Proportional assist versus pressure support ventilation in patients with acute respiratory failure: Cardiorespiratory responses to artificially increased ventilatory demand*

Dirk Varelmann, MD; Hermann Wrigge, MD; Jörg Zinserling, MSc; Thomas Muders, MD; Rudolf Hering, MD; Christian Putensen, MD

Objective: **To test the hypothesis that in response to increased ventilatory demand, dynamic inspiratory pressure assistance better compensates for increased workload compared with static pressure support ventilation (PSV).**

Design: **Randomized clinical crossover study.**

Setting: **General intensive care u nits of a university hospital.**

Patients: **Twelve patients with acute respiratory failure.**

Interventions: **Patients received PSV, proportional assist ventilation (PAV), and PAV+ automatic tube compensation (ATC) in random order while maintaining mean inspiratory airway pressure constant. During each setting, ventilatory demand was increased by adding deadspace without ventilator readjustment.**

Measurements and Main Results: **Cardiorespiratory, ventilatory, and work of breathing variables were assessed by routine monitoring plus pneumotachography; airway, esophageal, and abdominal pressure measurements; and nitrogen washout. After deadspace addition, tidal volume and end-expiratory lung volume increased similarly in all ventilatory modalities. Ventilator work, peak inspiratory flow, and maximum airway pressure increased significantly during PAV+ATC when compared with PSV after deadspace addition. However, increase in ventilator work did not result in a smaller increase in patients' work of breathing with elevated ventilatory demand during PAV+ATC (PSV 807 ± 204 mJ/L, PAV 802 ± 193 mJ/L, and PAV+ATC 715 ± 202 mJ/L, $p = .11$). Increase in patients' work of breathing was mainly caused by a significantly higher resistive workload during PAV and PAV+ATC.**

Conclusion: **In patients with acute respiratory failure, dynamic inspiratory pressure assistance modalities are not superior to PSV with respect to cardiorespiratory function and inspiratory muscles unloading after increasing ventilatory demand. The latter might be explained by higher peak flows resulting in nonlinearly increased resistive workload that was incompletely compensated by PAV+ATC. (Crit Care Med 2005; 33:1968–1975)**

KEY WORDS: acute lung injury; spontaneous breathing; functional residual capacity; lung; partial ventilatory support; work of breathing

Pressure support ventilation (PSV) is commonly used to decrease work of breathing (WOB) in patients requiring ventilatory assistance (1, 2). During PSV, the ventilator applies constant pressure for every detected patient's inspiratory effort. In contrast, proportional assist ventilation (PAV) provides dynamic inspiratory pressure assistance in linear proportion to patient-generated volume and flow (3, 4). In theory, by adjusting the proportionality between applied pressure and both actual volume and flow, the ventilator should selectively unload the patient's inspiratory muscles for increased elastic and resistive WOB. Endotracheal tube resistance (R_{et}) imposes an undesirable inspiratory muscle load that is nonlinearly dependent on flow and should, therefore, not be entirely compensated by linearly flow-dependent support with PAV or constant PSV. Automatic tube compensation (ATC) (5) provides ventilatory assistance of each spontaneous breath by increasing airway pressure (Paw) during inspiration and lowering Paw during expiration aiming at compensating nonlinearly flow-dependent R_{et} (6, 7). Based on these considerations, PAV and the combination of PAV and ATC should better adapt the dynamic inspiratory pressure assistance to variations in ventilatory demand than PSV (8).

We hypothesized, that, in response to an increase in ventilatory demand, patients' WOB increases less during PAV+ATC compared with PAV alone or PSV, Therefore, we examined WOB and cardiopulmonary function in patients with acute respirator failure (ARF) and unrestricted breathing with equivalent levels of pressure support during PSV, PAV, and PAV+ATC during normal breathing and after a provoked increase in ventilatory demand.

MATERIALS AND METHODS

Patients. After approval by the Bonn University Ethics Committee, informed consent for inclusion in the study was obtained primarily from the next of kin of 12 mechanically ventilated patients with ARF meeting acute lung injury criteria (9) and secondarily from the patients themselves after recovery. Patients with a history of chronic lung or heart disease and those with mean arterial blood pressure <60 mm Hg and/or need for >5 μg/min epinephrine or norepinephrine were excluded. Severity of illness was assessed with

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From the Department of Anesthesiology and Intensive Care Medicine, University of Bonn, Germany.

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the Simplified Acute Physiology Score (10) at inclusion in the study.

Cardiovascular Measurements. Routine clinical management of all patients included electrocardiogram, the use of a radial artery catheter, and a thermistor-tipped quadruple-lumen pulmonary artery catheter (CCO 746HF8, Baxter Edwards Critical Care, Irvine, CA), the latter in ten of 12 patients. Cardiac output was continuously monitored using thermal dilution (Vigilance, Baxter Edwards Critical Care). Cardiac index, systemic vascular resistance index, and oxygen delivery index were calculated using standard formulas.

Ventilatory and Lung Mechanics Measurements. Spirometric variables were determined as described in detail elsewhere (11). Esophageal pressure (P_{es}) was measured with a balloon catheter (International Medical, Zutphen, The Netherlands) connected to differential pressure transducers (SMT, Munich, Germany). The validity of the esophageal balloon measurements in the supine subject was tested with the occlusion method (12, 13). When the slope of the P_{es}/Paw tracing differed from 1, P_{es} was corrected according to Brunner and Wolff (14). Intra-abdominal pressure (P_{ab}) was measured intermittently in the urinary bladder as described previously (15). All signals were sampled with an analog/digital converter board (PCM-DAS16S/12, Mansfield, MA) and stored on a personal computer.

Before the study, all patients were placed in a semirecumbent position and received time-cycled pressure-controlled ventilation with unrestricted spontaneous breathing (SB) in the airway pressure release ventilation (APRV) mode (Evita 4, Dräger, Lübeck, Germany), which is our standard ventilatory mode. The ventilatory setting was selected as previously described (16). An SB trial with PSV was initiated to record tidal volume (V_T) and respiratory rate (RR). The pressure level was set to avoid rapid shallow breathing (7.5 ± 3.0 mbar). To measure dynamic respiratory system resistance (R_{rs}) and elastance (E_{rs}), the patients were briefly switched to controlled mechanical ventilation (CMV) without SB at the positive end-expiratory pressure level used at inclusion in this study. The RR and V_T were set to match those of the SB trial setting to imitate the patients' spontaneous breathing pattern, and the inspiratory flow was set at 1 L/sec (17, 18). The inspiratory to expiratory time ratio was 1:2. To suppress SB during this CMV period, the patients were briefly sedated with propofol (1–2 mg/kg).

RR, inspiratory time (T_I), and duty cycle (T_I/cycle time) were determined from the gas flow signal. Mean airway pressure and mean inspiratory ($P_{insp,\ mean}$), minimum (Paw_{min}), and maximum airway pressures (Paw_{max}) were determined for each respiratory cycle. All ventilatory variables were averaged over a period of 5 mins.

Calculation of Work of Breathing Indexes. The patient's inspiratory work of breathing (WOB_{pat}) was calculated as the area under the P_{es}/V_T curve incorporating chest wall compliance as described previously and further divided into WOB against elastic and resistive (viscous) properties ($WOB_{pat,el}$ and $WOB_{pat,visc}$, respectively) (11, 19–21). Elastic and resistive ventilator WOB ($WOB_{vent,el}$ and $WOB_{vent,visc}$) was determined accordingly. The P_{es} values at zero-flow points were considered as the beginning and end of expiration. The area under the P_{es}/V_T curve was only considered if P_{es} was below baseline at end-expiration to ensure that the pressure change results from patient activity (22). WOB was considered as the average of breath-by-breath calculations during 5 mins and indexed for minute volume (in mJ/L). Power of breathing (POB) was calculated as WOB indexed for time (mJ/min).

In addition, diaphragmatic pressure time product (PTP_{di}) was determined from transdiaphragmatic pressure ($P_{di} = P_{es} - P_{ab}$) as the area under the P_{di}/time curve (Fig. 1), which was, again, only taken into calculation if P_{di} was below a baseline value defined at end-expiration (23, 24). The esophageal pressure time product (PTP_{es}) was determined accordingly.

All ventilatory variables were averaged over a period of 5 mins; on average each mode was studied for 25 mins.

Gas Analysis. Arterial blood gases and pH were determined immediately after sampling with standard blood gas electrodes and oxygen saturation by spectrophotometry (ABL 620 and OSM, Radiometer, Copenhagen, Denmark). Fractions of inspired and expired oxygen, CO_2, and N_2 were measured continuously with mass spectrometry (Random Access Mass Spectrometer M-100, Marquette Hellige, Freiburg, Germany).

Determination of End-Expiratory Lung Volume (EELV) and Serial Deadspace. For the calculation of EELV, the multiple breath nitrogen washout method was used as described in detail previously (24, 25). Mean values of two consecutive EELV determinations were used for the analysis; the coefficient of variation was 6.5%.

Serial N_2 deadspace was calculated as previously described by Brunner et al (26). To allow comparisons of EELV with and without artificial deadspace, serial N_2 deadspace was subtracted from EELV.

Protocol and Ventilator Settings. After inclusion into the study, patients remained supine and continued to receive infusions of sufentanil (10–20 μg/hr) and midazolam as necessary, to achieve a Ramsay sedation score of 3 (16).

Before inclusion into the study, all patients were ventilated with APRV as described previously. APRV was used as baseline ventilation to restore lung history before each study mode.

Before randomization, pressure support levels in each patient had to be defined and matched between the investigated ventilatory support modalities: $P_{insp,mean}$ served as the independent variable (11). First, during PAV, volume assist and flow assist were adjusted to compensate for 50% of E_{rs} and R_{rs} previously measured during CMV. $P_{insp,mean}$ measured during this PAV setting was used as reference for the two other studied ventilatory modes.

ATC should compensate for R_{et} by increasing P_{aw} during inspiration and lowering P_{aw} during expiration in a nonlinearly flow-dependent manner to maintain a constant preset tracheal pressure (P_{tr}) during SB with continuous positive airway pressure. P_{tr} was estimated by the ventilator as $P_{tr} = P_{aw} - K_1 \cdot \dot{V}^2$ (27), which differs from the original ATC algorithm (5, 28). During PAV+ATC, ATC was added to the previously adjusted PAV setting. The resulting proportionality for P_{aw} regulation is then $Paw - V \cdot VA + \dot{V} \cdot FA + \dot{V}^2 \cdot K_1$. Because ATC compensates for parts of the resistive workload, flow assist was reduced while volume assist remained unchanged until $P_{insp,mean}$ was not different from $P_{insp,mean}$ during PAV alone. During PSV, the inspiratory pressure support was adjusted accordingly. Positive end-expiratory pressure was kept constant during all ventilatory modalities.

Patients were assigned to receive PAV, PAV+ATC, and PSV as stand-alone ventilatory modes in random order. Measurements and data collection were performed during stable conditions confirmed by constancy (±5%) of minute volume, arterial oxygen saturation, expiratory CO_2 fraction, mean arterial pressure, and cardiac index for ≥15 mins. After a first set of measurements in each mode, a deadspace of 150 mL was added between the Y-piece and the endotracheal tube to increase the patient's ventilatory demand while the ventilatory setting remained unchanged. Following another set of measurements during stable conditions (see previous criteria), the additional deadspace was removed and patients were returned to baseline ventilation (APRV).

Statistical Analysis. To detect differences in WOB and $Pa_{O_2}/F_{I_{O_2}}$ between the ventilatory settings with the given two-sided crossover design at a significance level of 5% ($\alpha = .05$) with a probability of 80% ($\beta = .20$) based on an estimated difference of 0.82 of the variable's mean within-patient SD, the number of patients to be studied had to be ≥12.

Results are expressed as mean ± SD. Data were tested for normal distribution by the Shapiro-Wilks' W test and analyzed by a two-way analysis of variance, with the ventilatory modalities as the between-groups factor and deadspace on/off as the repeated-measures factor. When a significant F ratio was obtained, differences between the means were isolated with the *post hoc* Tukey's multiple comparison test. Differences were considered to be statistically significant if $p < .05$.

RESULTS

The patients' demographic and clinical data are shown in Table 1.

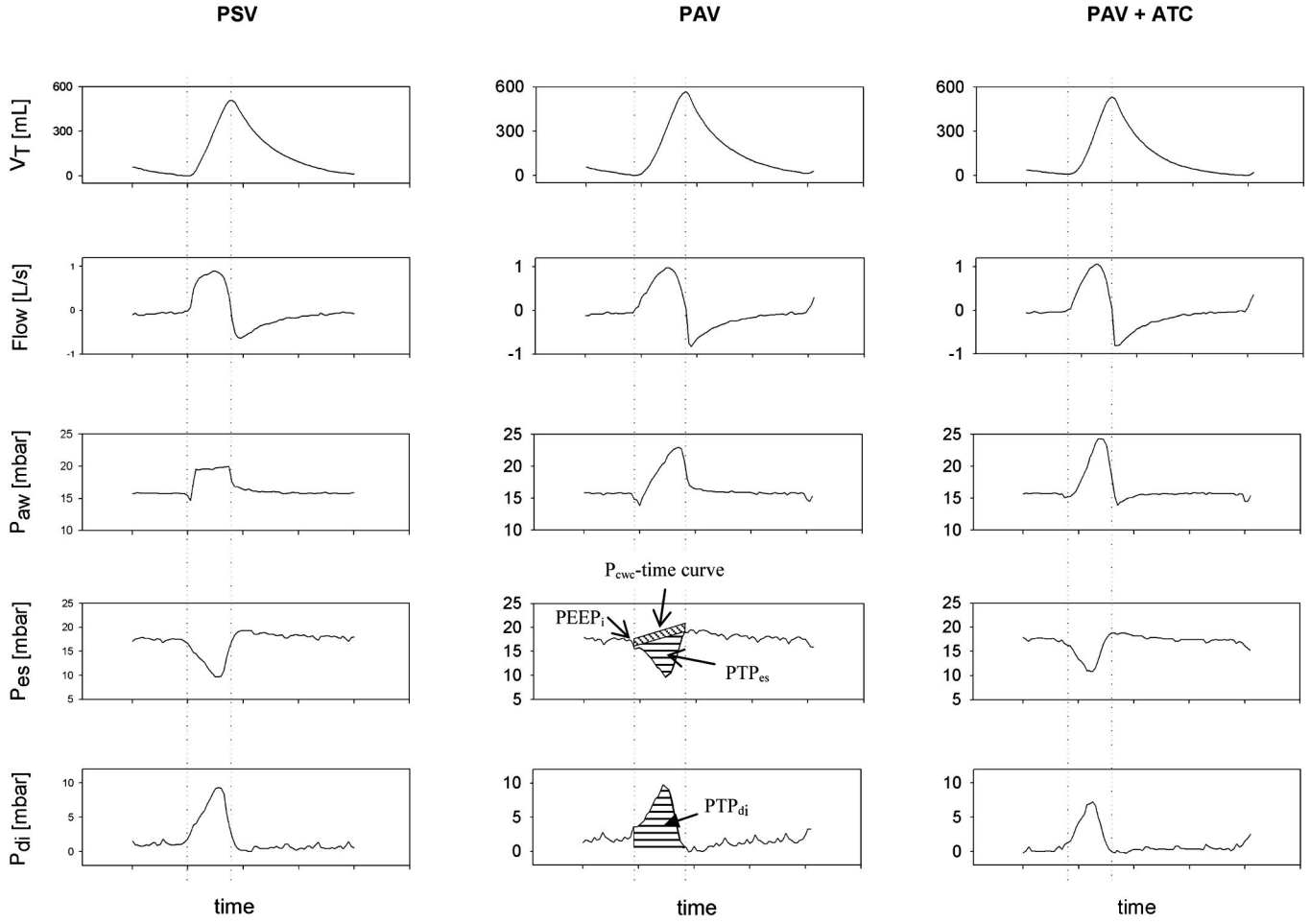

Figure 1. Tidal volume, flow, airway, esophageal, and transdiaphragmatic pressure tracings. The figure shows typical tidal volume (*VT) flow as well as pressure tracings (Paw, airway pressure;* P_{es}*, esophageal pressure;* P_{di}*, transdiaphragmatic pressure) in patient 3. Graphic measurements of esophageal and transdiaphragmatic pressure time product (*PTP_{es} *and* PTP_{di}*, respectively) of a single breath are exemplarily shown during proportional assist ventilation (*PAV*). PTP$_{es}$ is the horizontal and diagonal-hatched area subtended by the P$_{es}$. Diagonal-hatched area represents work imposed by intrinsic positive end-expiratory pressure (*PEEPi*). The horizontal-hatched area subtended by P$_{di}$ represents PTP$_{di}$.* PSV*, pressure support ventilation;* ATC*, automatic tube compensation;* P_{cwc}-time*, chest wall static recoil pressure over time.*

There were no significant changes in any of the cardiorespiratory variables measured during baseline ventilation with APRV before each of the studied ventilatory modes, indicating no systematic change in patients' condition during the study period.

Typical tracings of VT, flow, Paw, P_{es}, and P_{di} during the three different ventilatory modalities are shown in Figure 1.

Ventilation and respiratory mechanics variables are given in Table 2. According to the protocol, $P_{insp,mean}$ was comparable during all settings without additional deadspace. Addition of deadspace led to an increase in $P_{insp,mean}$ during PAV and PAV+ATC ($p < .05$). Lowering Paw during expiration with ATC resulted in a significantly lower Paw_{min} during PAV+ATC ($p < .05$) compared with PSV and PAV. Paw_{max} increased after deadspace addition during PAV and PAV + ATC ($p < .05$) and remained constant during PSV. All other ventilatory variables were not different before adding deadspace. Matching inspiratory assistance by using $P_{insp,mean}$ resulted in comparable workload of the patients' inspiratory muscles as indicated by work of breathing indexes (Fig. 2*B*), PTP_{es}, PTP_{di}, and POB_{pat}. In contrast, WOB_{vent} was higher during PAV+ATC compared with PSV ($p < .05$, Fig. 2*A*).

RR and VT increased after deadspace addition, leading to the significant increase in minute volume ($p < .05$) accompanied by higher inspiratory peak flows ($p < .05$) and $Paco_2$, whereas pH decreased during PSV, PAV, and PAV+ATC (Table 2). Peak flows during PAV with ATC were significantly higher than during PSV ($p < .05$). WOB_{pat}, $WOB_{pat,visc}$, PTP_{es}, and PTP_{di} increased after addition of deadspace ($p < .01$) during all tested ventilatory modalities. Not surprisingly, WOB_{vent} remained unchanged during constant inspiratory pressure assistance with PSV after addition of deadspace but increased during both forms of dynamic assistance ($p < .05$). WOB_{vent} during PAV+ATC without additional deadspace was as high as during PAV with deadspace. $WOB_{vent,el}$ was higher during PAV and PAT+ATC compared with PSV ($p < .05$) independently of deadspace addition. $WOB_{vent,visc}$ was lowest during PAV ($p < .05$) but increased after deadspace addition in all modes. EELV was comparable between all modes tested and increased after addition of deadspace ($p < .05$).

During PAV+ATC, patients showed the highest VT variability ($p < .05$).

Table 1. Anthropometric data

No.	Gender	Age, yrs	BMI, kg/m^2	Tube, et/tc	Tube Diameter, mm	Ventilator Days	F_{IO_2}	PEEP, mbar	E_{rs}, mbar/mL	R_{rs}, mbar/L/sec	SAPS	Diagnosis
1	M	35	20.2	et	8	10	0.4	14	48	23	28	Atypical pneumonia
2	F	70	24.5	tc	9	37	0.3	13	25	14	53	Sepsis
3	M	67	27.7	et	8	23	0.3	11	21	17	59	Peritonitis, sepsis
4	M	60	26.1	et	7.5	20	0.35	14	13	9	46	Pneumonia, sepsis, MOF
5	M	27	27.8	et	8	10	0.55	17	15	11	71	Aortic rupture, sepsis
6	M	58	26.1	et	7.5	5	0.35	13	14	9	61	Sepsis, pneumonia
7	M	57	29.2	tc	9	12	0.35	15	12	6	66	Rip series fractures, multiple trauma
8	M	61	39.6	et	7.5	12	0.35	15	14	10	76	Septic shock
9	M	76	29.9	et	8	7	0.35	12	13	7	74	Pneumonia, abdominal aortic aneurysm
10	M	64	15.9	et	7.5	8	0.35	18	14	8	53	ARF
11	F	45	35.4	et	7.5	8	0.3	13	30	12	59	Retroperitoneal hematoma
12	M	71	32.7	et	8	36	0.3	20	26	10	53	Sepsis, MOF
Mean		57.6	27.9		8.0	15.7	0.35	14.6	20.4	11.3	58.3	
SD		14.8	6.3		0.5	11.0	0.07	2.6	10.6	4.8	13.3	

BMI, body mass index; et, endotracheal tube; tc, tracheal cannula; PEEP, positive end-expiratory pressure; E_{rs}, elastance; R_{rs}, resistance of respiratory system; SAPS, Simplified Acute Physiology Score; F, female; M, male; MOF, multiple organ failure; ARF, acute respiratory failure.

This table contains anthropometric data of all patients in this study.

Table 2. Ventilation and respiratory mechanics

	PSV		PAV		PAV + ATC		
Mode Deadspace	−	+	−	+	−	+	ANOVA
RR, min^{-1}	17.6 ± 4.8	18.5 ± 5.9	17.0 ± 5.6	17.8 ± 5.6	17.0 ± 6.5	18.2 ± 5.7	[a]
V_T, mL	629 ± 171	708 ± 192	642 ± 196	751 ± 221	670 ± 239	719 ± 168	[a]
V_E, L/min	10.3 ± 2.0	12.4 ± 2.8	10.2 ± 2.0	12.6 ± 2.7	10.4 ± 2.3	12.4 ± 2.5	[a]
T_i/T_{tot}	0.27 ± 0.06	0.29 ± 0.07	0.28 ± 0.06	0.31 ± 0.07	0.29 ± 0.08	0.30 ± 0.08	[a]
$Flow_{max}$, L/sec	0.97 ± 0.20	1.02 ± 0.20	0.95 ± 0.22	1.08 ± 0.20	0.99 ± 0.23	1.13 ± 0.1[b]	[a,c,d]
Paw_{min}, mbar	13.4 ± 2.6	13.5 ± 2.6	12.6 ± 2.4	12.4 ± 2.4	11.1 ± 2.7[b]	10.8 ± 2.9[b]	[c]
Paw_{max}, mbar	19.8 ± 3.7	19.8 ± 3.6	22.0 ± 3.9[b]	23.5 ± 4.6[b]	23.6 ± 4.5[b]	25.1 ± 3.6[b]	[a,c,d]
$P_{insp,\ mean}$, mbar	18.2 ± 3.2	18.4 ± 3.3	17.7 ± 2.7	18.6 ± 2.9	18.1 ± 3.0	19.3 ± 2.6	[a,d]
$Paco_2$, mm Hg (kPa)	48 ± 11 (6.4 ± 1.5)	50 ± 13 (6.7 ± 1.7)	47 ± 11 (6.3 ± 1.5)	52 ± 16 (6.9 ± 2.1)	48 ± 11 (6.4 ± 1.5)	52 ± 16 (6.9 ± 2.1)	[a]
PTP_{es}, mbar·sec/min	66.3 ± 25.3	98.7 ± 35.4	62.0 ± 21.1	98.2 ± 19.5	64.7 ± 22.1	85.1 ± 29.2	[a]
PTP_{di}, mbar·sec/min	48.6 ± 22.8	75.8 ± 30.0	44.4 ± 20.4	69.3 ± 17.8	48.2 ± 20.0	58.8 ± 24.5	[a]
$WOB_{pat,el}$, mJ/L	274 ± 161	352 ± 180	206 ± 135[b]	286 ± 151[b]	246 ± 157	266 ± 181[b]	[d]
$WOB_{pat,visc}$, mJ/L	337 ± 149	437 ± 154	393 ± 184	524 ± 161	387 ± 139	467 ± 135	[a]
$WOB_{vent,el}$, mJ/L	238 ± 20	246 ± 24	333 ± 32[b]	389 ± 45[b]	347 ± 28[b]	387 ± 33[b]	[c]
$WOB_{vent,visc}$, mJ/L	352 ± 46	355 ± 44	250 ± 32	291 ± 41	336 ± 44	396 ± 35	[a,c]
POB_{pat}, mJ/min	6523 ± 2060	9931 ± 2264	6066 ± 2434	10156 ± 1913	6723 ± 2696	8990 ± 2597	[a]
EELV-V_{ds}, mL	2364 ± 1111	2517 ± 1095	2414 ± 1106	2612 ± 1171	2505 ± 1243	2725 ± 1238	[a]
V_D, mL	197 ± 79	331 ± 51	190 ± 323	323 ± 45	184 ± 79	316 ± 63	[a]
CV_{VT}, %	7.6 ± 4.0	5.7 ± 3.3	9.5 ± 5.8	7.7 ± 4.0	12.0 ± 6.7[b]	10.6 ± 6.9[b]	[c]

PSV, pressure support ventilation; PAV, proportional assist ventilation; ACT, automatic tube compensation; ANOVA, analysis of variance; RR, respiratory rate; V_T, tidal volume; T_i, duration of inspiration; T_{tot}, duration of respiratory cycle; $Flow_{max}$, inspiratory peak flow; Paw_{min}, minimum airway pressure; Paw_{max}, peak inspiratory airway pressure; $P_{insp,mean}$, mean inspiratory pressure; PTP_{es}, esophageal pressure time product; PTP_{di}, transdiaphragmatic pressure time product; $WOB_{pat,el/visc}$, ventilator work against elastive/resistive properties; POB^{pat}, patients' power of breathing; EELV, end-expiratory lung volume; V_D, serial deadspace; CV_{VT}, coefficient of variation of V_T.

[a] $p < .05$ effect of deadspace addition; [b] $p < .05$, vs. corresponding PSV (*post hoc*); [c] $p < .05$ effect of ventilatory mode; [d] $p < .05$ interaction of effects of deadspace addition and ventilatory mode. This table contains the ventilatory parameters and respiratory mechanics.

There were no differences in cardiovascular variables between the tested modalities (Table 3) despite a small but significant increase in heart rate after deadspace addition. Blood gas analysis values are also presented in Table 3. Pao_2/F_{IO_2} and the arterial oxygen saturation showed a difference neither between the investigated ventilatory modes nor before and after deadspace addition. After deadspace addition, pH values decreased in consequence to the rise in $Paco_2$. During PAV and PAV+ATC, pH values were lower compared with the corresponding PSV mode, and the interaction of change of ventilatory mode with deadspace addition led to an decrease in pH.

DISCUSSION

Inspiratory pressure assistance has been demonstrated to decrease WOB in patients with ARF during weaning from controlled mechanical ventilation (29, 30). It has been claimed that dynamic inspiratory pressure assistance with PAV will better adapt the degree of ventilatory

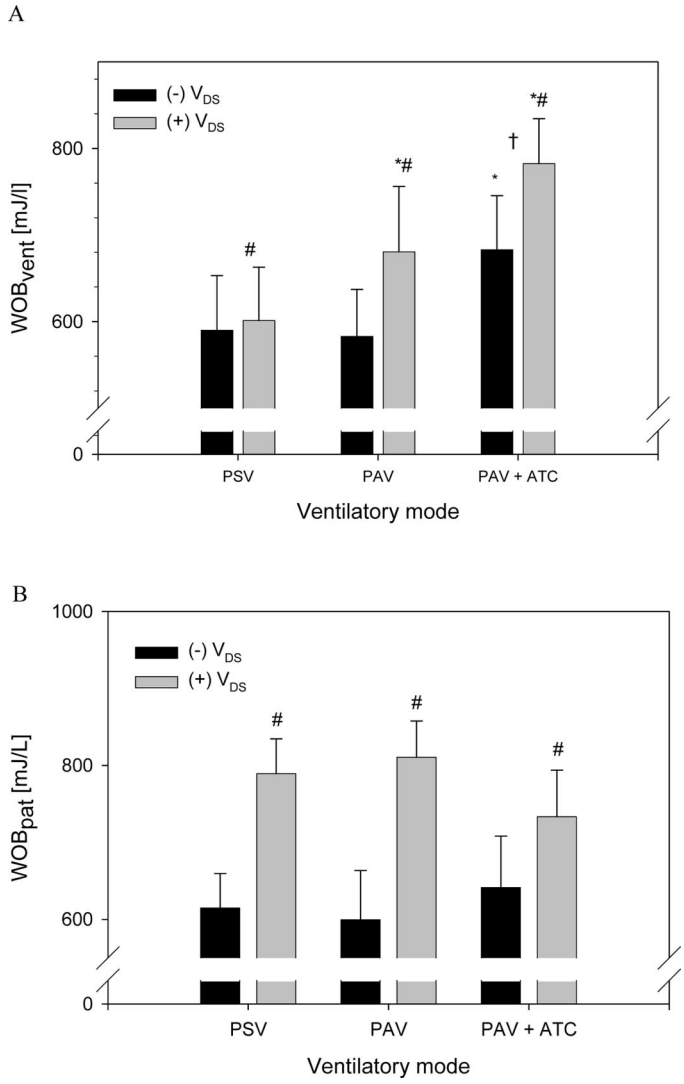

Figure 2. Patient and ventilator work of breathing during different ventilatory modalities, before and after addition of an artificial deadspace. *A*, work of breathing delivered by the ventilator (WOB_{vent}). *B*, patients' work of breathing (WOB_{pat}). V_{ds}, serial deadspace; *PSV*, pressure support ventilation; *ATC*, automatic tube compensation; *PAV*, proportional assist ventilation. Data are presented as mean ± SE. #$p < .05$ effect of artificial deadspace addition; †$p < .05$ effect mode vs. PSV, Tukey's honestly significant difference (HSD) test; *$p < .05$ interaction of effects deadspace addition and ventilatory mode, Tukey's HSD.

support to patients' actual demands than constant PSV and that this will improve patient-ventilator interaction and comfort of breathing (31–34). In this study, we investigated cardiorespiratory effects of different modalities of inspiratory pressure assistance in patients with ARF during normal breathing and after increasing ventilatory demand. Whereas we did not observe differences in patients' WOB indexes, EELV, and other cardiorespiratory variables while the level of inspiratory pressure assistance was matched, we expected better adaptation of dynamic inspiratory pressure assistance after artificial increase in ventilatory demand by adding a deadspace. Unexpectedly, after adding the deadspace, WOB_{pat} did not increase significantly less during PAV+ATC compared with PAV or PSV although WOB_{vent} was significantly higher during PAV+ATC.

The clinical use of PAV is limited by lack of routine measurement techniques of E_{rs} and R_{rs} during spontaneous breathing. We determined these values during CMV and used them as surrogate for setting PAV. Although this limited approach was used in previous studies (11, 35), measured E_{rs} and R_{rs} do not necessarily reflect the values expected during SB. Propofol used to suppress SB in the CMV period is also known to reduce R_{rs} in patients with chronic obstructive pulmonary (36) disease, which were not included in our study.

Because the delivered inspiratory pressure is constant and independent of the patient's inspiratory effort during PSV, a higher ventilatory demand must result in increased WOB_{pat}, as seen in our patients after adding deadspace. On the other hand, during dynamic inspiratory pressure assistance with PAV or PAV+ATC, inspiratory assistance should parallel increased inspiratory efforts resulting in less increase of WOB_{pat}. However, the preset proportionality between inspiratory effort and ventilatory assistance during PAV requires a linear behavior of the respiratory system (3). Based on the observations by Otis and Fenn (37), nonelastic WOB to overcome airway resistance also changes nonlinearly with flow. This is of increasing relevance with high inspiratory flow such as during increased ventilation. Differences in inspiratory flow pattern observed comparing the three modes may partially explain lack of differences in WOB_{pat}, PTP_{di}, and PTP_{es} between constant and dynamic inspiratory pressure with PSV and PAV, respectively (Fig. 3). Thus, although during PAV WOB_{vent} increased after deadspace addition, this did not result in a lesser increase in WOB_{pat} because WOB_{vent} was obviously absorbed by the higher nonelastic workload due to the higher peak flow and different flow pattern during PAV. This is also reflected by the significant increase in $WOB_{pat,visc}$ after deadspace addition. $WOB_{vent,visc}$ even decreased during PAV compared with PSV and was comparable during PSV and PAV+ATC, suggesting that compensation for resistive forces was insufficient during PAV and PAV+ATC. Interestingly, $WOB_{vent,el}$ increased more than $WOB_{pat.visc}$ during PAV and PAV+ATC, indicating that dynamic inspiratory pressure assistance might be more effective in compensation for increases in elastic workload.

Differences in flow pattern with higher peak flows may also explain that WOB_{vent} was always highest during the more aggressive regulation of inspiratory pressure assistance with PAV+ATC. This hypothesis is further supported by observation of significant correlations between differences of WOB_{vent} and differences of peak flow before and after deadspace addition during PAV ($r^2 = .18$) and PAV+ATC ($r^2 = .71$) but not during PSV ($r^2 = .003$). Because EELV was initially

Table 3. Hemodynamic variables

	PSV		PAV		PAV + ATC	
Mode Deadspace	−	+	−	+	−	+
HR, min^{-1}	96.8 ± 19.0	96.0 ± 20.5	92.9 ± 19.0	99.0 ± 21.1	93.1 ± 20.5	96.6 ± 15.3[a]
MAP, mm Hg	83.9 ± 15.3	87.0 ± 15.5	81.5 ± 15.9	83.7 ± 17.5	82.2 ± 14.8	82.7 ± 14.2
CVP, mm Hg	5.5 ± 4.8	5.3 ± 3.8	4.3 ± 4.4	4.3 ± 3.6	4.4 ± 3.5	4.5 ± 4.7
PAOP, mm Hg	7.2 ± 4.1	7.2 ± 4.1	6.6 ± 2.4	6.8 ± 3.2	7.3 ± 4.5	7.1 ± 4.4
CI, L/m^2	4.2 ± 0.9	4.4 ± 1.2	4.3 ± 1.1	4.7 ± 1.2	4.3 ± 1.0	4.2 ± 0.8
Svo_2, %	76.0 ± 6.8	75.9 ± 7.1	76.1 ± 7.9	77.0 ± 6.9	76.2 ± 6.8	76.6 ± 6.6
Ven. admix, mL	13.5 ± 4.5	12.4 ± 5.7	12.3 ± 5.9	14.1 ± 7.0	12.7 ± 5.3	14.4 ± 5.7
PAo_2/Fio_2, mm Hg (kPa)	346 ± 63	348 ± 83	363 ± 101	342 ± 79	357 ± 70	330 ± 76
	(46.1 ± 8.4)	(46.4 ± 11.1)	(48.4 ± 13.5)	(45.6 ± 10.5)	(47.6 ± 9.3)	(44.0 ± 10.1)
Sao_2, %	98.2 ± 0.4	98.1 ± 0.9	98.3 ± 0.7	98.1 ± 0.6	98.3 ± 0.8	98.0 ± 0.7
pH,	7.40 ± 0.06	7.37 ± 0.08[b]	7.39 ± 0.07	7.38 ± 0.08[b]	7.39 ± 0.06	7.37 ± 0.08[a,b,c]
$\dot{D}o_2I$, $mL/min/m^2$	582 ± 133	595 ± 178	593 ± 170	650 ± 182	588 ± 152	592 ± 124

PSV, pressure support ventilation; PAV, proportional assist ventilation; ACT, automatic tube compensation; HR, heart rate; MAP, mean arterial pressure; CVP, central venous pressure; PAOP, pulmonary artery occlusion pressure; CI, cardiac index; Svo_2, mixed venous oxygen saturation; ven. admix, venous admixture; Sao_2, arterial oxygen saturation; $\dot{C}o_2I$, index of oxygen delivery.

[a] $p < .05$, effect deadspace addition; [b] $p < .05$ interaction effect addition of deadspace and ventilatory mode; [c] $p < .05$, vs. corresponding PSV. In this table the hemodynamic variables of the participating patients are presented.

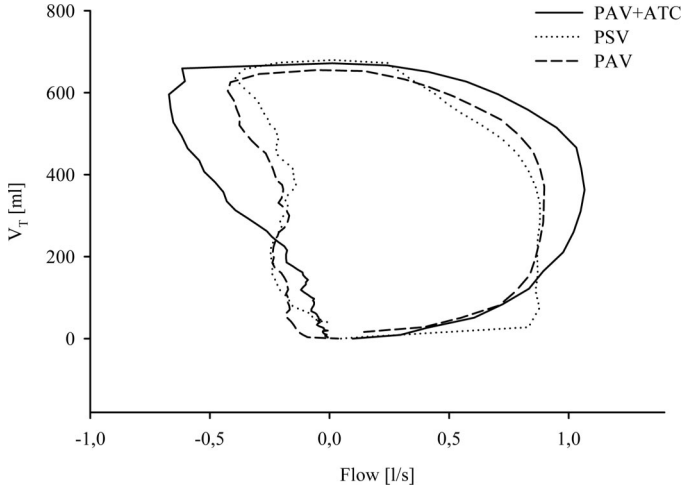

Figure 3. Flow-volume diagram during the three different ventilatory modes. Figure shows differences in flow pattern in all three applied ventilatory modes. Notably the inspiratory and expiratory flow during proportional assist ventilation (*PAV*) + automatic tube compensation (*ATC)* is markedly different from that in pressure support ventilation (*PSV*) and PAV. *VT, tidal volume.*

not different and increased by a comparable amount in response to deadspace, differences in elastic workload seem unlikely to explain the observed differences in the increase in WOB_{pat} among the three forms of inspiratory pressure assistance studied.

Although ATC should compensate for at least some nonlinearities of the resistance to flow (6, 38), PAV+ATC did not result in a significantly more inspiratory muscle unloading after deadspace addition. The failure of PAV+ATC to compensate for the increase ventilatory demand could be attributable to the fact that the algorithm or realization of ATC as employed in the ventilator is not sufficient in reducing the imposed work (WOB_{add}) caused by the artificial airway. This is in line with our previous observations of delayed pressure regulation during ATC as used in standard ventilators (39) and with *in vivo* studies by Elsasser and coworkers (40), who examined ATC performance of different commercially available ventilators. They showed that ATC as implemented in standard ventilators (including Evita 4 used here) is markedly less efficient in reducing WOB_{add} than the original experimental ATC system. This may be due to simplified algorithms employed in currently available ventilators and lack of negative pressure during expiration. The latter limitation was avoided by applying a sufficiently high positive end-expiratory pressure to allow unrestricted expiratory tube compensation by lowering end-expiratory pressure. Furthermore, the ATC algorithms are based on *in vitro* measurements of tube geometry and flow-dependent resistance, which cannot necessarily be transferred into *in vivo* situations (41). A possible method to estimate the tube's cross-sectional area noninvasively and therefore the WOB_{add} is described elsewhere (42, 43); however, we do not possess such a device. In line with these obvious limitations of ATC as currently realized in standard ventilators, Kuhlen and coworkers (44) found no difference in WOB between spontaneous breathing with a T-piece or ATC, whereas PSV reduced WOB significantly. Since different ventilators may implement ATC in different ways, the results may vary when other commercially available ventilator are used.

In a previous study in patients with ARF, Ranieri and coworkers (45) observed increased VT during PAV but increased RR with signs of dynamic hyperinflation during PSV in response to a higher ventilatory demand. In contrast, our patients were able to increase VT even during constant inspiratory pressure assistance with PSV and did not increase their RR in response to deadspace addition in any mode.

These inconsistent responses might be explained by differences in the degree of the patients' ventilator dependence at time of study. In addition, in the study by Ranieri et al. (45), the initial level of

In patients with acute respiratory failure, dynamic inspiratory pressure assistance modalities are not superior to pressure support ventilation with respect to cardiorespiratory function and inspiratory muscles unloading after increasing ventilatory demand.

pressure assistance was not matched between PSV and PAV, thus limiting a direct comparison of the breathing pattern during both ventilator settings.

PAV+ATC and PAV were associated with a higher V_T variability compared with PSV. Lefevre and coworkers (46) suggested that a higher variability in V_T in oleic acid injured pigs during volume-controlled ventilation resulted in improved oxygenation. Other authors failed to show an improvement in oxygenation when keeping mean Paw, CO, V_T, and other respiratory and cardiocirculatory variables comparable between groups (47). This is in line with our results, as we were not able to prove any difference in cardiorespiratory function between the three tested ventilatory modes as long as they are properly matched. A possible explanation could be that our patients were suffering from mild to moderate ARF. Patients with more severe lung injury could possibly benefit more from a high ventilatory variability.

CONCLUSION

In our patients with ARF we found no major differences in cardiorespiratory function between dynamic and constant inspiratory pressure assistance. The finding that inspiratory muscle unloading in response to an increased ventilatory demand was not significantly superior during PAV or PAV+ATC may be explained by nonlinearities of airway resistance that are not adequately compensated by PAV and ineffective implementation of ATC in the used standard ventilator.

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