Intensive Care Med (1999) 25: 790–798

ORIGINAL

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Proportional assist versus pressure support ventilation: effects on breathing pattern and respiratory work of patients with chronic obstructive pulmonary disease

Received: 21 October 1998
Final revision received: 23 March 1999
Accepted: 10 May 1999

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Abstract *Objective:* To investigate the breathing pattern and the inspiratory work of breathing (WOB_I) in patients with chronic obstructive pulmonary disease (COPD) assisted with proportional assist ventilation (PAV) and conventional pressure support ventilation (PSV).
Design: Prospective controlled study.
Setting: Intensive care unit of a university hospital.
Patients: Thirteen COPD patients being weaned from mechanical ventilation.
Interventions: All patients were breathing PSV and two different levels of PAV.
Measurements and main results: During PAV (EVITA 2 prototype, Dräger, Germany), the resistance of the endotracheal tube (R_{et}) was completely compensated while the patients' resistive and elastic loads were compensated for by approximately 80 % and 50 % (PAV_{80} and PAV_{50}), respectively. PSV was adjusted to match the same mean inspiratory pressure ($Pinsp_{mean}$) as during PAV_{80}. Airway pressure, esophageal pressure and gas flow were measured over a period of 5 min during each mode. Neuromuscular drive ($P_{0.1}$) was determined by inspiratory occlusions. Mean tidal volume (V_T) was not significantly different between the modes. However, the coefficient of variation of V_T was 10 ± 4.%, 20 ± 13 % and 15 ± 8 % during PSV, PAV_{80} and PAV_{50}, respectively. Respiratory rate (RR) and minute ventilation (V_E) were significantly lower during PAV_{80} as compared with both other modes, but the differences did not exceed 10 %. PAV_{80} and PSV had comparable effects on WOB_I and $P_{0.1}$, whereas WOB_I and $P_{0.1}$ increased during PAV_{50} compared with both other modes.
Conclusion: Mean values of breathing pattern did not differ by a large amount between the investigated modes. However, the higher variability of V_T during PAV indicates an increased ability of the patients to control V_T in response to alterations in respiratory demand. A reduction in assist during PAV_{50} resulted in an increase in WOB and indices of patient effort.

Key words Mechanical ventilation · Critical care · Chronic obstructive pulmonary disease · Patient-ventilator interaction · Proportional assist · Pressure support · Work of breathing physiology

Introduction

In the last decade, the early reinstitution of spontaneous breathing during the ventilatory support of intubated critically ill patients has become an important therapeutic option to avoid unwarranted side effects of controlled mechanical ventilation in more and more intensive care units. Potential reasons for this might be: (1) less sedation and no need for relaxation because of a better synchronization between the patient and ventilator during modern respiratory modes [1], (2) decreased airway pressure compared with controlled mechanical ventilation [2], (3) the possible beneficial effects of preserved diaphragmatic activity [3, 4, 5] and (4) earlier extubation as compared with controlled mechanical ventilation [6].

A recently developed mode of synchronized partial ventilatory support is proportional assist ventilation (PAV), during which the supportive pressure applied by the ventilator is proportional to the patient's inspiratory effort [7, 8]. During PAV, the ventilator delivers pressure in proportion to the inspired volume above functional residual capacity (FRC) and in proportion to gas flow. In theory, this dynamic pressure support should compensate for the patient's increased elastance and resistance and should normalize the relationship between the patient's inspiratory effort and the resulting ventilatory output [7]. This principle might be particularly important in patients with chronic obstructive pulmonary disease (COPD) requiring mechanical ventilation for acute respiratory failure. In these patients, respiratory mechanics are often impaired due to an increased resistance caused by airway obstruction and an increased elastic load caused by dynamic hyperinflation of the lungs. The latter results in an additional inspiratory load to overcome an intrinsic positive end-expiratory pressure (PEEPi) [9]. As the work due to PEEPi can be reduced by the application of an external PEEP (PEEPe) [10, 11], the elastic and resistive loads have to be compensated by ventilatory support. Pressure support ventilation (PSV) [12] and the more recently developed mode PAV [7, 8] have been successfully used to unload the respiratory muscles during partial ventilatory support in COPD patients [11, 13].

The aim of this study was to investigate the breathing pattern, inspiratory effort and work of breathing (WOB) of COPD patients during pressure support ventilation (PSV) and two different degrees of mechanical unloading with PAV.

Methods

Background

During augmented spontaneous inspiration the total applied pressure (P_{tot}) is the sum of the pressure generated by the patient's inspiratory muscles (P_{mus}) and the airway pressure by the ventilator (P_{aw}). The P_{tot} can be separated into a static and a dynamic component: pressure dissipated against the elastic recoil forces of the patient's respiratory system (P_{el}) and against the resistance to gas flow by the airways (R_{aw}) and the endotracheal tube (R_{et}): P_{res}. It follows

$$P_{tot} = P_{mus} + P_{aw} = P_{el} + P_{res} \quad (1)$$

P_{res} depends on total resistance (R_{rs}) and on gas flow ($\dot{V}$), whereas P_{el} depends on volume load above FRC (V) and elastance (E) of the respiratory system. R_{rs} can be separated into a component which is an approximation to the resistance of the patient's airways (R_{aw}) and a component which represents the endotracheal tube resistance (R_{et}). If elastance and resistance are constant, it follows:

$$P_{mus} + P_{aw} = P_{el} + P_{res} \cong \mathrm{V} \cdot E + \dot{V} \cdot R_{aw} + \dot{V}^2 \cdot R_{et} \quad (2)$$

The patient's inspiratory effort generated by the inspiratory muscles can be expressed by rearranging Eq. 2:

$$P_{mus} = \mathrm{V} \cdot E + \dot{V} \cdot R_{aw} + \dot{V}^2 \cdot R_{et} - P_{aw} \quad (3)$$

The resistance of the endotracheal tube (R_{et}) has been shown to change non-linearly with changes in flow [14]. To compensate for R_{et} as a part of total R_{rs}, the ventilatory mode automatic tube compensation (ATC) has recently been developed [15]. For the pressure drop across the endotracheal tube it follows [14]:

$$\Delta P_{tube} \cong \dot{V}^2 \cdot k_{tube} \quad (4)$$

where k_{tube} is the proportionality factor for the individual endotracheal tube.

If the pressure generated by the ventilator (P_{aw}) is a linear function of V and a linear as well as non-linear function of $\dot{V}$, which are all determined by the patient's inspiratory effort, it follows:

$$P_{aw} = V \cdot VA + \dot{V}\, FA + \dot{V}^2 \cdot k_{tub} \quad (5)$$

where VA is the constant proportionality factor between P_{aw} and volume load above FRC (volume assist, in cmH_2O/l) and FA is the constant linear proportionality factor between P_{aw} and gas flow (flow assist, in cmH_2O/l per s). According to Eq. 3 it follows that:

$$P_{mus} = \mathrm{V} \cdot (E\text{–VA}) + \dot{V} \cdot (R_{aw}\text{–FA}) + \dot{V}^2 \cdot (R_{et}\text{–}k_{tube}) \quad (6)$$

Equation 6 shows the proportionality between patient effort and the assistance of the ventilator depending on volume and flow. Additionally, the possibility to reduce the patient's effort selectively according to the measured elastance in proportion to the volume load by adjusting VA, according to the measured resistance in proportion to the inspiratory flow by adjusting FA and the compensation for the non-linearly flow-dependent resistance of the endotracheal tube is illustrated.

Subjects

Thirteen long-term mechanically ventilated COPD patients were studied. COPD was defined by medical history, clinical and radiological findings and chronic drug treatment for obstructive lung disease before admission. The patients were mechanically ventilated due to acute respiratory failure. During the measurements, all the patients were in stable circulatory and metabolic condition and in the weaning phase. The patients' characteristics are shown in Table 1. Informed consent was obtained from each patient or the next of kin. The investigative protocol was approved by the local ethics committee.

Measurement equipment and procedures

Gas flow was measured with a pneumotachograph (Fleisch no. 2, Fleisch, Lausanne, Switzerland) and a differential pressure transducer (Huba Control, Würenlos, Switzerland). After calibration with the patient's collected expired gas, the pneumotachograph was directly connected to a heat and moisture exchanger, HME (Humid-Vent 2, Gibeck Respiration, Väsby, Sweden) at the proximal end of the endotracheal tube. Airway pressure (P_{aw}) was measured at the same position with a second differential pressure transducer. A balloon-catheter (International Medical, Zutphen, Netherlands) connected to another pressure transducer of the same type was used to measure esophageal pressure (P_{es}). The correct balloon position was verified by an occlusion test [16, 17]. When the slope of the P_{es}/P_{aw} curve was different from 1, P_{es} was corrected according to the suggestion of Brunner and Wolff [18]. All data were sampled on-line by an analog/digital converter (DT 2801-A, Data Translation, Marlboro, Mass., USA) at a rate of 20 Hz and processed by a personal computer using a program based on a commercially available programming language (Asyst 4.0, Keithley Asyst, Taunton, Mass., USA). Volume was numerically integrated from the flow signal by off-line analysis and expressed for BTPS conditions. Respiratory rate (RR), tidal volume (V_T), minimum and maximum tidal volumes (V_T min and V_T max), minute volume (V_E), inspiratory time (T_I) and duty cycle (T_I/T_{TOT}) were calculated as means during the measurement period of 5 min. Dynamic intrinsic PEEP ($PEEPi_{dyn}$) was obtained after exclusion of artifacts as the pressure difference between the deflection in the esophageal pressure tracing and P_{es} at the initiation of inspiratory flow [19]. No abdominal muscle activity was observed during the study period.

During controlled mechanical ventilation, mean dynamic elastance was calculated as V_T divided by the end-inspiratory plateau airway pressure minus (PEEP + $PEEPi_{dyn}$). Resistance was obtained as the pressure difference between the inspiratory peak and initial inspiratory plateau airway pressure divided by inspiratory flow from the controlled breaths [20, 21]. The calculation of the patient's inspiratory work of breathing (WOB_I) based on the Campbell diagram [22] has already been described elsewhere [10]. WOB_I was considered as the average of breath by breath calculations during 5 min and related to V_T (expressed as mJ/l). The area under the P_{es}/V curve was only considered, if P_{es} was below baseline at end-inspiration to assure that the pressure change results from patient activity (Fig. 1)[23]. A patient's total inspiratory work was separated into work to overcome elastic forces (W_{EL}) and work to overcome the flow-resistive properties of airways, lung tissues and the ventilator system (W_{RES}) [24, 25]. As an index of patient effort, the neuromuscular drive ($P_{0.1}$) was obtained 5 times by an automatic maneuver integrated in the ventilator (EVITA 2, Dräger Medizintechnik, Lübeck, Germany) during each ventilatory setting [26, 27].

Technical design of proportional assist ventilation in the present study

In contrast to the ventilator described by Younes, which delivers pressure by a freely moving motor-driven piston [7], we used an EVITA 2 ventilator with prototype software, which applies the supportive pressure by microprocessor-controlled proportionality valves. Gas flow is measured inside the ventilator and volume is calculated by integration of the flow signal. The ventilator delivers pressure in proportion to the measured changes in the patient's effort and the preset proportionality factors. According to Eq. 5 the supportive pressure is a linear function of inspired volume with the proportionality factor VA and of inspiratory flow with the proportionality factor FA as well as a non-linear function of inspiratory flow and the tube constant k_{tube}. In contrast to the original PAV as described by Younes, FA in this prototype ventilator is performed as a dynamic pressure support changing with the squared measured gas flow and is thus a non-linear flow assist (qFA: quadratic FA) based on the same algorithm as ATC (Eq. 4). In contrast to ATC, qFA is not a characteristic constant for the endotracheal tube but was used in our study as a variable to adjust the level of support.

Experimental setting

Prior to the study all patients were mechanically ventilated in a semi-recumbent position in the PSV mode using the prototype EVITA 2 ventilator. The ventilatory setting was selected by the responsible physician according to the clinical requirements and is referred to as baseline PSV (PSV_b). To measure dynamic R_{rs} and E_{rs}, the patients were briefly switched to controlled mechanical ventilation without spontaneous breathing. The RR and V_T were set to match those of the PSV_b setting and a constant inspiratory flow of 1 l/s was used [28, 29]. The inspiratory to expiratory time ratio was 1:2 and the resulting inspiratory plateau time was 0.38–0.45 s. Static $PEEPi_{stat}$ was measured by an end-expiratory occlusion [30]. To suppress spontaneous breathing during this evaluation period of controlled ventilation, the patients were briefly sedated with propofol (2–4 mg/kg per min). After this evaluation period the patients were again ventilated with baseline PSV_b for a period of 15–20 min until steady state conditions were achieved. If necessary, the PEEP level was adjusted to meet 90 % of the measured PEEPi, but was never lower than 3 cmH_2O. The level of support during PAV was adjusted as follows: (1) the resistance of the patient's endotracheal tube (R_{et}, at a flow rate 1 l/s) was totally compensated by ATC and subtracted from the total R to unload the inspiratory muscles from this variable additional workload, which depends on the size of the endotracheal tube. (2) In order to avoid runaway phenomena, which can occur in positive feedback systems like PAV, the remaining resistance and the measured elastance were then compensated by only 80 % (PAV_{80}) or 50 % (PAV_{50}) using additional flow and volume assist, respectively. The level of pressure support (PSV) was chosen to match the same mean inspiratory pressure ($Pinsp_{mean}$) as measured during PAV_{80}. The pressure rise time during PSV was 0 s and inspiratory flow was cycled off at a flow of 25 % of its peak flow value [29]. During the study all patients were ventilated in the following order: PSV_b, PAV_{80}, PSV_b, PSV, PSV_b, PAV_{50}, PSV_b. A measuring period of about 5 min was performed during each setting, after stable conditions had been obtained. PSV_b was applied until V_E differed less than 10 % as compared with the previous PSV_b setting. During the initial PSV_b setting an arterial blood gas analysis was drawn and $PaCO_2$ was measured (ABL 505, Radiometer Control, Copenhagen, Denmark).

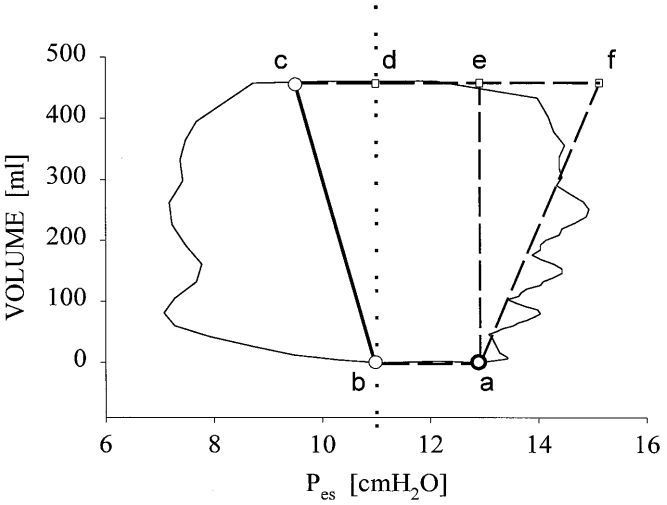

Fig. 1 Partitioning of work of breathing. P_{es}-volume plot of patient 11 during PSV. The patient's inspiratory effort starts at *a*, whereas inspiratory flow begins at *b* and ends at *c*. The area enclosed by the P-V curve and the line *bc* was used to calculate the patient's work of breathing dissipated against flow resistive forces (W_{RES}). The dotted line *bd* represents the P_{es} baseline pressure level at zero-flow condition and the P_{es} difference between *a* and *b* is $PEEPi_{dyn}$, the resulting rectangular area *abde* represents the patient's work to overcome $PEEPi_{dyn}$. The triangle *bcd* corresponds to the patient's work against elastic forces of the lung under the condition that P_{es} at *c* is below the dotted P_{es} baseline [23]. Since it is still difficult to obtain reliable pressure-volume curves of the chest wall during partial ventilatory support, we assumed chest wall compliance to be within normal values in our COPD patients [37] and calculated chest wall compliance as 4% of vital capacity per cm H_2O [38]. Values for vital capacity were taken from the literature and extrapolated for age [39]. Chest wall compliance is represented by the slope *af* in this figure. Thus, the triangle *aef* represents the chest wall component of the elastic inspiratory work. The sum of the areas *abde* plus *bcd* plus *aef* represents the total elastic work (W_{EL}). Please note that the absolute P_{es} values depend on (1) external PEEP, (2) the hydrostatic pressure of the tissue above the balloon catheter and (3) the pressure inside the balloon and, thus, the calculations are based solely on pressure differences

Statistics

The individual data of each patient were calculated as the mean values over the measurement period of 5 min after exclusion of artifacts. Additionally, the coefficient of variation (cv: SD*100/mean) was estimated for selected variables. After testing for normal distribution (Shapiro Wilk's W test) one-way analysis of variance (ANOVA) with subsequent post hoc testing of least significant difference (LSD) between means for multiple comparisons was used for statistical analysis. Probability values of less than 0.05 were considered as significant.

Results

Ventilatory variables

None of the variables during the four baseline PSV_b settings differed significantly, V_E was 12.4 ± 3.6, 12.6 ± 3.5, 12.3 ± 3.1 and 12.9 ± 3.5 l/min, respectively. Table 2 provides mean data characterizing the effects of PSV and PAV on the breathing pattern. As presumed by the study protocol, mean inspiratory pressure ($Pinsp_{mean}$) was the same during PAV_{80} and PSV. As T_I/T_{TOT} was not different between the two modes, the mean airway pressures (P_{mean}) were also comparable. During PAV_{50}, $Pinsp_{mean}$ was significantly lower compared to PAV_{80} and PSV, while P_{mean} tended to decrease but this did not reach statistical significance. Peak inspiratory pressure (P_{max}) was higher during PAV_{80} as compared with PSV and PAV_{50}. V_E and RR were significantly lower during PAV_{80} as compared with both the other settings. However, these differences did not exceed 10%. Despite comparable mean values for V_T in all ventilatory modes, the variability of tidal volumes was much higher during PAV as compared with PSV. An example of an original volume tracing is shown in Fig. 2. The coefficient of variation of V_T over a period of 5 min. was lower during PSV as compared with PAV_{80} and PAV_{50} (Fig. 3, Table 2). On the other hand, the variability of RR and T_I/T_{TOT} did not differ significantly between the modes (Table 2). In addition, no patient-ventilator asynchrony or wasted inspiratory efforts were observed in any of the studied ventilatory modes.

Work of breathing and patient effort

The patient's total WOB_I and the subparts W_{EL} and W_{RES} did not differ significantly between PAV_{80} and PSV (Table 2, Fig. 4). During PAV_{50}, W_{EL} increased by 36%, resulting in a mean increase in WOB_I of 22%, compared with both the other settings, whereas W_{RES} did not change significantly. $P_{0.1}$ did not differ significantly between the matched modes PAV_{80} and PSV, but increased significantly after the reduction of support during PAV_{50} (Table 2).

Discussion

Our study demonstrates that the differences of breathing pattern were small between the investigated modes when $Pinsp_{mean}$ was comparable. However, during PAV combined with ATC we observed a higher variability of V_T as compared with that during PSV. After reduction of mechanical unloading from 80% to 50% (PAV_{50}) the patients increased inspiratory effort and WOB_I to maintain a comparable ventilation.

Table 1 Patient characteristics and ventilatory support. $PEEPi_{stat}$: static PEEPi, E_{rs} and R_{rs}: elastance and resistance of the respiratory system (all measured during volume controlled ventilation), R_{et}: resistance of the endotracheal tube (as a part of R_{RS}, from [14]), VA: volume assist, FA: flow assist, ATC: automatic tube compensation, PSV: pressure support ventilation, PSV_b: baseline PSV, ARF: acute respiratory failure, COPD: chronic obstructive pulmonary disease, ACB: aorto-coronary bypass surgery, MAS: major abdominal surgery, LLL and RLL: left and right lower lobe of the lung, MOF: multiple organ failure

Patient No.	Sex	Age [yr.]	Ventilator Days	FIO_2	$PEEPi_{stat}$ [cm H_2O]	E_{rs} [cm H_2O/L]	VA 80 (50 %) [cm H_2O/L]	R_{rs} [cm H_2O/L/s]	R_{et} [cm H_2O/L/s]	qFA + ATC 80 (50 %) [cm H_2O/L/s]	PSV (PSV_b) [cm H_2O/L/s]	$PaCO_2$ at PSV_b [mm Hg]	Precipitating Cause of ARF
1	m	71	7	0.3	3	15	12.0 (7.5)	15	5.5	13.0 (10.0)	12 (10)	43	Exacerbation of COPD
2	m	66	15	0.3	3	16	13.0 (8.0)	10	5	9.0 (7.5)	9 (10)	45	ACB + MAS, fatigue
3	m	62	7	0.3	9	18	14.5 (9.0)	7	6.5	7.0 (7)	10 (10)	39	Atelectasis LLL
4	m	74	5	0.3	3	15	12.0 (7.5)	7	4.5	6.5 (5.5)	8 (5)	55	MAS, fatigue
5	m	71	20	0.4	4	22	17.5 (11.0)	6	4.5	5.5 (5.0)	10 (7)	51	RLL-resection
6	m	58	3	0.4	9	23	18.0 (11.5)	19.5	8.5	17.5 (14.0)	10 (5)	38	Pneumonia
7	m	72	4	0.4	3	17	13.5 (8.5)	13	7.5	12.0 (10.5)	7 (10)	49	MAS, fatigue
8	m	90	3	0.3	6	21	17.0 (11.0)	21	8.5	19.0 (15.5)	13 (10)	44	Multiple trauma
9	m	84	8	0.4	3	28	22.0 (14.0)	15	8.5	13.5 (12.0)	17 (15)	38	Pneumonia
10	m	64	10	0.4	4	12	10.0 (6.0)	12.5	6.5	11.5 (9.5)	4 (5)	46	MOF, pulmon. edema
11	m	61	7	0.4	5	20	16.0 (10.0)	15	5.5	13.0 (10.5)	13 (15)	43	Pneumonia
12	f	66	7	0.3	10	20	16.0 (10.0)	16.5	11.5	15.5 (14.0)	9 (7)	49	Pneumonia
13	f	50	3	0.4	7	14	11.0 (7.0)	18	8.5	16.0 (13.5)	17 (15)	51	Emphysema

In a comparative study of PSV and PAV it is crucial to apply equivalent levels of support. Ideally, the degree of respiratory muscle unloading should be the same in the two modes. Although this variable can be directly chosen in the PAV mode when elastic and resistive impedance is known, during PSV the level of muscle unloading has to be estimated. In the present study, we used $Pinsp_{mean}$ to match ventilatory support between PAV_{80} and PSV. Thus, $Pinsp_{mean}$ did not differ significantly between PAV_{80} and PSV, but decreased after reduction of support from PAV_{80} to PAV_{50}.

An adequate unloading of P_{mus} during PAV requires knowledge of the patient's elastance and resistance. One major drawback of the clinical application of PAV is that no accepted method for the measurement of elastance and resistance during partial ventilatory support is currently available [13]. One solution is the measurement of respiratory mechanics during controlled mechanical ventilation. Although this approach has been used in several recent investigations [13, 28, 31, 32, 33], it has limitations: the determination of resistance depends on the method used [21] and on the individual flow profile and elastance is not defined during assisted spontaneous breathing. Therefore, the measured respiratory mechanics during controlled mechanical ventilation in sedated patients are only approximations of the mechanics during partial ventilatory support. Consequently, the degree of unloading can also only be an estimate of the effective amount of unloading. Additionally, as the ventilator prototype used in this study delivers non-linear instead of linear FA, less compensation for inspiratory flow below 1 l/s and more compensation for inspiratory flow above 1 l/s occurs than with linear FA. Since inspiratory peak flow was approximately 1 l/s during all settings, the use of non-linear FA might have caused a certain lack of support of the inspiratory effort when inspiratory flow decreased at the end of the inspiratory cycle. This is another reason for the fact that

Table 2 Ventilatory variables, WOB and inspiratory effort[a]

		PSV	PAV_{80}	PAV_{50}
RR	[min^{-1}]	22.3 ± 6.9	20.8 ± 6.0 †	23.1 ± 6.6 † ‡
V_E	[L/min]	13.1 ± 3.3	11.9 ± 3.5 †	12.9 ± 3.5 † ‡
V_T	[mL]	618 ± 150	591 ± 153	579 ± 134
V_T min	[mL]	547 ± 128	451 ± 143 ††	468 ± 130 ‡
V_T max	[mL]	692 ± 177	727 ± 189	679 ± 165
Peak flow	[L/s]	0.90 ± 0.19	0.96 ± 0.26	0.99 ± 0.23
T_I	[s]	1.07 ± 0.25	1.09 ± 0.24	0.96 ± 0.25 †
T_E	[s]	1.92 ± 0.85	2.05 ± 0.75	1.83 ± 0.58
T_I/T_{TOT}	[s]	0.37 ± 0.07	0.36 ± 0.07 †	0.35 ± 0.06 ‡
PEEP	[cm H_2O]	6.5 ± 2.3	6.5 ± 2.3	6.5 ± 2.3
$PEEPi_{dyn}$	[cm H_2O]	2.0 ± 0.7	1.8 ± 1.0	1.8 ± 0.8
P_{mean}	[cm H_2O]	10.1 ± 1.8	10.1 ± 2.0	9.6 ± 2.1
$Pinsp_{mean}$	[cm H_2O]	13.8 ± 3.5	13.6 ± 2.8	12.1 ± 2.7 †† ‡‡
P_{max}	[cm H_2O]	18.7 ± 3.5	21.4 ± 4.7 †† ‡‡	18.0 ± 3.9
cv of V_T	[%]	10 ± 4	20 ± 13 ††	15 ± 8 †
cv of RR	[%]	12 ± 9	11 ± 7	10 ± 6
cv of T_I/T_{TOT}	[%]	11 ± 8	11 ± 6	8 ± 2
WOB_I	[mJ/L]	786 ± 334	799 ± 305	957 ± 330 † ‡
W_{VIS}	[mJ/L]	444 ± 201	466 ± 145	490 ± 159
W_{EL}	[mJ/L]	343 ± 175	333 ± 200	467 ± 204 † ‡‡
$P_{0.1}$	[cm H_2O]	2.02 ± 0.92	2.02 ± 1.00	2.67 ± 1.17 † ‡

[a] all values are means ± SD; †: $p < 0.05$, ††: $p < 0.001$ versus PSV, ‡: $p < 0.05$, ‡‡ $p < 0.001$ PAV_{80} versus PAV_{50}

the given percentage values of mechanical unloading during PAV are only estimates. However, since the two different ventilatory modes were matched by $Pinsp_{mean}$, this does not affect the comparability of PAV_{80} and PSV in this study.

As the degree of unloading P_{mus} can only be chosen during PAV but not directly during PSV, PAV_{80} had to be applied first to determine the $Pinsp_{mean}$ and to match the level of PSV afterwards. Thus, the administration of the ventilatory modes has not been randomized. However, to minimize the bias due to the lack of randomization, PSV_b was applied between the different ventilatory modes to ensure the same lung history.

During PAV_{80}, mean RR and V_E were significantly lower than during PSV and PAV_{50}, although these differences did not exceed 10% and, therefore, the clinical relevance of this finding is presumably low. However, the lower respiratory rate during PAV_{80}, as compared with PSV, during quiet breathing might reach clinical importance if the ventilatory demand is increased. This was recently demonstrated by Ranieri and co-workers, who compared the effects of an increased ventilatory demand by a CO_2 challenge on breathing pattern during PAV and PSV in patients with mild-to-moderate pulmonary dysfunction [31]. In their study the increase in V_E due to acute hypercapnia was induced by changes in V_T modulated by variations in inspiratory muscle effort during PAV without a considerable change in RR. In contrast, during PSV, the increase in V_E resulted from a higher RR which caused an increase in PEEPi, greater muscle effort and patient discomfort.

Although inspiratory peak flow did not differ significantly in all the settings of our study, P_{max} was higher during PAV_{80} as compared with both the other settings. This is because P_{aw} is greatly influenced by the mode of support: with a preset pressure support during PSV, P_{aw} remains relatively constant whereas, during PAV, there is a positive relationship between P_{mus} and P_{aw} (Eq. 5) [34]. Thus, the higher absolute values of V_T due to the higher variability of V_T during PAV_{80} resulted in the higher P_{max}. Despite these differences, all other variables did not differ considerably between the two modes (Table 2).

Our study demonstrates that a comparable $Pinsp_{mean}$ as an index of equivalent ventilatory support during PSV and PAV_{80} results in a comparable breathing pattern, a comparable inspiratory effort (as measured by $P_{0.1}$) and comparable WOB_I. The reduction of ventilatory support during PAV_{50} did not change the breathing pattern appreciably. However, to maintain the same ventilatory targets, the patients had to increase their inspiratory effort and WOB to compensate for the reduction of assist. This finding is consistent with the results of a previous study by Marantz et al. [35], who studied different levels of PAV.

It has been demonstrated that FA and VA are able to unload the resistive and elastic components of total WOB_I separately [32] and ATC can effectively compensate for the additional WOB imposed by the endotracheal tube [15]. In this study, during PAV_{50} WOB_I increased mainly by an increase in W_{EL} (Table 2). This is not surprising, since the R_{et} was 56 ± 16% of the total resistance and, therefore, according to our study protocol, a substantial part of the total resistance was still completely compensated by ATC during PAV_{50}. Thus, the reduction of ventilatory support from PAV_{80} to

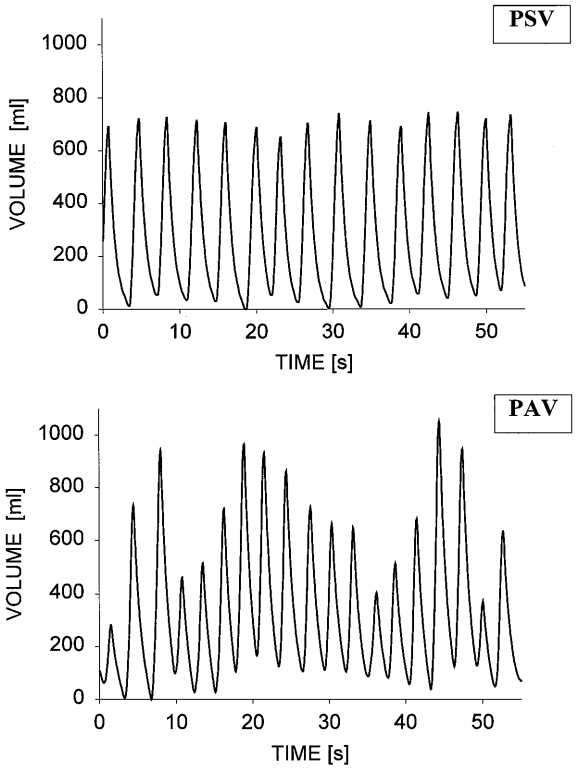

Fig. 2 Original volume tracings of patient 8 over a period of 1 min. *Top*: PSV, *bottom:* PAV_{80}. Note the differences in V_T variability

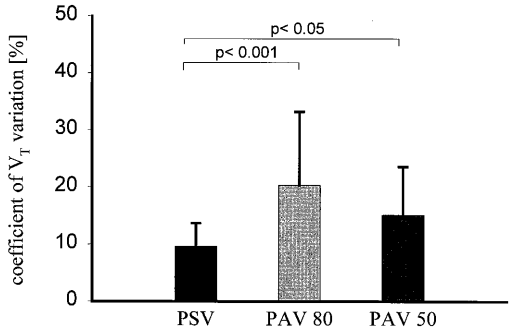

Fig. 3 Variability of V_T over a period of 5 min during PSV and PAV_{80} matched by $Pinsp_{mean}$ and after reduction of support during PAV_{50}. *Boxes* are means and *bars* represent SDs

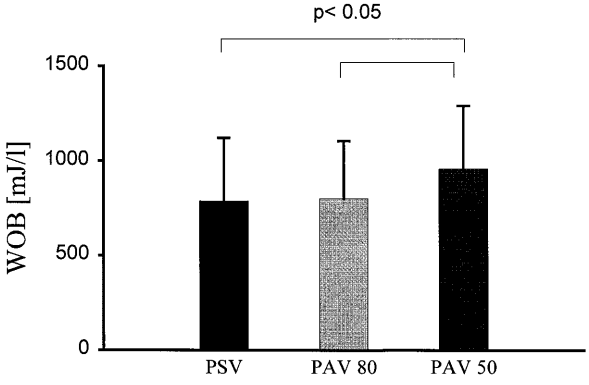

Fig. 4 Inspiratory work of breathing (WOB_I) at PSV and PAV_{80} matched by $Pinsp_{mean}$ and after reduction of support during PAV_{50}. *Boxes* are means and *bars* represent SDs

PAV_{50} is mainly caused by a reduction in volume-assist resulting in a higher W_{EL} in our study. It has to be kept in mind that the calculation of the patient's WOB in a mode with pressure support by the ventilator is the lower limit of the real mechanical work done by the patient. The pressure generated by the patient and the pressure applied by the ventilator counteract, so that the real P_{mus} generated by the patient might be lower than the measured esophageal pressure, but never higher. This fact results in an underestimation of the inspiratory work that is really supplied by the patient.

The most obvious difference between PSV and PAV was the higher variability of the V_T during PAV as compared with PSV (see Fig. 2 and 3). This indicates that, during PAV, the patient has the capability to change V_T by modulation of his inspiratory effort. This is different from PSV: during PSV any inspiratory effort is always augmented with a constant inspiratory pressure. Thus, in the case of changes in the respiratory demand, the patient's ability to modulate the V_T is limited and the patient has to change RR to reach the actual ventilatory target [31]. In our patients with mild-to-moderate respiratory failure no differences in $PEEP_i$ between the modes have been observed. However, it has been demonstrated that an increased ventilatory demand can result in a higher RR during PSV, which can increase $PEEP_i$ WOB and can cause discomfort in patients during weaning from mechanical ventilation [31].

In a study of breath-to-breath variability over a period of 15 min in 65 spontaneously breathing subjects, Tobin and co-workers [36] observed higher coefficients of variation in V_T ($33 \pm 14.9\,\%$) as compared with RR ($20.8 \pm 11.5\,\%$) and T_I/T_{TOT} ($17.7 \pm 6.5\,\%$). These data suggest that, in physiologic states, the rhythm generated from the respiratory control system is more constant than the drive component of the system. Thus, the higher variability of V_T observed during PAV in our study might indicate a more physiologic breathing pattern and a closer patient-ventilator interaction, although the variability was still below that observed in healthy subjects. Although we did not observe patient-ventilator asynchrony or wasted efforts in any ventilatory mode in this study, a better patient-ventilation interaction during PAV might have the potential to avoid these problems in difficult-to-synchronize patients.

In conclusion, mean values of ventilatory variables and respiratory work of breathing did not differ by a large amount during PAV and PSV if the $Pinsp_{mean}$ was

comparable. A reduction in ventilatory support during PAV increased the patient's inspiratory effort and WOB, but did not change the breathing pattern appreciably. However, there were significant differences in the variability of V_T, which was higher during both levels of PAV. This might reflect an increased ability of the patients to change V_T as a physiologic response to alterations in respiratory demand and a closer patient-ventilator interaction.

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