), the main reason for this to occur with PSV is the tendency for ventilator T_I to outlast neural T_I , particularly when the mechanical time constant (R/E) is long. This results in reduction in the time available for expiration, and hence inadequate emptying prior to the onset of the next effort. Computer simulations have also shown that the extent to which ventilator T_I exceeds neural T_I , and hence the frequency of unsuccessful efforts, should increase as the level of PSV increases (6, 7). This prediction is also borne out by the present results: ΔRR progressively increased with PSV level.

In a previous study using different levels of PAV, we observed that RR_{pat} covered a wide range (18 to 33 min⁻¹) despite high levels of assist (15). The present results confirm these previous findings and extend them in two respects. First, the same conclusion applies during PSV if one considers the patient's rate as opposed to RR_{vent} . Second, the range of RR_{pat} observed in the current study is considerably larger. Thus, at the highest assist level, RR_{pat} ranged from 12 to 46 min⁻¹ with PSV and 8 to 46 min⁻¹ with PAV (*open circles*, Figure 4). More importantly, in several patients with marked tachypnea at low levels of support, RR_{pat} changed little over the entire range of assist (Figure 4). This suggests that in some patients tachypnea may be largely due to abnormal tachypneic influences unrelated to respiratory load.

Differences in tidal volume response. Although V_T increased with level of assist in both modes, the increase was substantially more in the case of PSV (Figure 3). The large increase in V_T with PSV cannot be attributed to unusually high levels of PSV; even at PSVmax, PSV level was well within the range used in practice both in terms of absolute pressure (20.4 ± 3.6 cm H₂O) (Table 2) and in terms of associated V_T (10.2 ± 2.2 ml/kg). Likewise, the small increase in V_T with PAV was not due to low levels of assist (*see TECHNICAL CONSIDERATIONS*).

We believe that the difference in V_T response with the two modes is largely related to different patient-ventilator interactions. While with both modes inspiratory effort decreases progressively as assist level increases (16–19, 23–25), the response of the ventilator to this downregulation of Pmus is very different in the two modes. The results of computer simulation carried out here (Figure 5), where patient characteristics were matched to those of the average patient in this study and ventilator characteristics were similar, provide a framework for interpreting the experimental results. For simplicity, only the changes between minimum and maximum assist will be discussed. At PAVmin average V_T was 0.45 L at an average assist level of approximately 45%. This is represented by the *solid circle* on the 45% line (Figure 5, *right panel*). Increasing the

assist to an average of 75% (actual increase was to 77%) would, in the absence of downregulation of Pmus, immediately result in doubling of V_T with continued 1:1 synchrony (*open square*, Figure 5, *right panel*). Pa_{CO_2} would rapidly decrease as a result of the increased \dot{V}_E and decreased V_D/V_T (due to larger V_T). Peak Pmus decreases as a result, causing V_T to decrease along the 75% line. A new steady state is reached (*open circle*) at a point where the decrease in Pa_{CO_2} is commensurate with the decrease in Pmus (as governed by CO_2 responsiveness) and the change in \dot{V}_E is commensurate with the change in Pa_{CO_2} . It can be seen from this analysis that a substantial increase in V_T with PAV is possible only if RR decreases substantially, thereby minimizing the decrease in PCO_2 , or Pmus fails to downregulate as PCO_2 decreases (e.g., in the presence of important nonchemical sources of drive).

In our patients, V_D/V_T decreased slightly, while metabolic rate did not change as a result of increasing PAV support from minimum to maximum (Table 3). As a result of the small decrease in V_D/V_T , Pa_{CO_2} decreased by 2.8 mm Hg, despite a small reduction in \dot{V}_E (13.4 to 12.6 L/min) (Table 3). Alveolar \dot{V}_E actually increased from 5.6 to 5.9 L/min, which accounts for the decrease in Pa_{CO_2} . RRpat decreased from 30 to 26.4 min^{-1} , likely the result of the decrease in mechanical load and/or the small decrease in Pa_{CO_2} . Had RRpat decreased less, V_T would have increased even less than it did. The opposite, of course, would occur if RRpat decreased more. The decrease in estimated Pmus between PAVmin and PAVmax (14.0 cm H_2O to 8.2 cm H_2O , Figure 5, *right panel*) is likely related to the decrease in Pa_{CO_2} , although a reduction in other sources of respiratory drive cannot be ruled out.

The *solid circle* in the *left panel* of Figure 5 represents the case at PSVmin (average $V_T = 0.44$ L at PSV of approxi-

mately 10 cm H_2O) (Table 2). Increasing PSV from 10 to 20 cm H_2O would have, in the absence of Pmus downregulation, resulted in an increase in V_T to 0.73 L with maintained 1:1 synchrony (*open square*, Figure 5, *left panel*). Pa_{CO_2} would decrease sharply and Pmus would decrease accordingly. As a result, V_T would initially decrease sharply. However, if V_T at the trough of the transitional phase is not commensurate with a steady state, Pmus continues to decrease. V_T rises again, along with development of increasing degrees of nonsynchrony and prolongation of mechanical T_I . The final steady state would again be reached when the decrease in Pa_{CO_2} is commensurate with the decrease in Pmus and the increase in alveolar volume is commensurate with the decrease in Pa_{CO_2} . In the average patient represented in Figure 5, the trough of the V_T response at PSV 20 would not be consistent with a steady state. V_T at this point was 0.58, 26% greater than V_T at PSVmin. Even ignoring the lower V_D/V_T , this would have resulted in a 10 mm Hg reduction in Pa_{CO_2} . Pmus could not stabilize at the trough level and must decrease further, forcing the nonsynchrony and the secondary increase in V_T . The equilibrium point thus occurs at a much higher V_T . On average, in our patients at this equilibrium point (PSVmax), approximately one-half of inspiratory efforts failed to trigger ($\Delta RR = 12.1$, RRpat = 25.3 min^{-1}) (Figure 3). It is of interest to note that according to the simulation presented here, mechanical T_I would increase from 0.9 s to 1.9 s between PSVmin and PSVmax, despite a constant neural T_I in the simulation. This is quite similar to what was actually observed (0.9 to 2.1 s) (Table 2).

The simulation data shown in Figure 5, *left panel*, also provide an explanation for the occasional occurrence of rapid dramatic changes in ventilator output during PSV. Figure 6 provides an example. In this case, breathing pattern, as judged by

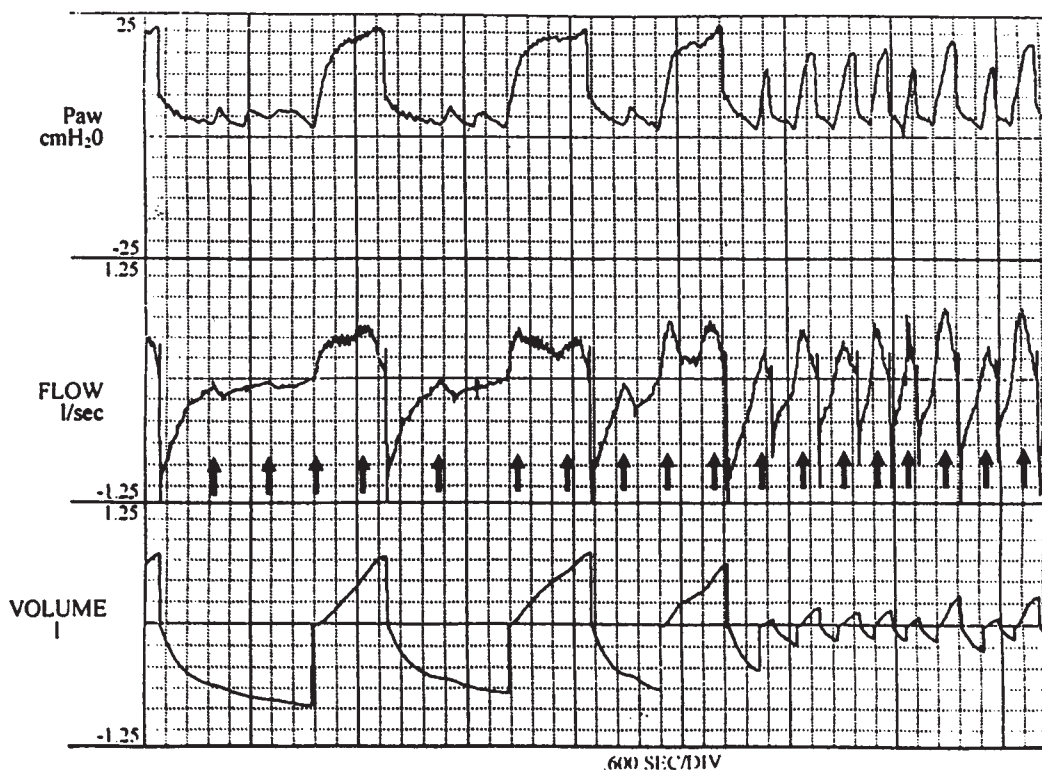


Figure 6. An example of a rapid spontaneous change in V_T and ventilator rate. Arrows indicate the patient's efforts and reveal that much of the increase in RRvent was due to improved synchrony (3:1 \rightarrow 1:1). V_T decreased markedly as synchrony improved. The change in ventilator output from a slow, deep pattern to a rapid, shallow pattern was likely the result of a small increase in the patient's inspiratory effort.

ventilator output, suddenly and spontaneously changed from slow, deep breathing to rapid, shallow breathing. The increase in ventilator rate was substantially greater than the increase in RR_{pat} (arrows), reflecting better synchrony. The improved synchrony was, in turn, likely related to an increase in patient effort. Note that with improved synchrony, V_T decreased. The transitional zone demonstrated by the computer simulation implies that small changes in P_{mus} may cause large changes in ventilator V_T and RR_{vent} when they occur in a critical P_{mus} range.

The above analysis indicates that the differences in the experimental results can be readily explained by the different patient-ventilator interactions in the two modes. It is to be noted that the expected increase in V_T upon transition from PAV_{min} to PAV_{max} in the absence of P_{mus} downregulation (difference between *solid circle* and *open square*, Figure 5, *right panel*) is substantially larger than the corresponding expected increase upon transition from PSV_{min} to PSV_{max} (0.43 L in *right panel* versus 0.26 L in the *left panel*, Figure 5). This further supports our contention that the smaller V_T response with PAV was not due to a relatively smaller range of assist.

Clinical Implications

1. The present study, along with earlier theoretical (6, 7) and experimental (20–22) findings, indicates that RR_{vent} should not be used as a surrogate for RR_{pat} in the PSV mode, whereas RR_{vent} is a reliable surrogate of RR_{pat} during PAV support.
2. A high RR_{pat}, as high as 46/min, on either PAV or PSV need not reflect inadequate support. In some patients respiratory rate is fairly insensitive to level of support. This conclusion is further supported by recent findings that respiratory rate is not a good predictor of work of breathing or pressure-time product during PSV (16, 26).
3. During PSV, particularly in patients with high resistance, breathing pattern, as judged by ventilator output, can undergo dramatic changes in response to minor changes in the patient's respiratory motor output or PSV level. These changes may be artifactual and should not be interpreted as a major change in the patient's inherent pattern of breathing or level of distress without independent confirmation.
4. Although synchrony between patient and ventilator is much better preserved with PAV, the clinical significance of this feature is not clear. There is very little impact on Pa_{CO₂} and it does not appear that synchrony, or lack thereof, materially affects gas exchange as judged by the Pa_{O₂}/F_{I_{O₂}} ratio.

In summary, the breathing pattern response to changes in assist level with PSV and PAV are substantially different. These differences are, however, largely artifactual and have little impact on gas exchange. The present study also confirms that breathing pattern at high levels of assist is highly variable with some patients displaying respiratory rates in the forties with very small V_T (approximately 0.3 L). Such patterns in the course of weaning need not signify excessive work.

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